A Process Mining Driven Framework for Clinical Guideline Improvement in Critical Care

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Abstract. This paper presents a framework for process mining in critical care. The framework uses the CRISP-DM model, extended to incorporate temporal and multidimensional aspects (CRISP-TDM^n), combined with the Patient Journey Modeling Architecture (PaJMa), to provide a structured approach to knowledge discovery of new condition onset pathophysiologies in physiological data streams. The approach is based on temporal abstraction and mining of physiological data streams to develop process flow mappings that can be used to update patient journeys; instantiated in critical care within clinical practice guidelines. We demonstrate the framework within the neonatal intensive care setting, where we are performing clinical research in relation to pathophysiology within physiological streams of patients diagnosed with late onset neonatal sepsis. We present an instantiation of the framework for late onset neonatal sepsis, using CRISP-TDM^n for the process mining model and PaJMa for the knowledge representation.

Keywords: Critical care, physiological data streams, process mining, knowledge discovery, clinical guidelines, patient journey modeling

1 Introduction

The neonatal intensive care unit (NICU) is a complex critical care environment that must support collaborative decision making amongst different care provider roles based on information received from high volumes of heterogeneous real-time synchronous medical device data, as well as asynchronous data from hospital information systems. Information must be organized to enable efficient and effective clinical decision making on the many complicated diagnoses present in today's NICUs. This includes supporting both known clinical guidelines and the ability to modify and extend current clinical guidelines based on new research, for example the retrospective analysis of physiological data streams to establish new and earlier pathophysiological behaviours evident in seemingly unrelated physiological data streams is a growing research area.

This paper presents a framework for process mining in critical care. It provides a structured approach to the knowledge discovery of new condition onset

pathophysiologies of physiological data streams and constructs process flow mappings that can be used to update patient journeys as instantiated within clinical practice guidelines. We demonstrate the flexibility and multidimensionality of this framework within the NICU setting where there are multiple streams of physiological data being captured from multiple patients, being watched for the onset of multiple potential conditions that can occur concurrently with patients located in multiple NICU locations. We are currently performing clinical research in relation to pathophysiology within physiological streams of patients who were diagnosed with late onset neonatal sepsis (LONS). We present an instantiation of the framework for LONS, showing the interactions between the physiological data streams and the high level clinical decision. While this case study is presented within a NICU context, its flexible and adaptive nature makes it equally applicable to any critical care environment acquiring data streams and performing similar knowledge discovery.

The remainder of the paper is structured as follows: Section 2 presents background information, including an overview of patient journey modeling and process mining. Section 3 introduces our framework and Section 4 demonstrates the framework within the NICU context. The paper concludes in section 5 where limitations of this research and future research directions are discussed.

2 Background

2.1 Process Mining

Process mining is an emerging research area motivated by the goal of extracting knowledge from event logs recorded by an information system; an event log contains data on the order in which the events take place [1]. While event-based data has potential to provide new knowledge *'process mining provides a new means to improve processes in a variety of application domains'* [2], in most cases this potential is unrealized. By providing techniques for discovering process, control, data, organizational, and social structures from event logs, process mining attempts to overcome this limitation [3]; for a current process mining review please see [2].

Event log data can originate from diverse systems, including hospital information systems (HISs), and support diverse applications, including health care [4]. As an example, the NICU's HIS records data on many clinical processes, including admission, investigations, diagnoses, treatment and follow-up. The current research on process mining in health care is in its early stages. Mans et al. provide several case studies proving the applicability of process mining to health care. In one, they demonstrate that process mining can be used for obtaining insights related to careflows, also referred to as patient journeys, for gynecological oncology patients where each event refers to a service delivered to a patient [4]. In that work, process mining was used to derive understandable models for large groups of patients. They identified that process mining is limited in its ability to work with unstructured processes often found in hospital environments. In a separate study, Mans et al. study two datasets for stroke patients, one of which encompasses the clinical course from admission to discharge, and the second focuses on pre-hospital behaviour [5]. They

found that process mining can be used both to construct models for a whole data set, or for only aspects that are of interest; for example, in the NICU context, only the investigation, diagnosis, or treatment process pathways. By focusing on specific process paths and using discovery process mining, they were able to identify differences in treatment strategies between different hospitals.

