Intelligent Decision Support System for Precision Medicine: Time Series Multi-variable Approach for Data Processing

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Abstract: This study has introduced a new approach to clinical data processing. Clinical data is unstructured, heterogeneous, and comes from various resources. Although, the challenges associated with processing such data have been discussed widely in literature, addressing those aspects is fragmented and case-based. This paper presents the initial outcome of applying the Time series Multi-Variables model (TsMV) to 12 different datasets from Intensive Care Units (ICU), medications, and laboratories. TsMV supports the development of an Intelligent Decision Support System for PM (IDSS4PM) by preparing effective data. Moreover, the CRISP-DM methodology was employed, and based on the proposed solution, we have adjusted the significant steps to CRISP-DM, where those extra phases are essential for taking future works.

1 INTRODUCTION

While, growing the aging population, consumerism, increasing the availability of patient data and limited human-cognitive for timely decision-making, in addition to the economic pressure have challenged the old model of clinical decision-making, big data, and analytics have provided the opportunity for developing Precision Medicine (PM). Although there is various definition of PM, the US National Library of Medicine, referred it to as "an as emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person" (Hulsen et al., 2019),(Y. Zhang, Silvers, & Randolph, 2007). Hence, not only biological factors are taken into the consideration, but also environmental, lifestyle, and patient's condition and preferences are important for releasing the best possible treatment (Fenning, Smith, & Calderwood, 2019),(Williams et al., 2018).

The advantages of Artificial Intelligence (AI) and analytics to reduce medical errors and increase the performance of clinical decision-making are extensively highlighted in the literature (Jiang et al., 2017). While descriptive, diagnosis and predictive analytics discover insights from data, prescriptive analytics focuses on optimal decision-making (Mosavi & Santos, 2020). Even though such promising technologies are advanced to extract, and interpret meaningful information from raw data, there are major challenges and limitations associated with data acquisition and processing in the context of the adoption of PM. Based on that, current studies have not demonstrated practical and valid frameworks to address the limitations in processing diverse and complex data (McPadden et al., 2019). This paper aims to present TsMV approach for filling the identified gaps in clinical data processing which is essential for the development of IDSS4PM.

IDSS4PM is a framework from the concept of "Decision Support Systems", where AI and analytics pioneer the development of PM to propose an optimal outcome for clinical decision-making.

The Time series Multiple-Variables Approach for Precision Medicine (TsMVs4PM) is designed to address the challenges such as infrequent registration of data, dimensionality, variety, velocity, and integration aspects.

From a general point of view, the key limitations and restrictions that have challenged the adoption of PM are classified into three categories: "Definition of

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PM", "Data source/Data Management" and "Validity/Reliability of clinical practice". Although there are wide contributions to explaining PM, the terms have evolved and it requires time and practice to emerge with the best possible performance. Moreover, issues related to the variety and types of data that come from diverse resources resulted in limitations in data integration. Even though there are defined standards for data exchange, stakeholders and potential adopters need to cooperate to employ the available policies (Sadat Mosavi & Filipe Santos, 2021). In addition, dealing with data quality, privacy, dimensionality, integration, and interoperability have provided remarkable research opportunities under the category of "Data Management" (Liu, Luo, Jiang, & Zhao, 2019). Finally, the shift from the traditional protocol of clinical decision-making to the new one needs valid and reliable practices in the area of AI and Machine Learning (ML). This effort mostly depends on overcoming the limitations of data sources, handling big data, and data processing. However, policies and regulations of data privacy, cost of project development, multidisciplinary cooperation, and technology acceptance by the professionals must be considered to facilitate the fusion of PM (Sadat Mosavi & Filipe Santos, 2021).

The TsMV method supports the development of an analytical dashboard to monitor and analyze all the clinical transactions from the time of admission to discharge. This solution addresses infrequent data registration and provides an integrated/unique platform for the decision maker to analyze the clinical background. Where It facilitates future works (clustering prediction and optimization).

Furthermore, since the objective is to maximize the rationality of clinical decision-making via adopting analytics, we have employed Simon's model of decision-making as the theoretical foundation. Intelligence-Design-choice, introduced by Simon has been identified as the most common framework in decision making where the "Intelligence" phase is about identifying the problem, searching and collecting relevant information, and "Design" is associated with generating alternatives and developing possible courses of action. Furthermore, evaluating the consequences of each option and choosing the optimal performance are related in the "Choice" phase (Mosavi & Santos, 2021).

