Managing COPD Exacerbations with Telemedicine

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Abstract. Managing chronic disease through automated systems has the potential to both benefit the patient and reduce health-care costs. We are developing and evaluating a monitoring system for patients with chronic obstructive pulmonary disease which aims to detect exacerbations and thus help patients manage their disease and prevent hospitalisation. We have carefully drafted a system design consisting of an intelligent device that is able to alert the patient, collect case-specific, subjective and objective, physiological data, offer a patient-specific interpretation of the collected data by means of probabilistic reasoning, and send data to a central server for inspection by health-care professionals. A first pilot with actual COPD patients suggests that an intervention based on this system could be successful.

1 Introduction

Increasing demands on health-care and continuous pressure from health-care authorities and insurance companies to reduce costs has created a situation in which automated patient assistance by telemedicine has become an attractive idea. Specifically in the context of chronic disease management, where patients are continuously at risk of deteriorating health, automated monitoring can relieve work-load of health-care workers, while helping patients self-manage their disease. These possible benefits are worth to be investigated, to establish whether or not telemedicine can effectively help.

Chronic obstructive pulmonary disease, or COPD for short, is a chronic lung disease with high impact on patient well-being and with considerable health-care related costs [1]. Exacerbations – acute events of worsening of symptoms – are important events in the progression of COPD, such that monitoring patients in a home setting to detect exacerbation onset may be warranted [2]. In this paper we describe a research project on detecting and managing the occurrence of exacerbations of COPD at an early stage. We aim to decrease the impact of chronic obstructive pulmonary disease on the patient's quality of life by means of a monitoring system that collects and interprets data by a probabilistic model to assess the exacerbation risks. This should help patients with self-management and prevent unscheduled doctor visits and hospitalisation due to exacerbations, as the monitoring system enables a faster response to their occurrence. In

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the research described here, we report on work on the construction of such a system and a study of its technical and clinical feasibility with a number of COPD patients.

An important feature of the system is that we use smartphones for the monitoring, thereby foregoing the need for a personal computer (PC) with internet connectivity. This has the advantage that whereas most people are used to responding to phone alerts, sending reminders via a PC may have little effect on the patient's behaviour. Most important, perhaps, is that data interpretation is performed directly on the smartphone enabling instant feedback to the patient. This is different from earlier work (e.g. [3]) in which telemonitoring data was analysed remotely by hand.

From a clinical point of view the importance of the research lies in empowering patients to monitor their disease and in providing timely intervention if needed. It also provides the nurse or physician with a means to stay informed on the patient's COPD-related health status. There exists some work on telemonitoring for COPD [4,5], however these systems are not as extensive as the support system we are developing now, including automated intelligent interpretation of questionnaire answers and sensor readings.

The rest of this paper is structured as follows: first in Section 2 we describe in more detail our current application domain COPD, followed by a description of the monitoring system being developed in Section 3; then in Section 4 we describe the model used to estimate exacerbation risk; Section 5 presents some initial pilot results; finally we conclude and note some future work that remains.

2 Chronic Obstructive Pulmonary Disease

Chronic obstructive pulmonary disease currently affects some 210 million people worldwide[1] and is one of the major chronic diseases in terms of both morbidity and mortality. COPD affects airways and lungs, decreasing lung capacity and obstructing airways, thus interfering with normal breathing. Patients often suffer from a combination of emphysema and chronic bronchitis, causing shortness of breath and therefore reducing their capability of performing day-to-day activities. The main cause of COPD is exposure to tobacco smoke, followed by severe air pollution. COPD is currently not curable, but treatment does reduce the burden considerably (for further information on COPD see e.g. the Global Initiative for Chronic Obstructive Lung Disease (GOLD)[2]).

An important aspect of COPD which is particularly relevant in the present context is the progressive nature of the disease. Specifically acute deterioration has a profound impact on patient well-being and on health-care cost [1]. These exacerbations are mainly caused by infections resulting in symptom worsening [6]. Important to note is also that patients with frequent exacerbations usually have faster disease progression, which makes exacerbation prevention a particularly interesting goal. Additionally, a faster treatment response to exacerbations leads to better recovery [7].