We see strong linkages between the real-time physiological data streams continually recorded in critical care settings and the event logs used in process mining; in critical care the processes of interest are the implementation of clinical guidelines, for which we seek to support process improvement and obtain new insights. However, process mining in health care has not yet been considered within the context of critical care and towards the improvement of care pathways and clinical guidelines through the inclusion of new pathophysiological behaviour analysis from complex and interrelated physiological data streams analysis.

2.2 Patient Journey Modeling

The Patient Journey Modelling Architecture (PaJMa) was designed specifically for health care, providing a visual representation of the processes, information and technology involved in a patient journey for different clinical scenarios. Recent work has implemented PaJMa in diverse hospital settings, proving that this technique is a highly applicable method of health care modeling for use within critical care [6]. PaJMa makes use of horizontal information layers containing independent information on different aspects of the patient's journey; layers are read vertically from left to right, with each process step moving across the page [7].

Working from the top-down, each layer provides important information related to the patient journey, specifically: 1) the patient's point of entry into the journey and subsequent interactions with the roles and processes contained in the journey; 2) the roles involved; 3) processes and possible decisions that comprise the action items of the journey; 4) information required or obtained by each process; 5) technology used; 6) underlying infrastructure support; 7) patient needs, policies, guidelines, and strategic objectives that are relevant to the various processes; and 8) optional metrics. An example PaJMa model instantiated for the diagnosis of LONS is provided in Section 4's case study. Experience indicates that PaJMa is effective at modeling different health care roles and their associated processes, as well as representing the use of technology to support the processes. However, to date PaJMa has not been used to support the event based activities that constitute clinical guideline models, where responses to events can trigger ad hoc pathways of patient journeys. In this work, we extend the current PaJMa modeling technique to show how it can support process mining of temporally abstracted physiological data streams.

2.3 CRISP-TDM

The CRoss Industry Standard Process for Data Mining (CRISP-DM) [8] was developed in 1996, with the goal of being industry, tool and application-neutral. Repeated references to the methodology by analysts have established it as the de facto

standard for data mining and KDD [9]. The model breaks the life cycle of a data mining project into six phases: business understanding, data understanding, data preparation, modeling, evaluation and deployment.

Analysis of the current CRISP-DM 1.0 Process and User Guide [8] identified that phases 1 (business understanding), 2 (data understanding), 4 (data modeling), 5 (evaluation) and 6 (deployment) of the current CRISP 1.0 model were all limited in their ability to describe: 1) clinically relevant and population-based information in the business understanding phase; 2) temporal aspects of the multidimensional data and the clinical study in the data understanding phase; 3) temporal abstraction of relevant details and knowledge management in the data modeling phase; 4) system integration in the data modeling phase, where CRISP 1.0 concentrates on applying several data mining techniques to arrive at one which offers the best results, rather than providing support for integrating techniques, such as data mining and temporal abstraction; 5) assessment of process mining results based on temporally abstracted data in the evaluation phase; and 6) storage issues, knowledge sharing and representation issues in the deployment phase, including mechanisms used for knowledge representation, such as adherence to health care standards [10].

Fig. 1 represents the enriched CRISP-DM model for reporting results of clinical investigations, for a detailed discussion please see [10]; the extended model is labeled CRISP-TDM^n to highlight its support of temporal (*T*) and multidimensional (*n*) clinical data. The first branch following a phase definition represents a task output for a CRISP-TDM^n phase; all lower branches in the hierarchy represent attributes of a task output for a CRISP-TDM^n phase. Tasks and attributes from the original CRISP 1.0 model are not presented in these figures, only those extensions relevant to the CRISP-TDM^n methodology are shown; extended tasks are marked with * and extended attributes with **. In this work, CRISP-TDM^n is used in conjunction with PaJMa to develop a framework for process mining of physiological data streams.

