Analyzing Sepsis Treatment Variations in Subpopulations with Process Mining

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Abstract: Healthcare processes frequently deviate from established treatment protocols due to unforeseen events and the complexities of illnesses. Many healthcare procedures do not account for variations in treatment paths across different diseases and patient subpopulations. Understanding the similarities and differences in treatment paths for different patient groups can provide valuable insights and potential process enhancements for various subgroups of concern. For hospitals, understanding various patient populations, such as severe or non-severe cases, is key for enhancing care paths. In this paper, we aim to compare treatment procedures for different subpopulations of patients using process mining techniques and identify indicators to improve the care path. We utilize the process mining for healthcare (PM^2HC) methodology to identify variations in treatment paths among different patient subgroups. We conducted a case study on sepsis, a complex illness with a wealth of available data, for in-depth analysis. Our findings indicate that various subpopulations exhibit different outcomes, offering promising directions for further research.

1 INTRODUCTION

Hospital Information Systems (HISs) contain a wealth of data on healthcare processes (Mans et al., 2013). These processes, while partially structured, frequently involve multiple stakeholders and exception handling, which can lead to ad hoc decision-making (Mans et al., 2015). The information stored in a HIS can reveal valuable insights into how healthcare processes are actually carried out in practice (Mans et al., 2013).

This research focuses on sepsis, a life-threatening condition typically resulting from infections, with a mortality rate ranging from 20% to 50% (Gyawali et al., 2019). The elderly are particularly vulnerable to this condition. The mean mortality rate of hospital-based sepsis is 35%. Approximately 10 out of 1000 patients are diagnosed with sepsis, and 30% of them develop Multiple Organ Dysfunction Syndromes (MODS) (Polat et al., 2017). In addition to the high mortality rate, sepsis has the second-highest readmission rate, with $18-26\%$ of patients returning to the hospital within 30 days (Mans et al., 2008).

Process mining techniques present methods for analyzing sepsis data and pinpointing the procedures involved in sepsis treatment. Despite prior research demonstrating the effectiveness of process mining in analyzing sepsis event logs (Hendricks, 2019), to our knowledge, there has been no exploration of the differences in treatment and care pathways for various subpopulations. While researchers have discovered how sepsis can impact a patient (Gyawali et al., 2019), the question of how to learn from best treatment practices remains to be addressed. As an initial step, we can investigate subpopulation comparisons, emphasizing specific subgroups to understand best practices better. Subpopulations based on attributes such as age (Martin et al., 2006), severity (Mans et al., 2008), and Systemic Inflammatory Response Syndrome (SIRS) criteria (Comstedt et al., 2009) have been demonstrated to be reliable predictors of sepsis.

The exploration of processes within electronic health record event data provides insights into patient flows. Ongoing research continues to explore these processes across various sub-populations (Marazza et al., 2020). This paper contributes to the aforementioned research direction by systematically identifying and comparing patient sub-populations. In this paper, we aim to analyze and contrast treatment procedures across diverse patient subpopulations using process mining techniques. Our goal is to identify key indicators that could significantly enhance patient care path trajectories. To achieve this goal, we first categorize subpopulations by identifying distinct

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treatment procedures based on attributes discovered through literature search and data exploration. We then apply process mining discovery techniques to these subpopulations and compare the resulting process models to examine the efficacy of care paths. Acknowledging the limitations of solely visual comparisons, we supplement our analysis with quantitative evaluations. We guide our process mining project using the PM^{2}HC methodology (Pereira et al., 2020) and select appropriate tools/plug-ins for comparing the process models. The results of this comparison can provide insights into best practices for each subpopulation, facilitating the design of more personalized and efficient treatments and thereby improving the overall quality of care for sepsis patients.

Our contributions are as follows: (1) we introduce an approach that incorporates a well-established PM^{2}HC methodology for conducting a process mining project, with the added step of subpopulation analysis; (2) as an evaluation, we perform a case study on sepsis using the proposed approach and a real-world dataset, providing valuable insights into optimal care paths.

