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Executive Summary

The aim of this task was to define the myAirCoach test campaign strategy, in order to develop a system that assists patients in recognising worsening of symptoms and function and to timely adjust behaviour or treatment. Two test campaigns will be organized: first, a quantification campaign running from Sept-Oct 2015, aimed at the parameterization/instantiation of the WP4 computational models and to evaluate the usability and acceptability of potentially relevant self-monitoring procedures, including sensor devices; and second, an evaluation campaign at a later stage (Jan 2017), aimed at the evaluation and validation of the final myAirCoach DSS and coaching framework.

This report is a living document and provides an overview of the sensor devices and measurement procedures that will potentially be included in the first quantification campaign. The current selection of methodologies is based on careful selection of potentially interesting parameters with respect to asthma self-management and technologies that are available within and outside the myAirCoach consortium. In addition, in this document we will present the design and planning of the both test campaigns. These need to balance the scientific wish list of data on the one hand and the feasibility of measurements by patients and costs on the other. The final choices on the methodology of the first quantification campaign will be made in the first week of July 2015. Based on these a detailed research protocol will be established and submitted for approval to UK and Dutch Medical Ethics Committees. The definitive methodology of the second quantification campaign will be established in 2016, since this will be partly based on the experience and results of the first campaign and the results of other workpackages.

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List of abbreviations and acronyms

(*in alphabetic order*)

ACD	Asthma Control Diary
ACQ	Asthma Control Questionnaire
APF	Advisory Patient Forum
AQLQ	Asthma Quality of Life Questionnaire
BAN	Body Area Network
DSS	Decision Support System
EBT	Exhaled Breath Temperature
ER	Emergency Room
FeNO	Fractional concentration of exhaled Nitric Oxide
FEV1	Forced expired volume in 1 second
GINA	Global Initiative for Asthma
QoL	Quality of Life
RR	Respiratory Rate

1 Introduction

The aim of this task is to define the myAirCoach test campaign strategy. The overall myAirCoach aim is to develop intelligent Quality of Life (QoL) technologies that assist patients in recognising worsening of symptoms, function or an impending threat. This system will support patients to timely adjust behaviour or treatment accordingly and the correct use of asthma medications and by alerting when to seek medical attention. To that end, two test campaigns will be organized:

1. A quantification campaign running from Sept-Oct 2015, aimed at the parameterization/instantiation of the WP4 computational models and to evaluate the usability and acceptability of potentially relevant self-monitoring procedures, including sensor devices.
2. An evaluation campaign at a later stage (starting in Jan 2017), aimed at the validation of the final myAirCoach DSS and coaching framework.

In the first quantification campaign, we will collect data from patients with mild to moderate asthma including an intensive one month home-monitoring period. Data that will be collected will range from online questionnaires on asthma-related quality of life and daily diaries of asthma control to daily home measurements of lung function and sensor data from a Body Area Network (BAN) and sensors in the patients' environment. In this campaign, we will use a number of monitoring devices that generate potentially relevant data streams for patients with asthma. Based on the modelling work in WP4 and the usability and technology acceptance by patients a decision on devices and data streams that will be incorporated in the myAirCoach system will be made.

The second campaign will be aimed at the evaluation of the myAirCoach sensor-based monitoring and coaching system. Thus, not only data streams will be collected in the campaigns of this work package in order to assess the performance of the WP4 computational model initialization/parameterization, but it will also be aimed at the evaluation of the clinical effectiveness, usability and acceptance of the myAirCoach system.

The current task was dedicated to investigate and specify potentially appropriate physiological, behavioural and environmental markers, which might have significant predictive value for asthma apart from those already known in order to recognise threats and predict episodes of controlled and uncontrolled asthma. In addition to data for predictive modelling, the first quantification campaign will provide data on usability and acceptability of the sensor devices by patients. These results, together with the technical aspects of the measurement devices and procedures will guide the final decision whether to integrate these in the myAirCoach platform.

This report provides an overview of the sensor devices and measurement procedures that will be included in the first quantification campaign. In addition, we will present the design and planning of the two test campaigns.

2 Assessment of asthma control and QoL

2.1 Background

Asthma is a heterogeneous condition. Its natural history includes acute episodic deterioration (exacerbations) against a background of chronic persistent inflammation and/or structural changes that may be associated with persistent symptoms and reduced lung function[1]. Trigger factor exposure combines with the underlying phenotype, the degree of hyperresponsiveness and of airflow obstruction, and the severity of airway inflammation to cause wide variability in the manifestations of asthma in individual patients. In view of current knowledge about the multiple domains of asthma and asthma control, no single outcome measure can adequately assess asthma control. Its assessment in clinical studies and in clinical practice should include components relevant to both of the goals of asthma treatment, namely achievement of best possible clinical control and reduction of future risk of adverse outcomes[1]. Therefore, in this section we describe the devices, procedures and data sources that will be used to assess the different aspects of asthma control and define the clinical state that is to be predicted by the WP4 computational models.

2.1.1 Asthma control tools

Asthma symptoms such as wheeze, chest tightness, shortness of breath and cough typically vary in frequency and intensity, and contribute to the burden of asthma for the patient. Poor symptom control is also strongly associated with an increased risk of asthma exacerbations[2]. Asthma control can be assessed by a consensus-based categorical GINA symptom control tool or numerical 'asthma control' tools which can be used to guide treatment decisions. Numerical 'asthma control' tools provide scores and cut-off points to distinguish different levels of symptom control, validated against health care provider assessment. Many translations are available. These scores may be useful for assessing patient progress and are commonly used in clinical research, but may be subject to copyright restrictions. Numerical asthma control tools are more sensitive to change in symptom control than categorical tools[2]. Examples are:

- *Asthma Control Diary (ACD)* [3]. Daily scores range from 0-6 (higher is worse). A score of 0.0-0.75 is classified as well-controlled asthma; 0.75-1.5 as a 'grey zone'; and >1 .5 as poorly controlled asthma. The ACD score is calculated as the average of 5, 6 or 7 items: all versions of the ACD include five symptom questions; ACD-6 includes reliever use; and in ACD-7, a score for pre-bronchodilator FEV1 is averaged with symptom and reliever items. The minimum clinically important difference is 0.5.
- *Asthma Control Questionnaire (ACQ)* [4]. This questionnaire was based on the ACD but requires a period of one week. Scores range from 0-6 (higher is worse). A score of 0.0-0.75 is classified as well-controlled asthma; 0.75-1.5 as a 'grey zone'; and >1 .5 as poorly controlled asthma. The ACQ score is calculated as the average of 5, 6 or 7 items: all versions of the ACQ include five symptom questions; ACQ-6 includes reliever use; and in ACQ-7, a score for pre-bronchodilator FEV1 is averaged with symptom and reliever items. The minimum clinically important difference is 0.5.

