Towards Process Mining of EMR Data
Case Study for Sepsis Management

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Abstract: Imagine you have cold shivers and a racing heartbeat and high fever. Clear thinking is impossible! Ceiling lights flash by as you are rushed to the emergency department (ED). You feel your body is getting even sicker. Doctors are doing their utmost to treat this acute and threatening condition, while they work piece together all small parts of evidence to set the diagnosis and start targeted treatment. In this situation, the clinical staff depends on a clinical pathway protocol to streamline communication and deliver care according to the latest medical evidence. Today, such clinical pathways are mainly executed and tracked using paper. Hence, there is ample opportunity for technology in a supportive role. Automated process analysis can help improve these processes of delivering standardized care beyond their current level. In this paper, we provide insight into the steps required to perform process mining to EMR data in the challenging domain of sepsis treatment and provide learnings from our preliminary analysis of these data using process mining techniques.

1 INTRODUCTION

Sepsis is a potentially life-threatening complication of an infection, where inflammatory responses throughout the body are triggered, which can lead to damage of multiple organ systems, causing them to fail. Sepsis is a condition with a very big impact on patient condition, and has high mortality rates. It is also characterized by high annual incidence rates, e.g., in the US 3-10 in 1000 people are hospitalized with sepsis (Kempker and Martin, 2016). The associated healthcare costs are also high; in 2011 it accounted for $20.3 billion, which is 5.2% of total US hospital costs, therewith the most expensive condition treated (Torio and Andrews, 2013).

The management of sepsis is complicated by the difficulties of detecting the condition. Recently, the community adopted a new definition of sepsis and a strategy for screening was proposed (Singer et al., 2016). As we evaluate our methods on data collected before 2016, this paper focuses on the method commonly accepted until that date, where screening for Systemic Inflammatory Response Syndrome (SIRS) symptoms is used to evaluate starting the treatment for sepsis. Hence, we adopt the 1992 definition from the American College of Chest Physicians / Society of Critical Care Medicine (Bone et al., 1992): "Sepsis is the Systemic Inflammatory Response Syndrome (SIRS) to the presence of infection". A patient is screened positive for SIRS if two or more of the following criteria are met:

- Temperature $>$ 38°C or $<$ 36°C
- Heart rate $>$ 90/min
- Respiratory rate $>$ 20/min or $PaCO_2 < 32$ mmHg (4.3 kPa)
- White blood cell count $>$ 12000/mm^3 or $<$ 4000/mm^3 or $>$ 10% immature bands

Patients are considered to be septic when the SIRS criteria are satisfied in combination with a suspected or established infection. As the SIRS criteria are not specific, many patients meeting the SIRS criteria will, however, not have or develop sepsis (Lord et al., 2014). When sepsis is complicated by organ dysfunction, it is called severe sepsis, which can turn into septic shock when hypotension persists despite fluid resuscitation. Mortality rates vary strongly per

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geography, but are known to increase with the three levels of sepsis: up to 30% for sepsis, 50% for severe sepsis and 80% for septic shock over the timespan of 1 year (Jawad et al., 2012). A multi-center study in Brazilian Intensive Care Units (ICUs) showed rates of 34.7%, 47.3% and 52.2% at 28 days, respectively (Silva et al., 2004).

In 2002 the Surviving Sepsis Campaign (SSC) was launched as a global campaign to reduce mortality due to sepsis. The guidelines they published, along with the updates made over the last years, are now widely adopted in clinical practice (Dellinger et al., 2004; Dellinger et al., 2008; Dellinger et al., 2013). The SSC provided a care bundle that comprises the following steps:

To be completed within 3 hours of presentation:

- Measure lactate level
- Obtain blood cultures prior to administration of antibiotics
- Administer broad spectrum antibiotics
- Administer 30mL/kg crystalloid for hypotension or lactate $\geq$ 4 mmol/L

To be completed within 6 hours of presentation:

- Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) $\geq$ 65 mmHg
- In the event of persistent hypotension after initial fluid administration (MAP $<$ 65 mmHg) or if initial lactate was $\geq$ 4 mmol/L, reassess volume status and tissue perfusion and document findings
- Remeasure lactate if initial lactate elevated.

