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Predicting asthma attacks using connected mobile devices and machine learning; the AAMOS-00 observational study protocol

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Manuscripts

Predicting asthma attacks using connected mobile devices and machine learning; the AAMOS-00 observational study protocol

Kevin C.H. Tsang^{1,2}, Hilary Pinnock¹, Andrew M. Wilson^{1,3}, Dario Salvi⁴, Syed Ahmar Shah^{1,2}

1. Asthma UK Centre for Applied Research, Usher Institute, University of Edinburgh, Edinburgh, UK

2. Medical Informatics, Usher Institute, University of Edinburgh, Edinburgh, UK

3. Norwich Medical School, University of East Anglia, Norwich, UK

4. Internet of Things and People Research Centre, Malmö University, Malmö, Sweden

Correspondence:

Mr Kevin Cheuk Him Tsang

Usher Institute,

NINE BioQuarter, Little France Road,

Edinburgh, United Kingdom.

EH16 4UX

Email: k.c.h.tsang@sms.ed.ac.uk

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20

21 ABSTRACT

22 Introduction:

23 Supported self-management empowering people with asthma to detect early deterioration and take
24 timely action reduces the risk of asthma attacks. Smartphones and smart monitoring devices
25 coupled with machine learning could enhance self-management by predicting asthma attacks and
26 providing tailored feedback.

27 We aim to develop and assess the feasibility of an asthma attack predictor system based on data
28 collected from a range of smart devices.

29 Methods and Analysis:

30 A 2-phase, 7-month observational study to collect data about asthma status using three smart
31 monitoring devices, and daily symptom questionnaires. We will recruit up to 100 people via social
32 media and from a severe asthma clinic, who are at risk of attacks and who use a pressurised metered
33 dose relief inhaler (that fits the smart inhaler device).

34 Following a preliminary month of daily symptom questionnaires, 30 participants able to comply with
35 regular monitoring will complete six months of using smart devices (smart peak flow meter, smart
36 inhaler, smartwatch) and daily questionnaires to monitor asthma status. The occurrence of asthma
37 attacks (definition: ATS/ERS Task Force 2009) will be detected by self-reported use (or increased use)
38 of oral corticosteroids. Monitoring data will be analysed to identify predictors of asthma attacks. At
39 the end of the monitoring, we will assess users' perspectives on acceptability and utility of the
40 system with an exit questionnaire.

41 Ethics and Dissemination:

42 Ethics approval was provided by the East of England - Cambridge Central Research Ethics Committee.
43 IRAS project ID: 285505 with governance approval from ACCORD (Academic and Clinical Central
44 Office for Research and Development), project number: AC20145. The study sponsor is ACCORD, the
45 University of Edinburgh.

46 Results will be reported through peer-reviewed publications, abstracts, and conference posters.
47 Public dissemination will be centred around blogs and social media from the Asthma UK network
48 and shared with study participants.

49 **Key Words**

50 Asthma Attacks, Machine Learning, mHealth, Smart Monitoring Devices, Prediction

51

52 ARTICLE SUMMARY

53 **Strengths and limitations of this study**

- 54 • This study combines objective data collected from multiple smart monitoring devices
55 available on the market.

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- Stratified analysis and individualised asthma attack prediction models are not expected, due to the limited number of participants and study period.
- Participants are limited to patients with severe asthma at risk of acute attacks, and to those using a pressurised metered dose relief inhaler that fits our smart device.

For peer review only

61

62 INTRODUCTION

63 Asthma is a variable condition, affecting around 5.4 million people in the UK.[1] Every 10 seconds in
64 the UK alone, someone has an asthma attack. Some of these attacks are life-threatening with over
65 1400 annual deaths estimated in the UK.[1,2] Since there is no known cure for asthma, self-
66 management is a key part of patient care; this involves detecting deterioration and taking
67 appropriate action to maintain control and prevent the threatened attack.[3] The most common
68 symptoms of asthma are wheezing, cough, chest tightness and shortness of breath.

69 Traditional self-management action plans use symptom scores, sometimes supplemented by peak
70 flow measurements, to determine a patient's asthma condition.[4–6] Keeping track of relief inhaler
71 usage can also help measure asthma control.[7] However, patients may regard this level of
72 monitoring as tedious as it involves high levels of active engagement on their part.

73 Increasingly, smart monitoring devices and “mobile-health” (mHealth) technologies are being
74 developed to support asthma self-management.[8] Some notable examples include myAsthma [9]
75 and Asthma MD.[10] myAsthma stores personalised action plans, includes instructional videos about
76 inhaler techniques, tracks symptoms and peak flow, and provides local weather forecasts.
77 AsthmaMD [10] has similar features to support self-management and can provide customised
78 notifications. However, these tools still require a high level to active engagement to monitor one's
79 asthma.

80 There has been an increasing number of mHealth studies to predict asthma attacks and develop
81 passive monitoring to support asthma self-management, including the use of smart peak flow
82 meters,[11] activity tracking,[12,13] smartphone administrated questionnaires,[6,14] and weather
83 data.[15,16] However, the combined use of the monitoring devices available to asthma patients to
84 develop asthma attack prediction models is largely unexplored. In addition, whilst there have been
85 some studies that explored the use of machine learning algorithms for chronic disease management
86 with home-monitoring data,[17] there is still no mHealth system that is widely used by asthma
87 patients. One of the key bottlenecks for the limited progress is the difficulty of collecting asthma
88 monitoring data and the lack of availability of such datasets from existing studies. Apart from the
89 Asthma Mobile Health Study,[18] no other asthma mHealth dataset is publicly available to be able to
90 investigate the development and validation of asthma attack prediction algorithm.

91 In this study, we will collect novel asthma monitoring data that will facilitate the development of an
92 asthma attack prediction algorithm leveraging available, approved asthma monitoring devices in the
93 market. This study will also enable us to test whether unobtrusive, passive monitoring and machine
94 learning could help minimise the need for active patient data collection whilst maintaining accuracy
95 for predicting attacks. We envisage that an mHealth system that leverages machine learning to
96 predict asthma attacks with passive monitoring will enhance patient adherence and improve patient
97 self-management.

98 The overarching aim of this study is to develop and assess the feasibility and acceptability of an
99 asthma self-management system using existing smart devices, collect novel monitoring data and
100 leverage machine learning to develop asthma attack prediction algorithm.

101

METHODS AND ANALYSIS

Study population

To maximise the chances of collecting data related to attacks in a short time-span, we will focus on patients with moderate to severe risk of attacks. Two key predictors are a recent history of attacks and people with severe asthma.[19,20] We will thus focus on adult asthma patients who have had at least one course of oral corticosteroid for an acute asthma attack in the past 12 months, and people attending a secondary care severe asthma clinic. See Table 1 for inclusion and exclusion criteria.

Social media recruitment consists of sending tweets on Twitter and posting on Facebook via the Asthma + Lung UK and Asthma UK Centre for Applied Research (AUKCAR) accounts, which total around 175,000 followers. The Norfolk and Norwich University Hospital will help identify potentially eligible patients for the study and direct them to the online information and expression of interest.

Table 1: Inclusion and exclusion criteria

Inclusion criteria:	<ul style="list-style-type: none"> • Aged 18 and above • Self-reported or doctor-diagnosed asthma • Possession of a smartphone (from 2016 onwards) that can support the Mobistudy and FindAir mobile apps (Android 4.4+, iOS 10+) and has Bluetooth capabilities • Has had at least one course of oral corticosteroids for an acute asthma attack in the past 12 months • Prescribed with pressurised metered dose relief inhaler that is compatible with FindAir ONE (e.g. Ventolin and other versions of salbutamol if the inhaler is a compatible shape inhaler as Ventolin; Salamol; Airomir; Fostair; Budiair)[21]
Exclusion criteria:	<ul style="list-style-type: none"> • Comorbidities that have overlapping symptoms (e.g. wheezing, cough, chest tightness and shortness of breath) • Aged under 18 • Unable to provide valid consent (e.g. cognitive impairment, learning disabilities) • Unable to use an app and respond to questions in English

Potential participants will complete an online questionnaire to identify whether they are eligible to participate. Informed consent will be collected via Online Surveys, a secure online platform for collecting questionnaire data. Potential participants will be given time to read the participant information sheet before deciding whether to participate.

121 Sample size calculation

122 To achieve the objectives of this study, we need to collect sufficient data need to train an asthma
123 attack prediction model.

124 In the study population of UK Optimum Patient Care Research Database (OPCRD) and Clinical
125 Practice Research Datalink (CPRD), 41% of the patients who had multiple (2 or more) attacks in the
126 baseline year also had multiple attacks in the following year.[20]

127 Based on 30 participants with daily monitoring, 3,470 recordings (= 30 people × 30 days × (89%
128 adherence at baseline, 58% adherence at 3 months, 52% adherence at 6 months [22])) for each of
129 the daily measurements can be expected in phase 2. Also, 12 recorded asthma attacks are expected,
130 assuming an average of one attack observed per participant in 41% of phase 2 participants during
131 the study period.[20] To use the novelty detection algorithm iForest (which can be trained even if
132 the data collected does not include any attacks), a sample of 256 recordings or data points would
133 suffice.[23] Other machine learning classification algorithms will also obtain high accuracy on this
134 sample size.

135

136 Recruitment strategy

137 Using a similar recruitment method, Hui et al. recruited 87 participants using social media alone, the
138 majority within the first month after the initial invitational message, although the number of those
139 who continued to use the app dropped to 15 (17% of the total initially recruited participants) after
140 30 days.[24] Moreover, only 5% of identified participants through practices agreed to join their study,
141 which totalled 28 participants from five practices.[24] However, the attrition rate for participants
142 recruited through practices was lower, 63% vs 83% reduction in social media participants; only 25%
143 of users were still using the app after 30 days.[24] The eligibility criteria (≥16 years, an asthma
144 prescription in the previous year, registered with a UK general practitioner) is more relaxed than the
145 proposed criteria. However, this study incentivises entry of data in the first 28 days by giving
146 adherent participants access to phase 2 which is likely to result in much more than 25% passing 30
147 days of participation.