- *Asthma Control Test (ACT).* This test evaluates asthma control over a period of 4 weeks. Scores range from 5-25 (higher is better). Scores of 20-25 are classified as well-controlled asthma; 16-20 as not well-controlled; and 5-15 as very poorly controlled asthma. The ACT includes four symptom/reliever questions plus a patient self-assessed level of control. The minimum clinically important difference is 3 points.

Since we aim to predict episodes of controlled and uncontrolled asthma, we will use the ACQ and related ACD framework that was developed by Juniper in the first myAirCoach quantification campaign. For both instruments, there are online versions available from the author in English[5]. Validated online Dutch versions of both the questionnaire and the diary are available within the PatientCoach asthma monitoring system[6].

2.1.2 Forced expired volume in 1 second (FEV1)

Since one of the items of the ACQ and ACD is the FEV1, we will include home-spirometry in the first myAirCoach quantification campaign. The FEV1 will be measured once daily by the patients using the PiKo-1 device. Patients will be instructed to report the highest FEV1 value out of 3 measurements. For technical specifications and operation details see Appendix 1: Forced expired volume in 1 second (FEV1). There is a webform in Dutch available within the PatientCoach asthma monitoring system[6].

2.1.3 Asthma exacerbations

- *Severe Asthma Exacerbations.* Severe asthma exacerbations are events that require urgent action on the part of the patient and physician to prevent a serious outcome, such as hospitalization or death from asthma[1]. The occurrence of severe asthma exacerbations is an important marker of poor asthma control. Severe asthma exacerbations are defined by the occurrence of at least one of the following:
    - Use of systemic corticosteroids (tablets, suspension, or injection), or an increase from a stable maintenance dose, for at least 3 days. For consistency, courses of corticosteroids separated by 1 week or more should be treated as separate severe exacerbations.
    - A hospitalization or ER visit because of asthma, requiring systemic corticosteroids.
- *Moderate Asthma Exacerbations.* A moderate asthma exacerbation is an event that, when recognized, should result in a temporary change in treatment, in an effort to prevent the exacerbation from becoming severe[1]. Moderate asthma exacerbations are defined by occurrence of at least one or more of the following:
    - deterioration in symptoms,
    - deterioration in lung function,
    - and increased rescue bronchodilator use.

These features should last for 2 days or more, but not be severe enough to warrant systemic corticosteroid use and/or hospitalization. ER visits for asthma (e.g., for routine sick care), not requiring systemic corticosteroids, are also classified as moderate exacerbations.

2.1.4 Quality of life (QoL)

Asthma related quality of life describes the problems that adults with asthma experience in their day-to-day lives. A complete review of all available instruments is beyond the scope of this report. In myAirCoach we will measure asthma related QoL instruments that are developed by Juniper[7,8]:

- *Asthma Quality of Life Questionnaire (AQLQ).* This 32-item questionnaire constitutes of 4 domains: symptoms, environment, emotions, activities, and covering a 2 week period. Scores range from 0-6 (lower is worse). The AQLQ score is calculated as the average of domain items. The minimum clinically important difference is 0.5.
- *Mini Asthma Quality of Life Questionnaire (mini-AQLQ).* This 15-item questionnaire is a short version of the complete 32-item questionnaire, but constitutes of the same 4 domains: symptoms, environment, emotions, activities, and covering a 2 week period. Scores range from 0-6 (lower is worse). The mini-AQLQ score is calculated as the average of domain items. The minimum clinically important difference is 0.5. This version has been developed to meet the needs of long-term monitoring, where efficiency may take precedent over precision of measurement.

For both instruments, there are online versions available from the author in English[5]. Validated online Dutch versions are available within the PatientCoach asthma monitoring system[6]. In the first myAirCoach quantification campaign, QoL will be home-monitored by the patients on a monthly basis.

3 Monitoring predictive factors of asthma control

3.1 Background

Monitoring predictive factors of asthma control includes (bio)markers that can be measured and trended within an individual to provide advance warning of an event, in the same way that oil temperature and pressure gauges give an indication of engine well-being. In this task, we have explored several potentially appropriate physiological, behavioural and environmental markers that are available for monitoring, which might have significant predictive value for asthma in order to recognise threats and predict episodes of controlled and uncontrolled asthma. In this section, we describe the devices, procedures and data sources which could be used in order to collect these physiological, behavioural and environmental data that will then be used as input for the WP4 computational models.

3.1.1 Medication usage

Asthma is characterised by several different elements: airway inflammation, tightening of the muscles around the airways and a build-up of mucus inside the airways. In combination, they make it harder for air to circulate in and out of the lungs and cause the common symptoms such as coughing, wheeze and shortness of breath. These characteristics are reversible either spontaneously or with treatment. Treatments address different elements of these underlying characteristics:

- reliever inhalers (typically blue inhaler, also known as ‘rescuer’) – provide bronchodilator to relax the muscles around the airways and relieve asthma symptoms in the short term – e.g. during an asthma attack, when coughing, during exercise.
- preventer inhalers (typically brown inhaler, also known as ‘controller’) – provide corticosteroid medication to treat the inflammation inside the airways. It takes some time (up to 14 days) for the treatment to build in the system meaning that they need to be taken regularly, not just when you’re feeling unwell. If left untreated, inflammation can become more permanent and may become irreversible – meaning you will have symptoms permanently.

In addition to these two inhaler types, there are also combination inhalers – combining some preventer and some reliever medications. Therefore, with respect to monitoring medication usage it is highly relevant to make a distinction between reliever, preventer or combination inhalers. Underuse of a preventer inhaler might indicate that a patient might have an increased risk of loss of asthma control and (over)use of a reliever inhaler might indicate the occurrence of increased asthma symptoms and loss of control. It is of key importance that medication usage is registered in the first quantification campaign and in the final myAirCoach system. However, the final myAirCoach inhaler device is not available during the first campaign. Therefore, the patients will be asked to register their medication usage in an online webform or app. A dedicated medication diary will be available in Dutch within the PatientCoach asthma monitoring system[6]. A similar online diary will be used for the UK setting.

3.1.2 Airways inflammation

Airways inflammation is one of the hallmarks of asthma. Therefore, monitoring of airways inflammation might provide relevant information about the underlying disease activity. Airways inflammation cannot be directly non-invasively measured. However, there are a few surrogate markers that allow indirect assessment of airways inflammation.

- *Fractional concentration of exhaled nitric oxide (FENO).* Patients with allergic airway inflammation generally have higher than normal levels of nitric oxide (NO) in their exhaled breath. By measuring the concentration of NO in an exhaled breath (fractional exhaled nitric oxide or FeNO), one can evaluate allergic airway inflammation in patients with underlying asthma. The exact relationship between the fractional concentration of exhaled nitric oxide (FENO) and the underlying pathologic process in asthma remains unclear. The increasing use of FENO as a surrogate marker for the presence of clinically relevant eosinophilia is based on significant correlations between FENO measurements and eosinophilic airways inflammation.