Simon in "Bounded Rationality" identified that the decision-maker chooses the first attention which is good enough without evaluating alternatives, but the optimum option cannot be the best decision as there is a difference between decision making and searching for the best (Barros, 2010),(Gigerenzer, 2001). Following the assumptions to decide rationally, the decision-maker should know all the alternatives as well as the consequence of each alternative. In addition, the decision-maker should be able to compute with perfect accuracy. Hence, optimization is one step closer to normative decision-making. In other words, optimization identifies the best course of action; maximizing the value between alternatives(Hertog, 2015),(Delen, 2020).

This paper has employed the CRISP-DM methodology, so it is organized based on the six phases of this methodology to present the initial result in the data processing phase. Therefore, the first three-phased are explained and the last three are planned as future work for developing the final framework of IDSS4PM.

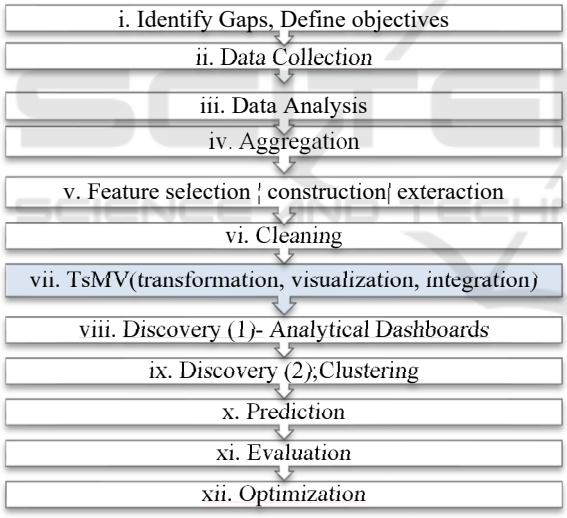
2 CRISPS_DM METHODOLOGY

CRoss-Industry Standard Process for Data Mining refers to the process of applying intelligent techniques to data to extract patterns and identify valid and useful information (S. Zhang, Zhang, & Yang, 2003). It is a multidisciplinary subject, leveraging various techniques such as ML, statistics, and data analytics (Leprince, Miller, & Zeiler, 2021). Whereas Fayyad considers DM as one of the phases in the Knowledge Discovery from Database (KDD) process for searching and discovering patterns(Fayyad & Uthurusamy, 1996), CRISP-DM guides people to know how DM can be applied in practice in real systems (Ipp, Azevedo, & Santos, 2004). This is a standard methodology used to support translating business problems or application requirements and objectives into data mining projects. Regardless of the type of industry, CRISP-DM helps the effectiveness of the outcome by extracting knowledge from the raw data (Pete et al., 2000). This methodology was introduced in the late 90s for Knowledge Discovery from Database (KDD) (Grady, 2016) and was developed by the means of the effort of a consortium initially composed of Daimler-Chrysler, SPSS, and NCR. The six phases of CRISP-DM 0.1 include "Business/Application Understanding", to identify problems or to define objectives. This phare requires domain knowledge and consists of various tasks and reports. "Data Understanding" includes activities such as data collection, exploration, and quality verification. The third phase, "Data Preparation", includes different activities to prepare data for modelling. Moreover, in "Modelling", the most promising and potential ML algorithms will be applied. In addition, "Evaluation",

uses techniques to assess the accuracy of the result, and finally, in "Deployment", the most suitable algorithm will be selected for practical use (Pete et al., 2000). This paper presents the result of the first three steps of developing IDSS4PM. This road map is adjustable to analytics where Simon's model of decision-making is taken into consideration.

According to table 1, the first step is "Business Understanding"; identifying scientific gaps and defining objectives. Moreover, data collection and analysis are associated with "Data Understanding". In addition, major activities are required to prepare effective data such as data aggregation, feature engineering, transformation, and cleaning. Furthermore, TsMV as an integrated approach is necessary for performing the discovery and prediction. Accordingly, prediction and evaluation are associated with "Modelling" and "Evaluation". Finally, we have justified "Optimization" as the part of "Modelling "and "Evaluation" phases for obtaining the sub-optimal result.

Table 1: Workplan According to CRISP-DM.