148 Following the previous research, which recruited participants through Asthma UK's social media (at
149 the time of writing had 175,000 followers), around 87 participants are expected to be eligible and
150 join this study. In addition, around six participants identified and invited via are expected to be
151 eligible and join from Norfolk and Norwich University Hospital. Of which, 47 people (50% of 93
152 respondents) are expected to complete phase 1. Thus, including 30 participants is achievable using
153 the outlined recruitment method.

154

155 Outcomes

156 Primary endpoints

157 The primary endpoints of this study are severe asthma attacks, as defined in the American Thoracic
158 Society (ATS)/European Respiratory Society (ERS) Task Force 2009 statement.[25] The definition is as
159 follows:

- 1
2
3 160 • *Severe asthma attacks* are events that require urgent action on the part of the patient and
4 161 physician to prevent a serious outcome. Such attacks are defined as a deterioration
5 162 requiring use of systemic corticosteroids (or an increase from a stable maintenance
6 163 dose).[25]

7
8
9 164 Severe asthma attacks will be identified using the use of systemic corticosteroids question on the
10 165 weekly self-reported questionnaire. Courses of corticosteroids separated by 1 week or more will be
11 166 treated as separate severe attacks.

13 167 Secondary endpoints

14
15 168 The secondary endpoints of this study are moderate asthma attacks, as defined in the ATS/ERS Task
16 169 Force 2009 statement.[25] The definition is as follows:

- 17
18 170 • A *moderate asthma attack* is an event that, when recognised, should result in a temporary
19 171 change in treatment to prevent the attack from becoming severe. Such attacks are defined
20 172 as a deterioration that does not require use of systemic corticosteroids.[25] Moderate
21 173 asthma attacks include a deterioration in symptoms, lung function, and/or increased rescue
22 174 bronchodilator use that lasts for 2 days or more but are not severe enough to warrant
23 175 systemic corticosteroid use.

24
25
26 176 Moderate asthma attacks will be identified using the questions about relief inhaler usage, symptoms
27 177 (day symptoms, nocturnal symptoms, interference with usual activities, shortness of breath,
28 178 wheezing), and unscheduled care (GP, emergency room, and hospitalisations) in the daily and
29 179 weekly self-reported questionnaires.

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31 180

33 181 Data collection

34 182 The data collection period is split into two phases:

- 35
36
37 183 1. *Questionnaire monitoring, daily for one month.*
38
39 184 2. *Smart device and questionnaire monitoring, daily for six months.* 30 participants who keep a
40 185 regular diary in phase 1 will be given three smart devices (smart inhaler, smart peak flow
41 186 meter, smartwatch) to collect data automatically as they use the devices, in addition to
42 187 completing daily and weekly questionnaires. We will choose participants for this phase with
43 188 a range of ages, gender, and smoking status, and with different types of asthma triggers.

44
45
46 189 At the end of phase 2, we will send a questionnaire asking for feedback about using the smart
47 190 devices and whether participants think they could be useful to help them look after their asthma.

48
49 191 We will be using Mobistudy to centralise most of the data collection, only the smart inhaler usage
50 192 and exit questionnaire will not be collected via Mobistudy (see Figure 1).

51
52 193

54 194 Data collection mobile app (Mobistudy)

55 195 Mobistudy [26] is an open-source platform facilitating mHealth studies available on Android and iOS
56 196 managed by Malmö University, Sweden. The platform has three key components: a mobile app for
57 197 participants, a REST API server, and a web portal for researchers (see Figure 2). The platform

198 supports multiple studies and participants of the AAMOS-00 study will be given a study invite code
199 to join the AAMOS-00 study within Mobistudy.

200 Each daily and weekly assessment, such as questionnaires and peak flow measurement, will appear
201 as an individual task of the home page on the participant's app (see Figure 3). Once the task is
202 completed, it will be removed from today's to-do list and the data is sent directly to the server via
203 the phone Internet connection. In real-time, the research team will be able to view the collected
204 data via the online web portal for researchers.

205

206 Phase 1

207 There will be a total of four questionnaires:

- 208 • A daily questionnaire that asks six questions about daily symptoms experienced, medication
209 usage, and the triggers encountered. This will take around 2 minutes to complete.
- 210 • A weekly questionnaire that asks 10 questions about asthma symptoms in more detail,
211 medication usage, and healthcare engagement. This will take around 5 minutes to complete.
- 212 • A questionnaire that asks 11 questions at the start of phase 1 about current asthma
213 condition and history.
- 214 • A questionnaire that asks five questions about race and smoking status. Additionally, some
215 demographic information will be collected from the Mobistudy profile of participants, such
216 as height, weight, and age.

217 The completion rate (50%) of the daily and weekly questionnaire will be used to determine the
218 eligibility of a participant to join phase 2.

219

220 Phase 2

221 In addition to the daily and weekly questionnaires (see Figure 4), in phase 2 participants will be
222 asked to collect data using three smart monitoring devices: Smart Peak Flow Meter (by Smart
223 Asthma [27]), FindAir ONE (by FindAir [21]) smart inhaler, and MiBand3 (by Xiaomi [28]) smartwatch.

224 Participants will be given the smart peak flow meter to take a peak expiratory flow measurement
225 twice a day, once in the morning and once at night; each measurement takes the best of three tries
226 (see Figure 5). They will also be provided in-app written instructions before each set of
227 measurements on using the peak flow meter. Furthermore, participants recruited through the
228 Norfolk and Norwich University Hospital have been trained to use a peak flow meter by the practice.
229 To connect the smart peak flow meter to the smartphone, participants can either use the audio-jack
230 connection or a Bluetooth adapter.

231 The FindAir ONE smart inhaler attaches to the top of pressurised metered dose relief inhalers, it
232 records the time at which the inhaler is used. The device can be moved to a new inhaler if
233 participants change medication. The device will be connected to participants' smartphone by
234 Bluetooth to the FindAir mobile app. The data will be transferred from the FindAir server and thence
235 to the research team using FindAir's Application Programming Interface (API). The data collection
236 will happen in the background once the participant has set up the connection between their mobile
237 app and the AAMOS-00 study.

238 Using the MiBand3, we will collect minute-by-minute data on heart rate, step count, activity
 239 intensity, and activity type. The watch will connect to the participant's smartphone via Bluetooth
 240 and to the Mobistudy app. Participants will be asked to upload the data from the watch at least once
 241 every three days. This also gives a chance for users to review their activity (see Figure 6).

242 Local daily weather reports will be obtained using the phone's location combined with the data from
 243 Open Weather Maps' [29] and Ambee's [30] API. The weather data will include the temperature,
 244 humidity, clouds, wind, air quality index, and pollen levels of grass, tree, and weeds measured at a
 245 one-kilometre resolution (see Figure 7).

246

247 Exit questionnaire at the end of Phase 2

248 At the end of phase 2, a survey will gather data regarding users' perspective of the acceptability and
 249 utility of the monitoring system. The survey combines validated questionnaires on usability and
 250 acceptance (SUS [31] and uMARS [32]) with questions about motivations to use technology (mTEI
 251 [33]) and desired features in an asthma management system.

252 See Table 2 for a summary of the study's activities.

253

254 Table 2. Summary of data collection

Assessment	Screening	Day 1 baseline	Phase 1	Day 31 baseline	Phase 2	Study Exit
Assessment of Eligibility Criteria	Once			Once		
Written informed consent	Once					
Demographic data, contact details		Once				
Weight/height		Once				
Known triggers		Once				
Peak flow					Twice daily	
Heart rate					Automated	
Activity					Automated	
Location, air quality and allergens					Daily	
Inhaler Usage			Daily & Weekly		Automated	
Symptoms			Daily & Weekly		Daily	
Triggers encountered			Daily		Daily	
Healthcare Usage			Weekly		Weekly	

Feedback						Once at the end
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256 Data analysis plan

257 Feasibility (from usage data)

258 Combining the usage data from phase 1 and 2 of questionnaire completion and device usage will
 259 compute compliance to the monitoring regime to assess if it is feasible for patients to use the
 260 monitoring devices in their daily lives.

261 We will also use activity logs on the server, and communication over email with patients, to identify
 262 major technical issues and shortcomings of the technology.

263

264 Acceptability (from survey data)

265 The data from the final questionnaire will be mostly ordinal data, with some free text answers. Free
 266 text will be processed for thematic text analysis, identifying overall acceptability and recurring topics
 267 present in the feedback. The ordinal data from answers on a Likert scale will provide measures of
 268 acceptability.

269

270 Prediction of asthma attacks (using monitoring data)

271 Severe asthma attacks will be identified by the reports of oral corticosteroid usage (or an increased
 272 dose from normal). Moderate and severe asthma attacks will be identified from the daily and weekly
 273 data, to observe a change in control from the norm lasting two days or more. Sensitivity analysis will
 274 be conducted using different features to define an asthma attack, such as hospitalisations and
 275 changes in peak flow.

276 The methods of linear fit and bin-algorithms will be used to collate and produce summary variables
 277 over irregular time-series and to handle missing data;^[6] though, the longitudinal data collected in
 278 this study are likely to be more complete than the Asthma Mobile Health Study.^[34] Data collected
 279 from participants who have withdrawn from the study will be used up to the last recording. After
 280 processing the data, machine learning classifiers will be trained to predict asthma attacks.

281 The primary classifiers that will be used in the study include Bayesian networks, decision trees,
 282 iForest, logistic regression, and support vector machines.^[35,36] From the classifiers, a severe
 283 asthma attack predictor will be built on the device and questionnaire data, at a patient-level and
 284 population-level. Also, feature selection will be used to identify the most useful features in the
 285 prediction models.