As these guidelines provide a recommendation, hospitals implement these guidelines adapted to their standards of care. These guidelines are translated into clinical pathways (CPs), which are "complex intervention[s] for the mutual decision making and organisation of care processes for a well-defined group of patients during a well-defined period" (European Pathway Association, 2016). In this field, Key Performance Indicators (KPIs) are often described in terms of adherence to such guidelines.

During the interpretation and translation process, the guidelines are made actionable for the clinical staff: tasks and responsibilities are defined and a communication structure around the pathway is put in place. CPs are implemented in different areas of health care, such as acute care (e.g., for chest pain in the emergency room (ER), stroke diagnosis), integrated oncology care and chronic disease management (e.g., coordination of care for heart failure patients). Often, the clinical pathway of a patient is managed using a paper sheet. However, this leads to double data entry as the status needs to be recorded in the Health IT system as well as on paper. Moreover, the current phase on the pathway, when represented on paper, is only available to those accessing the sheet, typically at the bed side.

In this research, we are interested in solutions to monitor the status of the patient in a clinical pathway by analyzing data from the Electronic Medical Record (EMR). To this end, we model the clinical pathway in a computer interpretable format. The events in this model are associated with data from the EMR. However, there might not always be in one-to-one correspondence. For example, events such as *patient transferred to ICU* or *Vital Signs measured* may be associated with only single time-stamped entries in the patient record, but as we will see in the following, events such as *Blood Volume Expansion performed* might be more complicated to retrieve.

Process mining is the technique to extract information from event logs (van der Aalst, 2011). In general, the scientific field is concerned with two research areas: process discovery and conformance checking. Process discovery deals with identifying a model that describes the behavior as observed in a set of event logs. In process discovery, the challenge is to identify a model that is not too general but is also not overfitting the behavior as encountered in the set of event logs. In conformance checking, on the other hand, a collection of event logs is compared with a reference model with the aim to research whether the observed behavior is matching the expected behavior. In particular, common deviations or delays in processes can be analyzed. As many KPIs are based on times-to-event or performing actions in a certain order, results from conformance checking can be used as input to KPI analysis.

Applying process mining to event logs obtained from EMRs is known to be a challenging topic, as was concluded in several studies in the application of process mining techniques domains such as oncology, surgery, cardiology, diabetes and clinical images (Rojas et al., 2016). Already in 2008, Mans et al. describe explorations to discover process models from hospital data on stroke care (Mans et al., 2008). Nonetheless, these past attempts were performed on relatively straightforward clinical processes with homogenous patient populations, or incorporated prospective data collection. To the best of our knowledge, two other studies looked into applying process mining for sepsis, however results are limitedly published (Mannhardt et al., 2016; Mcgregor et al., 2011).

