Personalized alerts for patients with COPD using pulse oximetry and symptom scores

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Abstract— **Chronic Obstructive Pulmonary Disease (COPD) is a progressive chronic disease, predicted to become the third leading cause of death by 2030. COPD patients are at risk of sudden and acute worsening of symptoms, reducing the patient's quality of life and leading to hospitalization. We present the results of a pilot study with 18 COPD patients using an m-Health system, based on a tablet computer and pulse oximeter, for a period of six months. For prioritizing patients for clinical review, a data-driven approach has been developed which generates personalized alerts using the electronic symptom diary, pulse rate, blood oxygen saturation, and respiratory rate derived from oximetry data. This work examines the advantages of multivariate novelty detection over univariate approaches and shows the benefit of including respiratory rate as a predictor.**

I. Introduction

Chronic Obstructive Pulmonary Disease (COPD), predicted to become the third leading cause of death by 2030 [1], is a progressive chronic disease that affects the lungs. It is caused by smoking or long-term exposure to lung irritants such as air pollution, dust or fumes. Symptoms include cough, breathlessness, wheezing, chest tightness, fatigue, and dizziness. Patients with COPD often experience an acute and sudden worsening of symptoms (an "exacerbation") [2], which if not treated promptly leads to hospitalization. Self-management can help patients to identify the early signs of an exacerbation, and to respond to these by taking appropriate medication, thus alleviating the COPD symptoms and the need for admission to hospital [3][4].

The medical literature suggests that daily self-reported symptoms correlate with patient deterioration [4]. A home-based digital health system can provide a solution for effective self-monitoring of symptoms and vital signs. The principal aim of avoiding hospital admissions caused by exacerbations could be achieved by augmenting such a system with early warning algorithms to prioritize those patients who require the specific attention of a Health Care Professional (HCP). In order to avoid large numbers of false alerts, any automated algorithm should be able to adapt to individual patients and their changing physiology.

Personalized algorithms which combine self-reported symptoms with vital sign data could help to identify the onset of deterioration, thereby alerting patients and/or HCPs before a full-blown exacerbation event. Given the constraints of the home-monitoring environment, a pulse oximeter (portable and non-invasive) provides a feasible solution to record pulse rate and peripheral arterial blood oxygen saturation (SpO_2). The use of a pulse oximeter also enables us to estimate the respiratory rate, which has previously been found to be useful in the early identification of exacerbations [5].

We compare each of the variables (diary score, pulse rate, SpO_2 and breathing rate) individually and jointly based on probabilistic novelty detection to help identify the onset of patient deterioration. Novelty detection enables us to identify abnormal data by building a model of normality from a set of normal data. It has previously been used in a number of applications including fault detection [6], detection of cancerous masses in mammograms [7] and patient monitoring in high-dependency care [8]. A recent review of novelty detection algorithms can be found in [9].

In this paper, we describe our m-Health system for use by COPD patients (Section II.A). We then introduce signal quality assessment (Section II.B), the algorithm used for breathing rate estimation from oximetry data (Section II.C), and the algorithms used for analyzing the self-monitoring data (Section II.D). In Section III we discuss our results and in Section IV we present some conclusions.

II. Method

We developed an m-Health system called EDGE (sElf management anD support proGrammE [10]), customized for COPD patients in collaboration with the Nuffield Department of Primary Health Care Sciences, University of Oxford. The system supports self-management for COPD patients by using a symptom questionnaire, Bluetooth-enabled pulse oximeter, and multi-media content. Additionally we aimed to design a scalable solution to monitor patients remotely and automatically generate alerts whenever the patient's well-being deteriorates. An initial pilot study involved 18 patients (see Table 1); during this initial phase, we developed and iteratively improved the Android tablet front-end and back-end algorithms based on feedback from HCPs and patients. The project is now in its second phase with a randomized control trial involving 165 COPD patients underway.

A. Data Collection

The 18 patients used our mobile tablet-based application on a daily basis to complete a symptom diary and record between

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30 and 40 seconds of pulse oximetry data using a Bluetooth-enabled finger probe. The pulse oximeter (Nonin Onyx II Model 9560) recorded both the pulse rate and SpO_2 with their values transferred via Bluetooth to the Android tablet (Samsung Galaxy Tab2). Additionally the oximeter was configured to record the photoplethysmogram (PPG) waveform (sampled at 75Hz). The PPG waveform represents the variation of blood volume in the finger with time. Validated self-reported symptom questionnaires were adapted to develop the COPD symptom diary shown in Table 2. All data were recorded on the Android tablet and transmitted to a secure remote server (behind the National Health Service firewall).