286 Furthermore, retrospective analysis will simulate the effects of limiting the use of active monitoring
 287 data, to simulate patients only taking active measurements (e.g., peak flow and symptom diary)
 288 when prompted. In other words, the training set will be considered as all data before a certain date
 289 in the study period and the test set everything after. Moreover, there will be simulation of the
 290 general population using samples of the data, where adherence to monitoring might be lower than
 291 the selected population. For assessing the performance of the models built in this study, we will use

1
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3 292 k-fold cross validation.[35] The performance metrics will include the common machine learning
4 293 metrics such as area under the receiver operating characteristic curve (AUC-ROC), sensitivity, and
5 294 specificity.
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10 296 **PATIENT AND PUBLIC INVOLVEMENT**

11
12 297 Patient and public involvement (PPI) is part of the project from the beginning. This study is nested
13 298 within the Asthma UK Centre for Applied Research and has been reviewed by their AUKCAR PPI
14 299 members.

15
16 300 All the participant and public-facing documents and study objectives have been reviewed by
17 301 AUKCAR PPI members before the start of the study and edited accordingly. Such a close PPI
18 302 involvement ensures that the participant and public facing material is accessible. As an example, we
19 303 attempted to explain several technical terms (such as “pMDI”) in more detail in the participant
20 304 documents and added pictures of pressured metered dose inhalers after feedback from PPI
21 305 members.
22
23
24 306

27 307 **DISSEMINATION**

28
29 308 We will be reporting the results in peer-reviewed journal publications and conference presentations.
30 309 Dissemination of the results will also include the AUKCAR network with blogs and social media to
31 310 reach an audience who is interested in the used of smart monitoring devices for asthma.

32
33 311 We will also be sharing links to publications and summaries with study participants.
34
35 312

37 313 **ETHICS**

38
39 314 This study has received ethics approval by the East of England - Cambridge Central Research Ethics
40 315 Committee. IRAS Project ID: 285505.
41
42 316

45 317 **DATA AVAILABILITY**

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47 318 At the end of the study, the anonymised research data will be stored at Edinburgh DataShare (a
48 319 digital repository of research data produced at the University of Edinburgh) in perpetuity.
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53 321 **CONCLUSIONS**

54
55 322 The present study will collect an important and novel dataset, where asthma patients use a
56 323 combination of multiple market-available mHealth monitoring devices in the real world. We plan to
57 324 use the rich dataset to improve existing asthma attack prediction algorithms and use the feedback
58 325 from participants to design a patient-centred asthma self-management system. This study is the first
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3 326 step in developing the Asthma Attack Management Online System (AAMOS) which will support
4 327 asthma patients with real-time tailored feedback based on machine learning driven by mHealth data.

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10
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16 335
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20 336 **AUTHOR CONTRIBUTIONS**

21
22 337 KCHT, HP, AMW, and SAS designed the study. SAS is the study guarantor. KCHT and DS set up the
23 338 data collection system. KCHT drafted the manuscript which was critically revised by HP, AMW, DS,
24 339 and SAS. All authors approved the final version of the manuscript.

25 340
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28

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30
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33 344 Foundation KK-stiftelsen.

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38 346 **COMPETING INTEREST STATEMENT**

39 347 None declared.

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440 FIGURE LEGENDS

441 *Figure 1. AAMOS-00 system overview*

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- 442 *Figure 2. Mobistudy system overview*
- 443 *Figure 3. Participant's app home page*
- 444 *Figure 4. Questionnaire delivered by Mobistudy*
- 445 *Figure 5. Smart peak flow meter task*
- 446 *Figure 6. Smartwatch data*
- 447 *Figure 7. Local weather data*
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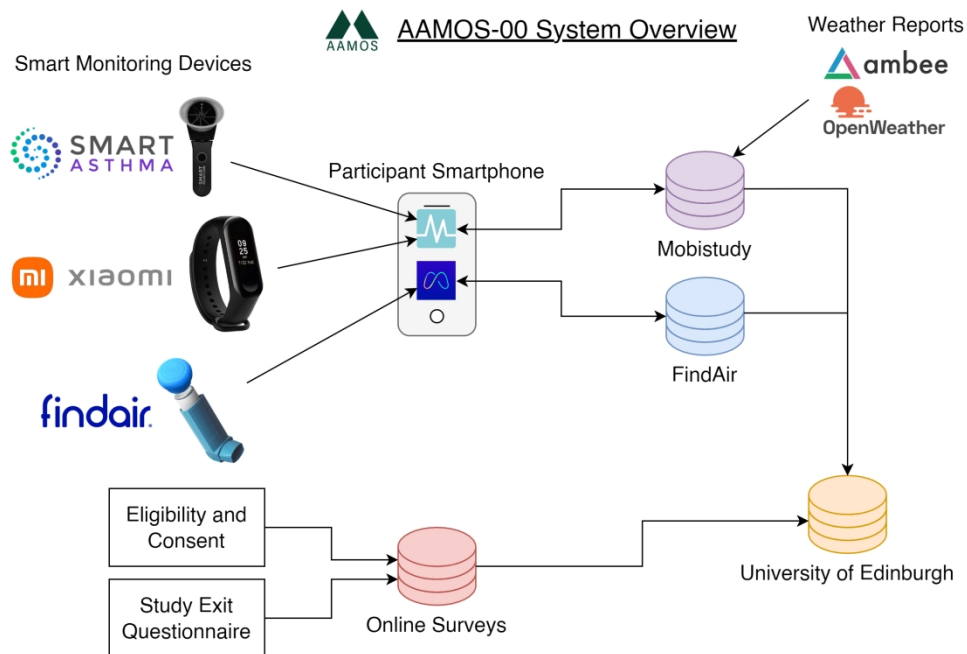


Figure 1: AAMOS-00 system overview

817x542mm (72 x 72 DPI)

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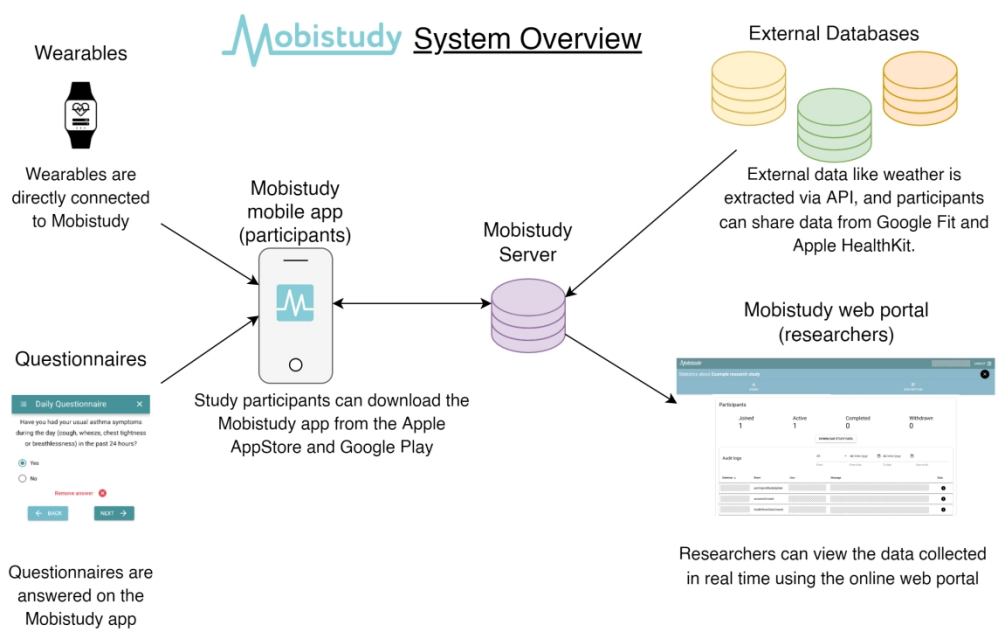


Figure 2: Mobistudy system overview

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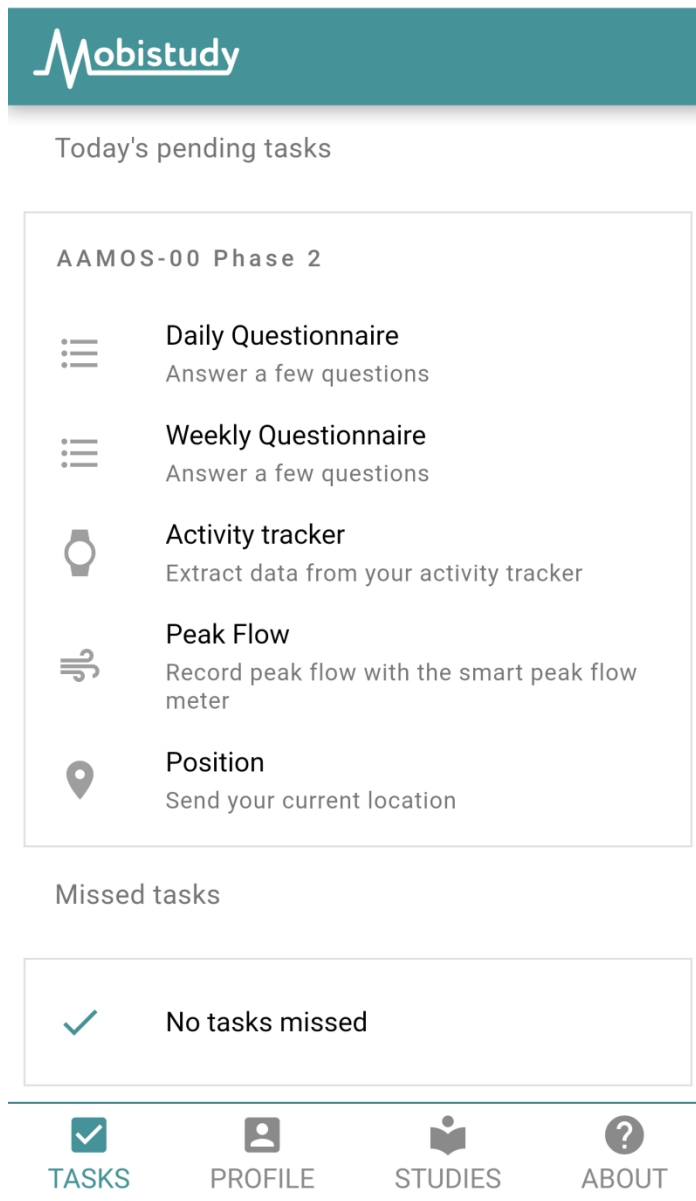


Figure 3: Participant's app home page

962x1649mm (38 x 38 DPI)

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☰ Daily Questionnaire ✕

Have you had your usual asthma symptoms during the day (cough, wheeze, chest tightness or breathlessness) in the past 24 hours?