In general, process mining techniques can only be

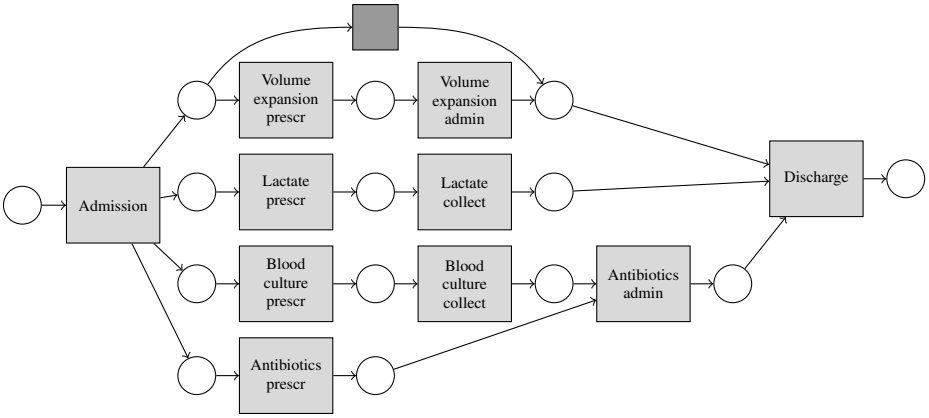

Figure 1: Petri net of the simplified model representing the clinical pathway for sepsis management, used for conformance checking.

applied if the event log describes a recognizable process. The event log for a patient from an EMR will contain events related to various processes and actions. The vast majority of these raw events will not be directly related to the care according to the reference pathway, but rather reflect routine sub-processes that the staff follows in usual care. Hence when analyzing the event log, a projection needs to be created of events that describe actions and data related to the pathway. In this paper, we are interested in exploring the potential of applying process mining techniques on a complete patient record from an EMR. We draw learnings from the modeling, data extraction and process mining steps.

2 METHODS

The data used in our study have been obtained from Hospital Samaritano, a private, Brazilian hospital having over 300 beds. For extracting the data from the Health IT system we identified the database tables and attributes that could represent the sepsis treatment activities from the ICU and emergency department (ED) processes. For the selection of sepsis hospitalizations, we considered hospitalization registries that had at least one diagnosis or death related to sepsis using an ICD, 10th edition (ICD-10) code list for sepsis (Canadian Institute for Health Information, 2009). Also, we included patients that were assigned a prescription template related to sepsis. The ICD-10 codings we selected, were validated by 3 Brazilian specialists and the sepsis selection method was validated by the physician responsible for the deployment of the sepsis protocol in the hospital. We extracted 4516 sepsis hospital encounters for a period of two years. To protect the identity of patients and caregivers, we pseudonymized the patient data. Important aspect with respect to the process analysis is that dates were shifted with a fixed amount of days per patient-encounter. Hence, the relative times between events per hospital admission were not altered. The data analysis was conducted with approval of the institution's ethics committee.

As indicated in the introduction, the raw data from the EMR requires interpretation or abstraction to bring it to the level of event analysis suitable to derive meaningful insights. The ultimate aim would be the analysis in terms of KPIs, however that would require more validation and comparison to the formal quality assessment procedure, which is beyond the scope of this paper. To this end, we focussed on the important elements in the first three hours of care as described in the SSC care bundle: Lactate measurement, obtaining blood cultures, antibiotics administration and volume expansion. The first two are relatively easily obtained from the data as they refer to procedures that are directly ordered as such and registered in the EMR. The antibiotics are retrieved in a similar method, using a long list of antibiotics names and active components. Volume expansion is, however, not directly registered as such in the EMR, but required interpretation of sequences of low-level events of administrating fluid. To this end, we collected all administrations of volume expanders and implemented a windowed thresholding that searches for sufficient fluid administration ($\geq 90\% * 30$mL/kg in 4 hours) such that it can be considered fluid administration with the purpose of volume expansion. For each of these four elements of care we collect the times of request and times of administration or collection, which gives 8 event types. To mark the start and end of event traces, we also include the moment of admission and discharge, yielding a total of 10 different event types.

In order to avoid that incomplete timestamps,

that only contain the date of the event, would negatively influence the results, we corrected timestamps of '00:00:00' in appropriate cases as we found that these timestamps referred to the midnight before the actual event must have happened. To allow for a more complete conformance checking, we chose to correct these timestamps as follows: if the event related to collection or administration and if the corresponding prescription event was present, we corrected the timestamp to one second after the corresponding prescription event. By doing so, we corrected the order of events, however it should be noted that these timestamps should still be considered imprecise and were thus excluded from any time-to-event analysis.

