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Toward Optimization of Medical Therapies with a Little Help from Knowledge Management

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Abstract

This chapter emphasizes the importance of identifying and managing knowledge from Informally Structured Domains, especially in the medical field, where very short and repeated serial measurements are often present. This information is made up of attributes of both patients and their treatments that influence their state of health and usually includes measurements of various parameters taken at different times during the duration of treatment and usually after the application of the therapeutic resource. The chapter communicates the use of the KDSM methodology through a case study and the importance of paying attention to the characteristics of the domain to perform appropriate knowledge management in the domain.

Keywords: knowledge management, knowledge discovery, informal structure domains, serial measurement, KDSM

1. Introduction

For decades, efforts have been made to endow computers with knowledge, i.e. valuable information, to support them in solving problems or needs in different domains that directly or indirectly affect humans. *Domain knowledge* has proven to be an essential component for human expertise, so intelligent software tools are only as good as they are programmed to be. Certainly, there are significant advances that allow *machine learning* tools to model, define rules, instances, and knowledge from the information they receive. These tools improve accuracy, adapting to domain-specific characteristics and sometimes extending their capabilities set out in their original programming. The results obtained with these tools have been promising, and applications are emerging every day in a wide variety of domains with certain types of intelligence. However, the challenge for the development of such intelligent solutions goes beyond the understanding and application of these intelligent technologies. The main challenge lies in understanding the domain and the ability to gain domain knowledge, which can be used as *a priori knowledge* for the training of many tools of *machine learning*. Therefore, *domain knowledge* is key to establishing the requirements for the development of these nowadays apps. This is most relevant when the construction of an intelligent solution is linked to an *Informal Structured Domains* (ISD) [1].

An ISD has the following characteristics:

1. The presence of one or more domain specialists who influence the domain from their particular backgrounds, perspectives, interests, and expectations,

bringing large amounts of wealth knowledge. Most of this knowledge is tacit, informal, and implicit; hence, only partial domain knowledge is formal, and therefore easily available. Moreover, this knowledge is often non-homogeneous, with varying degrees of specificity, and is also incomplete. In essence, knowledge in ISD depends on the domain specialists' experience in the domain.

2. Presences of one or more knowledge requirements engineers, responsible for the tasks of obtaining domain knowledge and translating to requirements, who generally are not involved in the domain. They usually have general technical knowledge about developing solutions.
3. A tangible or intangible solution developed on the knowledge that explains a behavior or solves or addresses a particular and unrepeatable situation. Such knowledge can be represented as a set of knowledge pieces or even as knowledge requirements.

In the medical domain literature, it is common to find different ways of doing knowledge management, as in ref. [2], and these different ways are due to the fact that often the characteristics of a medical ISD require particular treatment. Due to these characteristics, extracting truly useful information or knowledge from an ISD is a complex task and remains a relevant challenge, and requires the use of unconventional methodologies for their knowledge management. In particular, the characteristics of the medical domain case study presented in this chapter fit an ISD, where there is not enough *real a priori knowledge* to train powerful machine learning tools, and also contains in a particular way, unlike other medical ISDs, very short and repeated serial measurements with blocking factor. Some machine learning tools trained with very little *real a priori knowledge* or even using synthetic information could be employed and although the results could become congruent they cannot be valid for the medical domain due to intrinsic liability, so they could only be illustrative. On the other hand, by employing statistical tools, it is possible to obtain valid results. However, the knowledge that is lost can completely change the outcome of using a given medical therapy.

Of most of the current state-of-the-art architectures, only a few explore the frequency domain to extract useful information, identify time series patterns, and improve results. Many methods are based on a classification using deep learning models from Fourier analysis [3], a predictive method such as the autoregression model [4], or hidden Markov models [5]. However, these approaches, which are mainly based on a mathematical expression of the models, often do not provide an intuitive explanation of the results and are often difficult for humans or even machines to interpret. Even as they are based on general time series models that make use of many observations, they cannot deal with cases where there are few observations per series. In fact, when the number of observations per series is minimal, it is not possible to obtain convenient estimates from these models.

At the same time, some artificial intelligence approaches need a large amount of *real a priori knowledge* about the structure of the series or about the time patterns to be discovered [6, 7]. Unfortunately, this knowledge is often not available in real cases. From this point of view, a challenge that will always be interesting is to achieve the best possible characterization of the domain in which one is working. It is important to keep in mind that not all ISD will have a machine learning solution that is currently in fashion. If the real objective is to perform optimal knowledge management, sometimes it will be necessary to design a particular way to do it, as they say, *a tailor-made suit*.

The Knowledge Discovery Serial Measurements (KDSM) [8] is a hybrid methodology that uses machine learning and statistical techniques for the knowledge management and the benefit of using KDSM, in this particular study case where efficient handling of repeated measurements is desired as well as reliable knowledge management, is because it is the only methodology that is adapted to these particular characteristics to extract useful information, and that can be represented as *crisp rules*. KDSM also makes it possible to describe some behaviors to improve a medical therapy or treatment. In addition, the fact of being open allows it to adapt to the specific characteristics of the domain to be treated by assimilating tools to do so. However, it does not mean that it is the only way because each ISD challenges the knowledge manager to offer the optimal solution, and it is here when it can be said that it is an art to be able to do it. As it can be observed, knowledge management of a medical ISD with these characteristics is a complex task and remains a major challenge. Therefore, it is pertinent to communicate achievements and results of hybrid methodologies, AI, and Statistics, that treat medical ISD such as the one performed with the KDSM methodology. The results presented in this chapter illustrate why it is important to be open to this type of methodologies, as they have changed the paradigm of how to perform knowledge management for certain medical ISD; in addition, they motivate to continue working in this line of research.

The structure of the chapter is as follows: first, Section 2 summarizes the scope of the informally structured domains in which the KDSM methodology has been successfully used; its effects are also mentioned. Section 3 presents a formal description of the circumstances under which KDSM, using a combination of statistics and machine learning, can act as an optimal approach to obtain good knowledge results from patterns over repeated measurements in a very short time series with a blocking factor. In Section 4, a typical situation from an ISD in the medical field is shown, this section also briefly describes the knowledge management process, through KDSM, of the electroconvulsive therapy (ECT) domain: data characteristics used in the analysis, medical domain data is discussed through the KDSM phases, and results and conclusions derived from them. Section 5 reports the results of using the KDSM methodology in the situation described in the previous section. Finally, in Section 6 conclusions on the results and some interesting points for future work are mentioned.

2. Convenient knowledge management using KDSM

Today, every advanced medical institution is embedded in the digital era where the exponential growth of information and its management by data science methods is a complex process ranging from descriptive statistics to pattern recognition through machine learning and visualization techniques to support the interpretation of data to extract useful information from it. For acceptable knowledge management, it must be corroborated that the domain is really understood, and consequently, be able to establish how to work with the data, including data cleansing. This is essential as there is certainly useful hidden information that can be distinguished as patterns or converted to rules or to the most convenient representation for the manager to analyze the results obtained. In medicine, knowledge management must bridge the gap between data analysis and medical decision support to make medical work more efficient and effective. In addition, there are several medical domains whose characteristics make them complex because there is no structure with data and knowledge organized in a way that supports adequate knowledge management. For these reasons, making decisions about what is and what is not good knowledge in these domains is always a very difficult problem.