3 Framework for Process Mining and Process Representation in Critical Care (CRISP-TDM^n⇒PaJMa)

In this section we introduce our framework to enable process mining in critical care. The framework follows the principles of the CRISP-TDM^n approach to knowledge discovery and utilizes the Service based Multidimensional Temporal Data Mining (STDM$^n{}_0$) framework [11] to perform the process mining that enables knowledge discovery of new condition onset pathophysiologies from physiological data streams. It enables the construction of process flow/patient journey pathways within an extended PaJMa model based on the knowledge gained that can be used to update patient journeys as instantiated within clinical practice guidelines. The first subsection describes the components for knowledge discovery and the second details the representation of the new knowledge within the PaJMa model.

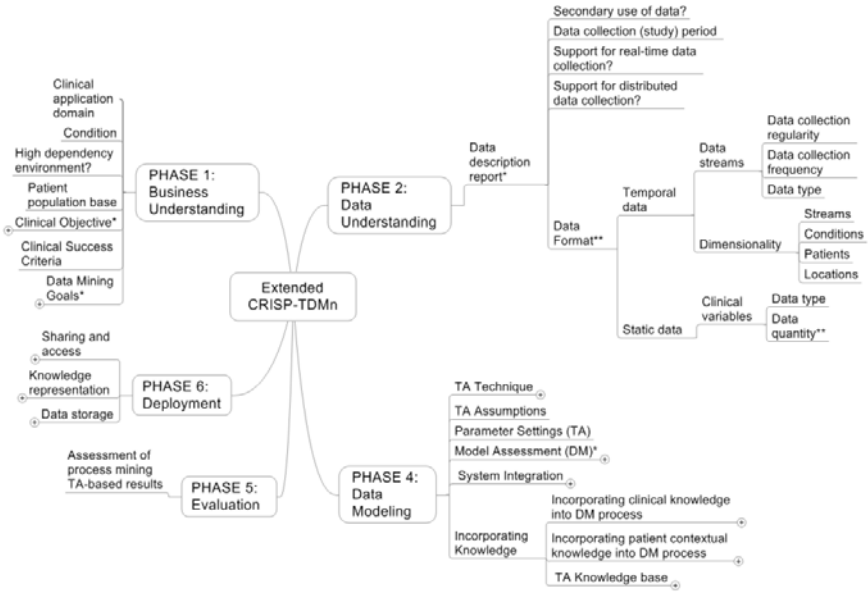

Fig. 1. Extended CRISP-TDM^n model [10]

3.1 Process Mining in Critical Care – Knowledge Discovery

This framework utilizes the extensions proposed to CRISP-DM for a standardised approach to temporal data mining. Following the principles of the CRISP-TDM^n, for process mining to occur a goal must first be determined as part of the *Business Understanding Phase*. The goal will be to determine whether new pathophysiological behaviours can be found in retrospective analysis of physiological data streams prior to the diagnosis of a selected clinical condition or clinical event of interest, where in each instance the condition or event will be quantified. During this phase ethics approval would normally be sought for the research.

The second phase of CRISP-TDM^n is to perform *Data Understanding*. Through the use of STDM$^n_0$ the data will have already been gathered by the STDM$^n_0$ processing agents and contained within the data management layer of the architecture. In addition, several temporal abstractions against that data will have already been run. The rules for which are contained in the temporal rules table, and the derived patient data is contained within the temporal abstraction tables. New temporal abstractions related to the study can also be performed on the data at anytime through the study process. As a result, CRISP-TDM^n *Data Preparation* is also completed.

The next step is to establish a study data subset for the process mining. Within STDM$^n_0$ this is performed by defining a new study. When a new study is defined, the clinical condition event of interest is defined and, associated with that, the rules for the selection of patients to be included in that retrospective study. As part of the data subset establishment and in support of patient anonymity, the data is relatively aligned

to represent a relative negative distance back in time from the point of the clinical condition or event of interest; this is performed by the Relative Agent. The rules for the study are stored within the study table and the data within the relative alignment table, encoded with the study id.