Our explorative analysis started with retrieving the times to event for each of the care elements as a step towards measuring KPIs. Note that we used the time of presentation (admission) as time zero to be able to measure all other timestamps relative to this time of admission. After that, we used the ProM software (van der Aalst et al., 2007) to perform conformance analysis of the model outlined by the SSC care bundle. To this end, we constructed the model as a Petri net, displayed in Figure 1, that represents the different steps that can happen concurrently, and the (time-wise) dependency between obtaining the blood cultures and administration of antibiotics. While this model might seem an oversimplification of clinical reality, it does contain all the critical steps outlined in the SSC care bundle (see Introduction) and provides a first step towards more elaborate pathway models. In the process of conformance checking, the event traces in the event log are aligned with the model and a distance is calculated for the alignment. We used the 'standard distance function' that assigns a cost of 0 in case log and model agree and 1 in case of disagreement (move on log or move on model) (van der Aalst et al., 2012).

3 RESULTS

The cohort extracted for the present analysis, using the inclusion criteria outlined in the previous section, consisted of 4516 patients. 4442 patients entered the hospital via the ED and were selected for the subsequent analysis. These patients have a median age of 37.7 years, 51.5% were male, median length of stay (LOS) was 5 hours, and 2.5% died in hospital. Further descriptive statistics can be found in Table 1.

3.1 Events

In total there were 37635 events extracted for the 4442 patient admissions. 4204 events had a timestamp of 00:00:00. The vast majority (4162) of these events were the collection of lactate. For 3700 events we could correct the timestamps using the aforementioned procedure, another 504 could not be corrected (no corresponding request event could be found) and were removed. Note that for the time-to-event analysis, we excluded all the 4204 events with imprecise timestamps.

Table 2 shows the number of events retrieved from the EMR. We observe that all event types are highly represented in the database, with at least 85% (lactate collection) and more than 95% of cases for the other obligatory event types. Volume expansion is less often represented, however this is also considered an optional (conditional) event, as specified in the model (Figure 1).

Figure 2 shows the histograms of time-to-event (from the moment of presentation) for each of the prescription and administration/collection events. Note that that the rightmost bars in the histograms (at 3 hours from presentation) contain all samples with times $\geq$ 3 hours. We observe that the vast majority of events happen within the first hour after presentation, with modes being 16 minutes for prescription of antibiotics and volume expansion, and 17 minutes for lactate and blood cultures. For administration/collection, the mode are 15 minutes for lactate, 19 for volume expansion, 21 minutes for antibiotics and 38 for blood cultures. The following fractions of prescription events happen outside of the window of 3 hours: Lactate (5.4%), Antibiotics (5.2%), Blood cultures (4.9%), Volume expansion (14.7%). Note that for lactate collection, the number of events found is much smaller than for the others due to the inaccurate timestamping mentioned earlier.

Conformance analysis using ProM yielded the results presented in Figure 3. The number of prescrip-

Table 1: Descriptive statistics of the patient population.

Name	Valid *N*	*N* (%) Median [25th-75th]
Age (year)	4442	37.5 [26.0-56.3]
Male	4442	2295 (51.7%)
LOS (hour)	4439	5.0 [3.4-75.2]
Died in hospital	4442	113 (2.5%)
Initial diagnosis	4442	
Missing		77 (1.7%)
Infections / Parasites		1041 (23.4%)
Respiratory		1631 (36.7%)
Abnormalities		953 (21.5%)
Other		740 (16.7%)