Such domains are included in what is referred to in [1] as Informal Structure Domains (ISD). The situation to be presented in Section 4 fits the definition of an ISD. Moreover, it presents some additional particularities that will determine its further analysis, such as the inclusion of short and serially repeated measurements over time, heterogeneous data describing objects that can be quantitative or qualitative where the second ones usually have a significant number of modalities, and declarative knowledge is available concerning relationships between attributes, classification targets. Therefore, finding a consistent way to manage these very short measures of observations, to extract useful information from them, and to be able to find profiles of this type of data linked to the rest of the patients' characteristics and those of their treatment is complex for both statistics and machine learning, especially if no *a priori knowledge* is available.

Very short, repeated serial measurements are very few records made of the same attribute at a given time [9, 10]. Such records have the following characteristics:

- the same attribute is measured on the same observed entity more than once; thus, the responses are not independent as they are in a standard regression analysis; and
- is more than one observed entity; thus, the responses do not form a classical time series.

Very short, repeated, serial measures are very often found in the domain of medicine (e.g. successive periods of illness and recovery under different treatment regimens). In many instances, medical research protocols, in humans, aim to measure the evolution of a disease or the performance of the treatment of a condition. This is done by collecting a set of serial measures of an attribute (e.g. symptoms), or some of them, over a period of treatment. The result of this process is a database containing one or more serial measures (one for each attribute of interest) for each patient included in the study. Thus, as mentioned above, several serial measures are available for a given attribute, and it is not correct to consider them all together. One of the most common ways to analyze serial measures of a continuous variable in a set of patients is to follow the proposal of Schober and Vetter [11]: (a) simplify sets of serial measures of records of the attribute in the observed entity to a single serial measure using some mathematical function (mean, area under the curve ...) and then (b) analyze the simplification using standard univariate methods. In addition, sometimes the structure of the records that make up the serial measures includes a blocking factor or the number of these measures is too small to use classical time series analysis.

Although the study reviewed in this chapter is from the psychiatric domain, the use of the KDSM approach is very feasible for any ISD in which a set of individuals is presented, and there are a variable number of occurrences of an event for each individual, all at different instances of time, and the measurement of an attribute to study its evolution—relative to the current individual—in a later time frame just after the occurrence of the event is of utmost importance. The attribute is measured a small fixed number of times, the same for all cases, and thus results in repeated and very short serial measurements (see **Figure 1**) for which each individual is a blocking factor. Basically, there are many medical circumstances for which it is necessary to record serial measurements of body functions, after repeated stimuli, of patients participating in a specific study to follow the effects of their therapy and their reaction to it. For example, changes in lung function are measured after repeated applications of a bronchodilator, serial tissue perfusion, or gut function measurements. Moreover, it should be noted that such situations are not exclusive

Figure 1.
Y measurements for all i after each occurrence of E.

to medical environments; in fact, repeated serial measurements of very short duration are often encountered, for example, in economic situations where many economic indicators have to be measured periodically especially after an unexpected event. Or even volcanology, when in an attempt to better understand volcanoes and improve disaster prevention programs, volcanoes are subjected to a special indicator monitoring system during critical periods when events such as seismic movements or emissions of gases and other substances or both are recorded.

3. Formal description of the ISD circumstances in which KDSM operates

This section formally describes the additional circumstances in an ISD that makes KDSM, a suitable tool for knowledge management.

3.1 Formalizing the situation in the ISD

The additional circumstances present in an ISD in which its knowledge management could be performed by KDSM can be formalized as follows:

Given:

- $I = \{i_1 \dots i_n\}$ a set of individuals,
- $X_1 \dots X_K$ a set of attributes (quantitative or qualitative) characterizing the set I ,
- $X = [x_{ik}]_{n \times K}$ a matrix, $i = \{1 \dots n\}$, $k = \{1 \dots K\}$, x_{ik} is the value of an attribute X_K for the individual i .

- $E = \{E_{ij}\}$ a set of events, where $i = \{1 \dots n\}$, $j = \{1 \dots n_i\}$, and $N = \sum_1^i n_i$, occur in the individuals of the set I being $\{E_{ij}\}$ the j th occurrence of E to the i th individual.
- $Z_1 \dots Z_K$ a set of attributes (quantitative or qualitative) characterizing the set E ,
- $Z = [z_{(ij)l}]_{NL}$ a matrix, $i = \{1 \dots n\}$, $j = \{1 \dots n_i\}$, $N = \sum_1^i n_i$, $l = \{1 \dots L\}$, $z_{(ij)l}$ is the value of the attribute Z_l for an event E_{ij} .
- $\{Y^t\}$ a group of attributes of interest that make up the serialized measures, where $i = \{1 \dots n\}$, $j = \{0 \dots n_i\}$, and $t = \{1 \dots r\}$,
- $Y = [Y_{ij}^t]_{N'r}$ the matrix containing all the serialized measures, $i = \{1 \dots n\}$, $j = \{0 \dots n_i\}$, $t = \{1 \dots r\}$, and $N' = \sum_1^i n_i + n$ and taking into account that
- individuals $I = i_1 \dots i_n$ act as a blocking factor in the records of matrices Y and Z ,
- $\{Y_{i0}^t\}$ are the baseline serial measurements of the individuals recorded before E_{i1} and with no values for any of the attributes in Z .
- the measurement recording moments $t = \{1 \dots r\}$ represent a fixed distribution overtime for all the serial measurements,
- number of records per series r is minuscule, and
- for each i there is a variable number of serial measurements n_i ,

In this particular ISD with serial measures Y , the KDSM methodology will be able to carry out knowledge management that provides:

- a pattern for the behavior of the serial measures $\{Y^t\}$ and
- the relationship between the serial measures $\{Y^t\}$, matrix X , and matrix Z .

In short, the KDSM is a hybrid methodology that uses machine learning and statistical techniques for the knowledge management of an ISD where the above circumstances are present.

3.2 Data structure

A generic description of the specific circumstances of ISD is shown in **Figure 1** by representing a series of individuals ($i_1 \dots i_n$) in which n_i occurrences of a given event E take place at different times ($E_{i1} \dots E_{in_i}$), $\{i_1 \dots i_n\}$. Connected to each event, there is an attribute (or set of attributes) of interest Y that affects the individual's behavior. When performing knowledge management through KDSM, the aim is to know the behavior of Y during a very short period of time $[t_1, t_r]$ immediately after each occurrence of E .

Therefore, a minimum number of serial measurements (r) of Y is fixed for each individual and each occurrence of E . In this particular case, the times at which Y will be recorded are fixed and will always be counted for all times E is presented.

In this sense, in the actual implementation of the Section 4, it is stated:

$I = \{i_1 \dots i_n\}$ is a set of patients $\{p_1 \dots p_n\}$,

E is the application of an electroshock ES to a given patient at a given time point. Thus, every patient has a ES sequence; then the electroconvulsive therapy $ECT_i = \{ES_{i1} \dots ES_{in_i}\}$.

Y are the attributes whose behavior is of interest to observe and which in this example corresponds to the reaction time RT of the patient to a given light stimulus presented at some point after each ES . Serial measurements of this attribute are recorded during the first 24 hours after each ES application, in particular after $t_1 = 2h$, $t_2 = 4h$, $t_3 = 6h$, $t_4 = 8h$, $t_5 = 12h$, and $t_6 = 24h$; ($r = 6$) then $Y = \{Y^2, Y^4, Y^6, Y^{12}, Y^{24}\}$.

