Physiological trajectory of patients pre and post ICU discharge[1]

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***Abstract*— The intensive care unit (ICU) admits the most severely ill patients, and the goal of the unit can be interpreted as stabilizing patient physiology. Once these patients are discharged from the ICU to a step-down ward, they continue to have their vital signs monitored by nursing staff. Early detection of physiological deterioration has been highlighted as a key step to reduce ICU readmission and improve patient outcomes. Vital signs were collected for a dataset of 98 patients admitted to an ICU and who survived to hospital discharge after their stay on a step-down ward. A model of physiological normality was developed using data from the day of hospital discharge, and patients were retrospectively evaluated throughout their stay using this model. We show that the physiology of patients being cared for in the ICU improves very rapidly in the three days prior to discharge, and furthermore, that this recovery continues during their stay on the ward, albeit at a slower rate.**

I. INTRODUCTION

Physiological abnormality is the hallmark of severity of illness, and failure to recognize adverse events has been linked to patient impairment and poorer outcomes [1]. In the intensive care unit (ICU), which provides care for extremely ill patients, many interventions are based upon abnormal vital signs. The goal of the unit is to stabilize patients, with continuous monitoring employed to ensure physiological deviations are detected ideally as often as they occur. Patients who survive their ICU stay are discharged to a step-down ward, usually the general ward in the UK. Early detection of physiological deterioration is very important on these wards, as it has been shown to reduce the rate of ICU readmission [2], which is associated with poorer patient outcomes [3], [2], [4]. Failure to recognize physiological indicators of worsening acute illness led the UK National Institute for Health and Clinical Excellence (NICE) to release a set of guidelines recommending the use of Track and Trigger (T&T) systems with critical care outreach services where possible [5], [6]. T&T systems involve the periodic collection of six vital signs (heart rate, respiratory rate, systolic blood pressure, oxygen saturation, tympanic temperature and a measure of consciousness) and calculation of an Early Warning Score (EWS). The EWS is used to convert the value of each vital sign into an integer score. These six scores are then summed to give the overall EWS score. If this score surpasses a certain threshold, care is escalated. While the use of these scores is seeing increased adoption in Europe, Australasia, and North America [7], the quality of evidence supporting the use of T&T has not been sufficiently established [7]. Problems with current EWS systems include the ranges of normality being set in an ad hoc manner, and scoring being performed independently for each vital sign, thereby ignoring clinically relevant interactions.

Novelty detection is an alternative to the integer, univariate EWS scores, in which a model of a patient is derived using vital-sign data collected from a set of "normal"observations. Patients who deviate from this multivariate model of normality display a high degree of "novelty", and can be considered as potentially abnormal. An extensive review of novelty detection can be found in [8]. There are many advantages to the use of novelty detection as an alternative to the current EWS systems. Firstly, the model of normality is fully data-driven, capturing the distribution of physiological variables for the population of interest. Secondly, as the model is multivariate and multimodal, the interactions between various vital signs can be modeled and assessed for normality. Data-driven models of normality have been successfully applied to track the trajectory of recovery in cancer patients following upper gastro-intestinal surgery [9].

Here we evaluate the physiological trajectory of patients both before and after ICU discharge using a kernel density estimate. The model is non-parametric and allows for the quantitative evaluation of the patient's physiological status with a single score. A similar method was employed to develop the patient status index, or PSI, for continuous monitoring of patients in critical care [10].

II. MATERIALS AND METHODS

A. Data

The data for this study were extracted from two sources. The first source of data was collected during the patient's enrollment in the Post Intensive Care Risk Alerting and Monitoring (PICRAM Phase 2) trial (approved by the local research ethics committee, REC reference: 12\SC\0357), at the John Radcliffe Hospital in Oxford, UK.

The aim of the on-going PICRAM Phase 2 trial is to create an early warning system which is capable of alerting when the vital signs collected during a patient's stay on the step-down ward are sufficiently abnormal. For the purpose of designing this system, the values of the vital signs recorded on the hospital's paper T&T charts were retrospectively transcribed by two research nurses. Demographics and statistics

[1]This paper is a tribute to Dr. Jonathan Burgess, who was the Research Assistant working in this project, but was sadly unable to see the work completed before his untimely death.

