PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	MyAirCoach – The use of home-monitoring and mHealth systems to predict deterioration in asthma control and the occurrence of asthma exacerbations; study protocol of an observational study.
AUTHORS	Honkoop, Persijn; Simpson, Andrew; Bonini, Matteo; Snoeck-Stroband, Jiska; Meah, Sally; Chung, Kian; Usmani, Omar; Fowler, Stephen; Sont, Jacob

VERSION 1 - REVIEW

REVIEWER	Cristoforo Incorvaia Cardiac/pulmonary Rehabilitation Unit, ASST Gaetano Pini/CTO, Milan, Italy
REVIEW RETURNED	28-Aug-2016

GENERAL COMMENTS	The study protocol is accurate and the data that will be obtained are likely to be useful for the management of patients with asthma. The only issue I see concerns the lack of an upper age limit. Elderly people (for example, aged more than 75 years) may find it difficult to use some of the devices on which the study is based. In addition, though “Comorbidities that cause overlapping symptoms such as breathlessness, wheeze, cough or other interfering chronic conditions” are reported in the exclusion criteria, to distinguish asthma from asthma-COPD overlap syndrome may be not simple. The algorithm proposed by Sin et al (Eur Respir J 2016 doi: 10.1183/13993003.00436-2016. [Epub ahead of print] could be used to exclude ACOS patients.

REVIEWER	Tiago Jacinto CUF Porto - Instituto & Hospital, Porto, Portugal CINTESIS, Faculty of Medicine of University of Porto, Portugal ESS - Porto Health School, Portugal
REVIEW RETURNED	22-Nov-2016

GENERAL COMMENTS	This is a very interesting project and a very well written protocol. I do however have some comments, that, in my perspective, may help improve the protocol. Feel free to address these points: Page 9, Line 9 - should have a better, more objective definition of asthma, in line with the objective measures in Table 1. Page 10, Line 10 - what's the timeframe for the patient to have performed the tests? Page 10, Line 43 - Please clarify, and better define how will you

	classify this. Page 11, Line 7 - Please clarify how will the patients be selected. Page 15, Line 18 - Please describe in more detail when, where and how FeNO measurements will be performed. Will the patients take the device home, etc? Methods - Protocol should list all the wearables, devices and PRO's that the patient will be asked to have / perform, and have a visit, or time within a visit, to be able to explain and test this, with the individual. Page 19, Line 22 - Are there plans to make the data publicly available? Page 21, Line 48 - Please consider, in the text, the usage of the term "correlation". Do you really mean correlation, or do you mean "association"? Figure 1 - Can be vastly improved to include more details. I don't think it is clear enough to understand the study design on its own, and being the main schematic of the study, it should speak for itself. This said I believe this will be a very important study with relevant outcomes for asthma care, and I hope the authors can successfully accomplish it.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Q1: The only issue I see concerns the lack of an upper age limit. Elderly people (for example, aged more than 75 years) may find it difficult to use some of the devices on which the study is based.

A1) We agree with the reviewer that elderly people will probably find it difficult to use the devices (and possibly a group of younger people as well). However, we did not wish to make an inclusion criterion along the lines of: sufficient ability to use electronic devices. This would prove to be a hard criterion to judge (when is it sufficient?), but more importantly if our devices prove to be too difficult to use it is also vital information (therefore we also ask feedback on the ease of use (with the After Scenario Questionnaire ASQ). We can use this feedback to improve ease of use in the future, if necessary.

Q2) In addition, though “Comorbidities that cause overlapping symptoms such as breathlessness, wheeze, cough or other interfering chronic conditions” are reported in the exclusion criteria, to distinguish asthma from asthma-COPD overlap syndrome may be not simple. The algorithm proposed by Sin et al (Eur Respir J 2016 doi: 10.1183/13993003.00436-2016. [Epub ahead of print] could be used to exclude ACOS patients.