Figure 2 is a graphical representation of the record of the reaction time RT observed in the 24 hours following the application of each electroshock to a set of patients. The rows Y^t_{i0} of the matrix Y are the RT curves for each patient before initiating ECT .

The X matrix contains quantitative or qualitative information regarding the patients (e.g. age, gender ...) and the Z matrix contains quantitative or qualitative information regarding each ES applied to each patient (e.g. energy level, impedance ...).

The data for this scenario is structured as follows:

- For each i a set of quantitative or qualitative characteristics $X_1 \dots X_K$ is available. This can be represented by a matrix-like as shown in **Table 1**.
 On matrix X , x_{ik} , where $i = \{1 \dots n\}$ and $k = \{1 \dots K\}$, is the value taken by X_K for an individual n .
 For example, if X_1 corresponds to the patients' age, then x_{11} must be the first patient's age and so on.
- Each time E occurs, measurements of Y are recorded at each fixed point in time. Let $E_{ij} \ i = \{1 \dots n\}$ and $j = \{1 \dots n_i\}$ be the j th occurrence of event E in the

Figure 2.
 Electroshocks applied to some patients.

		X_1	X_2	...	X_K
X=	i_1	x_{11}	x_{12}	...	x_{1K}
	i_2	x_{21}	x_{22}	...	x_{2K}
	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
	i_n	x_{n1}	x_{n2}	...	x_{nK}

Table 1.
Matrix X.

		t_1	t_2	...	t_r
Y=	E_{10}	Y_{10}^1	Y_{10}^2	...	Y_{10}^r
	E_{11}	Y_{12}^1	Y_{12}^2	...	Y_{12}^r
	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
	E_{1n_1}	$Y_{1n_1}^1$	$Y_{1n_1}^2$	...	$Y_{1n_1}^r$
	E_{20}	Y_{20}^1	Y_{20}^2	...	Y_{20}^r
	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
	E_{nn_i}	$Y_{nn_i}^1$	$Y_{nn_i}^2$	...	$Y_{nn_i}^r$

Table 2.
Matrix Y.

individual¹ i . Therefore, for a given individual i , there are n_i the number of occurrences of E . Considering that time resets to 0 at each occurrence of E , it is possible to set $t_1 \dots t_r$ as the moments in time at which Y will be recorded after each E occurs.

For example, if E_{11} corresponds to the first electroshock applied to the first patient, then Y_{11}^1 must be a record of the reaction time (attribute of interest) measured 2 h after applying the electroshock (instant t_1). By analogy, Y_{21}^3 must be the third record of the reaction time measured 6 h (instant t_3) after the first electroshock is applied ($j = 1$) to the second patient ($i = 2$).

The Y records form a second data matrix with the structure shown in **Table 2**.

3. Also for each E_{ij} , there are quantitative and/or qualitative characteristics, which are not serial measurements, $Z = Z_1 \dots Z_L$ that form a data matrix with the structure shown in **Table 3**.

In the matrix Z , $z_{(ij)l}$, where $i = \{1 \dots n\}$, $j = \{1 \dots n_i\}$ and $l = \{1 \dots L\}$, is the value Z_L has for the specific event E_{ij} . There are no $z_{(i0)l}$ values since $j = 0$ relates to the baseline measurements in Y , and are recorded before the first occurrence of the event.

For example, if Z_1 is the energy level of the electroshocks, then $z_{(23)1}$ is the energy level of the third electroshock applied to the second patient (E_{23}).

The attributes of interest are contained in Y , which contains serial measurements of the target attribute Y after each occurrence of E in each individual i . Thus, the cells of matrix Y are Y_{ij}^t , where $i = \{1 \dots n\}$ is the individual, $j = \{0 \dots n_i\}$

¹ Remember that $j = 0$ records the baseline serial measurements.

		Z_1	Z_2	...	Z_L
$Z=$	E_{11}	$z_{(11)1}$	$z_{(11)2}$	...	$z_{(11)l}$
	E_{12}	$z_{(12)1}$	$z_{(12)2}$	...	$z_{(12)l}$
	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
	E_{1n_1}	$z_{(1n_1)1}$	$z_{(1n_1)2}$	...	$z_{(1n_1)l}$
	E_{21}	$z_{(21)1}$	$z_{(21)2}$	...	$z_{(21)l}$
	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
	E_{nn_i}	$z_{(nn_i)1}$	$z_{(nn_i)2}$	...	$z_{(nn_i)l}$

Table 3.
 Matrix Z.

indicates the j th occurrence of E on the individual i and $t \in \{1 \dots r\}$ (where r is small) indexes the time recorded in Y after the occurrence of E_{ij} . It should be noted that *those moments of time for the measurement are all equal* in terms of the time of occurrence of all events for all individuals.

3.3 Characteristics of this particular ISD

In this subsection, the unique features of this ISD and possible approaches to calculate Y^t and the relationships between Y and X, Z are highlighted. Consequently, the convenience of using the KDSM is argued.

3.3.1 Incompatibility of X and Y

The purpose of using KDSM was to find:

- the pattern followed by the serial measurements $\{Y^1_{ij} \dots Y^r_{ij}\}$, and
- which characteristics of individuals ($X_1 \dots X_K$) and events ($Z_1 \dots Z_L$) are related to the time evolution of the records of the attribute of interest Y .

However, to relate Y s to X s and Z s, it is necessary to consider the following features:

- the characteristics relating to the individual are represented by a single row of the matrix X and for each individual
- there are n_i sequences of the records of the interest attribute Y freely placed along the timeline and are represented by n_i rows of matrix Y (as well as Z), which are not independent of each other.

Therefore, KDSM adequately handles the Y matrix regarding the X and Z matrices to analyze them in a global sense. The following paragraphs argue why not try other options for handling the relationships between these matrices.

3.3.2 Role of i as a blocking factor

All events E_{ij} occurring in the same individual ($j = 1 \dots n_i$) are affected by his/her individual characteristics (matrix X), which means that all serial measures related

to him/her including the baseline $\{Y_{ij}^1 \dots Y_{ij}^r\}, j = \{0 \dots n_i\}$ also receive this common influence.

Therefore, in the Y and Z matrices, the individual i can be considered as a *blocking factor*²; in the case of matrix Y , the individual i defines blocks of records that are *non-independent* of each other (see **Table 4**); in the matrix Z , the set I defines bundles of quantitative and/or qualitative non-serial attributes of each E (see **Table 5**), also non-independent.

Thus in the matrix Y , a block is constituted by all the records $\{Y_{ij}^1 \dots Y_{ij}^r\}, j = \{0 \dots n_i\}$ made after any occurrence of E in the same individual i (see **Table 4**). As mentioned before, these records establish a very small set of measurements over a

	t_1	t_2	...	t_R	
E_{10}	Y_{10}^1	Y_{10}^2	...	Y_{10}^r	
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	Block 1
E_{1n_1}	$Y_{1n_1}^1$	$Y_{1n_1}^2$	...	$Y_{1n_1}^r$	
E_{20}	Y_{20}^1	Y_{20}^2	...	Y_{20}^r	
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	Block 2
E_{2n_2}	$Y_{2n_2}^1$	$Y_{2n_2}^2$	...	$Y_{2n_2}^r$	
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	
E_{n0}	Y_{n0}^1	Y_{n0}^2	...	Y_{n0}^r	
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	Block n
E_{nn_i}	$Y_{nn_i}^1$	$Y_{nn_i}^2$	...	$Y_{nn_i}^r$	

Table 4.
Individual acting as a blocking factor for matrix Y .