In a proof-of-concept study in children with asthma van der Valk et al. analysed long-term daily measurements of FeNO by different types of mathematical techniques in order to look at periods of exacerbations relative to reference periods in the same patient[9]. The analysis showed that there are changes in FeNO before the onset of exacerbations compared to reference periods and they quantified some of these changes. However, the available sample size was small, namely 25 moderate exacerbations in 18 children. There were only 12 severe exacerbations in nine patients, which may have decreased the power to detect significant associations between daily FeNO and severe exacerbations. Their findings suggest that regular FeNO measurements in the home setting could help to detect and perhaps even help prevent loss of asthma control. Such monitoring could be especially useful in a selected population with frequent exacerbations. The authors state that further studies looking at changes in FeNO over time in selected populations are warranted to assess the role of FeNO for monitoring and risk prediction in asthma among other parameters [10,11]. In a recent study, Saito et al. reported that diurnal variation in FeNO assessed by morning and evening measurements can be used as a biomarker of asthma control and as a predictor of the risk of future exacerbation [12].

In the first myAirCoach quantification campaign FeNO will be home-monitored by the patients using the NIOX-VERO device. The duration of a FeNO test with NIOX takes only a few minutes, once the patient has done it a couple of times and is used to it. The exhalation procedure takes about 20 seconds and the result comes in 1 minute. For technical specifications and operation details see Appendix 2: Fractional concentration of exhaled nitric oxide.

- *Exhaled Breath Temperature (EBT).* Evaluation of the exhaled breath temperature (EBT) has been suggested as a new method to detect and monitor pathological processes in the respiratory system. The putative mechanism of this approach is based upon changes in the blood flow in the conducting airways that are characteristic of different disease states, which influence the

temperature of the exhaled gases. The first attempts to prove this concept were made in conjunction with measurement of exhaled nitric oxide fraction (FeNO) about a decade ago. They made use of an open-circuit, single-breath method in a closed indoor environment, and demonstrated associations between EBT on the one hand, and bronchial blood flow, FeNO and sputum cellular content on the other[13].

In the first myAirCoach quantification campaign EBT will be home-monitored by the patients using the X-halo device. The measurement procedure with the X-halo home device takes less than a minute to complete. For technical specifications and operation details see Appendix 3: Exhaled Breath Temperature.

3.1.3 Respiratory rate (RR)

Respiratory Rate (RR) is a very important physiological parameter to be monitored in people both in healthy and critical condition, as it gives meaningful information regarding their respiratory system performance as well as condition. The RR is defined as the number of breaths per minute. A typical RR at resting is 12 and its corresponding frequency is 0.2 Hz. During sleep, behavioural influences are minimal; hence, the fluctuations are primarily driven by underlying feedback control mechanisms. Furthermore, analysing respiratory variables during sleep allows one to collect large segments of data and to examine fluctuations over both short and long time scales. nocturnal worsening of asthma has been described for centuries and conveys a poor prognosis, although the underlying mechanism is unknown. Based on the notion that deep inspirations may be bronchoprotective, lack of breathing variability during sleep may be an important factor in promoting nocturnal bronchospasm or may be a marker for future asthma attack[14].

There are a few commercial options for self-monitoring of respiratory rate. Spire seems to be one of the most elegant devices that allows continuous measurements of inhalation and exhalation times, breath rate, deep breaths, apneaic events, steps and infers a patients stress level. Spire has an open programming interface that allows access to the raw data. In the first myAirCoach quantification campaign we will explore whether it is possible for (a subgroup of) patients to monitor their respiratory characteristics. An alternative approach for the measurement of respiratory rate is provided by the Speckled Computing research framework of the University of Edinburgh. For technical specifications and operation details see Appendix 4: Respiratory Rate.

3.1.4 Physiological monitoring by wristband

Possible candidates for self-monitoring physiological functions by wristbands in asthma are pulse rate, skin temperature or even oxygen saturation by companies like Fitbit and Seraphim Sense[15,16]**.** Although the added value of monitoring these parameters has not been established yet they potentially provide relevant information about the clinical state of asthma including the severity of exacerbations when evaluated in perspective with other clinical outcomes and exercise levels.

In the first myAirCoach quantification campaign patients will monitor their pulse rate and exercise capacity by the Fitbit Charge HR (heart rate) wristband. For technical specifications and operation details see Appendix 4: Respiratory Rate. The Fitbit can be connected to the solution of our partner CNET as well as to PatientCoach for patients in the Netherlands. In addition, we will explore whether the AngelSensor wristband is a better option for the final myAirCoach system, since it provides an open architecture and therefore allows full integration with myAirCoach apps. For technical specifications and operation details see Appendix 5: Pulse rate.

3.1.5 Environmental parameters

Environmental factors and stimuli have a major impact on the clinical state of patients with asthma. Therefore monitoring of environmental factors will be incorporated in both test campaigns.

- Air quality monitoring. In the UK, the website of the Department for Environment, Food and Rural Affairs (DEFRA) is linked to the UK-AIR (Air Information Resource) webpages providing in-depth information on air quality and air pollution in the UK[17]. A range of information is available, from the latest pollution levels, pollution forecast information, a data archive, and details of the various monitoring networks. The data provides an interactive monitoring map of the pollution levels in the UK from 300 monitoring sites in total across the UK which monitor air quality which are organized into networks that gather a particular kind of information, using a particular method. The data is also able to predict a 5-day forecast. The Automatic Urban and Rural Network (AURN) is the UK's largest automatic monitoring network. It includes automatic air quality monitoring stations measuring oxides of nitrogen (NOx), sulphur dioxide (SO2), ozone (O3) and particles (PM10 and PM2.5). These sites provide high resolution hourly information which is communicated rapidly to the public, using a wide range of electronic, media and web platforms.
- In The Netherlands the air quality monitoring network provides information on measured air quality at many points throughout the Netherlands[18]. The measurement points are managed by different authorities, including the Netherlands National Institute for Public Health and the Environment (RIVM). The Dutch air quality monitoring network provides a detailed hourly 2-day ahead forecast of PM10 and ozone values.

Figure 1. Measurement points of air quality in The Netherlands.

- *PM10.* The concentration of fine particulates (PM10) is higher around the morning and evening rush hour. The weather and traffic emissions have a great impact on the concentration. PM10 is a collective term for suspended particles that can be inhaled, with a maximum diameter of 0.01 millimetres. The legal limit value is an annual average of 40 (µg/m3). In addition, the daily average of 50 (µg/m3) may only be exceeded no more than 35 times per year.
- *PM2.5.* The concentration of fine particulates (PM2.5) is higher around the morning and evening rush hour. The weather and traffic emissions have a great impact on the concentration. PM2.5 is a collective term for suspended particles that can be inhaled, with a maximum diameter of 0.0025 millimetres. The legal limit value is an annual average of 25 (µg/m3). As PM2.5 particles are even smaller than PM10 particles they are able to penetrate even deeper into the lungs and are therefore more harmful from a health perspective.
- *Black smoke.* The concentration of black smoke is higher around the morning and evening rush hour. This substance is released when trucks, ships and industry burn fuel. The concentration of black smoke is an indicator of the number of soot particles in the air. Soot is the smallest particulate matter (PM2.5). There is no set legal limit value yet. As soot is

even smaller than PM2.5, particles are able to penetrate even deeper into the lungs and are therefore more harmful from a health perspective.

