

# Alert system for Timely Medication Administration

C. Puente<sup>1</sup>, A. Sobrino<sup>2</sup>, A. Villa-Monte<sup>3</sup>, J. A. Olivas<sup>4</sup>

<sup>1</sup> Advanced Technical Faculty of Engineering – ICAI, Pontificia Comillas University, Madrid, Spain, cristina.puente@comillas.edu

<sup>2</sup> Faculty of Philosophy, University of Santiago de Compostela, La Coruña, Spain alejandro.sobrino@usc.es

<sup>3</sup> Institute of Research in Computer Science LIDI, Faculty of Computer Science, National University of La Plata, Buenos Aires, Argentina avillamonte@lidi.info.unlp.edu.ar

<sup>4</sup> Information Technologies and Systems Dept., University of Castilla-La Mancha Ciudad Real, Spain, joseangel.olivas@uclm.es

**Abstract** – *Time has an extraordinary relevance in medicine. The diagnoses of diseases or prescription of medicines frequently presents temporary references. The etiology of a disease frequently depends on when such a symptom appeared and the prescription of some drugs is severely constrained to certain temporary annotations. Every year, the health of the patients suffers due to the bad administration of medicines and an appreciable amount of money is lost by that bad practice. In this paper we want to contribute to mend this problem. In that vein, we approach a release software for controlling the medicine doses administration with an intuitive traffic-light code in order to help the patient to consume the drugs according to the temporary restrictions indicated by the doctor. That software involves three steps. The first one encodes into a database the guidelines of the IHS BCMA for timely medication administration. The second part is in charge to locate the timely restrictions associated to a given illness. By last, the software display to the user the time alarms associated to a prescribed treatment.*

**Keywords:** AI, Copyright, Authorship, Copyright Ownership, Robots.

## 1 Introduction

The daily activity of patients, nurses and doctors involves causal time management. Diseases symptoms or prescription of medicines frequently presents temporary references. That is shown by typical sentences as Fever started two days ago, or Antibiotics should be taken after meals, being ‘two days ago’ and ‘after ’ temporal markers. The medical records and reports are full of temporary lexicon showing that, in medicine, time is a relevant matter. Imagine a visit to a doctor without temporal mentions and check that it is very unlikely. Time plays a leading role in our conversations, records, diagnoses or assessments and medicine shows that [11].

Time is a construct to determine the simultaneity or change of two events. Two events are simultaneous if they occur at the same instant. If it evolves from the past to the present or from the present to the future, then the change happens. Humans have invented calendars and clocks to control time, although not all those devices measure it in the same way, as relativity theory shows.

The doctor-patient interaction involves time references as an unavoidable factotum. Time-based decision making cover four areas of patient care [5]:

- (a) Prevention, that evaluates risk factors for patients who behave in a certain way (Smoking for a long time causes lung cancer).
- (b) Prognosis, for predicting the likelihood of a person’s survival (25% of patients with septic shock will die within 15 days).
- (c) Treatment, administration of drugs during certain periods of time or under certain temporary restrictions (The treatment is omeprazole and aspirin and omeprazole should be taken before aspirin).
- (d) Diagnosis, or the identification of the origin or cause of the disease (The diagnosis, according to the symptoms that he presents, is flu). Diagnosis is largely related to the cause-effect explanation in medicine [10].

Medical diagnosis is largely based on causal associations involving time dependence. Frequently, symptoms run over time making the illness a not static picture but a progressive one. Treatment is also time-dependent. Some drugs must be rigorously scheduled in order to harvest the intended benefits.

Time is a natural property, but also a social construct. Time in medicine is considered a social invention, i.e., a way to fix time-units, as seconds, minutes, etc., in order to inquiry medical information relevant to diagnose and treatment (He

has a fever for 5 days; Take 2 gr of aspirin after dinner). It can be also denoted by intervals (He had a high fever between 10:00 and 13:00 hours). Usually, time is represented by a line over there events are chronologically ordered (First he had episodes of fever and 2 hours later, seizures) and may evolves accordingly the following patterns: (i) branching, when several scenarios are open (After the operation, the leg can be recovered or demand amputation); (ii) parallel, when different lines progress at the same time (He was induced to a coma while receiving corticosteroids) or (iii) circular, when an event is repeated periodically (You need dialysis every two days) [6].