The state of the respiratory system is observable via symptoms including dyspnea, productive cough, wheezing breath and decreased activity due to breathlessness.

[1] World Health Organization `http://www.who.int/mediacentre/factsheets/fs315/en/index.html` Accessed: January 2011.

[2] `www.goldcopd.com`

Besides these symptoms a number of physiological signs are relevant, in particular the forced expiratory volume in 1 second (FEV_1) and blood oxygen saturation. FEV_1 measures airway obstruction by testing whether the patient can overcome obstructive and restrictive resistance during forced exhalation. A number of other indicators of deterioration exist, like blood-gas pressure, inflammatory proteins and white blood-cell count, however, measuring these factors requires hospital-grade equipment and incurs considerable inconvenience for the patient. Blood oxygen pressure can be observed by proxy, with a pulse-oximeter that measures blood oxygen saturation.

3 Patient Monitoring at Home

The long term nature of COPD and associated exacerbation risk requires that a monitoring system can easily be deployed in a home-care setting. Not only efficacy, but also usability is an important factor in the design. This section describes the current system design and some of the issues that arise.

3.1 System Description

In Fig. 1 a graphical representation of the exacerbation monitoring system-setup is shown. The monitoring system consists of a smartphone, a sensor interface (Mobi) to which a micro-spirometer and pulse-oximeter are connected, and a web-centre. Data is collected from the patient through the smartphone, which also communicates wirelessly with the sensor interface. The web-centre receives the data from the smartphone and provides data access for health-care workers.

Before going into more detail on the various components let us first describe the monitoring process. At regular intervals, adjustable in frequency and in time of the day, the patient gets an automatic reminder for data entry from the smartphone. The patient is presented with a simple touch-interface to answer a set of questions about COPD symptoms and is subsequently asked to perform a spirometry test and pulse-oximeter measurement. The results of the measurements are transmitted to the phone,

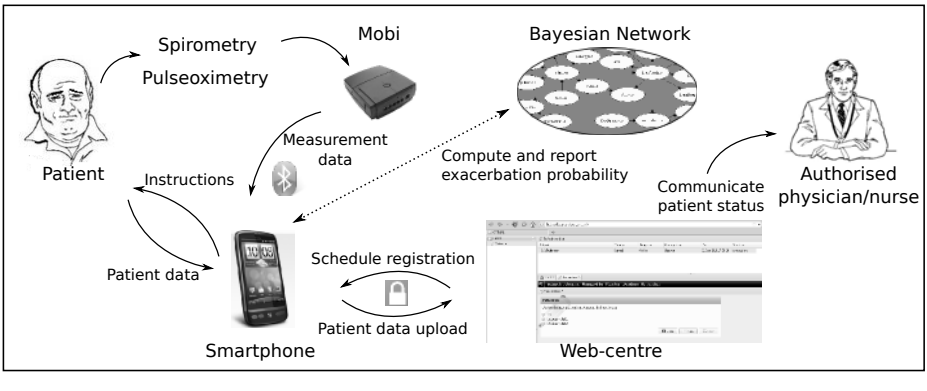

Fig. 1. Schematic of the system setup for COPD exacerbation detection and monitoring

and entered in a Bayesian network model (described in more detail in the next section) to obtain a probability of exacerbation. In addition, the data is synchronised with the web-centre, which allows the responsible health-care workers to examine the patient data; depending on the situation this may be a nurse specialised in lung diseases, general practitioner or pulmonologist. If necessary, the patient can be advised to take action, based on the model's prediction.

Technical Details

Smartphone. Currently our monitoring system runs on an HTC Desire smartphone as an application in the Android OS. In principle any Android phone with Bluetooth capability should suffice, which makes the platform fairly general. The application has been custom-made to provide the questionnaire functionality; manage communication with the sensors and web-centre; and compute the model predictions.