Table 1 Demographics of the COPD patient cohort in the pilot study

Characteristic	Value
Male/Female	9 / 9
Age[a]	71 (9)
Days in the study[a]	179.8 (0.3)
COPD Severity	6 moderate, 1 likely severe, 9 severe, 2 very severe
Pulse rate (beats/minute) [a]	83.2 (18.3)
Blood oxygen saturation (% SpO_2) [a]	93.5 (4.1)

a. values reported as mean (standard deviation)

A typical daily interaction with the COPD application on the Android tablet begins with patients reporting their symptoms using the diary and then using the pulse oximeter probe to measure SpO_2 and pulse rate. Since m-Health applications are used at home by the patients on their own, signal quality assessment is of utmost importance.

Table 2 Illustration of how answers to diary questions are mapped into a symptom score (higher score indicates worse symptoms)

Question	Range of values
How are you feeling today?	[0, 5]
How is your breathlessness?	[0, 5]
How is your wheeze or chest tightness today?	[0, 5]
Do you have a cough?	yes/no
How is your cough today?	[0, 3]
What color is your sputum?	[white, brownish]
Do you have a cold (such as a runny/blocked nose) or sore throat?	yes/no
Did you wake up last night due to breathing problems?	[0, 5]

B. PPG Signal Quality Assessment

Motion artifact has been identified as a major reason for the poor performance of various algorithms developed for the estimation of respiratory rate from PPG [11]. To obtain high-quality PPG recordings a series of strategies have been devised. On the Android tablet, information on how to use the oximeter (images, videos, and textual information) is displayed to patients to guide them while taking readings. The patient is advised to remain still while recording pulse rate and SpO_2 for 30 seconds. Movement artifact and incorrect positioning are flagged by the Nonin pulse oximeter. If there is an artifact at the start, recording is extended by up to another 10 seconds. If the recording is of poor quality, the patient is given the option of repeating the recording. Additionally, during the respiratory rate estimation, a PPG signal is marked as of low quality, and rejected, if it contains more than five occurrences of error flags from the oximeter. As a result of these strategies, very few recording sessions were found to have been corrupted by artifact.

C. Respiratory Rate Estimation

The respiratory rate estimation algorithm is based on autoregressive modeling (AR) applied to the amplitude modulation in the PPG signal [12]. Unlike previous work with AR modeling that aims to eliminate the dominant frequency (the cardiac frequency) in the de-trended PPG waveform before applying an AR model [13], we apply a low-order low-pass filter (Kaiser window based, pass-band cut-off=*0.5**cardiac frequency, stop-band cut-off=*1.2**cardiac frequency, attenuation of *40dB* at stop-band) to the waveform. The low-order filter allows attenuation of the cardiac frequency in the PPG signal while ensuring that there is no spectral leakage near the filter cut-off. The frequency spectrum of the processed signal includes a peak at respiratory frequency (generated by the amplitude modulation of the PPG waveform) and an attenuated peak at the cardiac frequency. In this work, a 7^{th}-order AR model is applied to the processed signal which returns three conjugate poles and a pole at $\omega=0$. Of the three conjugate poles, the pole at the lowest angle corresponds to the respiratory rate, the one at the highest angle corresponds to the pulse rate while the third pole accounts for spectral shaping of the filtered PPG signal. A model order of 7 was found to be the lowest possible model order to obtain accurate estimates of the respiratory and cardiac frequencies [16].

D. Novelty Detection

In conventional COPD monitoring systems, the alerting threshold is set to the same value for all patient data (for each variable), or an HCP sets a different threshold for each patient (often subjectively, without detailed knowledge of the patient's previous data). Unlike these systems, our approach automatically computes patient-specific thresholds. For every patient, 40 sets of data points (approximately 6 weeks of data) are used as the training set. Initially, a univariate approach is adopted, whereby the symptom score and each vital sign are considered independently, and then a multivariate approach is investigated. The six-week time period was chosen in collaboration with the HCPs in order to allow time for the patient to become familiar with the system, and for sufficient symptom and vital sign data to be collected to characterize that patient.