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relevant to the frequency of monitoring are provided in Table I. As enrollment in the trial is voluntary, not all patients discharged from the ICU are included in the dataset.

The second source of data is the set of vital sign values from the same patients enrolled in the trial during their stay in the John Radcliffe ICU prior to discharge to the step-down ward. This data was extracted using the electronic data management system currently in use at the John Radcliffe Hospital (the CareVue Clinical Information System from Philips). Data extracted consisted of the same vital sign measurements as for the step-down ward, except that there is no measure of consciousness. The frequency of data upload into CareVue varies from patient to patient depending on the intensity of monitoring provided at any given moment, however it is usually at least one set of vital sign measurements per hour. Note the trial only includes patients discharged alive from the ICU to a step-down ward. Five of these patients subsequently died in the hospital.

T&T data from 98 patients was retrospectively transcribed by the two research nurses and each set of vital-sign data (heart rate, respiratory rate, systolic blood pressure, oxygen saturation, tympanic temperature) was then matched to the respective ICU vital sign measurements for that patient. Of the 98 patients, 7 were excluded from the analysis as they died or were readmitted to the ICU within their hospital stay.

TABLE I
DEMOGRAPHICS AND STATISTICS OF INTEREST.

	In ICU	In Ward
Number of patients	91	
Age (mean ± SD)	61.48 ± 16.83	
Sex (male)	64.84%	
Length of stay (days)†		
Median ± IQR	1.92 ± 3.79	9.00 ± 17.00
25th percentile	1.00	4.00
75th percentile	4.79	21.00
Number of observations	38164	26201

B. Exclusions

Patients who were discharged for palliative care or unable to provide informed consent due to diminished capacity were not included in the study. As the physiology of paediatric patients is different from that of adult patients, and since the data was collected in adult ICUs, patients < 16 years of age were excluded from this study.

C. Data processing

After merging the vital-sign data recorded in the ICU with that collected on the step-down ward, the data is temporally centred about the time of ICU discharge. The data was then averaged into 24-hour bins. This resulted in a 5-dimensional evenly sampled time series for each patient. Data extended from -3 days (with respect to the day of discharge from the ICU), representing the average of vital sign values recorded between the 72nd and 48th hours before ICU discharge, to a maximum of 14 days post ICU discharge.

Data from the day of ward discharge for each patient was used to develop the model of normality. These vital-sign measurements correspond to the most "normal" physiology for that patient, being collected at the point where the patient is deemed healthy enough to leave the hospital. All sets of vital-sign measurements across each patient's last day on the ward were aggregated resulting in 336 prototype five-dimensional vectors. These vectors were used as the development, or training, dataset for the model of normality. It should be noted that not all patients stayed in the hospital for the same duration, and so the day of ward discharge varies from patient to patient.

D. Model of normality

The model of normality was developed using a dataset $\mathbf{X} \in \mathbb{R}^5$. A kernel density estimate (KDE) [11] was used to estimate the probability density function (pdf) of the five vital signs. This is a non-parametric technique, and thus no a priori assumptions about the underlying distribution were made. Our notation follows that of [9]. The data distribution $p(\mathbf{x})$ was modeled using the $N = 336$ set of observations, each with $D = 5$ dimensions, as shown in (1).

$$p(\mathbf{x}) = \frac{1}{N(2\pi)^{D/2}\sigma^D} \sum_{i=1}^{N} \exp\left(\frac{-|\mathbf{x} - \mathbf{x}_i|^2}{2\sigma^2}\right) \quad (1)$$

This is a weighted sum of Gaussian kernels, each with identical variance σ^2 (i.e., isotropic kernels), centred on observations $\mathbf{x}_1, ..., \mathbf{x}_N$.