Model Implementation. The Bayesian network has been developed using SamIam[3], and ProBT[4], which provides an implementation of the expectation-maximisation algorithm used for learning probabilities from data. For the monitoring application we used the lightweight reasoning engine EBayes[5], in combination with a custom Perl script to perform the necessary conversion in network representation. Since EBayes is written in Java the model inference could easily be integrated in the Android application. Due to the relatively small size of the Bayesian network and the processing power of modern smartphones it turns out that the inference does not have to be deferred to a server but can be performed on site. This has the advantage that even when mobile phone network coverage is suboptimal the application can still provide a probability estimate.

Sensor Interface. The phone communicates with the sensors via a Mobi, a Bluetooth-capable multichannel sensor-interface, from Twente Medical Systems International. In our case a Nonin pulse-oximeter and a custom micro-spirometer were connected to the Mobi. An important advantage of using the Mobi sensor interface is the availability of the communication-protocol specification, enabling us to integrate the sensor readings seamlessly into the Android application. Most of the other micro-spirometers on the market do not allow this, which makes them unsuitable for easy deployment in a home setting. The monitoring kit is shown in Fig. 2.

Pulse-Oximeter. The pulse-oximeter used in this study was a Nonin Medical 8000AA, which is an industry standard pulse-oximeter. SpO_2 accuracy is 70-100% ± 2 digits.

Spirometer. We used custom-made pneumotachograph micro-spirometer prototypes by Twente Medical Systems International. These spirometers are newly developed to

[3] Automated Reasoning Group, University of California, Los Angeles. `http://reasoning.cs.ucla.edu/samiam/` Accessed: April 2011.

[4] Probayes `http://www.probayes.com/index.php/en/products/sdk/probt` Accessed: April 2011.

[5] F.G. Cozman, `http://www.cs.cmu.edu/~javabayes/EBayes/index.html/` Accessed: April 2011.

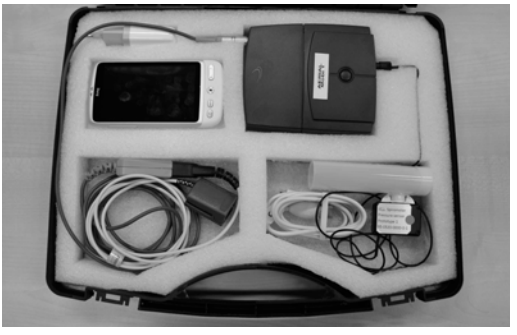

Fig. 2. The monitoring kit consisting of a smartphone, sensor interface and sensors

interact with the Mobi sensor interface and have the advantage of providing raw data such that analysing the spirometer readings is possible without requiring external software. This enables tight integration with our application, which is difficult or impossible with most commercial spirometers on the market.

Web-Centre. The web-centre provides an interface to the gathered data and is used to enrol patients, schedule registrations and similar practical issues. It is built using the workflow management system iTasks [8], which implements advanced features to generate and coordinate tasks and provides a generic (web)interface. Since the data management involved with patient monitoring is suitable to be represented as a workflow, iTasks provides a simple and effective way to construct the web-centre.

3.2 Design Considerations

Monitoring patients over longer periods of time requires a careful balance between costs and benefits. Specifically the intrusiveness of monitoring systems and costs both monetary and in terms of patient time investment result in a target population of patients with moderate to severe COPD and frequent exacerbations. These patients suffer greatly from the consequences of exacerbations, hence providing regular data to detect exacerbations in an early stage will in general be more acceptable. The most appropriate time to start the intervention would be directly after hospitalisation due to COPD, because then the goal of preventing hospitalisation is clearly relevant for the patient.

Due to the privacy sensitive nature of the data, all data transmission is encrypted (HTTPS). Also access-rights to the data in the web-centre have to be controlled and patients should give prior consent. Since these are general issues when working with patient data, we will not focus on them here, but they remain important.

