

Implementation of an Intelligent decision support System for Medication Review at European Hospital Pharmacy

Intelligent decision support System Medication Review Project (ISMRP):

A new tool for developing a Hospital Pharmacy basic competence

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1.- BACKGROUND:

The medication-use process has six components: ordering-prescribing, validation, procurement, preparation-dispensing, administration and monitoring (*HFAP Accreditation Standards for Pharmacy Services and Medication Use*). Safety issues arise in daily activity in relation with any of these components: prescribing challenges, validation of complex treatments in complex patients, procurement in an era of drug shortages, preparation and dispensing (includes sterile preparation), administration (timing, patient identification, medication verification) and routine medication use evaluations.

A recent report from the Institute of Medicine (*To Err Is Human: Building a Safer Health System (IOM, 2000)*) has revealed that a large number of patients die unnecessarily each year due to errors committed while delivering care. A large number of these errors are related to medication use. In fact, it is estimated that as many as 30% of all hospital admissions are due to the improper use of medications. These negative outcomes carry a high cost, first emotional to all those involved, then financial. Leape and colleagues (*Leape LL et al Systems analysis of adverse drug events. ADE Prevention Study Group. JAMA 1995*) reported in 1995 that medication errors occur at different concentrations depending on the stage of the medication or prescribing process. Most medication errors occur during physician ordering (39%) and medication administration (38%). Costs associated with adverse events are 4% and 5% of total health spending in the United States, respectively. The FDA analyzed fatal medication errors from 1993 to

1998, 41% of the errors were caused due to the administration of an inadequate dose or a wrong drug. In Spain, in specialized care, the percentage of medication errors published in the ENEAS study was 3%, and in primary care, according to the study APEAS is 5.38 ‰.

During the last years of the twentieth century, medical orders, including medication orders, were provided via a paper-based system. Medication orders were written in the patient's medical record on copy sheets. We improved the process after the implementation of a CPOE system. But CPOE systems only support medical prescription process helping resolve challenges coming from patient identification of duplicate therapies, drug-allergy alerts and drug-drug interactions (DDIs). Unfortunately the safety benefits of CPOE depends on the provision of clinical decision support in prescribing. The clinician is interrupted with alerts pertaining to allergies, duplications, potential drug/drug interactions, and inappropriate doses, but the burden of alerts is often high. The same alert is often presented several times during order entry, and many eRx systems require prescribers to provide a rationale for overriding the alert. [(Russ AL, Zillich AJ, McManus MS, Doebbeling BN, Saleem JJ. Prescribers' interactions with medication alerts at the point of prescribing: a multi-method, in situ investigation of the human-computer interaction. *Int J Med Inform.* 2012;81:232-243). Physicians and other users often suffer "alert fatigue" caused by excessive numbers of warnings. (Smithburger PL **A critical evaluation of clinical decision support for the detection of drug-drug interactions.** *Expert Opin Drug Saf.* 2011 Nov;10(6):871-82. doi: 10.1517/14740338.2011.583916. Epub 2011 May 4.)

During the last years of the twentieth century, prescription in hospitalized patients has been controlled by a pharmacist who analyzed the prescriptions using their professional judgment and rarely Intelligent support systems in order to improve the use of; we call this process: pharmacist validation. According with EAHP statements: "All prescriptions should be reviewed and validated as soon as possible by a hospital pharmacist. Whenever the clinical situation allows, this review should take place prior to the supply and administration of medicines" (*Eur J Hosp Pharm October 2014 Vol 21 No 5*). Whenever a pharmacist is going through a validation process is doing a research of drug-related problems (DRPs), particularly for the elderly who often take many medications simultaneously. Medication reviews have been demonstrated to improve medication usage, leading to reductions in DRPs and potential savings in healthcare costs. However, medication reviews are not always of a consistently high standard, and there is often room for improvement in the quality of their findings.

An Intelligent decision support system could directly support pharmacist providing medication reviews (*Bindoff IK, J Clin Ther 2007 Feb; 32(1):81-8**Development of an intelligent decision support system for medication review*). Rather than being based on static rules to trigger alerts, this system utilizes a multiple classification ripple-down rules approach, which allows the user to build rules incrementally and improve the accuracy of the knowledge base in identifying medication-related problems while the system is in use, with no outside assistance or training. The system contextualizes the potential drug therapy problems by taking into consideration the patient's demographics, and other medical condition and drugs.