Yes

No

Remove answer ✕

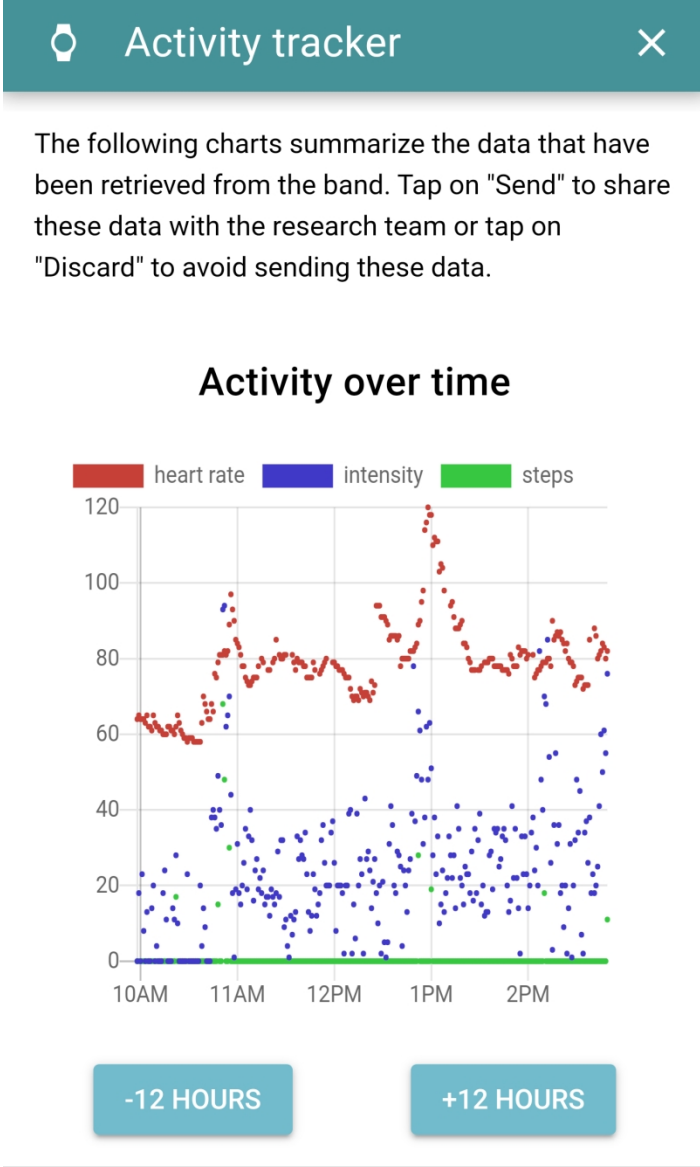
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Figure 4: Questionnaire delivered by Mobistudy

962x1647mm (38 x 38 DPI)

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Time spent in each activity

Figure 6: Smartwatch data

957x1637mm (38 x 38 DPI)

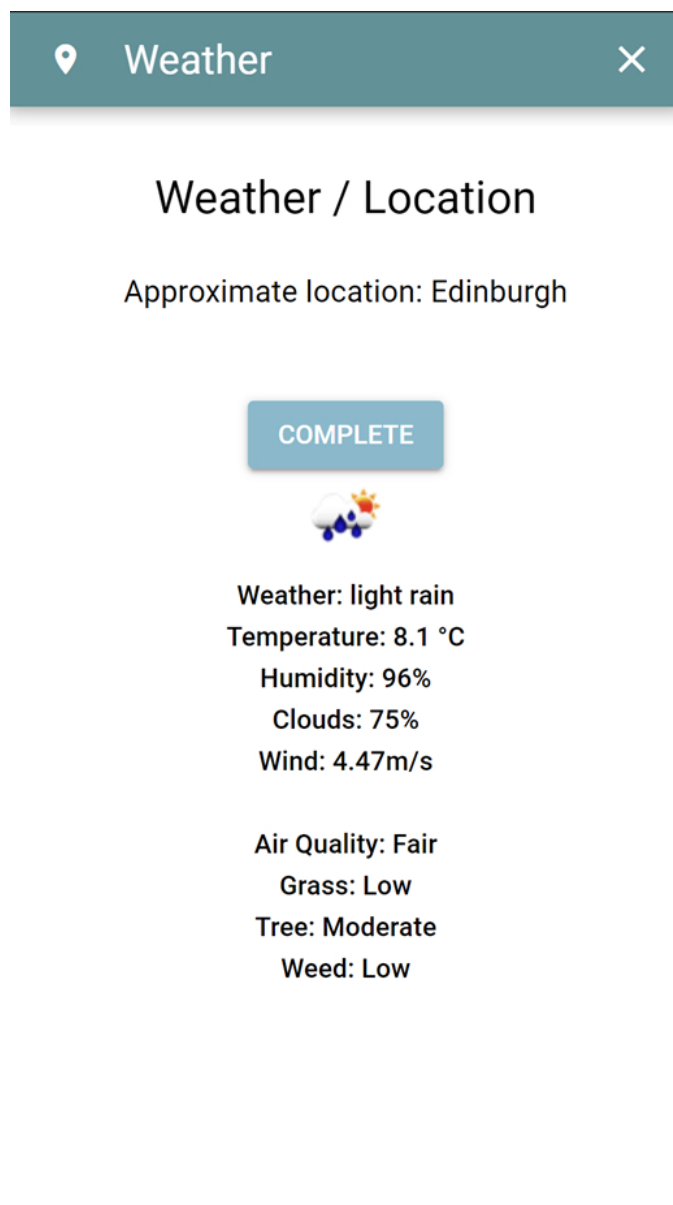


Figure 7: Local weather data

347x616mm (38 x 38 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	5
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7
Bias	9	Describe any efforts to address potential sources of bias	NA
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	10
		(b) Describe any methods used to examine subgroups and interactions	10
		(c) Explain how missing data were addressed	10
	NA	(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	10

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	NA
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	NA
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	NA
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	NA
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	NA
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	NA
		(b) Report category boundaries when continuous variables were categorized	NA
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	NA
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	NA
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	NA
Generalisability	21	Discuss the generalisability (external validity) of the study results	10
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Predicting asthma attacks using connected mobile devices and machine learning; the AAMOS-00 observational study protocol

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2022-064166.R1
Article Type:	Protocol
Date Submitted by the Author:	01-Sep-2022
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Primary Subject Heading:	Health informatics
Secondary Subject Heading:	Respiratory medicine, Public health
Keywords:	Asthma < THORACIC MEDICINE, Health informatics < BIOTECHNOLOGY & BIOINFORMATICS, Information technology < BIOTECHNOLOGY & BIOINFORMATICS, World Wide Web technology < BIOTECHNOLOGY & BIOINFORMATICS

SCHOLARONE™
Manuscripts

Predicting asthma attacks using connected mobile devices and machine learning; the AAMOS-00 observational study protocol

Kevin C.H. Tsang^{1,2}, Hilary Pinnock¹, Andrew M. Wilson^{1,3,4}, Dario Salvi⁵, Syed Ahmar Shah^{1,2}

1. Asthma UK Centre for Applied Research, Usher Institute, University of Edinburgh, Edinburgh, UK

2. Medical Informatics, Usher Institute, University of Edinburgh, Edinburgh, UK

3. Norwich Medical School, University of East Anglia, Norwich, UK

4. Norwich University Hospital Foundation Trust, Colney Lane, Norwich, UK

5. Internet of Things and People Research Centre, Malmö University, Malmö, Sweden

Correspondence:

Mr Kevin Cheuk Him Tsang

Usher Institute,

NINE BioQuarter, Little France Road,

Edinburgh, United Kingdom.

EH16 4UX

Email: k.c.h.tsang@sms.ed.ac.uk

Word count: 3544

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ABSTRACT

Introduction:

Supported self-management empowering people with asthma to detect early deterioration and take timely action reduces the risk of asthma attacks. Smartphones and smart monitoring devices coupled with machine learning could enhance self-management by predicting asthma attacks and providing tailored feedback.

We aim to develop and assess the feasibility of an asthma attack predictor system based on data collected from a range of smart devices.

Methods and Analysis:

A 2-phase, 7-month observational study to collect data about asthma status using three smart monitoring devices, and daily symptom questionnaires. We will recruit up to 100 people via social media and from a severe asthma clinic, who are at risk of attacks and who use a pressurised metered dose relief inhaler (that fits the smart inhaler device).

Following a preliminary month of daily symptom questionnaires, 30 participants able to comply with regular monitoring will complete six months of using smart devices (smart peak flow meter, smart inhaler, smartwatch) and daily questionnaires to monitor asthma status. The feasibility of this monitoring will be measured by the percentage of task completion. The occurrence of asthma attacks (definition: ATS/ERS Task Force 2009) will be detected by self-reported use (or increased use) of oral corticosteroids. Monitoring data will be analysed to identify predictors of asthma attacks. At the end of the monitoring, we will assess users' perspectives on acceptability and utility of the system with an exit questionnaire.

Ethics and Dissemination:

Ethics approval was provided by the East of England - Cambridge Central Research Ethics Committee. IRAS project ID: 285505 with governance approval from ACCORD (Academic and Clinical Central Office for Research and Development), project number: AC20145. The study sponsor is ACCORD, the University of Edinburgh.

Results will be reported through peer-reviewed publications, abstracts, and conference posters. Public dissemination will be centred around blogs and social media from the Asthma UK network and shared with study participants.