Ease of use is a critical requirement for any system that has to be used on a regular basis for a prolonged period of time. Since the interval between exacerbations is usually in the order of months, one should take care to reduce patient effort to a minimum, lest patients would stop entering data due to it being inconvenient. The patient population is relatively old on average – possibly not very experienced with technology – hence to facilitate understanding the web-centre provides the ability to do practice runs. The nurse will have a supportive role in training patients.

Depending on the health status of the individual patient the rate of data acquisition can be varied, which can be automated based on the acquired data and the model. As long as a patient has low risk of an exacerbation, monitoring can take place on a weekly basis, keeping the time investment at a minimum. If a patient is at risk according to model predictions, the system check-in can be scheduled daily to ensure the possible exacerbation is detected and acted upon appropriately. Unscheduled, patient initiated registrations are being implemented for the next pilot, facilitating self-management. Currently the system only advises to contact a physician, but further self-management supporting advice could be implemented. Advising to see a clinician does not interfere with current clinical practice guidelines, other advice will have to be implemented in accordance with the guidelines.

4 A Model for COPD Exacerbation Detection

4.1 Bayesian Network Structure

Data interpretation for exacerbation detection is performed by a Bayesian network, which is a probabilistic graphical model consisting of vertices representing random variables of interest and arcs representing dependencies between variables [9]. Each random variable has a quantitative part, denoting conditional probabilities of the type $P(X \mid pa(X))$, that is the probability that X takes on a specific value given the values of its parent variables. Probabilities of interest can be computed from the joint probability of all variables: in this case the probability of exacerbation given the evidence obtained from monitoring. An important observation is that although the model describes general relations between the variables of interest, all predictions are personalised by entering patient specific data. The model is thus capable of making predictions for individual situations, and can provide 'what-if'-predictions by entering virtual evidence.

The current COPD-exacerbation prediction model is depicted in Fig. 3. The main outcome variable is 'exacerbation', but the nature of a Bayesian network allows us to easily inspect probabilities for any variable. The network contains two 'hidden' variables, namely 'infection' and 'lung function' which cannot be observed directly, but whose values can be derived based on indirect measures, such as body temperature for infection and the forced expiratory volume in 1 second (FEV_1) for lung function. Other important variables are the symptoms that one might expect a patient to report, such as dyspnea (breathlessness), sputum volume and purulence, cough, wheeze and whether performing daily activities is difficult due to COPD. Additionally some clinical signs have been included such as the aforementioned FEV_1, blood oxygen saturation (SpO_2), CRP concentration, leukocytosis and blood gas and pH levels. Except for FEV_1 and SpO_2, these variables are mostly included for the sake of completeness, as they will not be observable in a home-care setting, which is the application's target.

4.2 Model Construction

The Bayesian network has been constructed in close cooperation with specialists of the Radboud University Nijmegen Medical Centre. A set of relevant variables that are

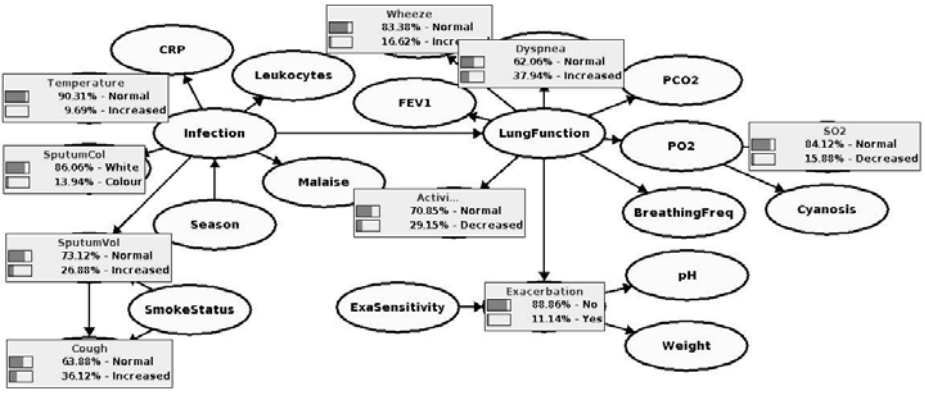

Fig. 3. Bayesian network for prediction of COPD exacerbations (probabilities partially shown)