Univariate: The univariate algorithm computes the personalized thresholds by estimating the probability density function (PDF) of the training data points using a Gaussian kernel, and integrating the PDF to obtain a cumulative density function (CDF). Finally, the percentile of interest is selected

and its corresponding value is used as a threshold to determine whether future data points are normal or abnormal.

Multivariate: The approach is based on Parzen windows, a non-parametric density estimation technique [14]. A model of normality is constructed using an Nx4 dimensional matrix, where N is the number of training data points (symptom score, pulse rate, SpO_2, respiratory rate). After normalization (using the zero-mean unit-variance transform), spherical Gaussian kernels are centered on each training data point in the 4-dimensional space and the probability of any data point is computed using equation (1). Since the Gaussian function is smooth, the resulting probability density estimated will also be smooth. In equation (1), σ is a smoothness parameter. It is set to be the mean of local variances, with local variance estimated by calculating the mean distance to the 10 nearest neighbors [15].

$$p(z) = \frac{1}{n}\sum_{j=0}^{n}\left(\frac{1}{2\pi^{3/2}\sigma^{3}}\right)e^{-\frac{|x-x_j|^2}{2\sigma^2}} \quad (1)$$

$$novelty\ score = -\ln(p(z)) \quad (2)$$

A higher value of $p(z)$ means that z lies close to the distribution of data points from the normal group (in the training set). A novelty score is then calculated according to equation (2) which ensures that lower values of $p(z)$ result in higher novelty scores [8].

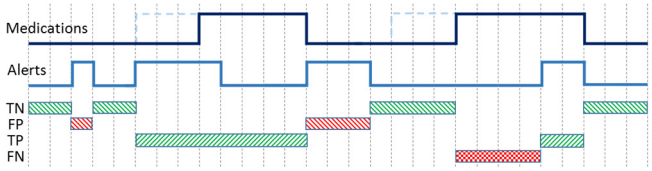

Figure 1 Illustration of how the true/false positives and true/false negatives are defined according to the patient's self-reported medication use

E. Performance Evaluation

To validate our alerting algorithms, we assumed that the self-reported use of medications was an indicator of deterioration (exacerbations). At the end of each interaction with the Android tablet, patients were asked about their medication intake (e.g. reliever inhaler, steroids, antibiotics). We identified the occasions on which a patient took any combination of the three medications (shown by the step change of the blue solid line in Figure 1) as medication events. For every medication event, a premonitory period of three days (marked by the blue broken line) was defined. The 3-day period was indicated by the HCPs as an appropriate time during which a potential exacerbation could be detected.

During the periods for which the patient is not taking any combination of medications, those days for which no alert is generated are marked as true negatives (TN). During those same periods, those days for which an alert *is* generated are marked as false positives (FP). During the premonitory period, if no alert is raised, all days in this period are marked as TN. If an alert is raised, then all days from the day of the alert until the end of the medication event are marked as true positives (TP). During the medication event, if an alert is generated, then those days from the day of the alert to the end of the medication event are marked as TP, while the days from the start of medication use until the day of the alert are marked as false negatives (FN).

To compare different methods, we compute the total numbers of TP, TN, FP, and FN for each threshold. Subsequently we combine these values to evaluate the true positive rate (sensitivity) and the false positive rate (1-specificity), and we plot the corresponding receiver operating characteristic (ROC) curves. In order to rank each method, we use the area under the curve (AUC).

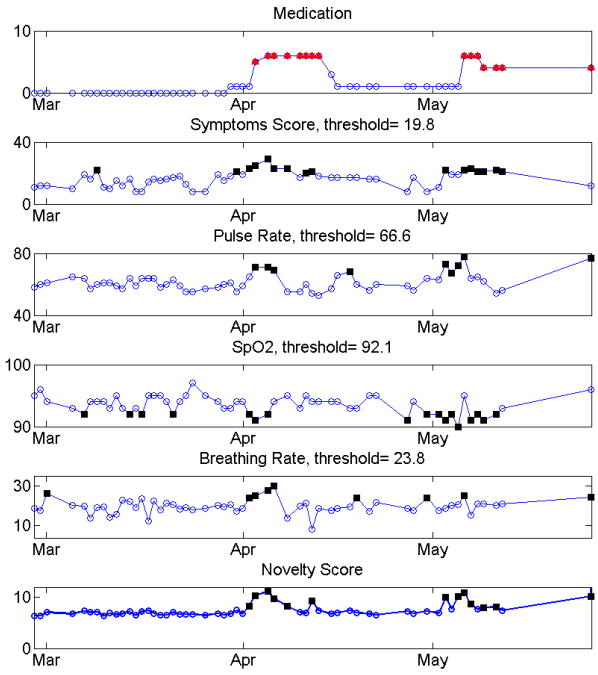

Figure 2 Alerts generated for a single patient during the study, using the univariate (Symptoms Score, Pulse Rate, SpO_2, Breathing rate) and multivariate approaches. The days when the patient takes any combination of antibiotics, relievers and steroids are marked in red.