The remainder of this paper is structured as follows. Section 2 discusses the background of this research. Section 3 presents the approach that is followed. Section 4 discusses the findings based on the case study. Section 5 provides a discussion. Finally, Section 6 concludes and discusses future work.

2 BACKGROUND AND RELATED WORK

Early diagnosis and optimal patient care are essential for the effective management of sepsis (Gyawali et al., 2019). Researchers have proposed a scoring system that uses biomarkers to assess the likelihood of developing sepsis (Samraj et al., 2013). This system can assist in early detection, pinpointing high-risk patients, and monitoring the disease's progression. One widely recognized biomarker is the SIRS criteria, which encompasses measurements such as temperature (below 36°C or above 38°C), heart rate (exceeding 90 beats per minute), respiratory rate (more than 20 breaths per minute), and white blood cell count (10^3/µL) either below 4 or above 12 (Comstedt et al., 2009).

Numerous academic studies have delved into the application of process mining in healthcare (Dallagassa et al., 2021; Munoz-Gama et al., 2022), also with a particular focus on contrasting processes among varied subpopulations. Research in process mining has been pivotal in evaluating care paths for sepsis, notably from bottleneck and performance viewpoints (Hendricks, 2019). One study (Partington et al., 2015) analyzed processes across four Australian hospitals, comparing service performance and efficiency. The authors devised a unified process model encompassing the paths of patients from all the participating hospitals. While this study provided valuable insights into healthcare processes, the visual representation of their comparative analysis was constrained. Further research is required to enhance these visualizations and to correlate observed processes with health outcomes (Partington et al., 2015). Another study (Mans et al., 2008) applied process mining techniques to analyze clinical data of stroke care across various hospitals and subpopulations. Similarly, another study (Marazza et al., 2020) contrasted cancer treatment processes across two hospitals employing process mining techniques.

However, on the whole, there has been a scant focus on contrasting these processes specifically within defined subpopulations. While factors like patient age, gender, and infection type can influence the prescribed care path (Quintano Neira et al., 2019), there is limited research on comparing subpopulations to identify the most effective care paths. In contrast, our study illustrates the delineation of sepsis patient subpopulations and the integration of subsequent analyses into a pre-existing process mining methodology. We employ a dataset with real-world case data and adapt the widely adopted PM2 methodology for process mining projects (van Eck et al., 2015) to discern and illustrate treatment variations across subpopulations.

3 APPROACH

The modified methodology is detailed below and visualized in Figure 1. Although our approach aligns with the PM^{2}HC methodology, which is specifically designed for the healthcare domain, we have made some modifications by introducing stakeholder roles and a subpopulation selection phase for simplification purposes.

3.1 Research Planning

In the first phase, a healthcare process is selected, and research goals are defined. During this phase, the scope and metrics to be used for comparing process models should also be determined. Additionally, one must select the tools and algorithms for process exploration and mining.

We selected the sepsis dataset (Mannhardt, 2016) for comparison using *BPMNDiffViz* and *ProM* (van