At present, no European intelligent system is available that allows to work in network and to review drug prescriptions coming from individual electronic records, evaluate and select by clinical relevance all drug medication error/drug related problem, and show them to pharmacist helping in the advising process that goes after validation. Network working transfers the experiences coming from every day work to the rest of pharmacists. Therefore, drug treatment validation is not performed by a single person; an intelligent system will propose clinical decisions that will help hospital pharmacist make their own decisions.

Soon, in the health sector fourth industrial revolution will take place. Therefore, it appears the need to create technology products that can operate in various hospitals and improve the efficiency of the verify process, the systems will automatically recognize the clinical relevance errors or opportunities for improvement. Fourth industrial revolution with labor integration between man and intelligent machines threatens millions of jobs in Europe. It is necessary to anticipate and integrate hospital pharmacists with intelligent systems that evaluate the patient pharmacological treatment making hospital pharmacist work more efficient.

2.- DESCRIPTION:

Intelligent decision support System for Medication Review Project (ISMRP)

We would like to present for evaluation to the EAHP Board the Intelligent decision support system for medication review project. This project is based in the virtual system ALTOMEDICAMENTOS® already developed in Spanish and ready to operate through homepage access: www.altomedicamentos.es

ALTOMEDICAMENTOS® is a virtual system that contains a database with relevant information about drugs, which helps in error detection and improved drug treatments. ALTOMEDICAMENTOS® works analyzing prescriptions and issuing alerts differentiated by their clinical relevance against the traditional system in which a pharmacist analyzes treatments according to their knowledge. In other sectors of technology, automated systems are used to improve security, such as in the automobile sector: Airbag, ABS, ESP, or in the future, self-directed cars. ALTOMEDICAMENTOS® automatically analyzes drug prescriptions. One of the novel aspects of ALTOMEDICAMENTOS® is that classifies the clinical significance of the actions to be performed at three levels: **Alert, Review and Informative**. That is, the system can automatically categorize the actions to be carried out according to individual clinical relevance based on the clinical condition of the patient. For example, in a patient of 75 years with a dose of 25mg of hydroxyzine, the system will indicate **review**; at doses of 75mg the system will indicate **alert**; while an adult under 65 years the system do not indicate any action to be taken, but it would warning you in a non-elderly adult with 125mg/day.

There have been two studies to evaluate the system's ability to detect possible interventions compared to traditional system validation, detecting 0.56% and 0.89% with the traditional system interventions and 1.55% and 1.13% with the automated system (ALTOMEDICAMENTOS®), in the first and second study respectively. That is, in the first study (*Comparison of the traditional pharmaceutical validation method versus an assisted pharmaceutical validation in hospitalized patients Farm Hosp 2016, http://www.sefh.es/fh/153_9960.pdf*), the number of interventions detected with the automatic system is 2.77 times the number of interventions detected with the traditional system and in the second study 1.27 times higher; the average of the two studies is 2.02.

These studies also noted a decrease in the time required to perform automatic validation over traditional validation. The time spent with the automatic system was 0.044 minutes per line treatment vs 0.214 minutes with the traditional system validation. So, the automatic system improves 4.84 times the time required to perform the validation of the treatments. Assuming that the cost of 1 minute of work of the pharmacist is € 0.59 (€ 58.215,76 per 1.645 hours). The cost associated to the validation of a treatment line in the traditional system is € 0.12626 vs 0.02596 € with the automatic system.

Additionally, the system detects double errors than the traditional system, without ALTOMEDICAMENTOS® these errors would not be detected and may reach the patient. The drug-analytic interactions (Na, K,...), which we are incorporating into the system, enhance the project's value even more.

Knowing the actual errors that occur in clinical practice of hundreds of thousands of patients can make early detection campaigns to avoid them. Time last to analyze 1000 patients and 9,000 treatments (15,000 lines of administration) is about 3 minutes, although it takes a few minutes more to anonymize them.

Effectiveness is 2.02 times higher with the automated system, time is 4.84 times quicker, so its cost is 4.84 times cheaper, as currently the system is free. Efficiency is 9.77 times higher in the automatic vs. traditional system validation. If we perform a sensitivity analysis with the best and worst times and the best and worst effectiveness, we found that in the worst situation the system would be 4.26 times higher than traditional system validation; and that in the best situation would be 33.78 times higher than traditional system validation.