Time uses a specific lexicon. Temporal sentences frequently include calendar-dating references (year/month/date; seasons, part of the day (morning, evening, ...)) and conjunctions and prepositions, as by, until, before, since, past, next. Causal phrases as 'secondary to' or 'because of' also denotes temporal causal influence. Frequently, temporal expressions are fuzzy, as in: A little before the admission, Few days ago he received a very high dose being 'A little before' and 'few days' vague temporal markers. Fuzzy time sentences include (i) fuzzy quantifiers (most of, a few (He was bleeding most of the previous days, he was discharged a few days later)), (ii) linguistic hedges (very, rather (He was admitted very early, It was rather sedentary than active)); (iii) temporal adjectives as 'subsequent', 'previous' or adverbs as 'lately', 'afterward'. Some particles as 'occasional', 'abruptly', or 'still' denotes also fuzzy time [12].

Time may be absolute (January 12, 2017) or relative (ten years ago, within the last month) and may be denoted by an instant or a period, being both of them primitives in its representation. Medical reports include both of them. An instant is usually denoted by a number (fever during 3 days, surgery at ten o'clock) and a period, by an interval (hospital admission between day 3 and 5). Intervals reflect some kind of uncertainty scheduling some act or action. Intervals denote a duration, illustrated by two points: the start point and the finish point. In some cases, the end point is not fixed to the line time (the evolution has been favorable for two days) and when exist, can be considered as a kind of anchor against which to refer the evolution (before the date of diagnosis) [9].

As previously quoted, treatment is a relevant factor in time-based patient care. This paper focuses on that subject. Drugs administration is a relevant area of medical aid. The Institute for Safe Medication Practices (Canada) published a 'List of High-Alert Medications in Acute Care Settings' [4]. This report showed that some drugs are very sensible to time administration and if those indications are not observed, they can cause serious harm to the patient, either because they are ineffective or because they provoke additional damage instead of the expected benefit. Damage can be extended to public institutions, as claims demanding compensations or extra hospital expenses, caused by the ineffectiveness of the treatments. Guo et al. reported that the estimated costs of

adverse drug events amounts 8,75 dollars per hospital stay (3,5 billion for 400,000 cases) in USA hospitals [7]. So, mistakes in the prescribed medication are not only a health problem, but also a financial one. In an aging population with diminished resources of memory, having alert systems to take medicines at the right time is of interest. In this paper we will approach a time caused alert system for aging people in a hospital environment or at home. This alert system can also be useful for Chronotherapy, i.e., the administration of drugs in coordination with circadian rhythms in order to increase their advantages and minimize their costs [8].

The rest of the paper is organized as follows: In section 2 we will describe the software design to control temporary restrictions in the administration of medicines. In section 3 we will detail an example of use and show some screens. Finally, in Section 4, we will summarize the main contribution of the paper and some lines of future work will be sketched.

## 2 Developing a Software to Hold Time Restrictions

To contribute to the management of time in treatments that must take into account temporary information, we have created a software to control temporary restrictions indicated by doctors when prescribing treatments for certain diseases. This problem affects all ranges of age, but our application is focused specially to old people, usually with memory impairments. To facilitate its use, we approach a very simple interface, with few components, but very easy to understand and control.

First, the system catalogued the medicines with critical time intervals. According to the Institute for Safe Medication Practices (ISMP), there are several 'time critical' medicines administration, either because: (i) time is key to obtain an optimal pharmacological effect, (ii) some drugs require repeated cycles or frequency or (iii) first and loading doses should be administrated in accordance with a time schedule. So, the first step was to control those restrictions. As a second step, the software detects the time-sensitivity medicines regarding to their active principles. To that end, a small parser detects those principles contained into the database automatically. Once detected, the interactions with other medicines are also annotated. Those actions permit to design an interface able to indicate the right time to take the medicine and if that medicine has or not interactions with others.