The nearest-neighbor method was used to estimate the variance [11]. Briefly, this method involves determining the squared Euclidean distance (Δ) for each observation to its 10 nearest neighbors (NNs), as shown in (2).

$$\Delta_i = \frac{1}{10} \sum_{j \in \{NNs\}} \|\mathbf{x}_i - \mathbf{x}_j\| \quad (2)$$

This quantity, Δ, is then used to estimate variance, σ^2, as shown in (3).

$$\sigma = \frac{1}{N} \sum_{i=1}^{N} \Delta_i \quad (3)$$

Estimation of the underlying pdf of normal vital-sign data provides a means of quantifying the degree to which a given set of observations is abnormal. The likelihood $p(\mathbf{x}|\mathbf{x}_i, \sigma)$, a measure which represents the probability of observing a set of measurements given a distribution, can be used for this purpose. Thus we define the novelty score as in (4).

$$z(\mathbf{x}) = -\log\, p(\mathbf{x}|\mathbf{x}_i, \sigma) \quad (4)$$

For normal data, the new observation $\mathbf{x}$ will be similar to previously-seen normal observations $\mathbf{x}_i$, and so the likelihood will be high. Consequently, the negative log likelihood will be low and so the novelty score will be low. Conversely, for abnormal data, the data will be dissimilar and the likelihood will be low, and so consequently the novelty score $z(\mathbf{x})$ will be high.

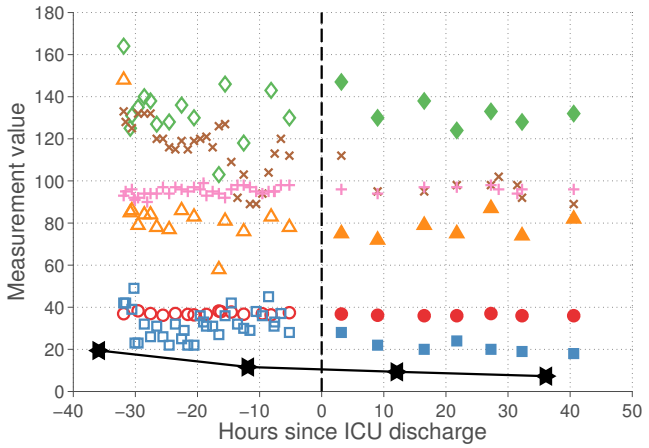

Fig. 1. Example of vital sign values recorded for one patient pre and post ICU discharge. Coloured in symbols indicate the measurement was made post ICU discharge. Vital signs plotted include temperature (red circles), respiration rate (blue squares), systolic blood pressure (green diamonds), diastolic blood pressure (orange triangles), heart rate (brown strikes), oxygen saturation (pink crosses), and novelty score (black stars). The black dashed line marks the patient's ICU discharge.

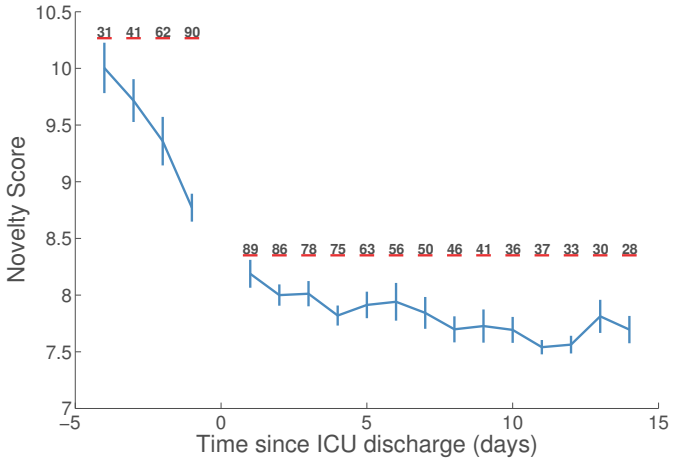

Fig. 2. Novelty score of patients pre and post ICU discharge. Underlined values indicate the number of patients with observations for that day. The score represents novelty with respect to a model of normality trained on vital-sign data from the day of hospital discharge.

III. RESULTS

Fig. 1 shows an example of vital-sign measurements for a single patient before and after ICU discharge. Note that the vital-sign observations are synchronous post-ICU discharge (manual observations made by nursing staff and recorded on T&T charts) and usually asynchronous on the ICU (pre-ICU discharge), depending on when each vital-sign value from the patient monitor is uploaded into the patient's record in the CareVue system.