The modeling component of CRISP-TDM^n is performed within STDM$^n_0$ by the Processing Agents. The evaluation component of CRISP-TDM^n is supported through the provision of support for null hypothesis testing. From this process mining activity, temporal abstractions within one or many isolated or interrelated physiological streams will be found to have strong correlations as pathophysiological indictors for the given clinical condition. A major strength of our approach for knowledge discovery from process mining is its multidimensional nature. We can support the instantiation of several studies around several clinical conditions, exploring different physiological streams, for data located in different locations, and of interest to different care provider roles. This multidimensional approach is represented in Fig. 2, illustrating the view for a neonatologist studying apnoea as a clinical manifestation of LONS. The next phase is to propose a mechanism for translation and representation of that new knowledge within a process model as detailed in the next subsection.

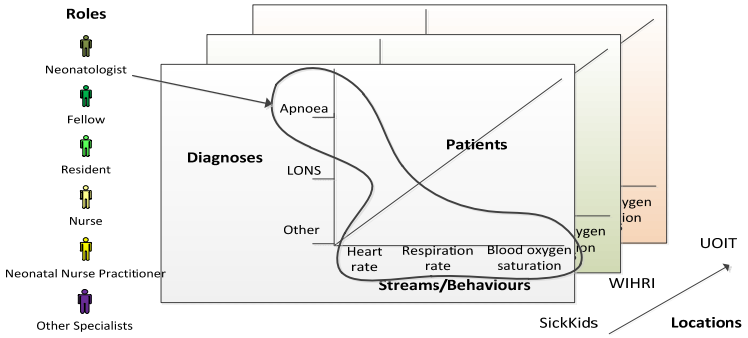

Fig. 2. Multi-dimensional nature of process mining environment – neonatologist's view

3.2 Process Mining in Critical Care – Knowledge Translation and Representation

For the representation of the new temporal abstraction knowledge within the process model we have chosen to use the PaJMa model. The information for the source physiological streams and the location of that data as it will be used in real-time is easily represented within the PaJMa model within the *Technology Used* and *Information* layers. In addition, the derived temporal abstractions that will need to be performed in real-time can also be represented within the *Information* layer of the PaJMa model. The clinical events that these abstractions work to support are represented within the *Process* layer of the model and the staff roles who will participate in these processes are included in the *Roles* layer.

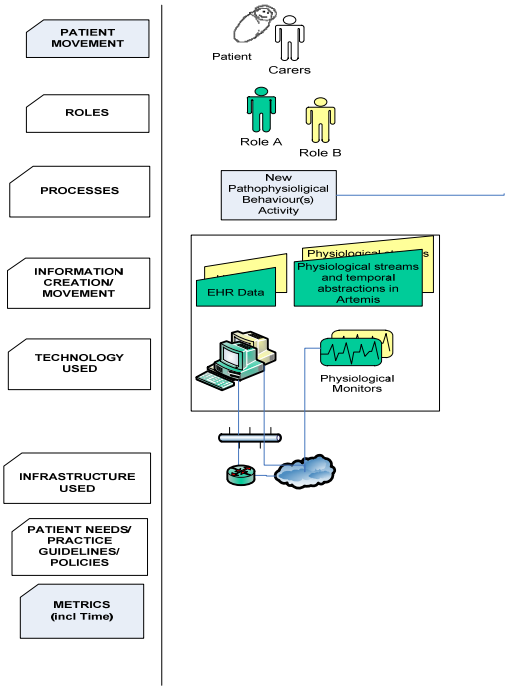

Fig. 3. Relationship between PaJMa layers and process mining in critical care components

Elements in the *Information* and *Technology Used* layer are colour coded to provide linkage to the roles. The relationship between PaJMa model layers and process mining in critical care is shown in Fig. 3. In previous work, we have demonstrated how the new knowledge in the form of temporal abstraction rules can be translated into a workflow engine designed to support the ingestion and analysis or real-time streaming sensor data and show its application to critical care. This instantiation is through the Artemis platform [12-14].