Key Words

Asthma Attacks, Machine Learning, mHealth, Smart Monitoring Devices, Prediction

ARTICLE SUMMARY

Strengths and limitations of this study

- This study combines objective data collected from multiple smart monitoring devices available on the market.

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- 58 • Stratified analysis and individualised asthma attack prediction models are not expected, due
59 to the limited number of participants and study period.
- 60 • Participants are limited to patients with severe asthma at risk of acute attacks, and to those
61 using a pressurised metered dose relief inhaler that fits our smart device.

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64 INTRODUCTION

65 Asthma is a variable condition, affecting around 5.4 million people in the UK.[1] Every 10 seconds in
66 the UK alone, someone has an asthma attack. Some of these attacks are life-threatening with over
67 1400 annual deaths estimated in the UK.[1,2] Since there is no known cure for asthma, self-
68 management is a key part of patient care; this involves detecting deterioration and taking
69 appropriate action to maintain control and prevent the threatened attack.[3] The most common
70 symptoms of asthma are wheezing, cough, chest tightness and shortness of breath.

71 Traditional self-management action plans use symptom scores, sometimes supplemented by peak
72 flow measurements, to determine a patient's asthma condition.[4–6] Keeping track of relief inhaler
73 usage can also help measure asthma control.[7] However, patients may regard this level of
74 monitoring as tedious as it involves high levels of active engagement on their part.

75 Increasingly, smart monitoring devices and “mobile-health” (mHealth) technologies are being
76 developed to support asthma self-management.[8] Some notable examples include myAsthma [9]
77 and Asthma MD.[10] myAsthma stores personalised action plans, includes instructional videos about
78 inhaler techniques, tracks symptoms and peak flow, and provides local weather forecasts.
79 AsthmaMD [10] has similar features to support self-management and can provide customised
80 notifications. However, these tools still require a high level to active engagement to monitor one's
81 asthma.

82 There has been an increasing number of mHealth studies to predict asthma attacks and develop
83 passive monitoring to support asthma self-management,[11] including the use of smart peak flow
84 meters,[12] night-time activity tracking,[13,14] smart inhalers,[15] smartphone administrated
85 questionnaires,[6,16,17] and weather data.[18,19] However, the combined use of the monitoring
86 devices available to asthma patients to develop asthma attack prediction models is largely
87 unexplored. In addition, whilst there have been some studies that explored the use of machine
88 learning algorithms for chronic disease management with home-monitoring data,[20] there is still no
89 mHealth system that is widely used by asthma patients. One of the key bottlenecks for the limited
90 progress is the difficulty of collecting asthma monitoring data and the lack of availability of such
91 datasets from existing studies. Apart from the Asthma Mobile Health Study,[21] no other asthma
92 mHealth dataset is publicly available to be able to investigate the development and validation of
93 asthma attack prediction algorithm.

94 A related study is the myAirCoach study,[22] which investigated asthma home-monitoring using
95 connected devices. However, their participants conducted daily monitoring for the first month with
96 an additional randomly allocated two weeks, compared to seven months in total proposed in this
97 study. To our knowledge, the dataset from myAirCoach is not publicly available and it has not yet
98 been used to test any machine learning-based algorithms for asthma attack prediction.[23,24]

99 In this study, we will collect novel asthma monitoring data that will facilitate the development of an
100 asthma attack prediction algorithm leveraging available, approved asthma monitoring devices in the
101 market. This study will also enable us to test whether unobtrusive, passive monitoring and machine
102 learning could help minimise the need for active patient data collection whilst maintaining accuracy
103 for predicting attacks. We envisage that an mHealth system that leverages machine learning to
104 predict asthma attacks with passive monitoring will enhance patient adherence and improve patient
105 self-management.

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2
3 106 The overarching aim of this study is to develop and assess the feasibility and acceptability of an
4 107 asthma self-management system using existing smart devices, collect novel monitoring data and
5 108 leverage machine learning to explore the feasibility of an asthma attack prediction algorithm based
6 109 on passive monitoring.
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11 111 METHODS AND ANALYSIS

12 112 Study population

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15 113 To maximise the chances of collecting data related to attacks in a short time-span, we will focus on
16 114 patients with moderate to severe risk of attacks. Two key predictors are a recent history of attacks
17 115 and people with severe asthma.[25,26] We will thus focus on adult asthma patients who have had at
18 116 least one course of oral corticosteroid for an acute asthma attack in the past 12 months, and people
19 117 attending a secondary care severe asthma clinic. See Table 1 for inclusion and exclusion criteria.

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22 118 Social media recruitment consists of sending tweets on Twitter and posting on Facebook via the
23 119 Asthma + Lung UK and Asthma UK Centre for Applied Research (AUKCAR) accounts, which total
24 120 around 175,000 followers. The Norfolk and Norwich University Hospital will help identify potentially
25 121 eligible patients for the study and direct them to the online information and expression of interest.
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29 123 Table 1: Inclusion and exclusion criteria

<p>31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49</p> <p>Inclusion criteria:</p>	<ul style="list-style-type: none"> • Aged 18 and above • Self-reported or doctor-diagnosed asthma • Possession of a smartphone (from 2016 onwards) that can support the Mobistudy and FindAir mobile apps (Android 4.4+, iOS 10+) and has Bluetooth capabilities • Has had at least one course of oral corticosteroids for an acute asthma attack in the past 12 months • Prescribed with pressurised metered dose relief inhaler that is compatible with FindAir ONE (e.g. Ventolin and other versions of salbutamol if the inhaler is a compatible shape inhaler as Ventolin; Salamol; Airomir; Fostair; Budiair)[27]
<p>50 51 52 53 54 55 56 57 58 59</p> <p>Exclusion criteria:</p>	<ul style="list-style-type: none"> • Comorbidities that have overlapping symptoms (e.g. wheezing, cough, chest tightness and shortness of breath) • Aged under 18 • Unable to provide valid consent (e.g. cognitive impairment, learning disabilities) • Unable to use an app and respond to questions in English

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3 125 Potential participants will complete an online questionnaire to identify whether they are eligible to
4 126 participate. Informed consent will be collected via Online Surveys, a secure online platform for
5 127 collecting questionnaire data. Potential participants will be given time to read the participant
6 128 information sheet before deciding whether to participate.

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10 130 Sample size calculation

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13 131 To achieve the objectives of this study, we need to collect sufficient data need to train an asthma
14 132 attack prediction model.

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16 133 In the study population of UK Optimum Patient Care Research Database (OPCRD) and Clinical
17 134 Practice Research Datalink (CPRD), 41% of the patients who had multiple (2 or more) attacks in the
18 135 baseline year also had multiple attacks in the following year.[26]

19
20 136 Based on 30 participants with daily monitoring, 3,098 recordings (= 30 people × 30 days × (85%
21 137 retention at baseline,[28–30] 50% retention at 6 months[28,29,31,32]) × 85% adherence[30,31]) for
22 138 each of the daily measurements can be expected in phase 2. Also, 12 recorded asthma attacks are
23 139 expected, assuming an average of one attack observed per participant in 41% of phase 2 participants
24 140 during the study period.[26] To use the novelty detection algorithm iForest (which can be trained
25 141 even if the data collected does not include any attacks), a sample of 256 recordings or data points
26 142 would suffice.[33] Other machine learning classification algorithms will also obtain high accuracy on
27 143 this sample size.

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30 145 Recruitment strategy

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33 146 Using a similar recruitment method, Hui et al. recruited 87 participants using social media alone, the
34 147 majority within the first month after the initial invitational message, although the number of those
35 148 who continued to use the app dropped to 15 (17% of the total initially recruited participants) after
36 149 30 days.[28] Moreover, only 5% of identified participants through practices agreed to join their study,
37 150 which totalled 28 participants from five practices.[28] However, the attrition rate for participants
38 151 recruited through practices was lower, 63% vs 83% reduction in social media participants; only 25%
39 152 of users were still using the app after 30 days.[28] The eligibility criteria (≥16 years, an asthma
40 153 prescription in the previous year, registered with a UK general practitioner) is more relaxed than the
41 154 proposed criteria. However, this study incentivises entry of data in the first 28 days by giving
42 155 adherent participants access to phase 2 (where participants are sent smart devices) which is likely to
43 156 result in much more than 25% passing 30 days of participation. The adherence to four weeks of
44 157 monitoring with daily questionnaires and activity monitors has seen values upwards of 95%.[30]

45
46 158 Following the previous research, which recruited participants through Asthma UK's social media (at
47 159 the time of writing had 175,000 followers), around 87 participants are expected to be eligible and
48 160 join this study. In addition, around six participants identified and invited via are expected to be
49 161 eligible and join from Norfolk and Norwich University Hospital. Of which, 47 people (50% of 93
50 162 respondents) are expected to complete phase 1. Thus, including 30 participants is achievable using
51 163 the outlined recruitment method.

52
53 164

165 Outcomes

166 Primary endpoints

167 The primary endpoints of this study are adherence to monitoring, which are defined by the
168 collection of data using different devices. For each task, we will measure the percentage of total
169 days completed.

170 Secondary endpoints

171 The secondary endpoints of this study are asthma attacks. Primarily, we use severe asthma attacks
172 as defined in the American Thoracic Society (ATS)/European Respiratory Society (ERS) Task Force
173 2009 statement.[34] The definition is as follows:

- 174 • *Severe asthma attacks* are events that require urgent action on the part of the patient and
175 physician to prevent a serious outcome. Such attacks are defined as a deterioration
176 requiring use of systemic corticosteroids (or an increase from a stable maintenance
177 dose).[34]

178 Severe asthma attacks will be identified using the use of systemic corticosteroids question on the
179 weekly self-reported questionnaire. Courses of corticosteroids separated by 1 week or more will be
180 treated as separate severe attacks.

181 We will also explore the use of moderate asthma attacks, as defined in the ATS/ERS Task Force 2009
182 statement.[34] The definition is as follows:

- 183 • A *moderate asthma attack* is an event that, when recognised, should result in a temporary
184 change in treatment to prevent the attack from becoming severe. Such attacks are defined
185 as a deterioration that does not require use of systemic corticosteroids.[34] Moderate
186 asthma attacks include a deterioration in symptoms, lung function, and/or increased rescue
187 bronchodilator use that lasts for 2 days or more but are not severe enough to warrant
188 systemic corticosteroid use.