III. RESULTS

From a total of 2523 sessions with diary and oximetry data, 144 PPG recordings (5.7%) were of less than 20 seconds of duration. Of the remaining 2379 sessions, only 71 PPG recordings (2.9%) were of low-quality. The mean respiratory rate from the 2308 PPG sessions was found to be 22.4 (with a standard deviation of 5.1) breaths per minute. Two of the 18 patients were discarded from further analysis since they were found to have been taking a combination of medication for over 60% (62% and 100%) of the time that they were in the cohort study. From the remaining 16 patients, there were 2108 sessions, divided into 640 training sessions (first 40 from each patient) and 1468 test sessions.

For illustration, Figure 2 shows the medication score, along with the symptom score, pulse rate, SpO_2 and the respiratory rate for one patient. In addition, the multivariate novelty score

is also shown in the figure. Based on a specific threshold (95% in this case), the data points with univariate alerts are also indicated. It can be seen that each of the variable generates alerts during the medication event, but the performance of the Parzen windows based method (multivariate novelty score) is superior to the rest as no false alerts are generated.

Table 3 Comparison of area under curve (AUC) for each of the personalized alerting methods used in the study

Method	AUC
Multivariate (with respiratory rate)	*0.91*
Multivariate (without respiratory rate)	0.88
Respiratory rate	0.88
Pulse	0.84
SpO_2	0.81
Symptoms score	0.76

Figure 3 shows the ROC curves for each of the univariate (SpO_2, pulse, symptoms score and respiratory rate) and the multivariate methods (with and without the addition of respiratory rate). To compare the overall performance of each method, we use the AUCs (Table 3). Multivariate novelty detection using Parzen windows improves performance (AUC rises to 0.88). Respiratory rate on its own performs as well as the combination of the other three variables. The addition of respiratory rate to the multivariate method leads to further improvement, giving an AUC of 0.91.

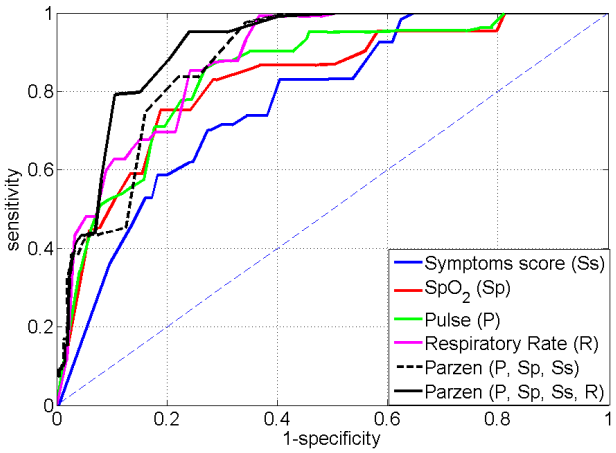

Figure 3 The ROC curves for the univariate and the multivariate alerting algorithms (with and without the addition of respiratory rate)

Since it is not feasible to obtain an objective measure of lung infection, we relied on the self-reported medication events as exacerbation indicators. However, relying on patients to identify exacerbation periods may be imprecise. Some patients could miss an event, while others might take medication even during normal periods. Future work could use information from healthcare professionals (e.g. hospital admissions) to help identify exacerbations more accurately.

IV. Conclusion

We evaluated both univariate and multivariate approaches using data from 16 COPD patients acquired over a period of six months using an m-Health system based on a tablet computer and a pulse oximeter. We have described a novelty detection framework for generating personalized alerts to prioritize patients for clinical review. We found that using a multivariate approach which includes estimates of respiratory rate gives the best result using retrospective analysis on pilot data. Future work involves the use of the multivariate approach in a randomized control trial with 165 COPD patients.

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