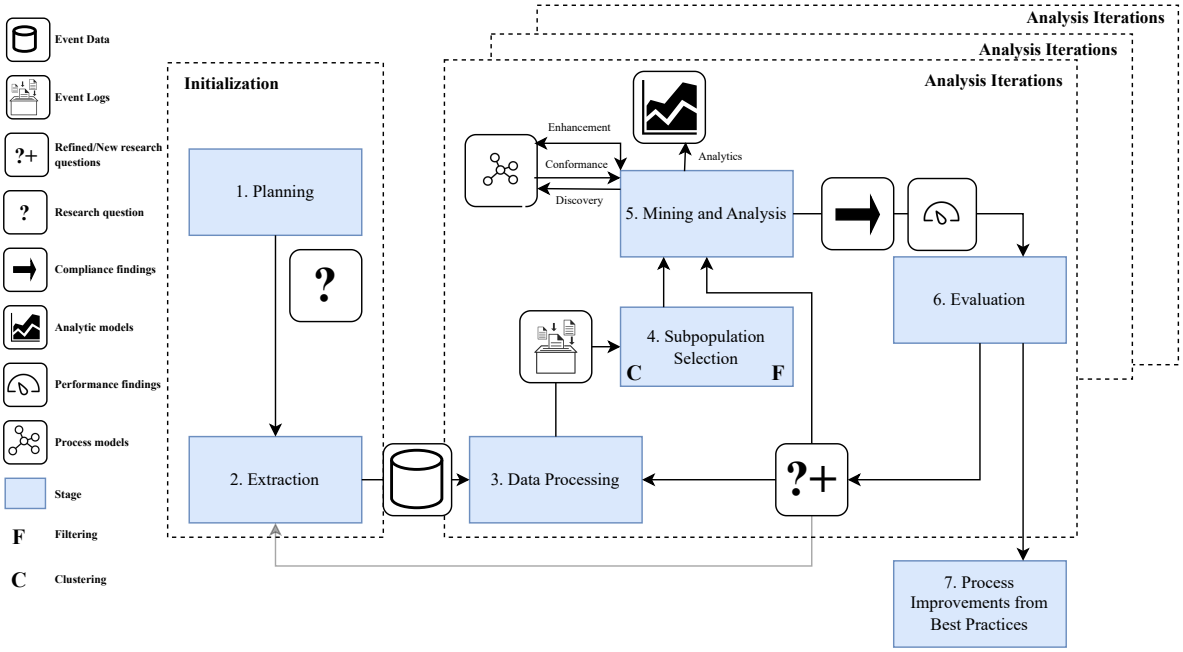

Figure 1: Visualization of the approach, based on the PM^{2}HC methodology (Pereira et al., 2020).

Dongen et al., 2005). Section 4.2 explains how we will use the graph edit distance (using the graph edit distance metric and conformance checking metrics).

3.2 Extraction

In the extraction phase, the study's boundaries are further determined. It involves selecting the relevant data and excluding irrelevant information. In this research, we extracted and retrieved event data related to sepsis cases from a hospital dataset (Mannhardt, 2016). The extracted data underwent cleaning and preparation. We performed data preparation steps as discussed by (Mannhardt and Blinde, 2017). We have limited the scope of the study to real-life data of patients who were admitted to the hospital's emergency room (Hendricks, 2019). Each case is represented by a trace, which records the patient's journey through the hospital. More information about the dataset can be found in Subsection 4.1.

3.3 Data Processing

This phase encompasses an iterative analysis process requiring iteration between the third, fourth, and fifth phases of our methodology. In this phase, the data is processed by creating visualizations of the processes (i.e., process discovery). The typical steps involved in this phase include aggregating events, filtering and enriching logs, and identifying performance indicators. These steps culminate in the outcomes of the third, fourth, and fifth phases.

The visualizations created in this phase provide more insight into the recorded events. We will use dotted charts and process model visualizations. To do this, we import the XES file containing the events logs into the ProM platform and then filter the file into subpopulations using the "Filter Event Log" and "Filter Log by Attributes" plugins.

3.4 Subpopulation Selection

The subpopulation identification phase is introduced as an additional step to the PM^{2}HC methodology for data processing. This step involves using the "LogVisualiser (LogDialog)" plugin to analyze the data and conduct literature research to identify relevant attributes (such as age, severity, process duration, etc.) that can be used to create subpopulations. As suggested by (Mamaliga, 2013), the data should be segmented into data cubes based on a combination of these attributes. A more detailed explanation of subpopulation selection and analysis can be found in Subsection 4.1.

3.5 Mining & Analysis

In the fifth phase, process-related data is mined and analyzed to gain insight into different treatment paths and care paths. The main objective of this phase is

to derive insights from the sepsis treatment processes. Performance analysis is conducted to gain insights, and the models created are evaluated through conformance analysis.

To further examine the process models, the "Inductive Visual Miner" plugin is employed. This tool helps to analyze the number of resources, such as individuals, following specific activities, identifying relative paths, and locating bottlenecks. Additionally, performance indicators are identified using the tool, which also enables performance and conformance analysis. Subsection 4.3 provides an explanation of the tool's implementation.

3.6 Evaluation

The primary objective of this phase is to gain insights into the processes involved in sepsis treatment. The numerical values obtained are translated into new learning perspectives and suggestions for improvement, ultimately leading to conclusive findings.