A2) The reviewer is correct to mention that the distinction between asthma and ACOS can be very difficult and the algorithm can be very useful. Unfortunately, since our research has been CME approved, we cannot add it as an additional exclusion criterion, but we can use it in practice to determine whether patients have ACOS or not. We have now added information that the decision whether or not a patient should be excluded based on comorbidity, should be made by the treating physician.

Reviewer: 2
Q1) Page 9, Line 9 - should have a better, more objective definition of asthma, in line with the objective measures in Table 1.

A1) We agree with the reviewer that this should be more clearly described. We changed this sentence to make it more clear. One hundred and fifty patients with a confirmed diagnosis of asthma (see Table 1 for criteria) will be recruited…

Q2) Page 10, Line 10 - what's the timeframe for the patient to have performed the tests?

A2) We have discussed the possibility to add a timeframe, but in the end we decided not to include any. If a patient's asthma has been confirmed in the patient's medical history, he/she will remain to be an asthmatic. Practically though, we should be able to find these details recorded somewhere, preferably in an electronic database, so this limits the timeframe to about ten years back.

Q3) Page 10, Line 43 - Please clarify, and better define how will you classify this.

A3) We agree with the reviewer that this could be clarified. We did not make a list of specific comorbidities that should be excluded, since whether or not to exclude doesn't only depend on which comorbidities exist, but also on their severity and if it has any influence in this particular patient. Therefore, we decided to leave this decision to the treating physician. To clarify this, we have included the following sentence in the table: The decision whether or not a patient should be excluded due to significant comorbidity is to be made by the treating physician.

Q4) Page 11, Line 7 - Please clarify how will the patients be selected.

A4) We added the following text to explain how patients will be selected:
One hundred and fifty patients with a doctors-diagnosis of asthma will be recruited from outpatient clinics and from general practices in the region of London and Manchester in the UK and Leiden in The Netherlands (50 patients per region). Patients will be informed by their pulmonologist, general practitioner or practice nurse about the study. A member of the study group will be available for additional information.

Q5) Page 15, Line 18 - Please describe in more detail when, where and how FeNO measurements will be performed. Will the patients take the device home, etc?

A5) The measurement is performed in the morning and evening and the device will be taken home. These details have now been provided in the text.

Q6) Methods - Protocol should list all the wearables, devices and PRO's that the patient will be asked to have / perform, and have a visit, or time within a visit, to be able to explain and test this, with the individual.

A6) During the introduction visit all tests and study procedures will be explained. After that, we are available in case of questions, but no further visits are specifically planned and participants will be treated by their own treating physicians. The introduction visit is now explicitly mentioned. Furthermore, a list is added of all wearables and devices.

Q7) Page 19, Line 22 - Are there plans to make the data publicly available?
A7) Certainly. In our research proposal for the Horizon 2020 grant, we stated:
Findings and results from our project will be submitted as abstracts to open access national and

international medical meetings under three main disciplines: (i) respiratory medicine, (ii) aerosol inhalation medicine and (iii) health technology. Furthermore, myAirCoach is aiming to produce outcomes of high importance to be published in scientific journals of high impact factor concerning the (i) development of the technology and also the (ii) clinical use of this technology by patients

Q8) Page 21, Line 48 - Please consider, in the text, the usage of the term "correlation". Do you really mean correlation, or do you mean "association"?
A8) we agree, it should be association. We changed it in the text.

Q9) Figure 1 - Can be vastly improved to include more details. I don't think it is clear enough to understand the study design on its own, and being the main schematic of the study, it should speak for itself.
A9) We changed figure 1 to include more detail.

VERSION 2 – REVIEW

REVIEWER	Cristoforo Incorvaia ASST Gaetano Pini/CTO, Milan, Italy
REVIEW RETURNED	22-Dec-2016

GENERAL COMMENTS	The paper was modified according to the reviewers' comments.

REVIEWER	Tiago Jacinto CUF Porto - Hospital & Instituto, Portugal CINTESIS - FMUP, Portugal
REVIEW RETURNED	20-Dec-2016

GENERAL COMMENTS	Thanks for your responses. I have no further comments. The only additional procedure would be an overall English revision.