4 Demonstration of the Framework within a NICU Case Study

NICUs provide critical care to newborn children, often prematurely born infants that are especially susceptible to infection [15]. In this case study we focus on process mining centred around two clinically significant and related neonatal outcomes: LONS and central apnoea. We instantiate the layers of the CRISP-TDM^n technique and present extended PaJMA models, illustrating the framework's approach to process mining and knowledge translation for new onset diagnosis of LONS.

Neonatal sepsis is a life threatening condition, with early diagnosis being significant; infants are often diagnosed only when seriously ill which decreases the probability for prompt, complete recovery with antibiotic therapy [16]. LONS is

typically defined as sepsis acquired as early as four days after birth and as late as 28 days after birth [15]; for the purpose of this work we use the definition that LONS refers to sepsis acquired on or after the fifth day of life. LONS occurs in approximately 10% of all neonates and in more than 25% of very low birth weight infants who are hospitalized in NICUs [17]. Numerous studies have linked sepsis to reduced heart rate variability (HRV) [16], [18-21]. Previous work has discussed our approach to analyzing HRV for use as an early indicator of neonatal sepsis [22].

Central apnoea is another clinically significant condition, episodes are first recognized as a lapse in respiration, identified either by a decrease in respiration rate below a predefined threshold, or by a drop in frequency of the impedance respiratory wave. Many studies have shown that apnoea duration is positively correlated with both a decrease in blood oxygen saturation and heart rate [23-26]; this pathological change is used as a marker to indicate the possible presence of apnoea in the absence of a confirmed clinical observation of apnoea. Previous work has presented our implementation of clinical guidelines for the real-time detection of central apnoea using Artemis [27]. Episodes of apnoea can be a pathophysiological onset behaviour for several of conditions, one of which is LONS.

Given the body of research showing the worth of knowledge discovery in physiological streams, there is a need to enable a multidimensional environment that enables knowledge discovery of new pathophysiological behaviours in physiological streams prior to the onset of a clinical event and a multidimensional mechanism to watch for these in real-time.

4.1 CRISP-TDM^n Business Understanding

The *Clinical Application Domain* is that of neonatal intensive care involving two collaborating NICUs, The Hospital for Sick Children, Toronto (SickKids) and Women and Infants Hospital, Providence, Rhode Island (WIHRI).

The *Clinical Objective* is the proposition of new physiological stream pathophysiological behaviours evident prior to the diagnosis of LONS with a higher sensitivity and specificity as compared to current clinical guideline pathophysiological measures. A secondary objective is that these new behaviours are evident earlier than the current clinical guideline pathophysiological measures. Research ethics board approval was received from the hospitals of the two collaborating NICUs.

The *Data Mining TA Goals* and hence the process mining goals are then to perform population-based retrospective supervised data mining of temporally abstracted behaviours of physiological streams of patients who had developed LONS. Within this paper, for the purposes of this demonstration we will limit our temporal data mining to the temporal abstractions of reduced HRV and mild, moderate and severe instances of central apnoea. Temporal abstraction involves transforming time stamped data into an interval-based representation of the data by extracting the most relevant features [28], such as identifying states, trends and temporal relationships. Then sections of data that hold true for certain criteria can be summarized with a start time and end time.

4.2 CRISP-TDM^n Data Understanding and Data Preparation

Data for this research was collected utilizing the Artemis platform, and the study into LONS represents the primary use of this data. Data collection from SickKids commenced in August 2009 and in April 2010 from WIHRI [12], [14]. Heart rate (HR), respiration rate (RR), and blood oxygen saturation (SpO_2) are collected from patients at SickKids at the rate of one reading a second (1Hz) for the duration of their stay in the NICU from the bedside Philips MP70 devices. In addition, an impendence respiratory wave (IRW) is also collected measuring the chest wall impedance to determine the presence of breathing, with a frequency of 125 Hz. Currently Artemis has been enabled at 8 bed spaces while the platform has undergone testing, but a hospital infrastructure upgrade will now enable us to utilize network ports at each bed space to collect from all 38 beds.