	Z_1	Z_2	...	Z_L	
E_{11}	$\mathcal{Z}_{(11)1}$	$\mathcal{Z}_{(11)2}$	...	$\mathcal{Z}_{(11)l}$	
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	Block 1
E_{1n_1}	$\mathcal{Z}_{(1n_1)1}$	$\mathcal{Z}_{(1n_1)2}$	...	$\mathcal{Z}_{(1n_1)l}$	
E_{21}	$\mathcal{Z}_{(21)1}$	$\mathcal{Z}_{(21)2}$	...	$\mathcal{Z}_{(21)l}$	
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	Block 2
E_{2n_2}	$\mathcal{Z}_{(2n_2)1}$	$\mathcal{Z}_{(2n_2)2}$	...	$\mathcal{Z}_{(2n_2)l}$	
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	
E_{n1}	$\mathcal{Z}_{(n1)1}$	$\mathcal{Z}_{(n1)2}$	...	$\mathcal{Z}_{(n1)l}$	
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	Block n
E_{nn_i}	$\mathcal{Z}_{(nn_i)1}$	$\mathcal{Z}_{(nn_i)2}$	...	$\mathcal{Z}_{(nn_i)l}$	

Table 5.
Blocks of non-serial attributes of each E .

² A blocking factor is a qualitative attribute with an effect on the response attribute even of no direct interest, but which must be taken into account in the experiment to obtain homogeneous comparisons between observations where the factor remains constant [12].

given time period. However, the number of records is the same after each event, and these are equally distributed over time, considering the occurrence of the event as the starting point. In particular, a set of *very short and repeated serial measurements with a blocking factor* is going to be analyzed.

In fact, these situations are also present in several domains but are more frequent in medical domains. In the context of serial measurements, a widely used method is to reduce each block of these series to a single series that simplifies the whole set for each individual, either using the *statistica mean* operation at each time point (*thick line in Figure 3(a)*), or by reducing each series to a small set of independent indicators as a *mean area* or a *mean trend* per series [11, 13].

For the Z matrix, in a similar form one would replace the rows $z_{(ij)}j = \{1 \dots n_i\}$ with $z_{il} = \frac{\sum_j z_{(ij)l}}{n_i}$ or some other suitable summary statistic. This would allow the rows of Y and Z to be reduced to a single row for each individual, and the X , Y and Z matrices would be made compatible, allowing classical analysis using multivariate data analysis or modeling techniques.

However, on several occasions, if the average series for each individual is built—*average* understood in the broad sense mentioned before—is used, very often *too much* relevant information will often be lost, since the variability depends both on each event and on each *individual effect*. It can therefore be inferred that by employing such transformations, the conclusions reached in such a study may be far removed from reality.

Once a pair (i, j) is determined, which is given by the j th occurrence of E on the i th individual, the measures of Y in the time period $t_1 \dots t_r$ (the rows of the matrix Y) can be graphically represented by *very short curves* (r is usually small) apparently independent of each other (see **Table 4**). Regarding the real target application, it is easy to illustrate this phenomenon with a relevant case of the above comments represented by the following figures:

Figure 3(a) shows lines joining the reaction times on a simple visual test (S5) measured at 2, 4, 6, 12, and 24 hours after each ES applied to the 1st patient, and the black line represents the average of these curves (average RT curve for 1st the patient). This patient receives an ECT of 6 electroshocks, and each curve represents his/her reaction-time evolution.

Figure 3(b) shows the 4th patient's ECT evolution for the reaction times of the simple visual test (S5), and the black line also represents the average of all the curves (average RT curve for 4th the patient). The patient receives an ECT of 5 electroshocks.

As can be seen in these figures, constructing a single prototype curve from the mean of the reaction times (*thick curve*) and having it represent the evolution of the patient is not convenient regarding proper knowledge management, as the variability due to ES is too high and too much relevant information is lost.

Figure 3.
Curves of test S5 from: (a) 1st patient; (b) 4th patient.

Furthermore, differences in patient reaction between different ES will be lost if only the prototype curve is considered for each patient. Nevertheless, this average is useful as it can give an idea of the general trend of the patient. In fact, there is a significant change in the curves from one patient to another and from one test to another. Therefore, it is difficult to establish a general pattern for the curves of a particular patient. Consequently, reducing the patient information to a single record in the Y and Z matrices is not the right way to proceed. Accordingly, it is in the interest of keeping all records for all patients in the same database, but paying attention to this patient effect for the analysis.

3.3.3 No underlying pattern on occurrences of E_{ij} given i

Each individual is independent of the others. As a result, the number of events and the instant at which they occur may differ from individual to individual without any underlying pattern.

There is no agreement among psychiatrists about the quantity of ES that must be applied to a given patient.

If a common pattern of occurrences E overtime, **Figure 4**, had been present in this domain for all individuals, then it would have been feasible to consider and analyze a single series per individual using, for example, an *intervention policy* [14] characteristic of statistical time series models, therefore, as our particular domain does not conform to this prior assumption it is not appropriate to use a classical temporal analysis.

For example, the Electroconvulsive Therapy (ECT) applied to a patient consists of a variable number of sessions depending on the patient's condition, and their distribution over time is decided according to medical criteria for each particular case (between 6 and 12 ES per therapy). The frequency of ES may not be constant throughout the therapy (it is usual to increase the time between sessions as the patient improves. Normally be 2 or 3 ES per week).

Therefore, it is necessary to keep the series n_i distinguishable for each individual.

Figure 4.
Common pattern of occurrences E over time.

3.3.4 Too small series

Derived from the above, the n_i series non-independent per individual must be treated separately, and no summary series will be constructed. Since the number of observations in each series is too small, and estimation of the time series model becomes impossible, as the number of parameters is larger than the number of observations. Therefore, a classical time series analysis is not the right approach for this problem. Consequently, KDSM formally works every Y_{ij}^t $t = \{1 \dots r\}$ given E_{ij} and r is too small.

3.4 The significance of treating ISD in a particular way

The above reasons explain why the handling of repeated very short and repeated serial measurements with a blocking factor does not allow to correctly analyze this type of situation with traditional methods:

- Using summaries of serial measurements implies a loss of relevant and unwanted information.
- The individual acts as a blocking factor on the measures and they cannot be treated together as an independent.
- Serial numbers, as well as time of occurrence, vary for any individual.
- Series is too short to be modeled by a formal pattern.

Definitely, to deal with the circumstances in subsection 3.1, and perform knowledge management by dealing with this type of databases and obtain:

- a pattern for the behavior of the serial measures $\{Y^t\}$, and
- the relationship between the serial measures $\{Y^t\}$, matrix X , and matrix Z , is indeed significant, and to make it so, the *Knowledge Discovery in very short repeated Serial Measurements (KDSM)* methodology was used.