In our case study, we evaluated the results obtained from the comparisons made using *BPMNDiffViz* and observations gleaned from the "Inductive Visual Miner" plugin. We have supported our evaluation through scientific literature.

3.7 Improvement & Support

In the final phase, the findings are evaluated, future implementation plans are developed, and suggestions for improvements are made. The aim is to provide an optimal path for future learning guided by best practices. During this phase, all results are evaluated and interpreted. However, as this is the final phase of the research, it excludes the execution of the actual implementation plan. For future research, we are in the process of obtaining a sepsis dataset from hospitals in the Netherlands. Stakeholders can use the results obtained from this phase as a reference scenario for data preparation and extraction in subsequent studies.

4 FINDINGS

This section describes the findings and the results of execution the steps described in the previous section.

4.1 Division of Subpopulations

As mentioned previously, subpopulations are classified based on specific attributes and their relation to the diagnosis of sepsis, as well as the severity level that the attribute suggests. The dataset comprises 31 attributes, primarily consisting of blood values and diagnoses. The attributes used for categorizing the data into different subpopulations are *age*, and the number of SIRS criteria met (SIRS criteria ≥ 2, which indicates an increased likelihood to be diagnosed with sepsis (Comstedt et al., 2009)). The division of subpopulations was based on age, given its role as an important risk factor in predicting sepsis cases (Li et al., 2022). Besides the SIRS criteria, the dataset used did not capture other risk factors. Therefore, age and the SIRS criteria were considered the most important risk factors for dividing the subpopulations. The subpopulations are named and summarized in Table 1. The first column lists the subpopulations, while the first row explains the criteria that define each subpopulation. For instance, the subpopulation that includes patients aged 65 and below is now labelled as *Age A*, and the subpopulation with patients who meet less than two SIRS criteria is called *SIRS A*. The nomenclature for the remaining subpopulations follows the same pattern.

Please note that the duration of a treatment process is not given beforehand and needs to be calculated. This duration is classified into two categories: Duration A, which denotes a treatment process that takes less than or equal 7 days, and Duration B, which denotes a process that takes more than 7 days. The duration is determined by considering the time when an activity starts or ends, but there is no single unit of time for all activities, and therefore, the total duration cannot be assumed. However, the duration can be calculated by finding the difference between the starting and ending times of the treatment process.

The recorded patient data has an average age of 70.07. In order to create subpopulations of roughly equal size, the event log is divided at the ages of 65 and 85, resulting in three subpopulations. The first subpopulation, Age A, includes process traces of patients who are 65 years old or below. The second subpopulation, Age B, includes patients who are between 65 and 85 years old. The third subpopulation, Age C, includes patients who are 85 or older.

In the United States, over half of the patients in the Intensive Care Unit are over 65 years old, and many suffer from life-threatening sepsis (Starr and Saito, 2014). Therefore, the age of 65 is used as a threshold for the first and second subpopulations.

Since the SIRS criteria can only be true or false, the dataset is divided into two cubes. The first subpopulation, SIRS-A, includes patients who meet 0 or 1 SIRS criteria. The second subpopulation, SIRS-B, includes patients who meet 2 or more SIRS criteria.

Table 1: Division of subpopulations.

Label	Age (years)	SIRS criteria ≥ 2	Process duration (days)
Subpopulation A	≤ 65	False	≤ 7
Subpopulation B	$65 < age < 85$	True	> 7
Subpopulation C	≥ 85	n/a	n/a

4.2 Comparison Tools

We utilized the *BPMNDiffViz* tool to compare the process models. This tool offers structural matching by visualizing the differences between graphs and provides statistics to facilitate difference analysis (Dijkman et al., 2011). It computes the minimum graph edit distance between two processes based on the number of transformations required to change one process into another using the event labels of activity nodes (Ivanov et al., 2015). Among other algorithms, we chose the Tabu Search algorithm due to its precise results and faster performance (Skobtsov and Kalenkova, 2019).

We performed conformance checking by comparing the percentage of total traces that perform a specific activity within a subpopulation. This analysis revealed which subpopulation is most likely to follow a particular activity.