The Space Labs bedside devices are used at WIHRI and a cloud computing implementation of Artemis [14] enables the transmission of a number of physiological streams including heart rate, respiration rate and blood oxygen saturation readings every minute to the Artemis cloud implementation located at the University of Ontario Institute of Technology (UOIT). Currently Artemis cloud has been collecting data from between 10-15 patients daily during performance testing, but the architecture could collect from as many bed spaces as the clinical research requires.

4.3 CRISP-TDM^n Data Modeling

This research performs quantitative analysis of the temporal abstractions performed on physiological streams as detailed in Table 1. The details of the temporal abstraction calculations are outside the scope of this paper. Our approach for reduced HRV temporal abstractions is described in [22] and the abstractions for neonatal apnoea are detailed in [27]. The flexibility of this approach enables various data mining algorithms, such as machine learning, that accommodate temporal data to propose and analyse correlations.

Table 1. Temporal abstractions for LONS Process Mining

Temporal Abstraction	Physiological Stream
Reduced HRV	HR
Mild Apnoea	IRW
Moderate Apnoea	IRW, SpO_2
Severe Apnoea	IRW, SpO_2, HR

4.3 CRISP-TDM^n Evaluation

For the purposes of this demonstration for process mining we will assume that the results of the data mining have demonstrated superior sensitivity and specificity when mining the temporal abstractions relating to reduced HRV and those that classify apnoea. The next step is to model results within the PaJMa model.

4.4 PaJMa Knowledge Translation and Representation

The PaJMa model provides the representation of the knowledge within the process model to support the enactment of this new knowledge in real-time. Each form of temporal abstraction that represents a clinical event found to be relevant in the process mining phase is represented within the PaJMa model as a vertical slice. For each vertical slice, the clinical event is represented in the *Processes* layer. The medical devices creating the physiological data are shown in the *Technology Used* layer. The temporal abstractions that relate to that clinical event are represented in the *Information Creation/Movement* layer. The roles interested in this event are shown in the *Roles* layer and the elements of the *Information Creation/Movement* and *Technology Used* layers are colour coded to link them with the roles. The *Infrastructure Used* layer demonstrates where equipment is connected to the hospital network and where that could be connected to a secure gateway for connection through the internet. The *Technology Used* layer demonstrates that Artemis is used for the temporal abstractions and role notifications to different user interface devices.

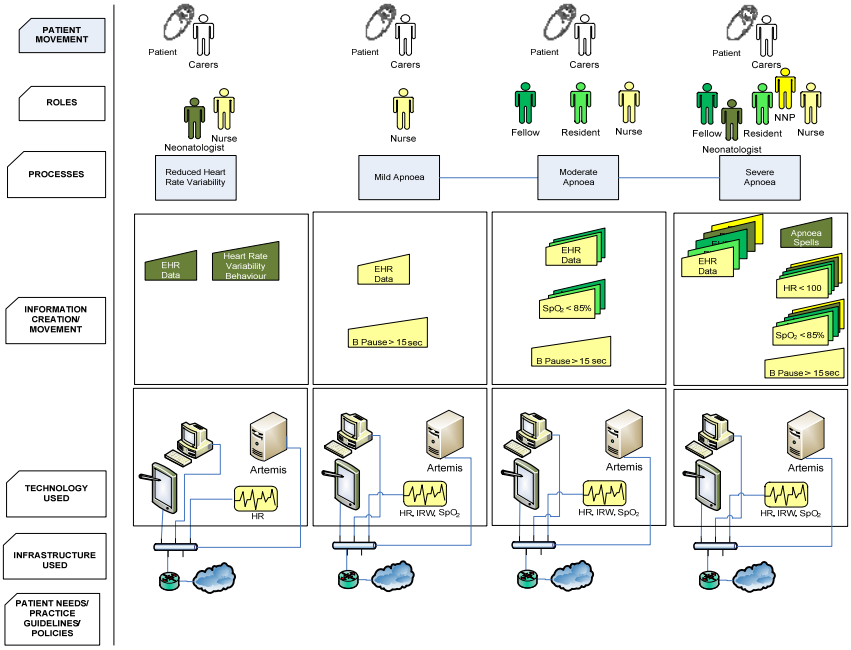

Fig. 4. PaJMa process model for LONS

5 Conclusions and Future Work

This research has presented a generalized framework to support process mining in critical care that enables knowledge discovery of new condition onset