As table 2 presents, phases 1,2,3, and 4 which are informative, are adjustable with the "Intelligence" phase in Simon's framework. Moreover, phases 1,2, and 3 are based on "Descriptive" analytics. phase 4 is associated with "Design" since in "Modelling" and "Evaluation", various algorithms will be generated, and different scenarios will be analysed and assessed. Finally, based on objectives and the outcome of the evaluation, the most potentials and suitable performance (algorithm) will be selected Hence, this step is about decision making and performance selection and it is related to "choice and prescriptive analytics.

Table 2: Towards optimal clinical decision making.

Tasks	CRISP_DM	Simon's Framework	Analytics
i	Phase (1)	Intelligence	None
i, iii	Phase (2)	Intelligence	Descriptive
iv,v,vi, vii	Phase (3)	Intelligence	Descriptive
viii, ix	NEW	Intelligence	Descriptive
x, xi	Phase (4,5)	Design, Intelligence	Predictive
xii	Phase (4,5,6)	Choice	Prescriptive

2.1 Application| Business Understanding

2.1.1 Precision Medicine

PM as a new approach in medical decision-making has been motivated by major opportunities and challenges such as the failed business model of "one size fits all" (releasing similar treatments for patients with similar symptoms) (Barros, 2010) which resulted in less effective medical performance. In addition, the cost of overtreatment, less balance between patient expectations and the quality of services, the global aging population growth, and an increasing number of new chronic diseases, need a supply of advanced scientific and medical commitment and technologies (C. Kennedy & Turley, 201AD). Besides, the availability of healthcare big data and advanced technologies such as AI, cloud computing, the Internet of Things (IoT), and analytics provide actionable and useful information for decision-making (Wu et al., 2017). Thus, it is expected, that by 2050, because of healthcare digitization under the influence of technological advancement, using patients' biological data for clinical decision-making will pioneer the adoption of PM (Khadanga, Aggarwal, Joty, & Srivastava, 2019). This shift from the traditional approach to the new way of clinical decision-making will effectively change the quality of treatment, especially for PM where IoT facilitates customized data collection for individual patients by considering the influence of heterogeneous data (Brown, 2016).

2.1.2 Scientific Gaps in Data Processing Phase

"As ever, where new technology promises "Big Advances," significant challenges remain" (Hulsen et al., 2019).

As it was mentioned above, whereas aspects related to data processing such as "data source and management" are identified as the major limitations

for standardizing the fusion of the "one-size-fits-all" model, other problems are related to terminology itself, and existing clinical practices. Although there is, a definition of PM released by the U.S national library of medicine, since literature is heterogeneous in terms of using the terminology of PM, there has not been a standard paradigm used to develop a data-driven DSS to conduct the protocol of PM (Sadat Mosavi & Filipe Santos, 2021). For example, some research works have considered genetic profiles as necessary data for obtaining precise treatment pathways, and others have defined PM as a process that needs to be evolved and completed over time. Therefore, by considering the general purpose of emerging PM in healthcare which is accepted as a process to develop the treatment pathway with more accuracy and transparency based on patient profile, research works and study designs strongly depend on the particular research questions (Hulsen et al., 2019).

On the one hand, features (heterogeneous, diverted, and unstructured) carried by clinical data have resulted in poor synchronization, particularly in data acquisition and integration phases (Y. Zhang et al., 2007). On the other hand, the lack of an integrated platform for considering multi-variable data paradigm caused useful data and trend information not able to be incorporated into a single model for further decision-making (C. E. Kennedy & Turley, 2011). One considerable reason is the diverse frequency of data registration from various resources. In addition, the different time granularity of data collection can result in ambiguous data correlation(Y. Zhang et al., 2007). For example, data from bedside monitoring has generally high frequency while clinical sampling and lab tests might be taken irregularly. Therefore, aspects such as frequency and regulations of data generation strongly influence the performance of the data processing phase (Wu et al., 2017). In addition, verification of data quality is a critical step in data processing. Data quality considerably depends on major factors such as the assessment of a patient's condition by the clinical team, misinterpretation of the original document, and mistakes in data entry(Brown, 2016). Also, Medical Waveforms (MW) such as electrocardiograms and electroencephalograms, which are widely utilized in physiological examination, might caries random noise and gaps(Khadanga et al., 2019).Therefore, deal with missing values is another point needs to be addressed in data cleaning and preparation (Adiba, Sharwardy, & Rahman, 2021).Finally, the validity and reliability of existing clinical practices in this area need maturity, and new policies, regulations, and cooperation pipelines between stakeholders to speed up the emergence of PM. In other words, successful and valid projects in scale affect positively the quality of performance in general and indirectly best practices boost problem solving associated with technical areas such as data processing aspects (Blasimme, Fadda, Schneider, & Vayena, 2018).