189 Moderate asthma attacks will be identified using the questions about relief inhaler usage, symptoms
190 (day symptoms, nocturnal symptoms, interference with usual activities, shortness of breath,
191 wheezing), and unscheduled care (GP, emergency room, and hospitalisations) in the daily and
192 weekly self-reported questionnaires.

193

194 Data collection

195 The data collection period is split into two phases:

- 196 1. *Questionnaire monitoring, daily for one month.*
- 197 2. *Smart device and questionnaire monitoring, daily for six months.* 30 participants who keep a
198 regular diary in phase 1 will be given three smart devices (smart inhaler, smart peak flow
199 meter, smartwatch) to collect data automatically as they use the devices, in addition to
200 completing daily and weekly questionnaires. We will choose participants for this phase with
201 a range of ages, gender, and smoking status, and with different types of asthma triggers.

202 At the end of phase 2, we will send a questionnaire asking for feedback about using the smart
203 devices and whether participants think they could be useful to help them look after their asthma.

204 We will be using Mobistudy to centralise most of the data collection, only the smart inhaler usage
205 and exit questionnaire will not be collected via Mobistudy (see Figure 1).

206

207 Data collection mobile app (Mobistudy)

208 Mobistudy [35] is an open-source platform facilitating mHealth studies available on Android and iOS
209 managed by Malmö University, Sweden. The platform has three key components: a mobile app for
210 participants, a REST API server, and a web portal for researchers (see Figure 2). The platform
211 supports multiple studies and participants of the AAMOS-00 study will be given a study invite code
212 to join the AAMOS-00 study within Mobistudy.

213 Each daily and weekly assessment, such as questionnaires and peak flow measurement, will appear
214 as an individual task of the home page on the participant's app (see Figure 3). Once the task is
215 completed, it will be removed from today's to-do list and the data is sent directly to the server via
216 the phone Internet connection. In real-time, the research team will be able to view the collected
217 data via the online web portal for researchers.

218

219 Phase 1

220 There will be a total of four questionnaires:

- 221 • A daily questionnaire that asks six questions about daily symptoms experienced, medication
222 usage, and the triggers encountered. This will take around 2 minutes to complete.
- 223 • A weekly questionnaire that asks 10 questions about asthma symptoms in more detail,
224 medication usage, and healthcare engagement. This will take around 5 minutes to complete.
- 225 • A questionnaire that asks 11 questions at the start of phase 1 about current asthma
226 condition and history.
- 227 • A questionnaire that asks five questions about race and smoking status. Additionally, some
228 demographic information will be collected from the Mobistudy profile of participants, such
229 as height, weight, and age.

230 The completion rate (50%) of the daily and weekly questionnaire will be used to determine the
231 eligibility of a participant to join phase 2.

232

233 Phase 2

234 In addition to the daily and weekly questionnaires (see Figure 4), in phase 2 participants will be
235 asked to collect data using three smart monitoring devices: Smart Peak Flow Meter (by Smart
236 Asthma [36]), FindAir ONE (by FindAir [27]) smart inhaler, and MiBand3 (by Xiaomi [37]) smartwatch.

237 Participants will be given the smart peak flow meter to take a peak expiratory flow measurement
238 twice a day, once in the morning and once at night; each measurement takes the best of three tries
239 (see Figure 5). They will also be provided in-app written instructions before each set of
240 measurements on using the peak flow meter. Furthermore, participants recruited through the
241 Norfolk and Norwich University Hospital have been trained to use a peak flow meter by the practice.

242 To connect the smart peak flow meter to the smartphone, participants can either use the audio-jack
243 connection or a Bluetooth adapter.

244 The FindAir ONE smart inhaler attaches to the top of pressurised metered dose relief inhalers, it
245 records the time at which the inhaler is used. The device can be moved to a new inhaler if
246 participants change medication. The device will be connected to participants' smartphone by
247 Bluetooth to the FindAir mobile app. The data will be transferred from the FindAir server and thence
248 to the research team using FindAir's Application Programming Interface (API). The data collection
249 will happen in the background once the participant has set up the connection between their mobile
250 app and the AAMOS-00 study.

251 Using the MiBand3, we will collect minute-by-minute data on heart rate, step count, activity
252 intensity, and activity type. The watch will connect to the participant's smartphone via Bluetooth
253 and to the Mobistudy app. Participants will be asked to upload the data from the watch at least once
254 every three days. This also gives a chance for users to review their activity (see Figure 6).

255 Local daily weather reports will be obtained using the phone's location combined with the data from
256 Open Weather Maps' [38] and Ambee's [39] API. The weather data will include the temperature,
257 humidity, clouds, wind, air quality index, and pollen levels of grass, tree, and weeds measured at a
258 one-kilometre resolution (see Figure 7).

259

260 Exit questionnaire at the end of Phase 2

261 At the end of phase 2, a survey will gather data regarding users' perspective of the acceptability and
262 utility of the monitoring system. The survey combines validated questionnaires on usability and
263 acceptance (SUS [40] and uMARS [41]) with questions about motivations to use technology (mTEI
264 [42]) and desired features in an asthma management system.

265 See Table 2 for a summary of the study's activities.

266

267 Table 2. Summary of data collection

Assessment	Screening	Day 1 baseline	Phase 1	Day 31 baseline	Phase 2	Study Exit
Assessment of Eligibility Criteria	Once			Once		
Written informed consent	Once					
Demographic data, contact details		Once				
Weight/height		Once				
Known triggers		Once				
Peak flow					Twice daily	
Heart rate					Automated	
Activity					Automated	
Location, air quality and allergens					Daily	
Inhaler Usage			Daily & Weekly		Automated	
Symptoms			Daily & Weekly		Daily	
Triggers encountered			Daily		Daily	
Healthcare Usage			Weekly		Weekly	
Feedback						Once at the end

268

269 At the end of the study, participants will be compensated for mobile data charges that may have
 270 incurred from participating in the study, £5 per month. Participants are also able to continue using
 271 the smart devices beyond the study.

272 Following ethics approval in December 2020, we aim to complete the study by June 2023.

273

274 Data analysis plan

275 Feasibility (from usage data)

276 Combining the usage data from phase 1 and 2 of questionnaire completion and device usage will
 277 compute compliance to the monitoring regime to assess if it is feasible for patients to use the
 278 monitoring devices in their daily lives.

279 We will also use activity logs on the server, and communication over email with patients, to identify
 280 major technical issues and shortcomings of the technology.

281

282 Acceptability (from survey data)

283 The data from the final questionnaire will be mostly ordinal data, with some free text answers. Free
284 text will be processed for thematic text analysis, identifying overall acceptability and recurring topics
285 present in the feedback. The ordinal data from answers on a Likert scale will provide measures of
286 acceptability.

287

288 Exploring asthma attack prediction (using monitoring data)

289 Severe asthma attacks will be identified by the reports of oral corticosteroid usage (or an increased
290 dose from normal). Moderate and severe asthma attacks will be identified from the daily and weekly
291 data, to observe a change in control from the norm lasting two days or more. Sensitivity analysis will
292 be conducted using different features to define an asthma attack, such as hospitalisations and
293 changes in peak flow. Data collected from participants who have withdrawn from the study will be
294 used up to the last recording.

295 The methods of linear fit and bin-algorithms will be used to collate and produce summary variables
296 over irregular time-series and to handle missing data.[6] After processing the data, machine learning
297 classifiers will be trained to predict asthma attacks. Evaluation of these classifiers will allow
298 comparison with the benchmarks set using daily questionnaires alone.[6] However, due to the
299 selection of participants with higher adherence to monitoring in phase 2 of this AAMOS-00 study,
300 the longitudinal data collected in this study are likely to be more complete than the data collected by
301 the wide range of participants in the Asthma Mobile Health Study.[43]

302 Using different subsets of the data and features, we will test the performance of predictions made
303 using different modes of monitoring, such as self-reported data alone, self-reported and objective
304 data (active and passive monitoring), and passive monitoring data only (see Figure 8). Our previous
305 analysis using only self-reported data achieved $AUC > 0.87$ and we expect the performance to
306 increase with the addition of objective data.[6]

307 There is no consensus on the optimal algorithm for classification as previous studies are not
308 comparable.[11] Therefore, we have taken a broad approach to use five state-of-the-art algorithm
309 classes including Bayesian networks, decision trees, iForest, logistic regression, and support vector
310 machines.[44,45] From the classifiers, a severe asthma attack predictor will be built on the device
311 and questionnaire data, at a patient-level and population-level. Also, feature selection will be used
312 to identify the most useful features in the prediction models.

313 Furthermore, if there are sufficient data, retrospective analysis will simulate the effects of limiting
314 the use of active monitoring data, to simulate patients only taking active measurements (e.g., peak
315 flow and symptom diary) when prompted. Moreover, there will be simulation of the general
316 population using samples of the data, where adherence to monitoring is lower than the select
317 population. For assessing the performance of the models built in this study, we will use k-fold cross
318 validation.[44] The performance metrics will include the common machine learning metrics such as
319 area under the receiver operating characteristic curve (AUC-ROC), sensitivity, and specificity.

320

321 **Strengths and limitations**

322 This study combines objective data collected from multiple smart monitoring devices available on
323 the market. Not only will this independently test the monitoring devices in the real-world, but also
324 patients will be able to continue using the devices they have found useful beyond the study. It also
325 allows other researchers to reproduce the study with the current or latest versions of the devices.

326 Due to the limited number of participants and study period, stratified analysis and individualised
327 asthma attack prediction models are not expected. However, seven months of daily monitoring per
328 participant will provide insightful data.