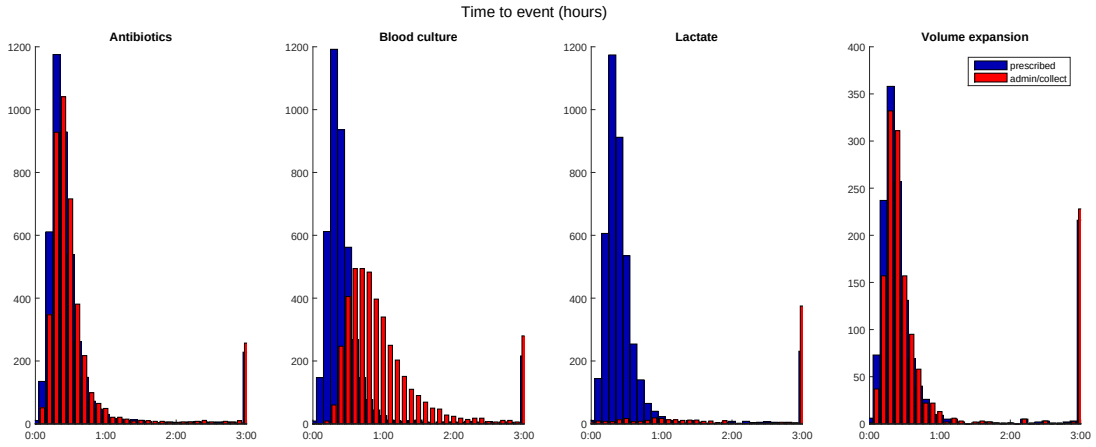

Figure 2: Distributions of time-to-event (from the moment of presentation) for the four care elements. The blue histograms represent the time to prescription, the red histograms represent the time to administration or collection. The horizontal axes represent time (hh:mm), the vertical axes represent counts.

tion events conforming to the model are the same as the number of (valid) events found in the time-to-event analysis. For the administration/collection events, we see different numbers of conforming events as compared to the numbers of events found in the time-to-event analysis. This is because the conformance checking does not only take into account presence of the events in the log, but also whether the order is according to the model. Here we see, for example, that there are 4352 blood culture prescriptions found in correspondence to the model versus 90 not; similarly, 1229 volume expansions that are in correspondence with the model. Note that volume expansion is, following the guidelines, an optional step if certain conditions are not met.

Table 2: Numbers of events found.

Event name	N (%)
Admission	4442 (100.0%)
Discharge	4431 (99.8%)
Blood culture prescr	4355 (98.0%)
Blood culture collect	4339 (97.7%)
Antibiotics prescr	4324 (97.3%)
Antibiotics admin	4309 (97.0%)
Lactate prescr	4231 (95.2%)
Lactate collect	3772 (84.9%)
Volume expansion prescr	1465 (33.0%)
Volume expansion admin	1463 (32.9%)

Volume expansion is only managed when clinically indicated (see also Figure 1).

If we now connect these numbers to the earlier found number of events logged (Table 2), we can derive, e.g., that for $3772 - 3751 = 21$ lactate collections there was a log-entry, however not in the order prescribed by the model. Similarly, we can see that for volume expansion there are $1465 - 1461 = 4$ prescriptions that are logged, however not in the way anticipated by the model. For antibiotics administration we observe many ($4309 - 252 = 4057$) not conforming events, which turned out to be caused by an order mismatch with the blood culture collection (i.e., antibiotics administered before blood cultures were collected). Potential reasons for these mismatches will be discussed in the next section.

4 DISCUSSION

In our analysis, we have first looked into time-to-event analysis, which looks at the number of events logged and can derive various statistics from the timestamps of these events. Although this can give a good insight into how processes are executed on average, and identify outliers with respect to time-to-event, it does not take into account correct order of events. Using process mining, and conformance checking in particular, we can also study the order in which events occur and study deviations in more detail. One particular challenge that we tried to address here, is that EMRs are general tools to support overall clinical processes and that fields in the EMR can be used for multiple conditions and are pathway aspecific by design. Often patients are concurrently evaluated and treated for a variety of conditions, and there is often little or no evidence of which data entries relate to which diagnosis; this relation has to be inferred. Also, it is important to stress that not all patient care activities are documented in the EMR.