- *CO.* The concentration of carbon monoxide (CO) in the air is normally around 500 (µg/m3). This compound is formed when a substance is burned at low oxygen levels. Traffic is a main source of carbon monoxide in the air. The legal limit is 40,000 (µg/m3). In ambient air this level is normally not reached.
- *O3.* The concentration of ozone (O3) depends partially on the weather. Slight smog occurs at ozone levels above 120 (µg/m3). Moderate smog occurs at ozone levels above a180 (µg/m3). Severe smog occurs at levels above 240 (µg/m3). This only occurs for a few hours each year, primarily during good summer weather.

- *Pollen counts and forecasts.* Approximately five percent of the population sometimes suffer from hay fever (pollinose) and this allergy is highly relevant in patients with asthma. This allergic reaction is caused by pollen from different species of plants (predominantly grass) and trees. When the symptoms (stuffy nose, running eyes, sometimes shortness of breath) become serious, patients can use their drugs or take other measures (i.e. stay indoors). In order to help these patients taking these measures a 5-day ahead pollen forecast is provided by the Leiden University Medical Center in The Netherlands. In the UK, the Meteorological Office (Met Office) manage the only pollen count monitoring network in the UK using information from their network, weather data and expertise from organisations such as the National Pollen and Aerobiological Unit[19] and Pollen UK to produce forecasts that help support allergy and hay fever sufferers through the most difficult time of the year[20].

- *Weather conditions and forecast.* Weather conditions are also relevant for patient with asthma. Therefore both in the UK and the Netherlands these data will be will be incorporated in both test campaigns.

- *GPS location.* In order to be able to interpret the environmental risks the final myAirCoach system should have insight into the location of the patient. Such location-aware healthcare is achievable as the location coordinates of the patients can be retrieved by GPS and sent to the myAirCoach server.

4 Quantification campaign methodology and planning

4.1 Background

In the first clinical myAirCoach study we will collect data in patients with mild to moderate asthma in order to develop intelligent QoL technologies[21]. The final intelligent myAirCoach system will assist patients in recognising worsening of symptoms or function or an impending threat. In addition the system will provide support to timely adjust behaviour or treatment accordingly and the correct use of asthma medications and by alerting when to seek medical attention. Data will be passively collected from medical registries, by using several sensors in a Body Area Network (BAN) and sensors in the patients' environment, and by active involvement of patients by performing daily home measurements and diaries during the first one month study phase and by less frequent measurements and questionnaires during the second phase. The aim of the first phase is to collect data in order to recognise threats and predict episodes of uncontrolled asthma and the second phase is aimed at prediction of (the onset of) full-blown asthma exacerbations.

4.2 Research questions

1. To what extent can sensor data from a Body Area Network (BAN) in combination with environmental (sensor) data and patient characteristics be used to recognise threats and predict episodes of uncontrolled and controlled asthma (with respect to Phase 1 and myAirCoach delivery D2.3)?
2. Is it possible to predict (the onset of) a full-blown asthma exacerbation (Phase 2)?

4.3 Aim

To develop models for intelligent QoL technologies that assist patients in recognising worsening of symptoms or function or an impending threat, in timely adjusting behaviour or treatment accordingly and using medications correctly and by alerting when to seek medical attention.

1. To collect data for modelling in order to recognise threats and predict episodes of uncontrolled and controlled asthma (Phase 1 with respect to delivery D2.3)
2. To collect data for modelling in order to predict (the onset of) full-blown asthma exacerbations (Phase 2)

4.4 Study design

This first campaign is designed as an observational study with a total duration of 12 month with 2 phases:

- Phase 1: 1-month period of daily monitoring of asthma (with respect to delivery D2.3)

- Phase 2: 11-month period of weekly monitoring of asthma control. Patients will be invited for a second 2 week period of daily monitoring spread over the remaining follow-up. The purpose of the second phase of daily monitoring is to assess the influence of seasonality (different seasons) on the patient's asthma .

0 xxxx 1 ------ 2 ------ 3 ------ 4 yy-- 5 ------ 6------ 7 ------ 8 ------ 9 ------ 10 ------ 11 ----- 12
Months FU

xxxx = first series of 4 weeks daily monitoring
------ = 12 months weekly monitoring
yy-- = example of second series of 2 weeks daily monitoring during month 5, in blocks of 12-13 patients per block. Blocks of patients will be randomised over month 2-9.

4.5 Study population

Population

One hundred and fifty patients with a doctor's diagnosis of asthma will be recruited from outpatient clinics or from general practices in London and Manchester regions 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, and additionally a member of the study group will be available for additional information.

In London and Manchester, participants will be recruited via secondary care hospital patients and also via primary care clinics with which the hospitals in London and Manchester both have links. Both London and Manchester have access to primary care networks that have been established through the NIHR (National Institute for Health Research) that are actively involved in patient-orientated research.

In the region of Leiden patients will be recruited via the LUMC pulmonary outpatient clinic and LEON primary care research network and the "Zorggroep Regionale Organisatie Huisartsen West Nederland (ROHWN)". This is a cooperation of 100 general practices that started in 2007 with a special focus on development of high quality care, including specific programmes for patients with asthma and COPD (since 2012).

Patients will be enrolled in 3 strata of asthma control, whereby one-third of the patients will have controlled asthma, one-third partly controlled asthma and one third uncontrolled asthma as based on the Asthma Control Questionnaire[8].

Inclusion criteria

(All of the following criteria)

- Doctors-diagnosis of asthma
- Atopic or non-atopic
- Asthma treatment step 2-4, need for controller medication, regular treatment
- Mobile phone and computer with internet access
- Age 18+

Exclusion criteria

- Well-controlled and without treatment most of the year
- Comorbidities that cause overlapping symptoms such as breathlessness, wheeze, cough or other interfering chronic condition
- Unable to understand English, Dutch

Sample size

With 150 patients daily monitoring for 6 (4+2) weeks we will obtain 150 * 6 * 7 = 6300 daily entries of measurements in this study. In addition to the daily monitoring, with 150 patients monitoring for 52 weeks we will obtain 150 * 52 weeks = 7800 weekly entries of measurements in this study. This is in addition to the total number of daily/hourly/quarterly data that are automatically generated by the wearables, including the wristband and the respiratory rate monitoring device.

Furthermore, in this quantification campaign we aim to include a subgroup of 60 patients with a history of a severe exacerbation in the previous year (20 per centre, total study group 150 patients). Severe exacerbations will be defined as a course of oral corticosteroids for at least 3 days, an emergency department visit or a hospitalisation due to increased symptoms of asthma. Given an history of 1 severe exacerbation per patient per year we expect to obtain in these patients with an exacerbation history already at least 60 severe exacerbations. However, there will be even a greater number of moderate severe exacerbations. This number of events is sufficient to allow us to build the predictive models.