329 This study is limited to patients with severe asthma at risk of acute attacks, and the findings may not
330 generalise to the wider asthma population. Furthermore, only participants using a pressurised
331 metered dose relief inhaler that fits our smart device are able to join the study, which is around 80%
332 of the UK's asthma population.[46] If there are sufficient data, we will explore the generalisability of
333 the results through simulating different adherence to monitoring.

334 The anonymised research data will be stored at Edinburgh DataShare (a digital repository of research
335 data produced at the University of Edinburgh),[47] which researchers can access for their own
336 research.

337

338 **PATIENT AND PUBLIC INVOLVEMENT**

339 Patient and public involvement (PPI) is part of the project from the beginning. This study is nested
340 within the Asthma UK Centre for Applied Research and has been reviewed by their AUKCAR PPI
341 members.

342 All the participant and public-facing documents and study objectives have been reviewed by
343 AUKCAR PPI members before the start of the study and edited accordingly. Such a close PPI
344 involvement ensures that the participant and public facing material is accessible. As an example, we
345 attempted to explain several technical terms (such as "pMDI") in more detail in the participant
346 documents and added pictures of pressured metered dose inhalers after feedback from PPI
347 members.

348 The findings about feasibility and acceptability will be interpreted with input from PPI members.
349 Furthermore, we plan to continue working with PPI members to develop a system that supports
350 asthma self-management.

351

352 **DISSEMINATION**

353 We will be reporting the results in peer-reviewed journal publications and conference presentations.
354 Dissemination of the results will also include the AUKCAR network with blogs and social media to
355 reach an audience who is interested in the used of smart monitoring devices for asthma.

356 We will also be sharing links to publications and summaries with study participants.

357

358 ETHICS

359 This study has received ethics approval by the East of England - Cambridge Central Research Ethics
360 Committee. IRAS Project ID: 285505.

361

362 DATA AVAILABILITY

363 At the end of the study, the anonymised research data will be stored at Edinburgh DataShare (a
364 digital repository of research data produced at the University of Edinburgh) in perpetuity.
365 Researchers will be able to access and download the data from the website for their own research.

366

367 CONCLUSIONS

368 The present study will collect an important and novel dataset, where asthma patients use a
369 combination of multiple market-available mHealth monitoring devices in the real world. We plan to
370 use the rich dataset to improve existing asthma attack prediction algorithms and use the feedback
371 from participants to design a patient-centred asthma self-management system. This study is the first
372 step in developing the Asthma Attack Management Online System (AAMOS) which will support
373 asthma patients with real-time tailored feedback based on machine learning driven by mHealth data.

374

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377 support with data collection. We thank Smart Respiratory Products Ltd for providing the Smart Peak
378 Flow Meter and associated software. We thank FindAir for providing the FindAir ONE devices and
379 FindAir's API. We thank Ambee for providing the pollen data. We thank Dr Sarah Brown (Edinburgh
380 Innovations, University of Edinburgh, UK) for organising the contracts required for the study.

381

382 AUTHOR CONTRIBUTIONS

383 KCHT, HP, AMW, and SAS designed the study. SAS is the study guarantor. KCHT and DS set up the
384 data collection system. KCHT drafted the manuscript which was critically revised by HP, AMW, DS,
385 and SAS. All authors approved the final version of the manuscript.

386

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391

COMPETING INTEREST STATEMENT

None declared.

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FIGURE LEGENDS

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5 514 *Figure 1. AAMOS-00 system overview*
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7 515 *Figure 2. Mobistudy system overview*
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9 516 *Figure 3. Participant's app home page*
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11 517 *Figure 4. Questionnaire delivered by Mobistudy*
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13 518 *Figure 5. Smart peak flow meter task*
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15 519 *Figure 6. Smartwatch data*
16 520 *Figure 7. Local weather data*
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18 521 *Figure 8. Exploring asthma attack prediction.*
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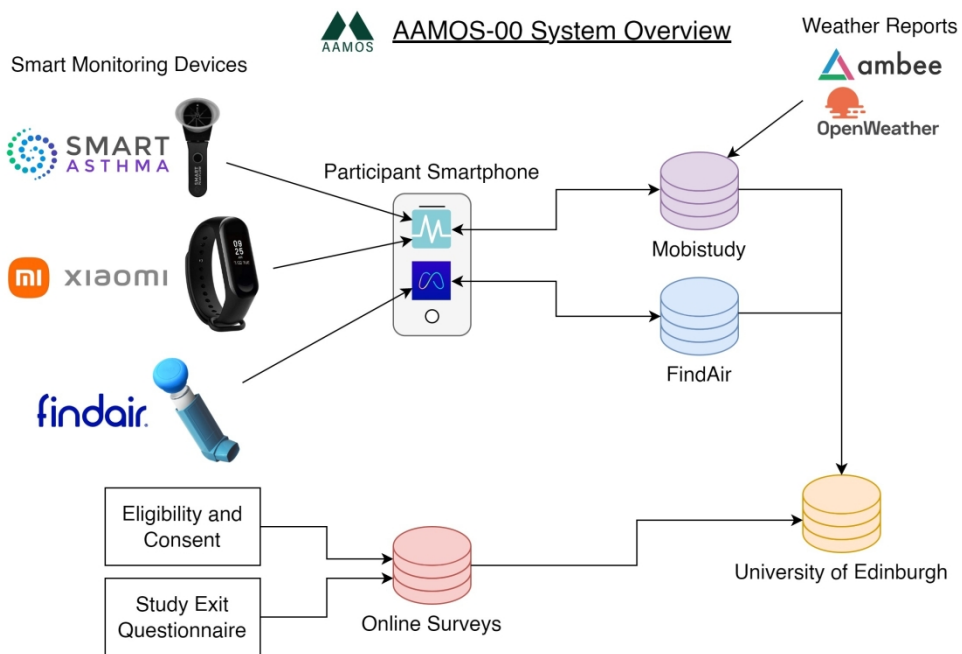


Figure 1: AAMOS-00 system overview

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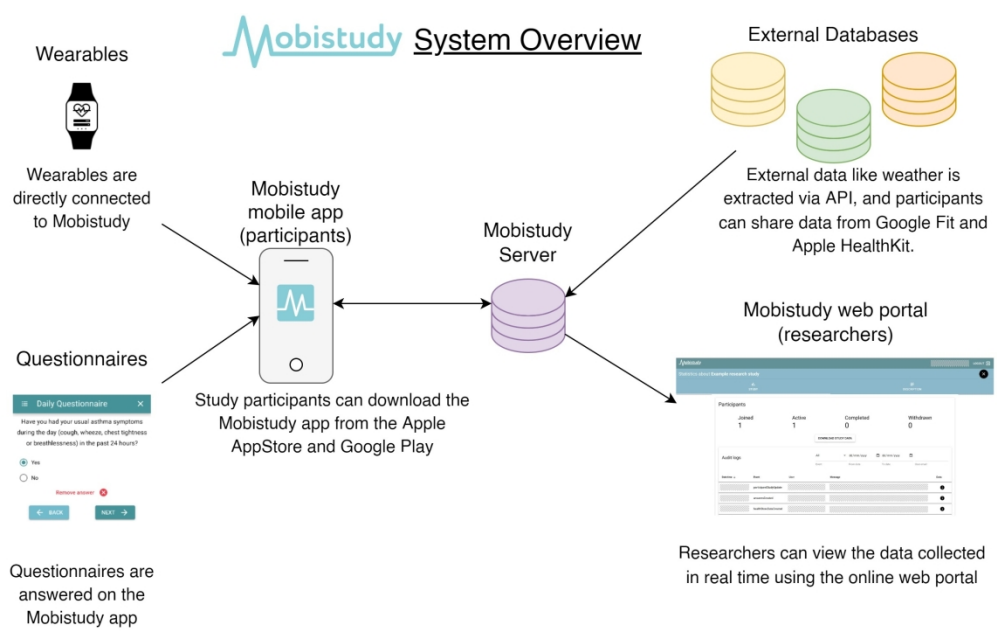


Figure 2: Mobistudy system overview

864x535mm (72 x 72 DPI)

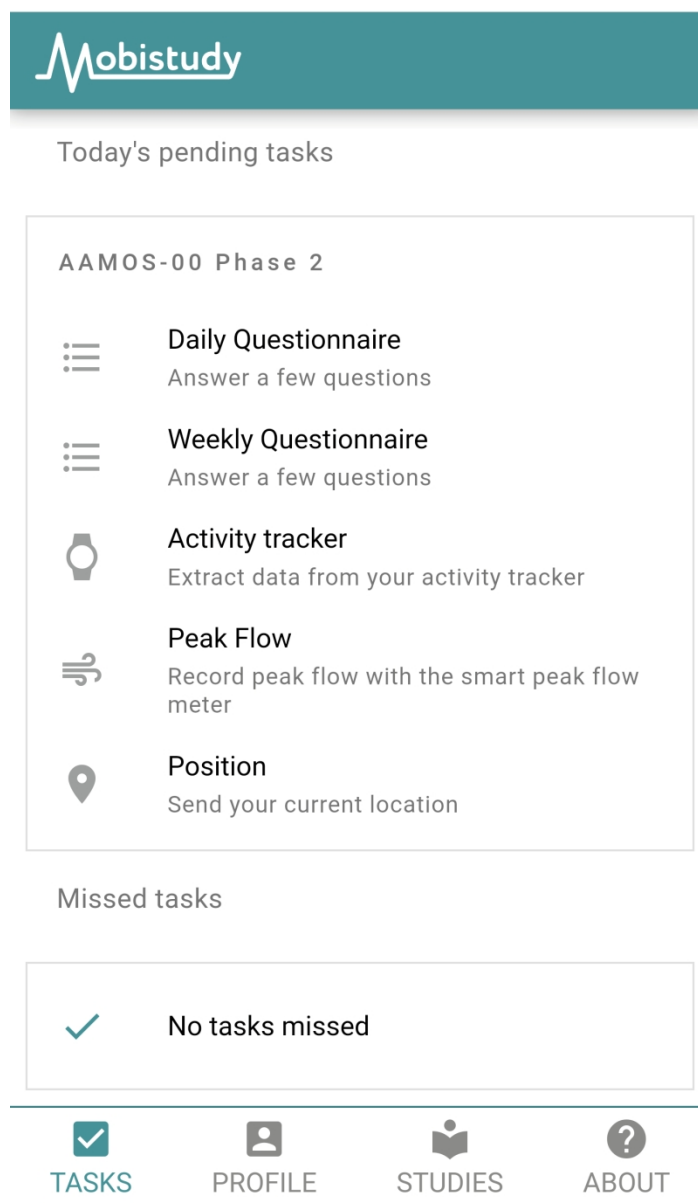


Figure 3: Participant's app home page

121x208mm (300 x 300 DPI)

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☰ Daily Questionnaire ✕

Have you had your usual asthma symptoms during the day (cough, wheeze, chest tightness or breathlessness) in the past 24 hours?