One common situation in digitized healthcare platforms is where various physiological variables of patients are continuously monitored and stored resulting in huge amounts of data collected. Whereas the integration of data collected at the bedside is required to study associated with other data generated during the patient's involvement with treatment, and other clinical aspects, outliers, and abnormal data present bias, and related data must be ignored in modelling and many cases data has to be filtered from the study(Seyhan & Carini, 2019). Hence, despite the promising start of Big Data analysis, manipulation, and interpretation in clinical research, which has seen a rising number of peer-reviewed articles, very limited applications have been used to overcome those aspects. A close future effort should be done to validate the knowledge extracted from clinical Big Data and implement it in clinical practice(Carra, Salluh, da Silva Ramos, & Meyfroidt, 2020).

Major studies that contributed to offering a promising framework have focused on time series data and addressed limitations in data preparation. One example is the "attention scores" technique for feature importance in time series clinical data. This method is complex and applicable for nonlinear (Johnson, Parbhoo, Ross, & Doshi-Velez, 2021). Another research works used summaries of patient time series data for 24-72 hour from ICU to examine the early prediction of in-hospital mortality. In this study, static observations and physiological data including labs and vital signs extracted based on hourly circumstances. This approach limited the data to vital signs and lab results and considered data extraction and integration of time series clinical data in the context of data aggregation (Johnson et al., 2021). Another limitation related to data management, and processing is storage and computing. Especially for handling data that is created with high frequency such as physiological indicators. Although this data is valuable for analyses, storing and managing such records needs high computation and storage facilities. The "Electron" framework is a solution offered to store and analysed longitudinal physiologic monitoring data (McPadden et al., 2019). Furthermore, the TDA approach is an effective way for large-scale datasets and employs algebraic topology to analysed big data

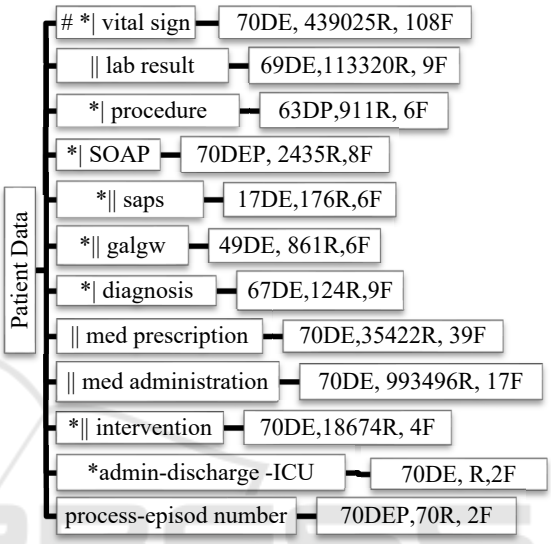
by reducing the dimension, particularly for geometric representations to extract patterns and obtain insight into them. In addition, to deal with data velocity, the "anytime algorithm "to learn from data streaming has been introduced as a useful approach for time series data which copies its growth over time. The effectiveness of this method depends on the amount of computation they were able to perform. Moreover, to deal with heterogeneous data (variety), although GNMTF is an efficient data integration framework, subject to the number of data types to be integrated the competencies complexity increased (Gligorijević, Malod-Dognin, & Pržulj, 2016). therefore, existing approaches have offered solutions to manage data such as time-series and case-based challenges such as feature importance, feature selection, dimensionally reduction, and velocity.

2.2 Data Understanding

According to table 2, there are 12 datasets collected as excel files. The "vital sign" includes 439025 records with 108 features and many of them came from biological sensors in ICU. Furthermore, "Lab Result" is a dataset that includes outcomes of laboratory exams. This table has113320 records with 9 features. "Procedure", with 911 records, and 6 features consisting of raw data associated with an action prescribed by the doctors. In addition, "SOAP" with 2435 records and 8 features, keeps key data about the SOAP framework (Subject, Object, Assessment, Plan). Gravity score or "saps" presents data about the level of gravity where it has 176 records and 6 features. Moreover, "Glasgow" carries 861 records and 6 features. The Glasgow table has data about the consciousness status of each patient. The "diagnosis" table with 124 records and 9 features is about signs, symptoms, and laboratory findings. While "prescription of medicine" addresses key information about medications prescribed by the clinician, "administration of medicine", with 993496 records and 17 features is associated with drug administration. The tenth table shows the intervention data of each patient. Finally, an "admin-discharge" dataset includes data on admission and discharge from ICU. In addition, there is a reference dataset that includes episode/process number exist in eleven datasets. Those two variables are key to linking datasets and are patient identifications.