Fig. 2 presents the patients' physiological status across the dataset as quantified by the novelty score. As patients have varying lengths of stay, the sample size used for each daily summary mean and standard deviation is provided above its respective data point. Each datapoint corresponds to data from an entire day. Thus 89 patients had data

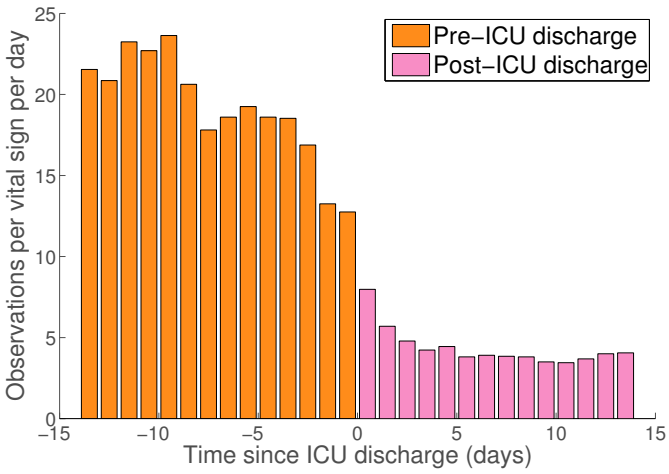

Fig. 3. Average number of observations per patient per day for each vital sign used in the novelty score.

available to calculate novelty scores on the first day post ICU discharge, and these novelty scores correspond to data collected between hour 0 and hour 24.

Fig. 3 contrasts the frequency of measurement in the ICU versus the frequency of measurement in the ward per patient vital sign.

IV. DISCUSSION

As expected, the frequency of vital-sign data recording in the ICU differs from that on the ward. This is visualized for the single patient in Fig. 1, and implied by the larger number of observations available pre ICU discharge as shown in Table I. Vital signs are recorded much more frequently in the ICU because of the need to sample unstable physiology much more frequently and a higher nurse-to-patient ratio.

Fig. 2 provides an excellent summary of the typical physiological trajectory for patients both during their ICU stay and after discharge to the ward. Patients have severe physiological derangement upon ICU admission, with longer ICU stays associated with higher initial physiological derangement. A clear return to normality (decrease in physiological novelty score) is then exhibited as a result of the treatment which patients receive in the ICU. This trend continues through discharge and onto the ward, where the patient continues to stabilize, albeit at a reduced rate. It should be noted that the novelty score presented is on a logarithmic scale, and thus physiology moves exponentially towards normality during the last three days on ICU. Furthermore, the timing of ICU discharge seems to occur at a mostly ideal time where the patient's physiology has almost returned to normality. Fig. 3 shows that patients are much more frequently monitored in ICU, and the physiological trend shown in Fig. 2 provides justification for the frequency of observation currently employed. In the ICU, where patient physiology is changing rapidly, the use of patient monitors and a much higher rate of recording are required. On the ward, where patients continue to recover but at a slower rate, less intensive monitoring (nursing observations of the vital signs every few hours) is

justified. Furthermore, the novelty score has applications for optimization of hospital resources, as more physiologically abnormal patients are likely to be higher-risk patients, and should be prioritized for post-ICU monitoring.

V. CONCLUSION

We have shown that data-driven modeling of physiology can effectively quantify patient status during the key period when patients are being stabilized on the ICU and then transferred to the step-down ward. We further demonstrate that the physiological trajectory of patients who survive to ICU discharge is one of rapid recovery in the ICU, followed by continued recovery in the ward at a lower rate. We believe that this is the first time that vital-sign observations recorded on hospital wards have been directly linked to the equivalent data in the ICU, thereby showing the overall rate of physiological improvement.

Knowledge of the typical recovery trajectory will now allow us to design an early warning system based on the individual patient's daily novelty scores as they move from the ICU to the general ward. Alerts will be generated whenever the patient's recovery does not follow the expected trajectory, i.e. the novelty score is higher than expected for that day post-discharge.

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