Before reflecting on the results obtained, we would like to emphasize that this experiment of gath-

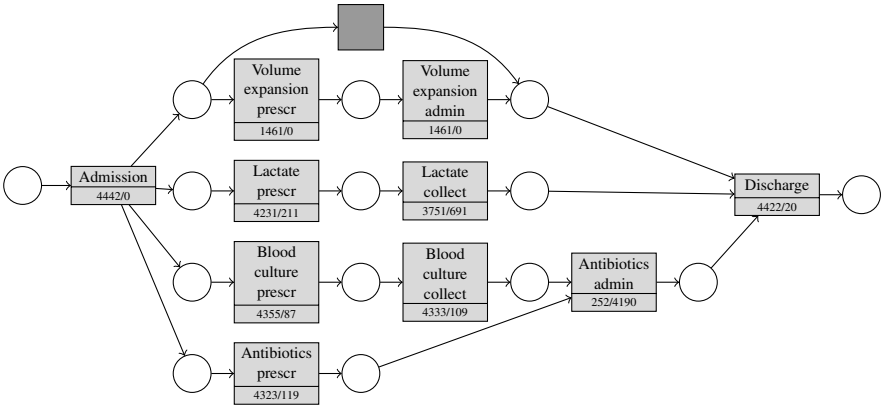

Figure 3: Output of conformance analysis in ProM, showing per event type the number cases that conform to that step in the model versus that do not.

ering KPI information directly from EMR data without a thorough, manual, quality analysis is likely to provide an underestimation of guideline adherence compared to reality. This is due to the following list of potential causes for our analysis not picking up adherent behavior:

- Not logged: Action has been performed but not logged
- Incorrect timestamping: Action has been performed but with incorrect or imprecise timestamp
- Incomplete querying: The query used for interpreting the EMR data can miss certain cases

Hence, we should not interpret the outcomes of our current analysis as quality measure for the care performed before carrying out a more thorough quality analysis. We are also reporting intermediate results, and therefore cannot draw conclusions on the KPIs themselves, but our focus is to share the challenges relating to process mining on "real-life" EMR data.

Although the blood volume expansion does only happen when clinically indicated, the relatively low number of blood volume expansion events, might suggest that our interpretation of the EMR data is not completely covering the different ways these events are reflected in the EMR, rather than they are often not prescribed, or that they are prescribed, but not logged. Further analysis is required to analyze the volume expansion management of these sepsis patients. In any case, the quality of the logging influences the results. Bose et al. distinguish 27 classes of quality issues with event logs (Bose et al., 2013). In our data, we observe presence of the following classes of issues: missing events, missing timestamps, incorrect timestamps and imprecise timestamps. The first category has been reflected upon already, the missing, incorrect and imprecise timestamps typically reflect clinical reality as it is simply not possible to 100% accurately timestamp all events. Imprecise timestamping can be observed in the lactate collections where often only date information was information. Incorrect timestamping might be observed in, e.g., many antibiotics administration events that are found not conforming to the model (4195 out of 4304). This is further substantiated by the notion that the clinical staff at the hospital, at which the study was performed, is all well aware of the fact that antibiotics influence the results of the laboratory measurements from the blood samples. It might well be that there are differences in the actual time of performing the event versus the moment of logging in the EMR, or alternatively that we made incorrect assumptions in the interpretation of raw data. Further verification with the hospital's quality assurance process is required to find the reason of this mismatch.

The treatment of sepsis in the ED is a particularly challenging environment as the condition is life threatening and quick responses are required, which we anticipated to potentially lead to problems in process mining with respect to the aforementioned quality issues. Despite that, we observed high levels of presence of events in the eventlog: at least 85% for all obligatory events. The inherently diverse group of patients with sepsis poses a challenge to process analysis techniques. We have shown that for a relatively simple model, we can successfully apply process mining techniques, with the ultimate aim of measuring KPIs. This provides a good outlook in the possibilities to also analyze the sepsis pathway at a finer grain. It remains, however, topic of research what the optimal level of detail in the process modelling is for a given purpose. The heterogeneity of sepsis patients might become more prominent in more detailed analysis and require some form of clustering before performing process analyses on the subgroups. Patients can be clustered on patient or on process characteris-

tics (see, e.g., (de Medeiros et al., 2007)).