4. Study for the optimization of the ECT

In this section, characteristics of the electroconvulsive therapy (ECT) domain are reported to identify why it is appropriate the usage of the KDSM methodology to manage the knowledge in this particular domain and to subsequently use it in the optimization of the ECT, with special emphasis on the reaction time parameter and others strongly related to it.

4.1 Background

An interesting field of psychiatric study concerns therapies for various severe and treatment-resistant psychiatric disorders, such as major depression or schizophrenia. ECT is used worldwide as a safe, effective, rapid, valuable, and widely used treatment for patients with major depression, bipolar disorder, psychosis. ECT is a biological treatment procedure that involves the brief application of an electrical stimulus to produce a generalized seizure appropriate to the therapeutic response

and improve the psychiatric condition, which, for example, in the case of intractable catatonia and neuroleptic malignant syndrome, ECT could be life-saving. For patients who do not tolerate or respond poorly to medications and who are at high risk of drug-induced toxicity or toxic drug–drug interactions, ECT is the safest treatment option [15, 16]. Even in certain conditions associated with neuropsychiatric disorders, such as parkinsonism, dementia, and stroke, ECT is effective. Currently, the aim is to optimize the use of ECT and, in correlation with other biological and psychological treatments, to reduce the impact of side effects, prevent relapses and the recurrence of symptoms. Although several of the brain biological events related to its efficacy are still unknown, the physiological response to ECT has been studied through heart rate, blood pressure, electrocardiogram effects, cardiac enzymes, electroencephalogram effects, or hormonal response among others. However, for the time being, there is no formalized technique applied to this therapy and one interesting avenue is the study of the neuropsychological effects of ECT on psychophysiological parameters such as reaction, decision, or motor times. These effects are cognitive changes related to orientation, attention and calculation, memory loss and recall [17], and the aim is to make progress in identifying the factors that cause them, a direct influence in the cognitive state of the patient, by analyzing the effect on reaction times related to visual and audible stimuli after ECT application.

Some studies in similar situations in psychiatry, neurology, or various areas of medicine have reviewed everything from simple comparisons of treatments to longer-term effects or pre-post responses to several treatments or medications. Increasingly, there is a need to detect more subtle or domain-specific effects that add complicating factors. In these situations, simplifying serial measures to summary statistics can facilitate analysis by removing the time element. This approach of using summary statistics does facilitate clear communication of the main results, both in simple terms for the public and with full reporting of individual responses to the scientific community. However, the graphical presentation of serial measures in a line graph does not allow for easy plotting of individual or paired responses. Measures of central tendency can illustrate group effects in graphs and figures, but individual responses to each experimental condition are presented and lost from view, especially when sample sizes are minimal and do not facilitate the critical evaluation of the data [18].

4.2 Data description

For this case study, information was available for 183 patients with very severe depressive disorder or schizophrenia, according to both ICD-10 and DSM-5 criteria, for whom ECT was indicated and who gave informed consent to undergo ECT and participate in the study. Information is available on patients' main characteristics, conditions, somatic status, routine hematological and biochemical tests, chest X-ray, electrocardiograms, history of alcohol or other drug abuse or dependence, anesthetic risk, comorbidities, age, weight, education ... It is worth mentioning that the dataset belongs to the Health Research Unit <https://www.uis.com.mx/index.php> which is a private organization. Therefore, the characteristics and attributes of the dataset are detailed only in small extracts in order not to make inappropriate use of the support provided by the aforementioned organization.

Standard practice optimizes the therapeutic relationship, in the selection of electrical stimulus parameters such as energy level, stimulus duration, pulse width, and pulse rate. In addition, multiple patient responses are monitored by electroencephalogram, electrocardiogram, and electromyogram, including a rigorous assessment of the patient's neuropsychological effects. For the measurement of

psychophysiological parameters, the Vienna Test System (VTS) was used at 2, 4, 6, 12, and 24 h after each electroshock (ES) application. The VTS provides various stimuli and records the ability to react to them, recording reaction time (RT) for single-choice and compound-choice stimuli. Different modes of light and sound stimuli are available, with a choice of red, yellow, or white, so that different combinations of stimuli can be created simultaneously or sequentially for reaction time measurement. The VTS offers 8 test forms:

- S1: Simple reaction, yellow—reaction to critical stimulus.
- S2: Simple reaction, tone—reaction to critical stimulus.
- S3: Choice reaction, yellow/tone—reaction to critical stimulus combination.
- S4: Choice reaction, yellow/red—reaction to critical stimulus combination.
- S5: Choice reaction, yellow/tone, yellow/red—reaction to critical stimulus combination.
- S6: Simple reaction, white under monotonous conditions.
- S7: Measurement of alertness—simple reaction, yellow (with acoustic cue).
- S8: Measurement of alertness—simple reaction, tone (with optical cue).

The use of a rest key and a reaction key makes it possible to distinguish between reaction time and motor time. The main areas of use are those in which reaction times are measured, such as traffic psychology, personnel psychology (safety assessments), sports psychology, and psychopharmacology. In recent years, the use of reaction time measurements has also increased in neurology, psychiatry, rehabilitation, and occupational medicine. The way to interact with the VTS is for study participants to react, as quickly as possible, to visual or acoustic stimuli. The reaction is recorded after pressing or releasing a button when presented with a stimulus, which can be a yellow or red light, an audible tone, or a combination of these stimuli. The following measures were recorded for this particular study: erroneous decisions, erroneous reactions, absence of reactions, incorrect reactions, correct reactions, decision times, driving times, and reaction times [15, 19] and, these measurements were made for four specific tests: simple visual (e5: S1), simple auditory (e6: S2), complex visual (e7: S4), and complex visual–auditory (e8: S5).

4.3 Description of the situation presented in the ECT ISD

In this domain of ECT, a representation of a set of patients as $(i_1 \dots i_n)$ in which a n_i occurrences of a given ES take place at different times $(E_1 \dots E_n)$. Connected to the occurrence of each electroshock, there are psychophysiological parameters denoted by Y (for this particular case the reaction time, RT) that reflect the performance behavior of the patient. Therefore, a few Y measurements are taken for each patient and each ES occurrence. For this particular case, r is a very small fixed number of times, moments in time, that Y will be measured each time just after an ES is applied. The measurement record is made during the first 24 h after application, in particular at 2 h, 4 h, 6 h, 8 h, 12 h, and 24 h after an ES. The recording and monitoring of RT are of particular interest for the study of side effects resulting from ECT. Such a scenario generates three types of information that can be organized in 3 matrices:

- Matrix X contains a set of quantitative or qualitative characteristics $X_1 \dots X_K$ of each patient.
- Matrix Y contains sets of very short serial measurements of a parameter of interest, in this case RT , at all the fixed time points for each ES occurrence.
- Matrix Z contains a set of quantitative or qualitative characteristics $Z_1 \dots Z_L$ of each ES.

The number of *ES* and the timing of their application may differ from patient to patient without any underlying pattern. However, all applications of *ES* to the same patient are influenced by patient characteristics, which means that all *RT* measurements on the same patient are influenced by patient characteristics. Therefore, in matrices *Y* and *Z*, each patient acts as a blocking factor, establishing, in the matrix *Y*, bundles of records of measurements of the attribute of interest, very short and repeated serial measurements, which follow the application of each *ES* on the same patient and which are not independent of each other. Consequently, the characteristics of matrices *X* (patient characteristics $X_1 \dots X_K$), *Y* (serial measurements of the parameter of interest *RT*), and *Z* (ECT characteristics $Z_1 \dots Z_L$) differ and the knowledge that interrelates them is non-trivial and complies with the previous description of the ISD (section §3).