4.3 Comparison of Treatment Processes

The comparison was based on the attribute by which each subpopulation was segmented. We also conducted a detailed analysis of certain activities within the process models and compared them for conformance. All the models were created using *ProM* and the *BPMNDiffViz* tools and were saved on an online data repository [1]. Next, we will discuss the main findings of our analysis.

4.3.1 General Observations

In general, the process models consist of 12 to 16 activities, with most models containing either 14 or 16 activities. In all models, *ER Registration* and *ER Triage* occur at the beginning in parallel. The activities that describe the patient discharge (*Release Activities A, B, C, D, E*) are typically found at the end of the treatment event(s). Only the activity *Return-ER* occurs after a patient has been discharged in any form.

Of all patients, 63.8% go through *Release-A*, while *Release B*, *C*, *D*, and *E* combined are followed by only approximately 5.5% of all patients. This also

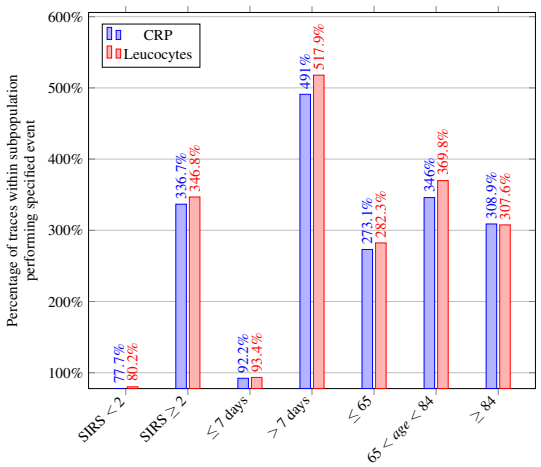

Figure 2: Conformance checking activity comparison for CRP and Leucocytes.

implies that the patients not covered by those statistics did not finish the process, for example, because they were still in the hospital. The activities *CRP* (i.e., c-reactive protein level checking a blood sample) and *Leucocytes* are the most frequently accessed activities in all processes, often occurring more than once in a single process.

To compare the process models of subpopulations, we calculate the Graph Edit Distance (GED). This metric indicates the transformations required to convert one process model into another. We have presented the results of these comparisons in Table 2. Furthermore, we have analyzed the number of traces following the events related to *leucocytes* and *CRP*. To analyze this, we use a metric called the number of traces, which is the total number of occurrences of an event by a subpopulation divided by the total number of patients in that subpopulation. As some events occur multiple times within one process, the resulting percentages may exceed 100%. We have visualized the values of all processes for *CRP* and *leucocytes* in Figure 2.

Compared to most diseases, patients with sepsis have higher mortality and readmission rates (Mans et al., 2008). Therefore, in this study, we focus on the discharge activity and the readmission of patients to the ER for different subpopulations. For illustration purposes, we analyze the process traces following Release-A and Return-ER using the metric, num-

[1] this url will be made available upon acceptance

Table 2: GEDs retrieved by comparing process models.

Attribute	Subpopulation 1	Subpopulation 2	Number of edits (transformations)
Age	≤ 65	$65 < age < 85$	72
Age	≤ 65	≥ 85	42
Age	$65 < age < 85$	≥ 85	60
SIRS criteria	≥ 2	< 2	58
Process duration	≤ 7 days	> 7 days	98

ber of traces, as described in the previous section. We also compare the number of traces following Release-A that eventually lead to readmission to the ER across different subpopulations. Figure 3 visualizes our results.

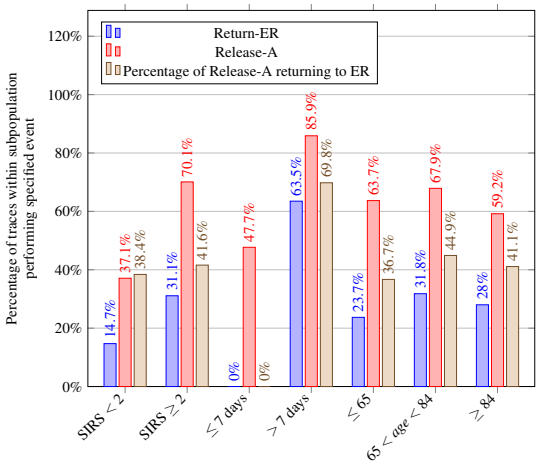

Figure 3: Conformance checking activity comparison for Release-A and Return-ER.