One particular issue that we faced when interpreting the EMR data was that we observed the need to interpret the purpose of actions performed from the event logs rather than purely the actions themselves. As an example, the administration of fluid in itself can happen for a multitude of reasons, however in order to interpret whether volume expansion was performed, we had to monitor whether a certain amount of fluid was prescribed in a certain amount of time. Similarly, for antibiotics we would like to know that they were prescribed and administered for the purpose of managing sepsis, however this intended purpose is not stored with the medication prescriptions. One way of obtaining more information on the purpose of certain actions performed is through careful analysis of clinical notes, where typically the intend of the medical staff is reflected. This will, however require the use of natural language processing (NLP) techniques to be able to extract structured information from these unstructured text data. Important to note in this respect is the lack of ground truth in such analysis of EMR data; the only evidence of what happened with the patient is the data in the EMR. Hence, the interpretation of raw EMR data should be given sufficient attention.

5 CONCLUSION AND FUTURE WORK

We have shown that we can successfully use process mining to follow selected events derived from the main KPIs for the sepsis pathway purely from EMR data. However, no conclusion should be drawn about the actual quality of care or adherence to these guidelines before verification with the clinical quality assurance process. It should be noted that it required a great effort in data preparation to create the event log and time-consuming manual quality checks to interpret the EMR data in terms of the concepts required for the pathway analysis. Using process mining techniques, we can analyze beyond the pure presence or absence of events and also address correct versus incorrect order with respect to a model that represents best practice. Applying these techniques on a dataset gathered at a large Brazilian hospital, we could analyze the data in terms adherence to the guidelines provided by the SSC. The reason for deviation in order of administering antibiotics and collecting blood cultures, however requires further research. In general, further follow up with the quality department would be required to quantify the accuracy of our assessment in comparison to the formal quality process that is in place in the hospital at hand. This actually highlights a big limitation of the data driven analysis of processes in general: it is impossible from event data alone to distinguish whether event logs are missing due to actions not being performed, performed actions not being logged or logged actions not being picked up by the data extraction and interpretation. For that reason, results should always be interpreted with care and at least a randomized sample should be analyzed through a formal quality assessment process in order to quantify the accuracy of the overall data-driven analysis results.

Although our analysis shows high levels of availability of time stamps (at least 85% per obligatory event type), there is room for improvement. The quality of the event log generated from the EMR data could be further improved by better support from the data entry module to allow for more accurate and timely data entry and the use of structured reporting over free-text notes. It should be noted, though, that this will remain difficult in busy environments such as the ER, where top priority is to provide acute care to the patient. It might require a change in the workflow to improve the precision of timestamps of time critical events such as lactate collection.

Our present analysis is limited to a relatively small and simple model to reflect sepsis care. Nevertheless, this model allows already for analysis in terms of various clinical KPIs. Future work includes the extension of the model used for conformance analysis in order to assess the clinical pathway in further detail. In our future aim of extending the model to cover more detailed steps in the sepsis care pathway, we expect that more elaborate data interpretation might be required. While many steps have already been taken to digitize hospital data in structured fields, rich information can also be found in non-structured text fields such as clinical notes. The analysis of such data will require NLP approaches to reliably retrieve structured information from text. Being able to analyze adherence to such a more detailed model would open up further analysis of conformance to and deviations from the best practice. The application of process discovery techniques can also provide a bottom-up view of the process as it is performed by the clinical practitioners. A root cause analysis into the reasons for deviation could help to further improve the guidelines and standard of care for sepsis.

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