Furthermore, it is very easy to appreciate the inconvenience of simplifying *RT* measurements to a single serial measurement for each patient, as shown in **Figures 5 and 6**, the mean *RT* curve (black line), since potentially relevant information is lost, as the variability depends on both *ES* and patient characteristics and the efficacy of ECT may be affected. This action would modify the structure of the matrices to allow for a classical analysis, although such an action is not recommended.

Moreover, the loss of potentially relevant information is easily observed, as the variability is linked to both *ES* and patient characteristics and, consequently, the efficacy of ECT is affected. Even the variability is significant between curves, making it difficult to find a general pattern. However, for representing knowledge and communicating it, it is possible to do so using the mean curve and visualize a very general trend of the evolution of the patient’s response to ECT. And as there is no fixed number of *ES* applications applied to a patient, the effect it exerts must be considered. Considering the above, and due to the lack of *a priori knowledge* for the training of machine learning tools, knowledge management must be performed by KDSM.

4.4 Knowledge management by KDSM

KDSM is a methodology for Knowledge Management and Knowledge Discovery in Informally Structured Domains where very short and repeated serial measurements with a blocking factor are presented (see **Figure 7**). Following good knowledge management practice, KDSM is developed in three phases:

Figure 5. VIC graphic of RT curves of the e8 test of the 1st patient. It shows the evolution of the RT through its curves for a 6 ES ECT applied to the 1st patient. The RT correspond to the complex visual-audible (e8) and was measured at 2, 4, 6, 12, and 24 hours after applying each ES.

Figure 6.
VIC graphic of RT curves of the e8 test of the 4th patient. It shows the evolution of the RT through its curves for an ECT of 5 ES applied to the 4th patient. The RT correspond to the complex visual-audible (e8) and was measured at 2, 4, 6, 12, and 24 hours after applying each ES.

Figure 7.
Three phases of KDSM methodology for knowledge discovery in informally structured domains where very short and repeated serial measurements with a blocking factor are presented.

1. **Individuals Baselines Analysis (BLA):** Initially, baselines and their relationship with the X matrix are studied to identify different initial profiles of individuals to be used as *a priori knowledge*.
2. **Event Effects Analysis (EEA):** The knowledge induced from the previous phase is used as input to study the effect of a given event E on the attribute of interest Y . Subsequently, different patterns on Y related to the individuals that are affected by E are identified.
3. **Knowledge Production (KP):** Finally, the results obtained in the previous phase are crossed with the X and Z matrices to find relationships between them, and to determine which individual and relevant event attributes constitute the patterns found.

In short, the methodology will carry out the next tasks:

BLA: Individuals Baselines Analysis

- The baseline matrix is extracted from the matrix containing the record of all serial measurements.
- Hierarchical clustering of patients using baseline matrix.
- Use of patient characteristics to interpret the classes obtained.
- Induction of rules from the comparison between classes and patient characteristics. The rules obtained form a KB.

EEA: Event Effects Analysis

- Management of the blocking factor to eliminate its effect on the serial measures and to be able to review the effect of the ES application through the RT attribute.
- Rule-based clustering of the serial measures, now without the blocking factor, using the KB knowledge base obtained previously.

KP: Knowledge Production

- Interpretation of resulting classes.

4.4.1 BLA phase

Baseline serial measurement records were analyzed for the simple visual (e5) and auditory (e6), visual and categorization (e7), visual and auditory, and categorization (e8) tests. To classify these patient reaction times, the hierarchical clustering technique was used, as these represent the baseline condition of the patients (using the hierarchical reciprocal neighbors method with Ward’s aggregation criterion and Euclidean distance). Subsequently, those patient characteristics that are relevant to the partition chosen by the domain specialist are determined in order to proceed to derive rules. The classification technique suggested partitions into 2, 3, 4, and 5 classes that group different patients according to their baseline reaction times. According to the domain specialist’s experience, he/she chose a cut-off into three classes (C1, C2, and C3, see **Table 6**).

The characteristics of each class were then analyzed with the information obtained from the classification. **Figure 8** shows the general trend of the baseline RT records for each class, i.e. it shows the initial conditions of the patients with respect to RT. It is possible to observe a consistent response of reaction times in

Class ^a	Record ^b
Class 1	22 patients: 063059, 499,969,..., 997,938.
Class 2	68 patients: 437289, 522,175,..., 997,877.
Class 3	85 patients: 505652, 782,035,..., 999,464.

^aPatient class label.

^bPatient record number.

Table 6.
The table shows a partial view of the arrangement of patient records in the three-cluster partition corresponding to the hierarchical cluster. The clustering technique indicates the varying baseline conditions of the patients.

Figure 8.
BLA phase, VAC plot showing the variability between classes regarding the basal TRs.

classes C1 (blue), C2 (orange), and C3 (gray) having essentially the same level for all tests. In all tests, both simple e5, e6, complex e7, and e8, the reaction times of classes C2 and C3 show a noticeable increase compared to class C1.

As previously noted, patient-specific information is available in the *X* matrix (102 attributes), and this information is used to find those attributes that identify patterns that clearly characterize the selected partition. Quantitative and qualitative attributes that are statistically significant for the partition are distinguished from patient characteristics using the non-parametric H-test and the χ^2 -test, both ($p < 0.05$). In addition, multiple boxes and bar charts were used to visualize the distribution of the data and how these attributes of the *X* matrix interpret the chosen 3-class partition.

The information obtained from the tests and graphs was reviewed by the domain specialist to determine which attributes he/she was interested in observing, including some that were not statistically significant. Subsequently, after attribute selection and personal interpretation by the domain specialist, rules (expert knowledge) are derived from the graphs. These are crisp rules, representing all the attributes selected by the specialist, e.g. height, weight, number of cigarettes per day ... They also constitute the initial and partial knowledge base (*KB*) of this domain.

Figure 9 shows the distribution of the age attribute in the 3-class partition. It can be seen that the BLA C1 class includes all baseline records of the youngest patients (up to 29 years) and the BLA C2 and BLA C3 classes include baseline records of patients older than 29 years. The attribute age was the first of the 40 statistically significant attributes to be selected based on the specialist's extensive experience and the fact that this attribute is one of the attributes that exerts a strong influence on psychophysiological testing [20] consistent with clinical evidence. Therefore, three classes of patients are described: younger patients (BLA C1) with smaller and regular baseline RT for all tests (e5-e8) and younger (BLA C2) and mature (BLA C3) patients with longer baseline RT, in particular with much longer times in the

Figure 9. The distribution of the attribute age in each class and partition stands out for its clear delimitation and symmetry. This attribute is relevant because it clearly differentiates the reaction times of younger patients from those who are older. Here it can be seen that the younger patients are in BLA class 1, with a smaller baseline RT than both BLA class 2 and the mature patients in BLA class 3.

complex tests (e7 and e8) than in the simple ones (e5 and e6). The next step is to integrate the 103 rules from the KB knowledge base, obtained from the selected significant attributes (**Table 7**). The specialist determined it appropriate to include this knowledge for the EEA phase, with separate processes for *younger*, *young*, and *mature patients*.