4.3.2 Age

The age attribute segments the data into three distinct subpopulations, each represented by its own model. Figure 4 includes the model comparing subpopulations Age A (≤ 65)and Age B ($65 < age < 85$), which resulted in a GED score of 72.

When comparing processes for individuals aged ≤ 65 to those aged between 65 and 85, a GED of 72 suggests a notable difference between the two processes. This suggests that the processes for these two age groups are considerably different. For individuals aged ≤ 65 compared to those aged ≥ 85, the GED is 42. This is somewhat counterintuitive, as one might expect a larger difference between the youngest and oldest age groups. However, the processes for these two age groups are more similar than the previous comparison. The processes for the age groups $65 < age < 85$ and ≥ 85 have a GED of 60, indicating a moderate difference between the two processes.

Figure 5 shows a segment of the process model for subpopulation Age A, where *Leucocytes* and *CRP* are the most commonly accessed activities. In Age A, the activity of *Leucocytes* has been performed in 282.30%, and CRP 273.1% of the time, as indicated in Figure 2. For Age B, CRP has been performed 346% of the time and Leucocytes 369.8% of the time. Finally, for Age C, CRP has been performed 308.9% of the time and Leucocytes 307.6% of the time.

When comparing the three models' patient discharge strategies, the most significant differences are observed between Age A and Age B. In Release-A, the highest number of traces following the events are associated with 'Age >65 and <85' for both Returns to the ER and Overall Return ER events. Age C follows closely for both ER events. Conversely, Age A has the lowest rate of return to the ER among the three age groups.

4.3.3 SIRS Criteria

The GED, resulting from the comparison of two models, (a) 'SIRS < 2' and (b) 'SIRS ≥ 2', is denoted as SIRS-A and SIRS-B, respectively. The processes for individuals with SIRS criteria ≥ 2 compared to those with < 2 have a GED of 58. This suggests a moderate difference between the processes for these two groups based on the SIRS criteria.

Upon examining the SIRS-A subpopulation, we observed that the mean number of included classes is 6, while for SIRS-B, it is 10. Thus, it can be concluded that the processes of patients for whom the SIRS criteria is higher than 2 include a larger number of different events overall.

In comparison to other subpopulations, the occurrences of CRP and Leucocytes in SIRS-A are lower, with events occurring in 78.2% and 80.7% of traces, respectively. However, for 'SIRS > 2', *CRP* events appear in 336.7% of traces, and *Leucocytes* events in 346.8%.

For patients in SIRS-B, 70.1% were discharged through *Release-A*, of which 41.6% returned to the ER. In the whole subpopulation, 31.1% returned to the ER. In both SIRS-A and SIRS-B subpopulations, all patients returning to the ER had been admitted to the NC earlier in their treatment.

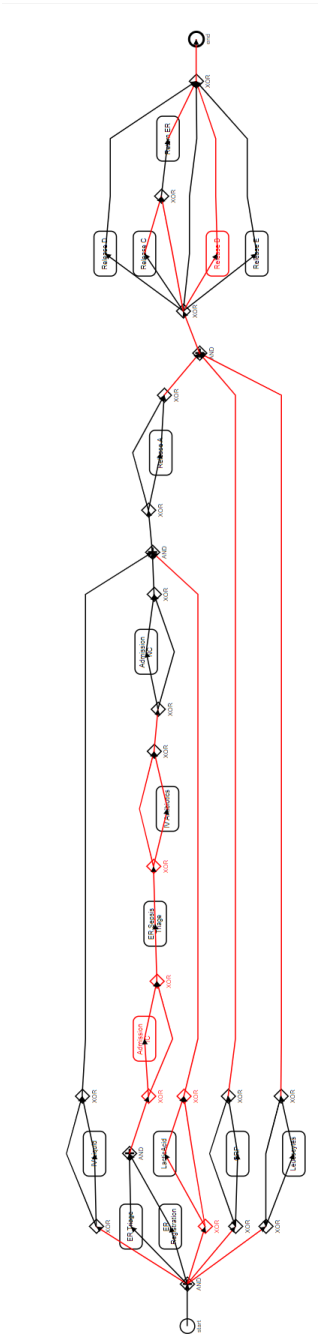

Figure 4: Comparison between process models of subpopulations A and B. Red lines highlight events that need removal to transform one model to the other, while black lines denote identical events. Further comparison models are available in an online data repository[1].

