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Explaining Anomalous Responses to Treatment in the Intensive Care Unit

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Abstract. The Intensive Care Unit (ICU) provides treatment to critically ill patients. When a patient does not respond as expected to such treatment it can be challenging for clinicians, especially junior clinicians, as they may not have the relevant experience to understand the patient's anomalous response. Datasets for 10 patients from Glasgow Royal Infirmary's ICU have been made available to us. We asked several ICU clinicians to review these datasets and to suggest sequences which include anomalous or unusual reactions to treatment. Further, we then asked two ICU clinicians if they agreed with their colleagues' assessments, and if they did to provide possible explanations for these anomalous sequences. Subsequently we have developed a system which is able to replicate the clinicians' explanations based on the knowledge contained in its several ontologies; further the system can suggest additional explanations which will be evaluated by the senior consultant.

1 Introduction

Intensive Care Units (ICUs) provide treatment to patients who are often critically ill and possibly rapidly deteriorating. Occasionally a patient may not respond as expected to treatment; this can be considered as anomalous. An anomaly can be defined as 'a counterexample to a previous model of the domain'[10]. For example, based on knowledge of the ICU domain, it may be reasonable to expect that when a patient is administered the drug noradrenaline, it should *increase* a patient's blood pressure. However, if a *decrease* in a patient's blood pressure is observed, this would be a counterexample and considered anomalous. Such scenarios can be challenging for a clinician, especially as a similar event may not have been experienced previously. The focus of this study is the analysis of explanations given by two ICU consultants of patients' anomalous behaviour. Based on these analyses we are in the process of implementing a tool to replicate these explanations. The rest of the paper is structured as follows: section 2 provides a literature review, section 3 presents explanations for anomalous patient behaviour in the ICU and section 4 outlines an ontology-based tool which suggests explanations for anomalous scenarios.

2 Related Work

It is recognized that the ICU is a challenging domain in which to perform decision making[9]. Several intelligent data analysis systems have been developed to aid decision making in the ICU, e.g. RÉSUMÉ[11] and VIE-VENT[8]. Some systems have been implemented 'live' in the ICU, such as those developed by the Pythia/MIMIC[1] project; others use data 'offline' for example, ICONS[2], a case based reasoning system. Despite the wide variety of decision-support systems implemented in the ICU, none have focused on providing support to clinicians when faced with anomalous patient behaviour.

The generation of medical hypotheses from data has also been discussed widely in the literature, of most relevance to this work is Blum et al[7] which created hypotheses from a knowledge base and then verified these using statistical methods applied to patient data.

From a cognitive science perspective, it is widely acknowledged that anomalous scenarios provide a key role in knowledge discovery; an anomaly can indicate to an expert that their understanding of a domain may require further refinement which in turn may lead to the discovery of new (clinical) knowledge[4]. It is also known that experts can differ in their strategies when faced with anomalous data[5][3].

3 Identifying and Explaining Anomalous Responses to Treatment

A senior consultant at Glasgow Royal Infirmary's ICU selected 10 patients from their repository and confirmed that a sizeable number of these records contained some anomalous sequences. Physiological data for these patients' complete stay in the ICU were made available to us from the unit's patient management system. A group of five further clinicians examined these datasets for sequences they thought involved anomalous behaviour. The clinicians were asked to 'talk-aloud' as they completed the task[6]. Protocol analysis[5] was performed on the transcripts by two analysts and yielded the following categories:

- **A** Anticipated patient responses to treatment, possibly with minor relapses (default if clinician does not provide any other classification)
- **B** Anticipated patient responses to treatment, with significant relapses e.g., additional bouts of sepsis, cardiac or respiratory failure
- **C** Patient not responding as expected to treatment
- **D** Odd / unusual set of physiological parameters (or unusual rate of change)
- **E** Odd / unusual treatment

In total, 65 anomalies (categories C-E) were identified by the clinicians. Figure 1 describes an anomalous response to treatment. As a further phase of this analysis, sequences which had been identified as including anomalous responses to treatment were presented to two further ICU clinicians, who were asked to provide as many explanations as possible for these sequences. A wide range of

"...but then we obviously do something because the cardiac output and the cardiac index get a bit better and the thing that we seem to have done is put the noradrenaline up to a high dose, but that isn't necessarily quite what we would expect from a high dose of noradrenaline"

Fig. 1. An anomalous response to treatment as detailed in clinician 2's transcript

hypotheses were proposed which were organised as the following broad categories: 1) *clinical conditions*, 2) *hormone regulation*, 3) *progress of the patient's condition*, 4) *treatment*, 5) *organ functioning* and 6) *errors in recordings*. For example, in response to the anomaly detailed in Figure 1, the first clinician suggested sepsis (*clinical conditions*), an improvement in the patient's condition (*progress of the patient's condition*) and a combination of sepsis and myocardial infarction (*clinical conditions*) as potential explanations (Figure 2)[3].