Figure 1 shows the database design approached for storing the guidelines of medication scheduling. Those that require an exact administration timing are of particular interest. This model consists of five tables that store the restrictions to timely administrate a scheduled drug. In particular, and from a given medication, it stores its doses and restrictions, taking into account the period of the day and the waiting time (in minutes), respectively ("day moment" and "timing" tables).

The approached design was applied to the document edited by ISMP, based on nurses experiences in 2010 regarding the CMS “30-minute rule” [2]. In this work, the list of time-critical scheduled medications was used. That list was analysed in detail and loaded into the database. Its content and structure allowed correctly record the information of the document.

With the data design proposed here, the timely administration policy of drugs can be retrieved according to each particular case. Even, the original document can be re-built at any time using all information stored in the database. The process of loading document information to the database was carefully carried out so as to avoid altering its content.

The Data Base Management System used was MySQL. To modeling database, the Visual Database Schema Design3 in the MySQL Workbench software was used. The following SQL query allows to obtain the control rules for the administration of each medication:

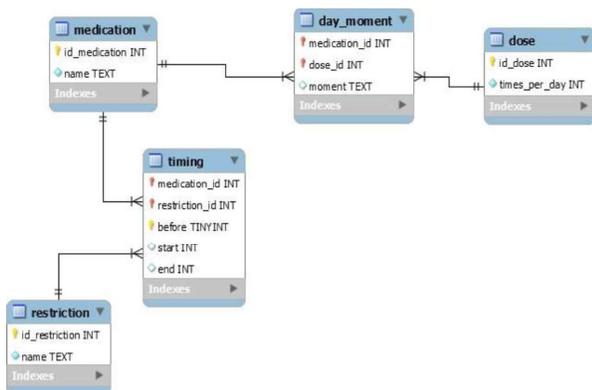


Fig. 1 Timely Admin Policy Sample Database.

To fill the information of the database, a very simple parser implemented in Python is suggested, using the library PLY [3]. That library allows us to program a morphological (the old Flex analyzer), and a syntactical analyzer (Yacc analyzer), so we can introduce some patterns to search for active principles into a web site.

In that case, using the database previously explained, we have looked into the Mayo Clinic website<sup>4</sup> to find drugs containing any of the words belonging to the table medication, i.e., to locate the active principles of each medicine and check if it is time dependent. Using that tool, the database is filled with critical information.

Once located a time critical medication, possible conflict in time with other medicines should be detected. These restrictions will be stored in the restriction table associated to each medicine.

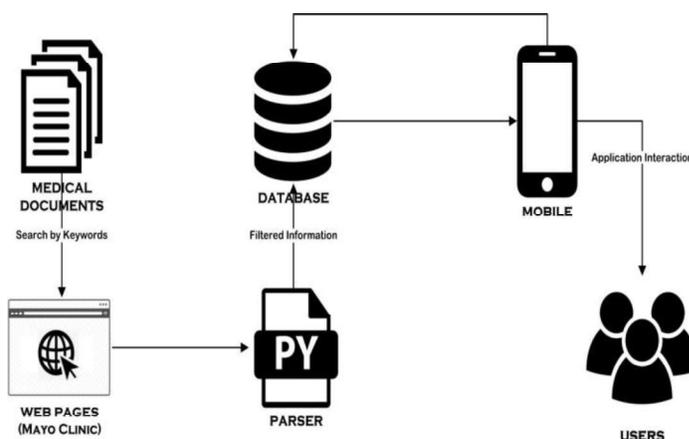


Fig. 2 Schema of the time administration of medicines control process.

Once the database has been filled with all these information, the interface will control the time as will be explained in the next section. Figure 2 shows a schema of the whole described process.