The only dataset including time-series data is a "vital sign" marked by #. Moreover, tables such as "vital sign", "procedure", "SOAP" and "diagnosis" are arked by | including time or date of admission. Based on that, others specified by ||, have both time and date (admission). In addition, tables marked by * consist of data from ICU. R means the number of records and F means the number of features. Also, two features include distinct values whether "Process Number" (DP) or "Episode Number" (DE). The "procedures" and "SOAP" include DP (distinct process number) and other tables have DE (distinct episode number).

Table 3: Data Collection/Initial Analysis.



2.3 Data Preparation

According to the CRISP_DM methodology, "Data Preparation" consists of activities to prepare data for the modelling phase. Since analytical dashboards and clustering (discovery) require integrated clinical data, TsMV performs to solve the limitation in the data processing. Thus, In addition to the initial data manipulation, TsMV method was applied. In this case, we have modified the CRISP-DM methodology by adding TsMV approach in data preparation and an extra step before modelling which is discovery.

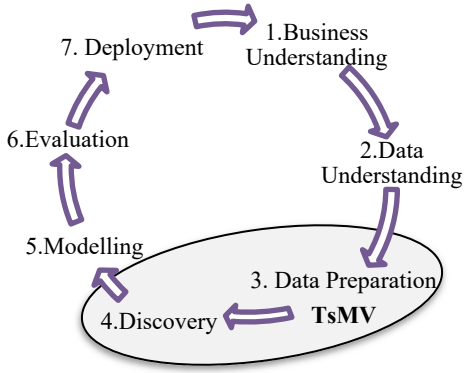


Figure 1: CRISP-DM - Adjusted for IDSS4PM.

2.3.1 Data Preparation- TsMV

As it was mentioned above, In addition to the initial data manipulation (feature engineering, data cleaning, data extraction, etc.,), specific data processing works were performed.

To solve the limitation associated with irregular data acquisition and synchronization, we aggregated physiological data (vital sign dataset) based on hourly circumstances. This solution addressed the diverse frequency of time series data registered by different sensors. In addition, because data generation from ICU (monitoring) has a high frequency compared with other data resources (medications, procedures, SAP, Glasgow, and intervention), therefore, to deal with fragmented and infrequent data generation, we performed a specific data transformation. where data has been transformed from the time/date dimension into a sequence dimension we called "Time Slot" (TS). According to the figure2, each patient has a Time Slot TS1 to TSn where the TS1 to TS23 includes one day of clinical transactions. In other words, each (TS+1)-TS= 1 hour Therefore, each patient with different episode numbers has TS from 1 to n where TS1 to TS23 shows transactions on the first day of admission and TS24 to TS71 is associated with the second day.

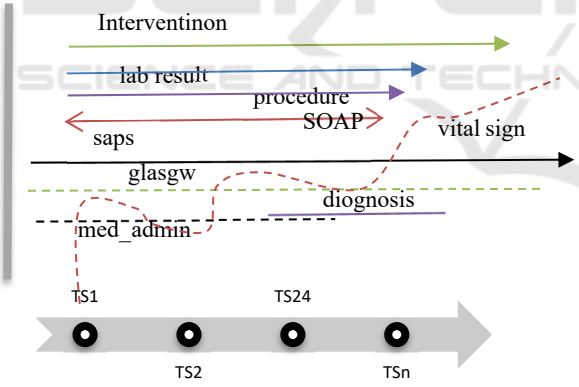


Figure 2: Timeline platform using TsMV model.

Data preparation is summarised in table 3 including transformation to TS, aggregation, feature engineering, selection, and data cleaning.

Transformation to TS: Each data set includes the time/date of admission. Hence, in the transformation from time/date to TS, each episode number has TS (1 to n).