4.4.2 EEA phase

To study the effect of each ES on reaction time and due to both the fact that the data in the matrix Y are ill-conditioned for classical statistical hypothesis testing, and the existing blocking factor in this matrix, this factor was treated. The treatment to remove the blocking factor consisted of transforming the Y matrix into a new matrix, but without the blocking factor. The transformation was carried out by performing the differences between *post-ES* and *pre-ES*. Then, on the transformed matrix, the rule-based hierarchical clustering technique (RBHC) [8] is applied.

Attribute ^a	Rules ^b
Age	If age > = 21 and < 30 then it is part of C1
	If age > = 60 and < 83 then it is part of C2
	If age > = 30 and < 60 then it is part of C3
Penthmed	If penthmed > = 200 and < 245 then it is part of C1
	If penthmed > = 118 and < 130 then it is part of C2
	If penthmed > = 130 and < 200 then it is part of C3
Sucme	If sucme > = 50 and < 67.7 then it is part of C1
⋮	
Hamtre17	If hamtre17 = 6 or > 10 and < 17 or > 17 then it is part of C3

^aPatient-specific attributes.
^bExtracted rules relating to the attribute.

Table 7. This table shows an abstract of crisp rules contained in the KB. Specifically, the rules for the age attribute.

Thus, the RBHC based on the rules contained in the *KB* suggests six classes of effect curves for each *ES* applied to the reaction times. The differences, in three of these classes, from *pre-ES* to *post-ES* are notable to slightly positive. In addition, they show a slightly more uniform pattern, where one class corresponds to younger patients, another to younger patients, and the last to mature patients. This means that reaction times are slower after *ES* application and would therefore be considered poor reactions. The remaining three classes present a more variable pattern corresponding to patients with faster reaction times after *ES* application. The differences between before and after an *ES* are negative, i.e. they are good reactions (see **Figures 10–12**) and there is a uniform trend in the EEA classes C1, C3, and C5 for an increase in RTs. Therefore, there is a tendency for patients in these classes to deteriorate. In contrast, in EEA classes C2, C4, and C6, a variable pattern is visualized in which the effect tends to decrease the RTs, i.e. a tendency toward the improvement of patients in these classes.

4.4.3 KP phase

In the Knowledge Production phase, relevant and interesting results were achieved in the opinion of the domain specialist. The non-parametric H-test and the χ^2 test were used both ($\rho < 0.05$) and box and bar graphs were made to visualize the distribution of the data. An arrangement of box plots corresponding to the statistically significant attributes of interest to the specialist, shown in **Table 8**, communicates the distribution of those attributes in relation to the partition. In **Table 8**, the attribute Enercon (seizure energy), figure (a, e), for all classes where patient behavior is more homogeneous (EEA C1, C3, and C5) is lower than in classes

Figure 10.
EEA phase, this graph shows the variability between classes, regarding the effects of each ES, employing two-class curves for tests e5 to e8 related to age rule 1.

Figure 11.
EEA phase, this graph shows the variability between classes, regarding the effects of each ES, employing two-class curves for tests e5–e8 related to age rule 2.

Figure 12. EEA phase, this graph shows the variability between classes, regarding the effects of each ES, employing two-class curves for tests e5–e8 related to age rule 3.

where patient behavior is variable (EEA C2, C4, and C6). And the impedance is low for the classes in which patients get worse, figure (b), EEA C5.

In addition, after the application of an ES, the blood pressure Caidao2t presents a range of lower values for class EEA 4, mature patients who improve, and a range of higher pressure values for class EEA 3 in which patients worsen. In fact, in figure (c, d) of **Table 8**, the classes where patients' behavior is more variable with a tendency to worsen (EEA 2) show a drop in oxygen (oximetry, oxygen drop) after the application of an ES. Regarding total seizure time (Tctotal) and Postcri, figure (e, f), the classes in which patients show variable behavior (EEA 2) show a lower energy level and time. Finally, in **Figure 7g** and **h** of **Table 8**, the lowest doses of both Pentothal and Succinyl were applied in the classes where patient behavior is most variable.

4.5 Analysis results

Due to the particular characteristics of this domain and for comfortable knowledge management it was necessary to use KDSM which provided an appropriate structure for the clinical data. The structure consists of a matrix containing the patient data, a second matrix containing the baseline and post-ES serial measurements, and a third matrix containing the ECT features.

The 3 KDSM phases were carried out with the following results:

1. Baseline Analysis of Individuals (BLA): Baseline reaction times were analyzed because they represent the initial conditions in which patients face the tests. The aim is to find the information useful for profiling patients prior to ECT treatment. In parallel, to find any *a priori* structure in the set of patients that could determine differences in the effects of ECT. In this phase, rules were obtained (see **Table 7**) that became a Knowledge Base (KB) and with them, the classes of *very young patients*, *young patients*, and *mature patients* were delimited.
2. Event Effects Analysis (EEA): To study the effect of electroshock in isolation, the blocking factor is removed, based on the differences in reaction times, and the difference matrix is obtained in which the rule-based hierarchical clustering technique using the KB is employed. KDSM improves the quality of the results even when making use of a small set of rules; as the interpretability of the final classes is improved by guiding the clustering process with the knowledge base due to the ability to incorporate specialist expertise for reaction time analysis. Regarding machine learning techniques, it is important to remember that they can not tackle this kind of domains with such a small KB. The domain specialist chose a partition of six classes where, on the one hand, there are three classes: *very young patients*, *young patients*, and *mature patients*. All three classes of patients show a tendency of deterioration in their

^{a, b}What is significant about this set of attributes is that, from the specialist's point of view, they can be modified to directly influence ECT performance.

Table 8.
As a result of the KP phase, this table shows an array of Box plots corresponding to those attributes that are relevant to the study that the specialist is carrying out.

reaction times and great variability of response to treatment. On the other hand, the other three classes showed a more homogeneous response throughout the treatment period and a relevant level of improvement.

3. Knowledge Production (KP): The attributes of the Z matrix were projected onto the six-class partition obtained in the previous phase and some valuable

attributes were identified. Some of them show differences between *young* and *mature patients*. Others between those that improve or deteriorate the patients' condition. Clearly, the last group is the most crucial for the expert, as it is possible to identify a set of factors associated with the fact that an ES improves the patients' condition. This result reveals the need for further studies on ECT, since, if these attribute trends are confirmed, the efficacy of ECT could be dramatically improved.

4.6 Conclusions from analysis results

The results of the previous analysis highlight some attributes of interest to the specialist in the field, in particular the reaction time of patients undergoing electroconvulsive therapy, at very specific time points and where the measurements constitute blocks relative to each patient. It should be emphasized that KDSM allows the management of patient knowledge from very short and repeated serial measurements, especially because it makes special management of management due to the presence of the blocking factor. In this respect, some interesting conclusions can be drawn:

1. 103 rules were derived and the groups of very young, young and mature patients are delimited by them with the validation of the specialist;
2. Rule-based clustering was carried out, using the rules chosen by the specialist, on the differences between RTs to directly observe the effect of electroshock, independent of patient influence. The specialist chose a partition of six classes into three groups of patients (the youngest, the youngest and the mature), patients with different responses, some more positive than others.