pathophysiologies using temporal data mining of physiological data streams and constructs process flow mappings that can be used to update patient journeys as instantiated within clinical practice guidelines. The research was demonstrated within the context of neonatal intensive care and specifically as it relates to LONS and the potential of reduced heart rate variability and apnoea to be pathophysiologies for that clinical condition. In this way, we have demonstrated the ability for this framework to be used by clinical researchers as a platform to perform knowledge discovery, to store that new knowledge, and to translate that knowledge to updated clinical guidelines.

While we have proven that PaJMa can easily represent the distinct activities and provide a rich set of information needed for the instantiation within real-time clinical care, the *ad hoc* nature of the event sequence was a challenge to represent, as it is with any business process modeling technique. We have commenced work on extensions to the PaJMa model to better support the event based nature of the ICU setting. The Guidelines Element Model (GEM) [29] has been proposed as a mechanism for knowledge representation of clinical guidelines. In future work we will show how the process mining phase can generate GEM representations which can then be represented within an extended PaJMa model.

To assess quality improvement in health care, the impact of changes to the clinical guidelines need to be assessed through either clinical trial or other metrics, such as in the case of LONS, a reduction in average length of stay. Formal models for evaluation need to be proposed for the analysis of these process mining driven changes to clinical guidelines.

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References

1. van der Aalst, W.M.P., Weijters, A.J.M.M.: Process Mining: a Research Agenda. Comput. Ind. 53, 231-244 (2004)
2. Van der Aalst, W.M.P.: Process Mining: Discovery, Conformance and Enhancement of Business Processes. Springer (2011)
3. Queensland University of Technology & Eindhoven University of Technology: Process Mining. http://is.tm.tue.nl/staff/wvdaalst/BPMcenter/process%20mining.htm
4. Mans, R.S., Schonenberg, M.: Application of Process Mining in Healthcare–A Case Study in a Dutch Hospital. In: International Joint Conference on Biomedical Engineering Systems and Technologies, pp 425-438. Springer-Verlag, Berlin Heidelberg (2008)
5. Mans, R., Schonenberg, H., Leonardi, G., Panzarasa, S., Cavallini, A., Quaglini, S., van der Aalst, W. Process Mining Techniques: an Application to Stroke Care. In: Proceedings of Medical Informatics Europe, pp 573-578. IOS Press (2008)
6. MacDougall, C., McGregor, C., Percival, J. The Fusion of Clinical Guidelines with Technology: Trends and Challenges. eJHI. 5, 2 (2010)
7. Percival, J., Catley, C., McGregor, C., James A. Modeling the Impact of Technology on Information Flows in Neonatal Intensive Care Units. Stud. Comp. Intell. 189, 147-169 (2009)