4.3.4 Process Duration

The comparison between processes with a duration of ≤ 7 days and those with a duration of > 7 days yields the highest GED of 98. This indicates a significant difference between the processes of these two groups. It suggests that the duration of the process has a substantial impact on the process model. However, it is worth noting that the maximum number of activities included in the two models differs. Treatments with a duration of less than or equal to a week include 12 different activities, while longer treatments include all 16 kinds of activities. ER returns are not included in shorter treatments, implying that no returns occur within the same week as a patient's hospital admission. Notably, the minimum time between admission and return is 7 days and 11 hours. On average, patients return after 91 days.

4.3.5 Concluding Remarks

The attribute with the most pronounced impact on process differences, as indicated by the GED, is 'Process duration'. Processes that last ≤ 7 days are considerably different from those lasting > 7 days. Age also plays a role in process differences, but the relationship is not linear. The processes for the youngest and oldest age groups are more similar than the processes for the youngest and middle age groups. The SIRS criteria also influence process differences but to a lesser extent than age and process duration.

In conclusion, this analysis provides insights into how different attributes influence process models. Such findings can be crucial for tailoring interventions or strategies specific to subpopulations based on these attributes.

5 DISCUSSION

While our preliminary research aimed to understand sepsis and its treatment, the involvement of medical experts would have enhanced the identification of treatment peculiarities. Collaboration with a hospital would have enabled a more detailed assessment of treatment processes, verification of our results, and ensured patient safety. Furthermore, we propose to enhance the discussion by incorporating interpretations provided by a medical professional. This has the potential to increase the depth of the findings and their applicability in real-world clinical contexts.

We used data from various sepsis treatment events within a hospital. However, the one-time assessment of attributes like age, blood rates, and diagnoses limited our ability to perform a detailed analysis of these differences during treatment. Anonymizing attributes in the dataset, such as patient gender, could have provided richer data and deeper insights, especially regarding processes leading to death due to the high