4.6 Methods

Diagnostic work-up

- Visit to the Lung function Laboratory to perform a spirometry before and after bronchodilations
- Online questionnaires

Diagnosis

Patients with asthma will be enrolled in the study if:

- History of episodic chest tightness and wheezing in the previous year
- Pre-bronchodilator FEV1 > 50% predicted
- Asthma control will be assessed by the Asthma Control Questionnaire (ACQ)[3]. A patient's asthma control status will be classified as Controlled (ACQ≤0.75), Partly Controlled (0.75<ACQ≤1.5) or Uncontrolled (ACQ>1.5)
- Atopy will be assessed by skin-prick test or measuring levels of specific IgE in serum

Baseline measurements

- Off-line clinical characteristics
    - Demographic data on the patient's age, gender, country,
    - Baseline weight, height, body mass index (BMI), body surface area (BSA)
    - Atopic status
    - Baseline lung function (spirometry and
    - Fractional exhaled Nitric Oxide (FeNO) by NIOX-VERO
    - Chronic sinusitis
    - Previous hospital admittance for asthma
    - Severe asthma exacerbation in the previous year
    - Inhalation technique
- Online patient characteristic questionnaire
    - Smoking status
    - Socio-economic status (SES)
    - Asthma Control Questionnaire (ACQ)[4]
    - Asthma Quality of Life Questionnaire (AQLQ)[7]
- Nutritional/diet questionnaire
- Online hospital anxiety and depression score (HADS)[22].
- Online self-management characteristics questionnaire (Health Education Impact Questionnaire (heiQ))[23]. This 40-item questionnaire includes the following domains: Health directed behaviour; Positive and active engagement in life; Emotional well-being; Self-monitoring and insight; Constructive attitudes and approaches; Skill and technique acquisition; Social integration and support; Health service navigation.

Phase 1 (first 4-week daily monitoring)

- Daily home spirometry (FEV1) via Piko-1
- Daily online Asthma Control Diary, (ACD-7, incl FEV1)[3]
- Daily online medication diary
- Weekly online mini Asthma Quality of Life Questionnaire (mini-AQLQ)[8]
- Daily, twice-daily Fractional exhaled Nitric Oxide (FeNO) by NIOX-VERO (in duplo)
    - 28x2=56 measurements/patient
- Daily, twice-daily Exhaled Breath Temperature (EBT) by X-halo (in duplo)
    - 28x2=56 measurements/patient

Phase 2 (month 2-12)

Weekly monitoring *(a fixed day during the week will be chosen for each patient to make it easy for them to remember when to undertake the measurements)*

- Weekly home spirometry (FEV1) via Piko-1
- Weekly online Asthma Control Questionnaire, (ACQ-7, incl FEV1) [24].
- Monthly online mini Asthma Quality of Life Questionnaire (mini AQLQ)[8].
- Weekly Fractional exhaled Nitric Oxide (FeNO) by NIOX-VERO (in duplo)
    - 48 weeks x 2 = 96 measurements/patient
- Weekly Exhaled Breath Temperature (EBT) by X-halo (in duplo)
    - 48 weeks x 2 = 96 measurements/patient

Second series of 2-week daily monitoring (start randomised)

- Daily home spirometry (FEV1) via Piko-1
- Daily online Asthma Control Diary, (ACD-7, incl FEV1)[3].
- Daily online medication diary
- Weekly online mini Asthma Quality of Life Questionnaire (mini-AQLQ)[8]
- Daily, twice-daily Fractional exhaled Nitric Oxide (FeNO) by NIOX-VERO VERO (in duplo)
    - 14x2=28 measurements/patient
- Daily, twice-daily Exhaled Breath Temperature (EBT) by X-halo (in duplo)
    - 14x2=28 measurements/patient

Both phase 1 & 2 (month 1 - 12)

- Continuous registration of sensor data via wearables (BAN)
    - pulse, exercise level via Fitbit wristband
    - breath rate via Respeck or Spire
- (Continuous) registration of environmental (sensor) data
    - Ozone (O3)
    - air pollution (PM10, PM2.5)
    - ambient temperature
    - Nitrous oxide (NO2)
    - Sulphur dioxide (SO2)
    - PM10 and Ozone forecast
    - Weather conditions and forecast
        - Mean temperature
        - Humidity
    - Relevant pollen counts and forecast
- Daily online symptom / medication diary is available
- Usability and Technology Acceptance questionnaire (3, 6, 12 months).

Data collection

Online questionnaires and data entry of home measurements can be performed by the patient using the monitoring and research modules of the self-management support internet application PatientCoach (only available in Dutch, see appendix).

Analysis

Main study parameter/endpoints

- Phase 1: asthma control
    - (episodes of) uncontrolled asthma
    - (episodes of) controlled asthma
- Phase 2: asthma exacerbation
    - course of prednisone
    - emergency visit

Secondary study parameters/endpoints

- Asthma quality of life
- self-management skills and health education impact
- side effects
- motivation /usability and technology acceptance
- therapy adherence

Statistical analysis

Model 1

- dependent variable
  - onset of exacerbations (12 months) (model 1) and
- (potential) predictors
  - patient characteristics
  - baseline / regular measurements
  - sensor data
  - environmental data and forecasts

Model 2

- dependent variable
  - episodes of (un)controlled asthma based on ACD-7/FEV1 (1 month) (model 2
- (potential) predictors
  - patient characteristics
  - baseline / regular measurements
  - sensor data
  - environmental data and forecasts

4.7 Planning

- Protocol M7
- Medical Ethical approval M9
- Research infrastructure M9
  - Online data collection, CRF database available
    - *NL: PatientCoach monitoring system*
  - CRF database
  - Piloting data collection
- Start inclusion M10
- End inclusion M12
- End 1 month FU last patient M13
- Source dataset cleared M14
- Intermediate variables M16

5 Evaluation campaign methodology and planning

5.1 Background

The evaluation campaign at a later stage (starting Jan 2017) will be aimed at the validation of the final myAirCoach DSS and coaching framework. This second campaign will be instantiated with measurements provided by the myAirCoach sensor-based monitoring system. Thus, new data streams will be collected in the campaigns of this work package in order to assess the performance of the WP4 computational model initialization/parameterization.

5.2 Methods

In the second half of the project, they will involve pilot execution in three distributed pilot sites and will serve both model optimization and validation purposes and, critically, to identify redundant clinical assessments. Work will also focus on the clinical analysis of the results and the optimization/quantification of the developed models.

Once the myAirCoach prototype has been developed and undergone successful validation testing, it will be utilised in a structured two-stage pilot study with the objectives of testing feasibility of myAirCoach in everyday use, and secondly proof of concept that myAirCoach improves asthma control.