8. Chapman, P., Clinton, J., Kerber, R., Khabaza, T., Reinartz, T., Shearer, C. CRISP-DM 1.0, http://www.crisp-dm.org/download.htm
9. Shearer, C. The CRISP-DM Model: The New Blueprint for Data Mining. J. Data Warehousing. 5, 13-22 (2000)
10. Catley, C., Smith, K., McGregor, C., Tracy, M. Extending CRISP-DM to Incorporate Temporal Data Mining of Multidimensional Data Streams: a Neonatal Intensive Care Unit Case study. In: Computer-Based Medical Systems, pp. 1-5 (2009)
11. McGregor, C. System, Method and Computer Program for Multi-Dimensional Temporal Data Mining. Patent # 089705-0009; Canada, Gatineau Quebec (2010)
12. Blount, M., Ebling, M.R., Eklund, J.M., James, A.J., McGregor, C., Percival, et al. Real-Time Analysis for Intensive Care: Development and Deployment of the Artemis Analytic System. IEEE Eng Med Biol Mag. 29, 2, 110-118 (2010)
13. McGregor, C., Sow, D., James, A., Blount, M., Ebling, M., Eklund, J., et al. Collaborative research on an intensive care decision support system utilizing physiological data streams. In: Proc AMIA Annu. Symp. pp 1124-6 (2009)
14. McGregor, C., Catley, C., James, A., Padbury, J. Next Generation Neonatal Health Informatics with Artemis. Accepted for presentation at MIE 2011, Informatics Europe, Oslo, Norway.
15. Ganatra, H. a., Stoll, B.J., Zaidi, A.K.M. International Perspective on Early-Onset Neonatal Sepsis. Clin. Perinatol. 37, 2, 501-523 (2010)
16. Griffin, M.P., O'Shea, T.M., Bissonette, E.A., Harrell, F.E., Lake, D.E., Moorman, J.R. Abnormal Heart Rate Characteristics Preceding Neonatal Sepsis and Sepsis-like Illness. Pediatr Res. 53, 6, 920-926 (2003).
17. Beck-Sague, C.M., Azimi, P., Fonseca, S.N., Baltimore, R.S., Powell, D.A., Bland, L.A., et al. Bloodstream Infections in Neonatal Intensive Care Unit Patients: Results of a Multicenter Study. Pediatr Infect Dis J. 13, 12, 1110-1116 (1994)
18. Flower, A.A., Moorman, J.R., Lake, D.E., Delos, J.B. Periodic Heart Rate Decelerations in Premature Infants. Exp. Biol. Med. 235, 4, 531-538 (2010)
19. Griffin, M.P., Lake, D.E., O'Shea, T.M., Moorman, J.R. Heart Rate Characteristics and Clinical Signs in Neonatal Sepsis. Pediatr Res. 61, 2, 222-227 (2007).
20. Griffin, M.P., Lake, D.E., Moorman, J.R. Heart Rate Characteristics and Laboratory Tests in Neonatal Sepsis. Pediatrics. 115, 4, 937-41 (2005)
21. Griffin, M.P., Moorman, R. Using Novel Heart Rate Analysis. Pediatrics, 107, 97-104 (2001)
22. McGregor, C., Catley, C., James, A. Simplifying Complexity: Variability Analysis with Analytics Applied to Physiological Data Streams from the Neonatal Intensive Care Unit. Submitted for presentation at Annual Fall Symposium, AMIA (2011), Washington DC.
23. Finer, N.N., Barrington, K.J., Hayes, B.J., Hugh, A. Obstructive, Mixed, and Central Apnea in the Neonate: Physiologic Correlates. J. Pediatr. 121, 943-950 (1992)
24. Finer, N.N., Higgins, R., Kattwinkel, J., Martin, R.J. Summary Proceedings from the Apnea-of-Prematurity Group. Pediatrics. 117, S47-51 (2006)
25. Muttitt, S.C., Finer, N.N., Tierney, A.J., Rossmann, J. Neonatal Apnea: Diagnosis by Nurse Versus Computer. Pediatrics. 85, 713-720 (1988)
26. Upton, C.J., Milner, A.D., Stokes, G.M. Apnoea, Bradycardia, and Oxygen Saturation in Preterm Infants. Arch Dis Child. 66, 381-385 (1991)
27. Catley, C., McGregor, C., Smith, K., James, A., Eklund, J.M. A Framework for Multi-Dimensional Real-Time Data Analysis: a Case Study for the Detection of Apnoea of Prematurity. J. Comput. Mod. Alg. Med. (in press 2011)
28. Post, A.R., Harrison, J.H. Temporal Data Mining. Clin. Lab. Med. 28, 83-100 (2008)
29. Guidelines Element Model, http://gem.med.yale.edu/default.htm