Once the database with all the critical information was completed, a user-friendly app interface to display the restrictions and warnings when administrating doses along time is produced, following the next sequence: First, the interface asks the user for a set of simple questions like the medicine name (in the database we have just introduced only those critical medicaments according to [2]). Considering the type of medicament, the system is going to ask for a series of questions corresponding to its administration; for instance, if the medicine has to be taken 30 minutes before the first meal, the system will ask you for the time that you usually get up to set you an alarm 30 minutes before. This setup interface has to control if the user has to take more than one medicine, and its possible conflicts along time with it. So that it is demanded for the amount of medicaments to search into the database, in order to detect possible incompatibilities among them.

Once the setup information has been introduced, the APP will notify the user when he has to take the medicine according to the restrictions introduced. At the same time, a Traffic-light color will be displayed to indicate if he can get the medicine according to the time or not. In the next section, we have created a full example to explain how it works.

### 3 Example of use

One of the diseases that are especially sensitive to time-controlling is thyroid hormone deficiency, treated with the active substance, L-Thyroxine. According to the restrictions gathered in our database, that medicine has to be taken half an hour before breakfast. Concerning that drug, another restriction to control is that before surgery, the patient sometimes has to take calcium attending some special restrictions as the one showed by the Mayo Clinic website [1].

That restriction is time-sensitive as it affects the absorption of thyroid hormone replacement medications. According to the website, two restrictions concerning calcium should be considered in our application:

- “Don’t take calcium supplements or antacids at the same time you take thyroid hormone replacement”
- “Take any products containing calcium at least four hours before or after taking thyroid hormone replacement”

These two limitations are transformed in our database as “calcium cannot be administrated with L-Thyroxime four hour before.” The following figures show the screenshots representing that. The first one has two simple buttons to indicate if the user wants to introduce information (CONFIGURATION PANEL) or check if he can ingest any medication (CHECK TIME):

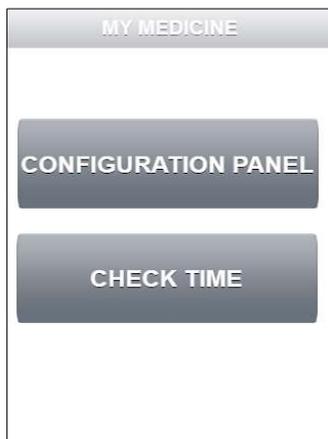


Fig. 3 Initial screen of the APP My Medicine

Once selected the configuration panel, the user introduces the number of medicines he are taking and its name. Then, questions about time restrictions are asked, as seen in figure 4 in the case of L-Thyroxine Tablet:

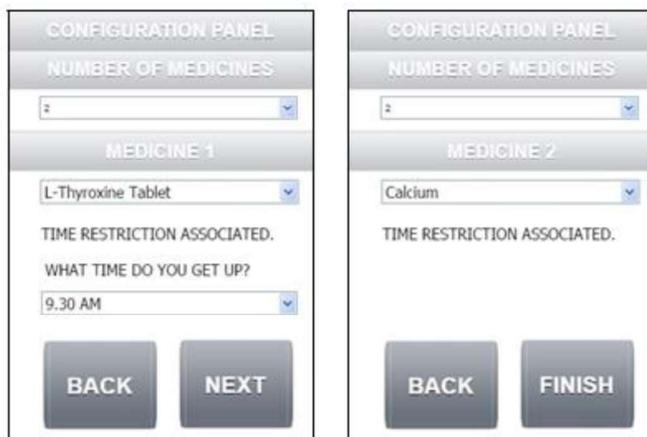


Fig. 4 Configuration Panel screens.

Associated to the L-Thyroxine medicine (medicine 1), a time restriction is posed and the system will ask for the waking time to program an alarm. Once the user presses the button NEXT, another screen will be displayed to ask for medicine 2. In this example, as Calcium has no questions associated, the restriction to control the time is displayed, but nothing else. Once the user has ended introducing the medicines, he clicks the button FINISH to save all the data.

In this example, if the user has introduced 9:30 as the time to wake up, the system will program an alarm half an hour before, as seen in figure 5, to alert that he has to take the L-Thyroxine medicine. A traffic-light color code is also displayed to indicate the user whether he can get, at the current time, other medicines or not. In this case, the message appears in green, denoting no conflict with other medicines yet.