Stage I. Feasibility study. The aim is to carefully investigate and highlight any potential issues that may impede implementation of myAirCoach. The prototype as delivered by WP5 (i.e. having already undergone pre-clinical and healthy-volunteer testing and validation) will be used in ten patients at each clinical centre (i.e. 30 patients in total). Each stage of the process will be evaluated carefully. Patients initially will attend the clinic for a demonstration of the system, and allowed to trial setting it up and using it independently, before taking it home for a two week period. During this period they will use it as instructed, with open access to the researchers by telephone or email for feedback. Patients will be contacted after two and seven days of use, before returning the equipment at day 14. Then patients will undergo a one-to-one debriefing session with a researcher, in order to record the user-experience of the myAirCoach procedure, from the initial set-up meeting through to home use. This will allow us to render any improvements to the user-instructions, and potentially to the device itself, prior to launching the stage II proof of concept study.

Stage II Proof of Concept Study. The aim of this study is to obtain pilot data on the effect of instigating myAirCoach on asthma related quality of life and asthma control, in order to inform the design of a future definitive clinical effectiveness study. We will use myAirCoach as refined (if necessary) following the feasibility study in a prospective three-month case-control study of 150 patients (50 per clinical centre, recruited in the first test campaign). Patients will be randomised 1:1 to either usual care or myAirCoach. The primary endpoints will be Juniper Asthma Quality of Life Questionnaire (AQLQ) and Asthma Control Questionnaire (ACQ) at three months. Secondary endpoints will be AQLQ and ACQ at month 1 and month 2, and medication use (average daily inhaled corticosteroid use and average daily reliever use), exacerbation rate (graded by severity) and spirometry (forced expiratory volume in one second (FEV1) and FEV1 / forced vital capacity ratio) at months 1, 2 and 3. Patients (in both groups) will attend at

baseline and end of study for instruction, baseline and end-of-study measurements. They will also have face-to-face or virtual (via videoconference) visits at month 1 and 2, in order to collect study data and provide refresher training for the myAirCoach group. Data will be analysed in order to provide estimates for effect size that will inform study design of a future effectiveness trial. The definitive methodology of the proof of Concept Study will be established in October 2016, since this will be partly based on the experience and results of the first campaign and the results of other workpackages.

5.3 Planning

Stage I. Feasibility study.

- Protocol M18
- Medical Ethical approval M21

Stage II Proof of Concept Study.

- Protocol M21
- Medical Ethical approval M24
- Research infrastructure M24
    - Online data collection, CRF database available)
        - *NL: PatientCoach monitoring system*
    - CRF database
- Start inclusion M25
- End inclusion M27

The planning of the evaluation campaign will be detailed in 2016.

Conclusion

In this living document, we describe the sensor devices and measurement procedures that will potentially be included in the first quantification campaign. The current selection of methodologies is based on careful selection of potentially interesting parameters with respect to asthma self-management and technologies that are available within and outside the myAirCoach consortium. The final decisions on the methodology of the first quantification campaign will be made in the first week of July 2015. These need to balance the scientific wish list of data on the one hand and the feasibility of measurements by patients and on costs. Based on the final choices a detailed research protocol will be established and submitted for approval to UK and Dutch Medical Ethical Committees in July 2015. The definitive methodology of the second quantification campaign will be established in October 2016, since this will be partly based on the experience and results of the first campaign and the results of other workpackages.

Appendix 1: Forced expired volume in 1 second (FEV1)

Forced expired volume in 1 second (FEV1) by PiKo-1®

PiKo-1 Measures peak flow and FEV1, considered by many asthma specialists to be a more reliable indicator of an impending asthma attack.

Recognized as the Best Over-the-Counter and Self Care Product at the US Medical Design Excellence Awards in 2003, PiKo-1 is more accurate in the measurement of peak flow than mechanical peak flow meters and is ATS/EU scale compliant.

Specifications

PEF:	Range: 15 - 999 l/min (1 l/min resolution) Accuracy: 5% or +20 l/min (whichever is greater)
FEV1:	Range: 0.15 - 9.99 liter (0.01 liter resolution) Accuracy: ±3% or 0.1 liter (whichever is greater)
Sensor:	Pressure/flow sensor technology, (patented)
Memory:	96 patient test scores
Memory Type:	Non-volatile
Color Zone:	3 Color Zones (Green, Yellow, Red)
Reference Values:	User defined
Quality Factor:	Warning & indicator for cough or abnormal blow
Sounds:	Four patterns for different indications and warnings
Communication:	Bi-directional IR port (RS232 format)
External Settings:	Possible settings using the optional PiKoNET Professional software: -Each Color Zone limits (in 10% increments)

	- Select Color Zones to relate to PEF or FEV1 or FEV6 (PiKo-6)
Battery Life:	One year (based on average of 6 blows per day)
Battery Type:	2 x type 357 silver oxide button cells (or equivalent)
Dimensions:	75 x 35 x 20 mm
Weight:	35 grams
Back Pressure:	<2.5 cmH2O/l/sec at 14 l/sec or lower
Operating Temp:	10 to 38°C (50 to 100 °F)
Storage Temp:	-20°C to 60°C (-4 to 140 °F)
Humidity:	0 - 100% relative humidity
Barometric:	550 to 780 mm Hg
Performance:	ATS1994 (monitoring), AS/NZS-4237: 1994, EN13826: 2003
Safety:	EN60601-1, EN60601-1-1, EN60601-1-2, EN13826:2003, and IPX4
Regulatory:	FDA - 510(k) for OTC; CE 0086, Class I with measurement function
Warranty:	Six months (batteries not included)

nSpire Health, Inc. Longmont, CO, USA, http://www.nspirehealth.com/

Appendix 2: Fractional concentration of exhaled nitric oxide

Fractional concentration of exhaled nitric oxide (FENO) by NIOX VERO®

NIOX VERO® is a point-of-care device for assessing airway inflammation in patients with respiratory problems such as asthma. NIOX VERO is a further development of NIOX MINO®, the most widely used device for measuring airway inflammation in clinical practice and clinical studies all over the world.

Expected characteristics for a point-of-care device

- Easy to use
- Quick results
- Reliable and accurate results
- Trouble free maintenance

Easy to use and quick results

- Designed with patients and health care professionals in mind to ensure best performance
- Can be used both for children and adults (provided patient cooperation)
- Short start-up time
- Quick analysis time, within a minute

Reliable and accurate results

- Internal check of electronics every time at start-up.
- Measurement result obtained only when the patient completes procedure correctly

- Good repeatability allows for one measurement only
- Follows ATS/ERS equipment recommendations
- CE marked

Trouble free maintenance

- Service and maintenance free device
- 5 years shelf-life and 15000 measurements
- No calibration required

Specifications

Measurement range: FeNO	5 to 300 ppb
Exhalation time	10 seconds (6 s for children ≤ 10 years
Measurement time	1 min
Accuracy	± 5 ppb or max 10%
Precision	<2 ppb of measured value <50 ppb <4% of measured value ≥50 ppb
Instrument memory capacity	15000 measurements
Dimensions (height x width x depth)	145 mm x 185 mm x 41 mm
Weight (including Sensor)	1 kg
Shelf-life (device)	Minimum 5 years at time of delivery, or 15000 measurements.