Yes

No

Remove answer ✕

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Figure 4: Questionnaire delivered by Mobistudy

121x208mm (300 x 300 DPI)

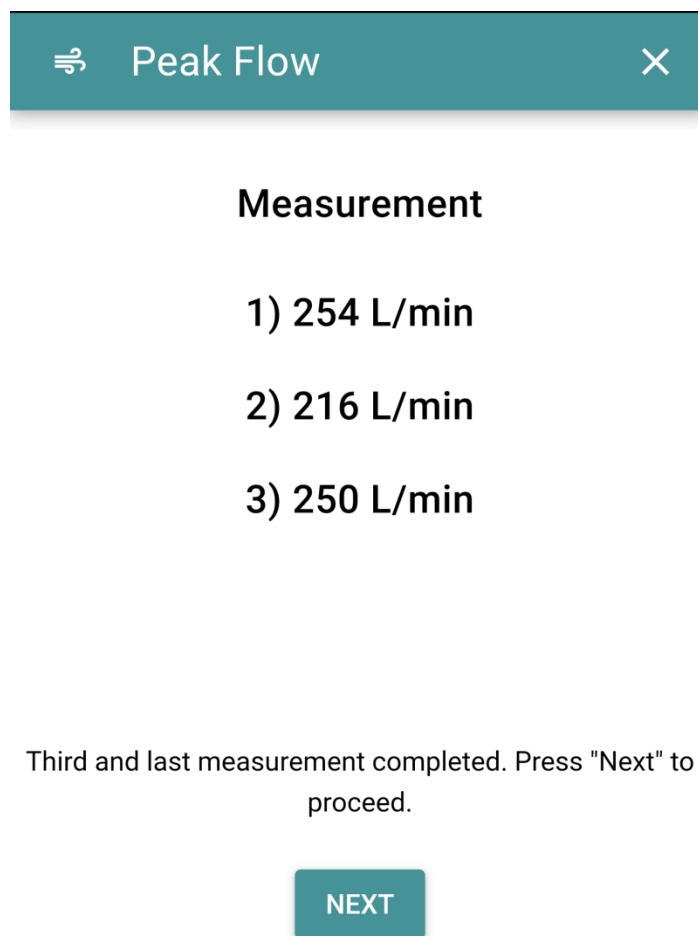


Figure 5: Smart peak flow meter task

121x208mm (300 x 300 DPI)

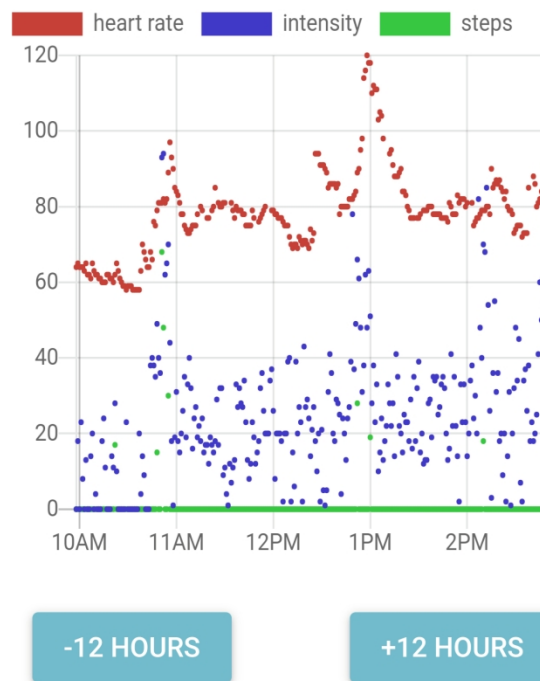


Activity tracker



The following charts summarize the data that have been retrieved from the band. Tap on "Send" to share these data with the research team or tap on "Discard" to avoid sending these data.

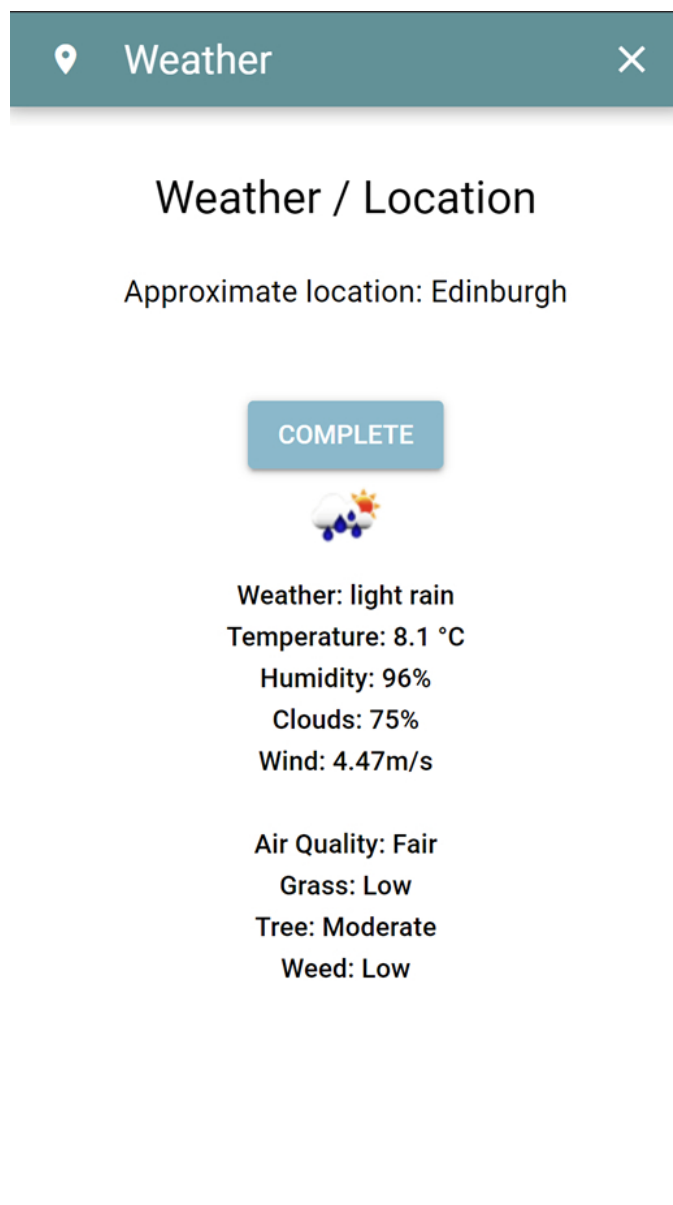
Activity over time



Time spent in each activity

Figure 6: Smartwatch data

121x207mm (300 x 300 DPI)



45 Figure 7: Local weather data

46 44x78mm (300 x 300 DPI)

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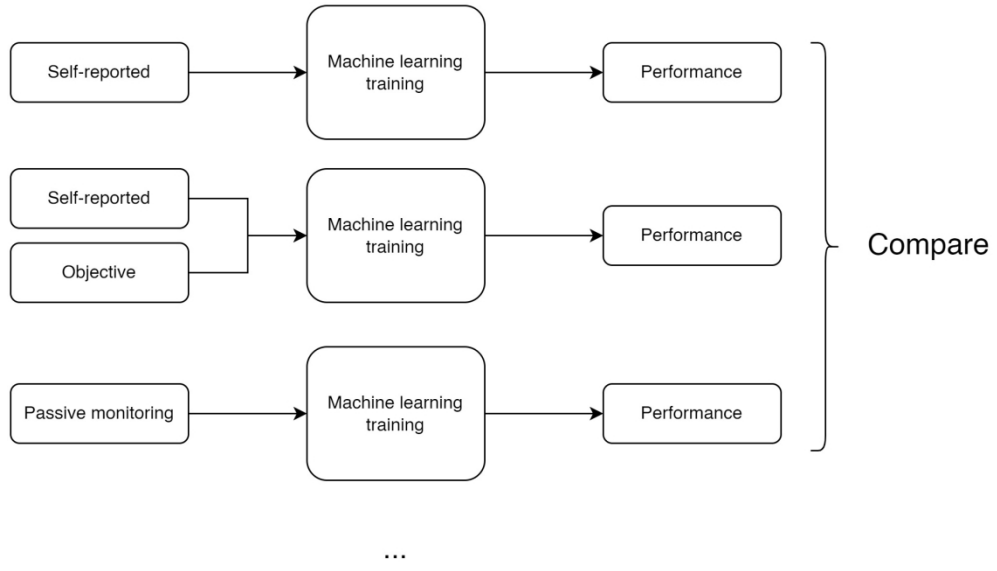


Figure 8. Exploring asthma attack prediction

714x407mm (72 x 72 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	5
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7
Bias	9	Describe any efforts to address potential sources of bias	NA
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	10
		(b) Describe any methods used to examine subgroups and interactions	10
		(c) Explain how missing data were addressed	10
	NA	(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	10

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60**Results**

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	NA
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	NA
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	NA
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	NA
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	NA
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	NA
		(b) Report category boundaries when continuous variables were categorized	NA
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA

Discussion

Key results	18	Summarise key results with reference to study objectives	NA
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	NA
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	NA
Generalisability	21	Discuss the generalisability (external validity) of the study results	10

Other information

Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12
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*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.