If the user takes its medicine and checks the system at 10:00, a message will be displayed indicating that there is a strong conflict with the second medicine introduced (in this example Calcium); so, the color code shown will be red, warning that he cannot take the medicine yet.

In the same example, if the user checks the time at 13:00, the system will indicate that the conflicting time between medicaments is about to finish, shown by the color code yellow. In case of long time periods between medicine administrations, as is four hours, the yellow color will appear 30 minutes before the time is up.

Once the conflicting time between medicines has expired (in this example that should happened at 13:30), the system will launch another alarm to indicate the user that Calcium can be taken now, turning the color code to green again, as figure 5 shows:



Fig. 5 Restrictions of time screens.

With this simple application the user can control throughout the day the medicines that he has to take, when he has to take and the conflicts or interactions, if any, between them.

## 4 Conclusions

In this paper we consider critical time in the administration of medicines, going in details to certain illness. Focused on elderly people that usually suffer several pathologies, we have created a program to prevent common errors in the time-dependent drugs administration, preventing the misuse of medicines and avoiding harmful interactions when several are prescribed. A very simple mobile app checks those conflicts and set a series of alarms to indicate the user what and when to ingest medicines.

As future work we would like to expand this app, using it not only in time conflicts medication, but also in the effect of many drugs varying according to the time administration in relation to our circadian clock. That is a matter of Chronotherapy, the subject that pursues the efficiency of medicines considering the time at the day at they are most effective and tolerate.

## 5 Acknowledgements

This work has been partially supported by the European Regional Development Fund (ERDF/FEDER, UE) and the State Research Agency (AEI) of the Spanish Ministry of Economy, Industry and Competitiveness (MINECO) under grant MERINET TIN2016-76843-C4-2-R, and under grant TIN2014-56633-C3-1-R, and TIN2017-84796-C2-1-R. A. Villa Monte thanks both the National University of La Plata (Argentina) and the University of Castilla-La Mancha (Spain) for supporting his co-tutelary PhD in Computer Science and Advanced Information Technologies respectively.

## 6 References

- [1] Hypothyroidism: Can calcium supplements interfere with treatment? <https://goo.gl/XQpxdA>, accessed: 2018-01-31
- [2] IHS BCMA Timely Admin Policy Sample, <https://goo.gl/VE8nFk>, accessed: 2018-01-31
- [3] PLY (Python Lex-Yacc) (2001), <http://www.dabeaz.com/ply/>
- [4] ISMP List of High-Alert Medications in Acute Care Settings. <https://www.ismp.org/tools/highalertmedications.pdf> (2014)
- [5] Augusto, J.C.: Temporal reasoning for decision support in medicine. *Artif. Intell. Med.* 33(1), 1–24 (2005)
- [6] Bardon, A.: *A Brief History of the Philosophy of Time.* OUP USA (2013)
- [7] Guo, J.W., Iribarren, S., Kapsandoy, S., Perri, S., Stagers, N.: Usability evaluation of an electronic medication administration record (emar) application. *Applied Clinical Informatics* 2(2), 202–224 (2011)
- [8] Ohdo, S.: Changes in toxicity and effectiveness with timing of drug administration. *Drug Safety* 26(14), 999–1010 (2003)
- [9] . Shahar, Y., Combi, C.: Timing is everything. time-oriented clinical information systems. *Western Journal of Medicine* 168(2), 105–113 (1998)
- [10] Thagard, P.: Explaining disease: Correlations, causes, and mechanisms. *Minds and Machines* 8(1), 61–78 (1998)
- [11] Zhou, L., Hripcsak, G.: Temporal reasoning with medical dataa review with emphasis on medical natural language processing. *Journal of Biomedical Informatics* 40(2), 183 – 202 (2007)

[12] Zhou, L., Melton, G.B., Parsons, S., Hripcsak, G.: A temporal constraint structure for extracting temporal information from clinical narrative. *Journal of Biomedical Informatics* 39(4), 424 – 439 (2006).