NIOX VERO® is CE-marked according to In Vitro Diagnostic Device Directive 98/79/EC and approved for clinical use in EEC Countries.

NIOX VERO® is 510(k) cleared by FDA.

As one of the myAirCoach consortium partners Aerocrine will make devices and sensors available to allow twice daily measurements for one month in @@@ patients.

Aerocrine AB, Solna, Sweden, http://www.niox.com/en/about-niox-products/about-niox-vero/

Appendix 3: Exhaled Breath Temperature

Exhaled Breath Temperature (EBT) by X-halo®

X-halo allows asthmatics to track their airway inflammation levels easily and quickly at home. Giving them the opportunity to take more control over their asthma management. X-halo precisely measures the temperature of the air in your lungs - called Exhaled Breath Temperature (EBT) - to within a tenth of a degree. When your lungs begin to get inflamed, your EBT rises and X-halo lets you know. X-halo is quick and easy. It takes less than 2 minutes a day to use and is suitable for everyone, children and seniors alike.

Specifications

Power supply	2 AAA batteries
Battery life	120 measurements or 2 months under normal use
Connections	Connects to smart phone, tablet, PC or Mac through an audio jack
App	Available free from the App store for iOS devices or Google play for Android devices and downloadable from www.x-halo.com for your PC or Mac
Measurement	Range: 25-42 *o*C
Accuracy	Sensor accurate to 0.1 *o*C in the temperature range specified
Storage	Temperature range: -20-60 *o*C; Humidity range: 10-90%RH
Usage	Temperature range: 10-35*o*C; Humidity: 30-80% RH
Characteristics	Non-predictive, no measurement offset and no-calibration necessary

Delmedica Investments, Singapore, www.x-halo-com

Appendix 4: Respiratory Rate

Respiratory Rate (RR) by Spire®

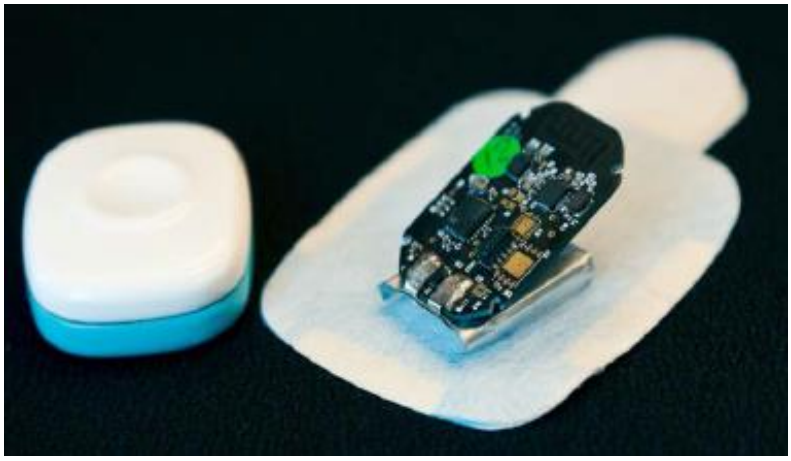
Spire allows continuous measurements of inhalation and exhalation times, breath rate, deep breaths, apneaic events, steps and calories. It analyses breathing patterns to infer state of mind (tense, calm, focus). Spire is suitable for regular daily use in daily life and supports customizable alerts, guidance, a rich API and back end storage making it perfect for continuous monitoring and interventions. Raw data is available.

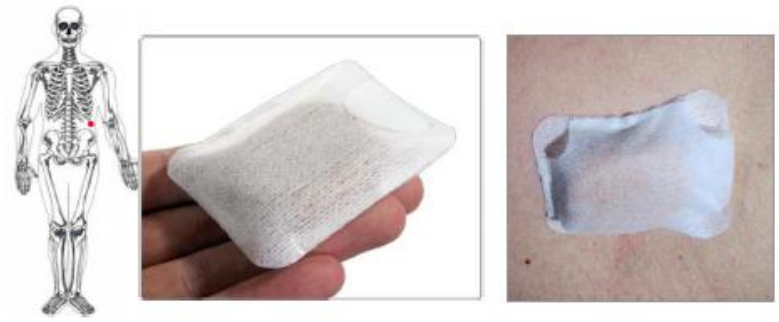
Specifications

- Spire captures respiratory characteristics on a per breath basis:
- Breath rate (on a per breath basis)
- Inhalation duration
- Exhalation duration
- Inhalation to Exhalation ratio (IER)
- Breath rate variability (BRV)
- Spire has been internally validated to be >95% accurate - this number varies during erratic physical activity (e.g., dancing). Spire's algorithms will throw away data that does not look like a breath - and infer data about those time segments.
- Spire differentiates between respiration and physical activity using the on-board 3-axis accelerometer.
- Spire is ideal for daily life situations where people alternate between physical activity and knowledge work.
- Raw data (respiration+steps) is transmitted to the phone and to Spire's HIPPA compliant cloud.
- Spire knows when it is not worn or when breaths are not clean enough to be analysed.

Spire, San Franciso, USA, www.spire.io

Respiratory Rate (RR) by RESpeck device





Specifications

- Specks: miniature devices combine sensing, processing and wireless networking
- Wireless patch for measuring respiratory rate, respiratory effort and activity
- Continuous remote monitoring which transmits data via a base-station to a secure server via a broadband interconnection
- Wireless patch with a three-axis accelerometer
- Sealed case and self-adhesive pouch
- Measures chest wall rotations as the wearer breathes
- Provides a respiratory effort waveform, respiratory rate and patient activity data
- Wireless patch worn on the torso
- Re-useable wireless sensor module
- Contained in a single-use sleeve for hygienic attachment to the torso
- Data collection and processing in a base-station via ultra low power wireless link
- Transmitted via broadband internet or via GPRS to server
- Remote respiratory monitoring service
- Daily reports summarising hourly trends
- Option to access historical data
- Respiratory rate, respiratory effort/flow, activity, heart rate, cough frequency, speech episodes
- Remote examination of patient's breathing in real-time

Patient-centric design

- Long-term wear
  - Light-weight - 17gms (incl. battery)
  - Unobtrusive - 4.5 x 3.7 x 1.3 cm
  - Battery lifetime - 12 months
- Ease of use
  - No recharging of batteries
  - Data stored on wireless patch and downloaded to the base-station when within range – no manual intervention

Centre for Speckled Computing, Edinburgh, UK, www.specknet.org

Appendix 5: Pulse rate

Pulse Rate by Fitbit Charge HR®

The Fitbit HR Charge allows monitoring of pulse rate automatically and continuously right on your wrist and to accurately track calorie burn. Like all heart rate monitoring technologies, accuracy is affected by physiology, location of device, and different movements.