related to exacerbations has been identified by domain experts – in this case two pulmonologists – supported with findings from current medical literature (e.g. [6]). As a second step the dependence relations between the variables have been elicited from the domain experts, resulting in the qualitative part of the model. Subsequently, probabilities have been estimated: starting from qualitative constraints we elicited probabilities from expert opinion and secondly, using a data set from an earlier project at the Radboud University Nijmegen Medical Centre, we estimated probabilities using the expectation-maximisation algorithm. Unfortunately, the data set does not include all variables of interest, therefore additional data (i.a. from [10]) will be used in a later stage for further evaluation of the probabilities. The expert opinion serves as an important comparison to make sure learned parameters are plausible.

4.3 Model Test

To get some feeling for the efficacy of the model we performed a preliminary evaluation with the available data consisting of questionnaire answers of 86 Dutch COPD patients, 54 of which had an exacerbation during the study. The data has been acquired biweekly during 2006-2007 via automatic telephone interviews, resulting in time series data with a total of 1922 data entries, of which 162 entries provided exacerbation data. It should therefore be noted that data correlation may influence the analysis result, as these temporal correlations were not taken into account. Data is only available for a subset of the variables in the model, specifically: exacerbation, dyspnea, sputum volume and colour, wheeze, cough, activity and season. We performed an ROC-analysis on this sub-model with expert opinion probabilities and with learned probabilities, using 10-fold cross-validation. In Fig. 4 the curves are shown for both the data and expert model, conveying that the predictions can indeed distinguish the exacerbation cases. For the data model we find a mean area under the curve (AUC) of 0.93; and for expert model a mean AUC of 0.97. It should be noted however that these results are based on cross-validation only and not on an independent test set; also the limited number of positive examples results in a rather large increase in true positive rate for each case classified correctly.

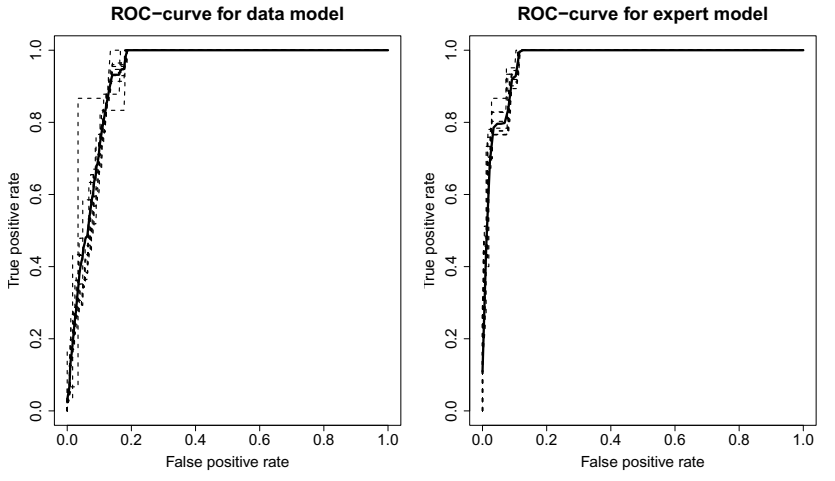

Fig. 4. ROC-curves, cross-validation results (dashed lines) and average (bold)

These first results indicate that we can at least detect exacerbations as they are happening, which is already useful. However, the more interesting task of actually predicting exacerbations still lies ahead, as currently we lack sufficient data to model the temporal progression. In further testing of the system we also plan to gather the necessary data to construct a temporal model, which requires trend analysis of time courses of symptoms and signs leading up to an exacerbation.