From the psychiatric perspective, the observations on the form of the data and the use of KDSM were corroborated, especially in the management of ECT measures, provided very satisfactory results from the point of view of the field in question. It has been shown that the behavioral curves of RT in each patient are neither inherent to the patient nor to the global observation of the whole therapy. On the contrary, all patients may react differently in each *ES* session. In fact, in many studies psychiatrists, even today, continue to treat ECT (the set of all *ES* applied to the same patient during the entire treatment period) as a single entity. Therefore, they analyze the effect of the whole therapy globally, i.e. they look at the situation of the baseline patient and how the patient completes the whole therapy [15]. It is worth emphasizing, again, that the management of serial measures, under these ISD circumstances, through a summary of measures implies the loss of too much information, hiding relevant situations, which affects the patient, as he/she reacts differently after each *ES* session. To demonstrate this, **Table 9** has been constructed that illustrates how, for the same patient, the effect on RT after the application of an *ES* is often different and does not even follow a specific order. This result is very relevant because it indicates that after an *ES* session the patient's condition improves or worsens, and this change does not depend only on the patient. *ES* can change the effect on the same patient throughout ECT.

With regard to the current state of the study, the psychiatrist specializing in the ECT domain, taking into account these results, works on the identification and analysis of possible causes external or internal to the patient that may or may not be present in each *ES* session. Thus, the knowledge acquired through KDSM is added to that of the specialist and immediately modifies the way in which the specialist obtains his or her interpretations of results in order to tackle this domain.

Patient ^a	Class 1 ^b	Class 2 ^b	Class 3 ^b	Class 4 ^b	Class 5 ^b	Class 6 ^b
063059					6	1–5
437,289			2–4	1,5		
499,969	5–6	1–4				
505,652					1,3,5	2,4
522,175					1–10	
682,257					1–5	
782,035					1–2,5–7	3–4
783,945			3,5	1,2,4		
789,145					1–7	
818,755					1–6	
822,836			1–2,8	3–7,9–11		
824,083					1,3–5	2
⋮	⋮	⋮	⋮	⋮	⋮	⋮
999,464						1–9

^aPatient label.
^bClasses 1 to 6 resulting from the EEA phase.

Table 9.
Sample table to demonstrate the relationship between a patient and the effect on RT of class-specific ES.

Today, there is still no standardized practice for dealing with ISD of the kind presented in this chapter.

The direct contributions of KDSM in knowledge management for this particular psychiatric domain can be summarized in that it allows medical praxis to reconsider how to study the effects of each *ES* applied throughout ECT, as these are not monotonic. It also highlights the risk of frequent use of measure summaries, as they directly affect the communication of treatment efficacy.

5. Discussion

The communication of case study results of knowledge management in Informally Structured Domains is a task that is more than a must, it is very fascinating. In this chapter, the way in which situations such as those presented in the section Knowledge Management in Informal Structure Domains were dealt with was shared. For, although management through *KDSM* is straightforward, analyzing very short and repeated serial measurements, at specific times, of an attribute of interest in these domains is not as simple as it seems.

Knowledge management of an *ISD* through *KDSM* yields the following results, it:

- provides knowledge to satisfy a need or solve a problem through tactics that include Machine Learning and Statistics, as it has an interdisciplinary orientation, combining *RBHC* with other statistical elements, such as statistical tests, knowledge representation, rule induction in Knowledge Base management ... ;
- corroborates why classical time series management is not very successful in this type of domain. It also considers a special type of data management—using

KDSM—which has never been considered before; it emphasizes that traditional management of serial measurements summarizes too much information and as a consequence loses sight of the fact that the attributes of each individual from which the measurements are derived exert an influence on the measurements after each event;

- proved easy and flexible to deal with very simple cases where even no serial measures are recorded, but it supports the interpretation of classes in general terms. Thus, *KDSM* enables the identification of novel, useful and relevant knowledge around domains that are characterized as ISD; and
- is not a simple *ad hoc* technique to deal with particular situations, but a general methodology that is useful to manage knowledge in any kind of domain where information is structured in three matrices *X*, *Y*, and *Z* that have the properties presented in section §3; it can be stated that, *KDSM* has been very successful in medical, economic, and labor domains.

Finally, the use of *KDSM* in the medical domain has made some valuable contributions; for example, for the psychiatric field at the level of medical praxis, it reconsiders how to study the effects of each *ES* of the *ECT*, as they are not monotonous.

6. Conclusion

As mentioned at the beginning of this chapter, the main challenge to carry out a proper Knowledge Management of an Informally Structured Domain, described in section §1, is based on both an excellent understanding of the domain and the ability to obtain knowledge from it. This action is key, to perform a suitably optimal intelligent data analysis or establish the knowledge requirements for the correct development of intelligent applications, or even for the proper representation of the knowledge of such domain. Since the knowledge management of an ISD is a complex task, but very often yields very interesting results, it is considered very relevant to communicate the use of the *KDSM* methodology and the results obtained through it, in a domain characterized as ISD, where very short and repeated serial measurements are presented, and there is not enough *a priori knowledge* to train machine learning tools. Moreover, as serial measurements are commonly found in a large amount of data from medical domains, it is doubly important to communicate successful *KDSM* practices in this type of domain, as this chapter aimed to do.

Thus, in this sense, the chapter reported on knowledge management related to certain attributes of interest to the domain specialist; in particular, the reaction time behavior of patients undergoing electroconvulsive therapy (section §2), at very specific times and where the characteristics of each patient constitute building blocks for serial measures. It is worth mentioning that thanks to *KDSM* a successful knowledge management of repeated and very short serial measurements of patients were achieved, as *KDSM* can be considered a special type of data management in the presence of a blocking factor. Consequently, some conclusions can be drawn: when conducting global analyses of situations that are characterized as ISD domains, the effect of using a summary of all serial measurements masks relevant information affecting the observed individual; that is, the use of the *KDSM* methodology, in domains where very short and repeated serial measurements with block factor are presented, have shown that the behavioral curves formed by serial measurements of an attribute of interest *Y* in each individual are neither inherent to the

individual nor the global observation of all measurements after each event E . On the contrary, all individuals may react differently after each event E . As exemplified and communicated through **Table 9**.

Finally, the frequent presence of this type of domain poses the risk that an inadequate characterization of the domain, the routine use of summary measures ... directly affect the performance and efficiency of the solution to a problem or satisfaction of a need that is intended to be satisfied through Knowledge Management.

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Nomenclature

I	a set of individuals
X	a matrix of attributes that describe I
E	a set of events occurring on the individuals of I
Z	a matrix of attributes which describe E ,
Y	a matrix containing all the serial measures
t	measurement time points represent a <i>fixed</i> distribution overtime for all the serial measures
r	number of observations per series, too small
p	a set of patients
ES	an electroshock
RT	reaction time
$e5$	simple visual test
$e6$	simple auditory test
$e7$	visual and categorization test
$e8$	visual and auditory and categorization test

Abbreviations

KDSM	Knowledge Management in Serial Measures
ISD	Informal Structured Domain
BLA	BaseLines Analysis
EEA	Event Effects Analysis
KP	Knowledge Production
ECT	Electro Convulsive Therapy.
RBHC	Rule-Based Hierarchical Clustering technique
VTs	Vienna Test System
DSM-5	Diagnostic and Statistical Manual of Mental Disorders

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