Specifications:

- Optical heart rate monitor
- 3-axis accelerometer
- Altimeter
- Vibration motor
- Display: OLED
- Battery life: lasts up to 5 days
- Battery type: Lithium-polymer
- Charge time: One to two hours
- Radio transceiver: Bluetooth 4.0

Environmental Requirements

- Operating temperature: -4° to 113° F
- Maximum operating altitude: 30,000 feet
- Memory: Tracks 7 days of detailed motion data – minute by minute.
- Tracks daily totals for past 30 days
- Stores heart rate data at 1 second intervals during exercise tracking and at 5 second intervals all other times

- Syncing: Charge HR syncs automatically and wirelessly to tablets, computers and 150+ leading iOS, Android and Windows smartphones using Bluetooth 4.0 wireless technology. Syncing range: 20 feet. Call notifications via Bluetooth 4.0 Syncing to computers requires Internet connection and USB port. Syncing to mobile devices requires Bluetooth and Internet connection. Syncs with Windows Vista and later, Mac OS X 10.6 and up, iPhone 4S and later, iPad 3 gen. and later, and leading Android and Windows devices.

Fitbit, Boston, USA, www.fitbit.com

Pulse Rate by AngelSensor®

Angel is a flexible wristband that can be worn 24/7. Angel Beta has three sensors (with an ulterior Blood Oxygen sensor in development) that monitor your vitals and provide you with data that can be used to inform lifestyle choices.

The metrics collected by Angel's advanced sensors can be transferred to devices and apps via Bluetooth Low Energy. The open platform allows developers the freedom to create and innovate, and allows our users access to many existing fitness apps.

Each of Angel's sensors applies advanced noise filtering and artificial intelligence algorithms to convert the signal into vital sign measurements. Our sensors provide raw waveform data that can be used for research and advanced processing.

Angel Sensor is easily integrated in Digital Health enterprises' products and services through its open SDK and drivers. Whether the objective is to lower costs or increase value, Angel Sensor gives enterprises complete freedom to innovate.

Specifications:

Dimensions

- Max width (A): 21.6 mm
- Min thickness (B): 3.9 mm
- Max thickness (C): 8.6 mm
- Weight: 39 g (Size L)

Wristband

- Surface materials: Stainless steel and silicon
- Water and dust resistant (more info)
- Available in white or black
- Li-Po Batteries (non-replaceable)
- Charge time: typically 1 hour
- 24/7 All-day monitoring
- Bluetooth Low Energy connectivity
- Updatable firmware

Modules

- Optical PPG sensor
- 3D Accelerometer
- 3D Gyroscope
- Temperature sensor
- NFC (Passive)

Seraphim Sense Ltd., Tel Aviv, Israel, www.angelsensor.com

References

[1] Reddel HK, Taylor DR, Bateman ED, Boulet LP, Boushey HA, Busse WW, et al. An official American Thoracic Society/European Respiratory Society statement: asthma control and exacerbations: standardizing endpoints for clinical asthma trials and clinical practice. Am J Respir Crit Care Med 2009 Jul 1;180:59-99

[2] GINA guidelines, 2015, www.ginasthma.com (Accessed 2015).

[3] Juniper EF, O'Byrne PM, Ferrie PJ, King DR, Roberts JN. Measuring asthma control. Clinic questionnaire or daily diary? Am J Respir Crit Care Med 2000 Oct;162:1330-4.

[4] Juniper EF, O'Byrne PM, Guyatt GH, Ferrie PJ, King DR. Development and validation of a questionnaire to measure asthma control. Eur Respir J. 1999 Oct;14(4):902-7.

[5] Measurement of Health-Related Quality of Life and Asthma Control. Available at: http://www.qoltech.co.uk/ (Accessed 2015).

[6] Patient Coach platform. Available at: http://www.patientcoach.nl/ (Accessed 2015)

[7] Juniper EF, Buist AS, Cox FM, Ferrie PJ, King DR. Validation of a standardized version of the Asthma Quality of Life Questionnaire. Chest 1999 May;115:1265-70.

[8] Juniper EF, Guyatt GH, Cox FM, Ferrie PJ, King DR. Development and validation of the Mini Asthma Quality of Life Questionnaire. Eur Respir J 1999 Jul;14:32-8.

[9] van der Valk RJ, Baraldi E, Stern G, Frey U, de Jongste JC. Daily exhaled nitric oxide measurements and asthma exacerbations in children. Allergy. 2012 Feb;67(2):265-71.

[10] Honkoop PJ, Taylor DR, Smith AD, Snoeck-Stroband JB, Sont JK. Eur Respir J. 2013 Jan;41(1):53-9. Early detection of asthma exacerbations by using action points in self-management plans.

[11] Frey U, Suki B. Complexity of chronic asthma and chronic obstructive pulmonary disease: implications for risk assessment, and disease progression and control. Lancet 2008;372:1088–1099.

[12] Saito J, Gibeon D, Macedo P, Menzies-Gow A, Bhavsar PK, Chung KF. Domiciliary diurnal variation of exhaled nitric oxide fraction for asthma control. Eur Respir J. 2014 Feb; 43(2) :474-84.

[13] Popov TA, Kralimarkova TZ and Dimitrov VD. Measurement of exhaled breath temperature in science and clinical practice. Breathe 2012; 8: 187-192.

[14] Campana LM, Owens RL, Butler JP, Suki B, Malhotra A. Variability of respiratory mechanics during sleep in overweight and obese subjects with and without asthma. Respir Physiol Neurobiol 2013 May 1;186:290-5.

[15] www.fitbit.com (Accessed 2015).

[16] Angel sensor. Available at :www.angelsensor.com (Accessed 2015).

[17] Department for Environment, Food and Rural Affairs (DEFRA) is linked to the UK-AIR (Air Information Resource) webpages at: http://uk-air.defra.gov.uk/ (Accessed 2015).

[18] Luchtmeetnet. Available at: www.luchtmeetnet.nl (Accessed 2015).

[19] National Pollen and Aerobiological Unit at: http://www.worc.ac.uk/discover/national-pollen-and-aerobiology-research-unit.html (Accessed 2015).

[20] Pollen UK to produce forecasts that help support allergy and hay fever sufferers through the most difficult time of the year at: http://www.metoffice.gov.uk/health/public/pollen-forecast (Accessed 2015).

[21] Schulz, R. Quality of Life Technology Handbook. CRC Press 2012.

[22] Snaith RP. The Hospital Anxiety And Depression Scale. Health Qual Life Outcomes 2003 Aug 1;1:29.

[23] Osborne RH, Elsworth GR, Whitfield K. The Health Education Impact Questionnaire (heiQ): an outcomes and evaluation measure for patient education and self-management interventions for people with chronic conditions. Patient Educ Couns 2007 May;66:192-201.