Explanations provided by Clinician 6

"So, the patient may have changed, there may have been more sepsis perhaps which causes systemic vascular resistance to fall or maybe the patient was just starting to get better. I think the patient is considerably better by the end of day 32, I think that's what happened, the patient's underlying condition has changed and the patient has just improved for one reason or another because they are a lot better at the end of day 32 than they were at the end of day 31."

"..I mean it may have been that there has been some event you see, the combination of sepsis and that after the myocardial infarction because they had a low cardiac index and a high systemic vascular resistance. So it's possible that they had a cardiac event, the explanation would be that sometime, a little bit previously, perhaps at the end of day 30 into 31 they had a cardiac event and 24, 48 hours they had recovered from this, that's a possible explanation in somebody who has got sepsis"

Explanation provided by Clinician 7

"The only thing that I can think of is that noradrenaline is actually an inotrope. In a low dose, it tends to be a vasoconstrictor, in higher doses it's an inotrope. So it might just be that, that dose for that particular patient is enough to, as well as causing a tightening, is enough to cause an increase force of contraction as well"

Fig. 2. Explanations given by Clinicians 6 and 7

These interviews were analysed further and a method of information selection and hypothesis generation used by the clinicians was proposed. Figure 3 illustrates this general model of hypothesis generation. Beginning with an anomaly, for example, *noradrenaline increased cardiac output and cardiac index*, it can be broken down into the treatment, '*noradrenaline*' and the effect '*increase cardiac output and cardiac index*'. The clinician then proceeds to explain any combination of the anomalous treatment and effects through the various routes shown. The clinician appeared to use domain knowledge about treatment, medical conditions and the desired physiological state of the patient to explain the treatment or effect. Further, the domain knowledge can also be applied whilst examining the

[3] Both clinicians also identified that the patient had an abnormally low systemic vascular resistance (SVR)

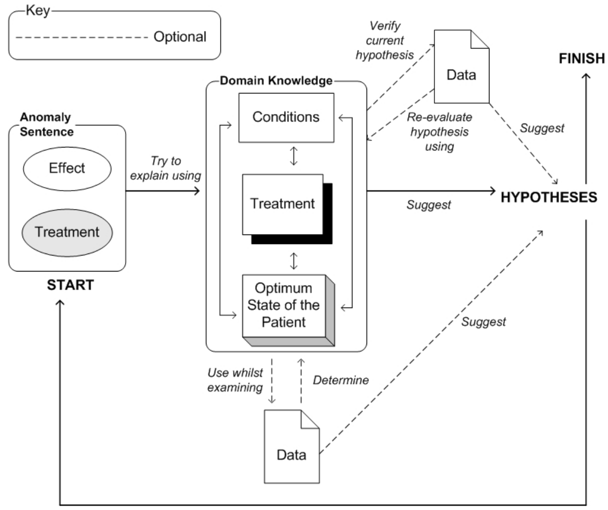

Fig. 3. General Model of Hypothesis Generation

data to determine facts; for example, the patient is suffering from a myocardial infarction. In addition, the patient's data can be used to eliminate hypotheses. For example, one of the explanations for the anomaly detailed in Figure 1 was that the patient may be getting better, if the data does not show this, the hypothesis could be eliminated. After suggesting a hypothesis, the clinician repeats the process until they are satisfied that all viable hypotheses have been proposed.

4 Ontology-Based Explanations of Anomalous Responses to Treatment

The model of hypothesis generation (Figure 3) forms the basis for an ontology-based hypothesis generation tool. In the initial stage, various methods (Figure 3) of querying the knowledge base and the patient data are used to generate a list of potential hypotheses for a given anomaly. The knowledge base comprises a set of ontologies coded in OWL containing the following concepts a) *Treatments* b) *Disorders* c) *Acceptable Parameters* and d) *Physiological Data*. The suggested hypotheses will subsequently be evaluated by an ICU clinician for clinical relevance. Building on this initial stage the work will be extended to explore the domain knowledge further. For example,

- Suppose: It had *not* been noted in the ontology that noradrenaline can, in high doses, increase a patient's cardiac output
- Observed Anomaly: The patient's cardiac output increased when the patient was on high doses of noradrenaline (as described in Figure 1)
- Known facts from knowledge base: *1)* Inotropes (a class of drugs) increase cardiac output *2)* Noradrenaline is a vasoconstrictor
- Conclusion: In this circumstance (high dose), noradrenaline is acting as an inotrope

5 Conclusions and Further Work

In this paper we have suggested a classification for the types of anomalies identified in the ICU domain and subsequently the types of explanations for such anomalies provided during interviews with domain experts. An initial system has been outlined to replicate the generation of these explanations. Planned future work involves a systematic evaluation of this system and enhancements namely a) the system could be extended to automatically detect anomalous scenarios in the patient data rather than rely on them being highlighted by a clinician and b) the system could explore more extensively both the data and the ontologies to suggest new hypotheses not currently contained in the knowledge base, for example, a new side effect of a drug not currently recorded in the treatments ontology.

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