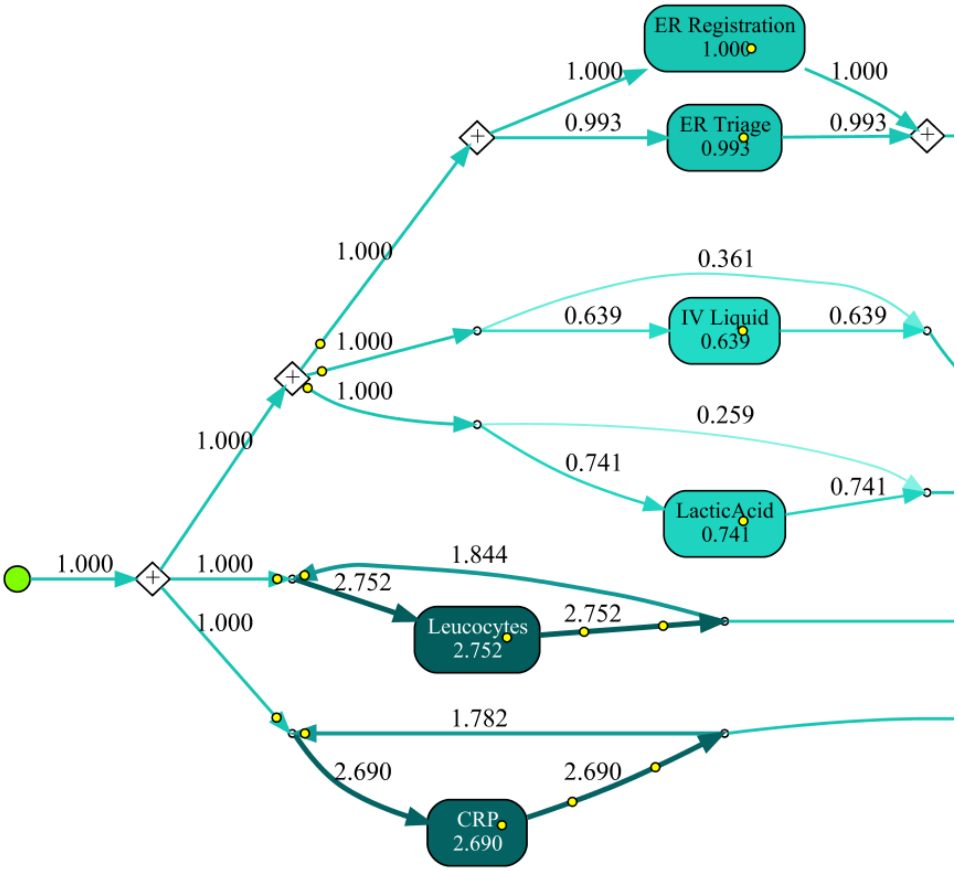

Figure 5: Process model abstraction of patients with age ≤ 65, using the Inductive Visual Miner (IvM) plugin. The complete process model and other models are available online[1].

mortality rate of sepsis. Furthermore, other features not included in the dataset (e.g., history or genetics) could also contribute to a more comprehensive result. In this study, we did not explore the generalizability of our findings or their applicability in other hospitals or for other sicknesses. Potential biases associated with the specific undisclosed hospital might have influenced the data. Nonetheless, our study highlights the feasibility of comparing process models within a hospital setting using GED and conformance metrics.

In our study, the metrics employed for comparison yield initial insights. Key to these insights is the utilization of the GED via *BPMNDiffViz*. The integration of *BPMNDiffViz* in GED computations facilitates visualization and discernment of the inherent structural variances between process models. This gains prominence in the context of subpopulation analyses, enabling a granular juxtaposition of process navigational patterns across varied groups. Additionally, the derivation of conformance metrics, anchored on the frequency of event execution by subpopulations, provides a lens to evaluate the alignment of these cohorts with established process models. While these metrics are useful, their role in comparing models across different subpopulations needs more research.

6 CONCLUSIONS AND FUTURE RESEARCH

In this study, we aimed to explore the challenge of contrasting subpopulations within healthcare treatment processes. Our focus was on sepsis, a condition characterized by a multitude of treatment procedures. We applied the PM^{2}HC methodology to a case study using real-world data.

Our investigation focused on the treatment trajectories of patients, taking into account factors such as age, severity, and SIRS criteria. Our findings revealed that distinct treatment processes were required for different age groups. Furthermore, we found that segmenting patients into two groups based on a duration threshold of seven days was beneficial for contrasting subpopulations. A notable correlation was iden-

tified between age group division and SIRS score, with the middle-aged subpopulation engaging in the most activities. The transformation from the process model for Age A to Age C required only 42 edits. In contrast, patients who met the SIRS-B criteria participated in approximately double the activities per patient compared to those in SIRS-A. In the subpopulation exceeding a seven-day duration, activities related to leukocytes, CRP, return-ER, and patient discharge were most prevalent. Our results suggest that treatment processes tailored to patient subpopulations based on age, severity, and SIRS criteria provide unique and promising insights.

Future studies should conduct an in-depth investigation of the performance of various subpopulations. This investigation could include both threshold and time-series analysis. Comparing outcomes across these subpopulations and benchmarking them against normative models of other healthcare providers could provide valuable insights. Furthermore, collaborative initiatives with hospitals to collect treatment data or explore challenges in the treatment process could enhance our understanding of the implications of this study. The conformance measures used in this study also warrant further scrutiny to validate their effectiveness. Lastly, we advocate for additional case studies on healthcare-related topics that employ comparative subpopulation analysis. The goal of these studies would be to generalize the implications of our findings to other hospitals and healthcare systems.

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