Feature Engineering | selection and Extractions: all tables had admission time in the format of seconds and data was extracted in the form of the hour to support TsMV solution.

The "vital sign" data set consists of time series data from ICU, considering data quality analysis, and based on studying the domain|literature, significant physiological features were selected for hourly aggregation. Hence, out of 108 features, specific biological indicators (pulse rate, temperature, oxygen, saturation, and heart rate) were chosen. In addition, a new conditional column was constructed where oxygen saturation value resulted in four categories: "actual danger to life", "critical-refer to a specialist", "decrease-insufficient", and "serve hypoxia hospitalization". This new feature will support clustering performance and the same type of constructed feature will be applied to other biological indicators too.

Lab result dataset includes features such as exam classification, detailed exam, and references associated with the value of the exam. This feature was split into min and max references to support the clustering phase. Moreover, result_status was created as a conditional column where it compares the result of the exam with the min-reference and max_refence, to show if the result is below the minimum or more than the maximum values. This new feature will be used in the clustering phase.

The "procedures" table includes "zona" (specific area of the patient body) and "DNOME" (in the category of ZONA). Furthermore, the "SOAP" table includes the subject, assessment, and plan.

The "saps", has a feature (valor) to show the value of the patient's gravity. Furthermore, in "Glasgow", The status of the patient's consciousness level is presented in a feature called valor.

In the "diagnosis" dataset, out of 124 features, 4 are selected where "SERVICE" shows the type of diagnosis, and "DIAG1" addresses the description of diagnosis for each episode number.

In addition, "medical administration" consists of features such as the dose of a drug used by the nurse, recommended dose, and the code of the drug.

Of the "medical prescription" with 14, out of 39 features, 10 effective ones were selected. Where the code of medication, prescriptions, dose, and unit of medicine are the essential ones. we have constructed a new feature: "Period of Stay" to analyse the period that a patient starts medication and finishes. This new feature will be used in clustering.

Finally, the "intervention" like other datasets has time|date of admission and episode number. Moreover, intervention service shows the type of service.

In terms of handling missing cells, in some tables such as "vital sign," we filled null cells with the average of previous and next values and in some other

datasets, we deleted null cells and marked some other null cells to decide on the modelling phase. In "lab result" we constructed three columns to mark null cells with zero where this method will be used in the modeling phase. In addition, in "SOAP" we deleted variables with the majority of missing values and marked missing cells associated with main features.

As it was discussed, all datasets include episid|process number, so this feature is used to link each table to the look-up table (the table consisting of the episode and process number was considered as the look-up).

Besides, features such as age, gender, and status (pre-operation, post-operation) are excluded to a new table called demographics.

Table 4: Summary of data preparation.

Dataset	Time/Date to TS	Aggregation	Feature Engineering| Selection	Missing Cells
Vital sign	Time	hourly	X	Filled
Lab result	Time	-	X	Marked
procedures	Date	-	X	Deleted
SOAP	Date	-	X	Marked
saps	both	-	X	Deleted
Glasgow	both	-	X	Deleted
Diagnosis	Time	-	X	Deleted
Med_admin	both	-	X	Deleted
Med_pres	both	-	X	Deleted
intervention	both	-	X	Deleted

3 CONCLUSIONS

This paper presents the initial result of TsMV approach to address the limitations and challenges identified in the clinical data processing phase.

12 datasets have been used under the guidance of CRISP_DM methodology to develop the framework of IDSS4PM.

The current study considered the literature gaps in integrating time series data from ICU and other clinical data resources which are multi variables. They proposed a solution by transforming time-dependent data to TS (independent of time). This solution not only provided a unique time sequence platform for analysing the whole clinical background from admission to discharge but also can solve challenges highlighted in literature such as infrequence data registration. In addition, having sync data in a unique platform will facilitate the clustering phase to classify similar patients by various indicators (medications, period of stay, laboratory results, vital signs, and SOAP). In addition, the modelling phase will be performed based on the outcome of the preparation phase. Based on that, the first three stages of CRISP-DM are discussed, and this methodology was modified by adding extra steps (TsMV, discovery).

Future work will be developed using the outcome of the fusion of TsMV for discovery phases (analytical dashboards and clustering) and predicting the best treatment pathway. Where optimization will present the sub-optimal outcome by considering the clinical objectives. Hence, "Discovery", "Modelling", "Evaluation" and "Optimization" will be performed as further steps to introduce an IDSS4PM.

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