5 Evaluation

5.1 Pilot Study

Careful evaluation of a number of different aspects is needed to assess the system's efficacy, ranging from usability to the accuracy of probabilities, overall effectiveness of predicting exacerbations and finally influence on disease management and health-care utilisation. We have carried out a initial feasibility study with COPD patients.

We performed a technical evaluation with a limited number of stable COPD patients, testing the monitoring equipment and data entry procedures to make sure they are bug-free, and usable from a patient perspective. This stage is described in more detail below. The second stage of evaluation consists of a small scale test in a home setting, supported by a nurse, to assess the full system and specifically obtain data to check the accuracy of the model and to construct a temporal model. The model accuracy testing will entail a side-by-side comparison of pulmonologists' assessment of exacerbations with model predictions, as well as a comparison with a data set with relevant measurements and exacerbation outcomes. If this stage turns out to be favourable, a follow-up project will have to test clinical validity.

5.2 Methods and Results

In order to test the technical feasibility and usability we conducted a pilot study with COPD patients recruited from the University Centre for Chronic Disease Dekkerswald in Groesbeek, the Netherlands.

Methods. For this study 5 stable patients were recruited by convenience sample from the lung rehabilitation program who gave informed consent to participate in the study. Using three exacerbation monitoring kits (as described in Section 3) patients were monitored for a duration of 9 days, starting in January 2011. Patients were contacted daily during this time to answer a set of questions and perform spirometry and oximetry measurement. The answers were entered as evidence into the Bayesian network model to determine the probability of occurrence of an exacerbation. These predictions have not been used for patient advice yet, as further model validation is required. Patients were asked to report malfunctioning which together with the received data and server-logs could be used to verify system performance. At the end of the monitoring period a semi-structured evaluation interview was held – both with the patient and with the health-care staff involved – to obtain qualitative feedback on the usability of the system. In the interview we established whether or not the patients understood the procedure and the questions and whether they found the phone-interface sufficiently usable. Also, we checked anomalous data we received (if any) and asked for suggestions for improvement. The evaluation results of the first 2 patients were used to improve the system before starting with the second group. As this was a technical feasibility test, the clinical data obtained were only used to check for errors in the application or obvious model inaccuracies, and checking the clinical accuracy of the model predictions is deferred to the next stage of experimental testing.

Results. The goal of the pilot test was twofold, first, to ascertain the technical feasibility of the system in a real but controlled test environment; and second, to obtain early feedback from end users on usability. As for the first goal, the pilot resulted in finding some inaccuracies in the server-side software specifically with respect to adequately recovering from connection errors, which could be amended and retested relatively easily. We can conclude that the system functions as designed at the technical level. With respect to the usability goal, some improvements became apparent at an early stage, such as response buttons being placed too close together for comfortable use and an unclearly worded question resulting in confusion. In the evaluation interview with the patients the consensus was that the system could be useful to gain insight in the disease, was easy to use and not found to be intrusive. In particular patients indicated that they would be willing to use such a system in a home-care setting, which will need to be verified more rigorously in the next pilot stage. It thus turns out that the patients' impression of the system after using it, is quite positive. Although the generalisability of these findings is limited (due to convenience sampling) it did provide us with early feedback from actual COPD patients, which we think is especially important because acceptance of this kind of systems is often a concern.

6 Conclusion

We have described the results of a feasibility study of the development of a smartphone-based home-monitoring system for COPD. The COPD exacerbation detection and monitoring system described in this paper uses probabilistic reasoning to automatically interpret patient specific data. Initial testing shows that applying the system is technically feasible and patients are capable and willing to use the system. The model is well-founded on expert knowledge, literature and data, providing exacerbation risk predictions that seem usable. We have thus produced and evaluated on a pilot scale an advanced system architecture for home monitoring of COPD exacerbations, with promising results. Future work will involve a more extensive test in a home-care setting, finally leading to a system capable of exacerbation detection in an early stage such that COPD exacerbation impact can be reduced.

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