The system consists in a database with relevant information about medications, which can help to detect errors and improve drug treatments.

ALTOMEDICAMENTOS® database contains 1.010.345 cells with information of 46.035 drugs:

- 563.678 cells with information on high doses in adults, elderly and pediatric (by age from infants to 12 years) of about 27.863 drugs.
- 42.460 cells with the dosage according to the route of administration, with doses in different units of measure.
- 4.368 cells with information on dosage in renal impairment of 1,224 active ingredients.
- 2529 cells with information on excessive duration of treatment.
- 276,204 cells with information marketed drugs and their active ingredients and routes of administration of pharmaceutical specialties.
- 43845 cells with information on drug interactions. These interactions are classified according to their clinical relevance (approximately 4,384 interactions).
- 3813 cells with information on the dosage of 954 active ingredients in liver failure.
- 67.537 cells with information on 8,442 drugs cannot be administered enterally, or where caution should be exercised.

- 5812 cells with information on correct administration route.
- 99 Cells for therapeutic duplication (grouped by therapeutic subgroups).

The information in the database has been obtained from different bibliographic sources with technical specifications of drugs and specific bibliography of each item analyzed: Summary of product characteristics (<http://www.ema.europa.eu/ema/>), British National Formulary for Children, Pediatric Dosage Handbook, Stockley 2016, Top 100 interactions 2016, The Renal Drug Handbook, Drug Prescribing in Renal Failure: Dosing Guidelines for Adults and Children, Lexicomp, www.uptodate.com,...

ALTOMEDICAMENTOS® checks:

- 1 Dosing
 - a. Based on age and route of administration.
 - b. Renal impairment (real or estimated)
 - c. Liver failure
 - d. Max and Min dosing
- 2 Treatment duration.
- 3 Suitable routes of administration for the drug.
 - a. Enteral route
- 4 Drug interactions.
- 5 Therapeutic duplication.

ALTOMEDICAMENTOS® needs for decision support solutions to get information from hospital pharmacy services (see section DATA REQUIRED BY ALTOMEDICAMENTOS).

ALTOMEDICAMENTOS® is already active in Spain, and the clinical integration between the hospital pharmacist and this intelligent system is already working in 50 Spanish hospitals in Madrid, Catalonia, Aragon (section 6 ACHIEVEMENTS). So, we propose through this project to get the same in Europe, to widespread a new way to do a basic task for hospital pharmacists, to build a very useful BIG DATA on pharmacists interventions and prevention of prescription errors, and finally to carry European Hospital Pharmacists to the new way of working in XXI century.

We are already preparing the system for Portugal, and we have made the first contacts to begin the analysis of the treatments with drugs included in Portuguese Vademecum, we have analyzed 20.000 drugs of this Portuguese Vademecum, and the first reunion

will be in one month, so two state of Europe will be working together with altomedicamentos.

3. OBJECTIVES

3.1 Primary objective:

- To offer a new tool for treatments validation by hospital pharmacists at European Hospitals with an intelligent system that improves the efficiency of the work of the hospital pharmacist and to integrate it in the model of work of the 21st Century (Integration with intelligent machines).
- To offer education and update about the use of ALTOMEDICAMENTOS, through the procedures already procured by EAHP: Congress, Academia, Seminars, etc....

3.2 Secondary objective:

- To adapt the program from Spanish to English and to make the relationships between the drug codes and Spanish master formulas with those of the countries where hospital pharmacist would like to participate in this project.
- To get a way to measure the hospital pharmacy profile in drug prescribing validation.
- To promote a BIG DATA structure.

4.- PRESENT OR FUTURE PROTECTION DEGREE FOR ALTOMEDICAMENTOS

We have the intellectual property of the database with 1 million cells of information. We do not give away the database or the decision algorithms.

Participants in the **(ISM RP)** will introduce their thousands of treatments, once anonymised to safeguard confidentiality, and the system informs them what actions to take and what their relevance is. In other words, we do not deliver the database, we let it use it, just like Google does, it gives you the result of your search not all of its database and its decision algorithms.

Each hospital saves the results obtained in excel or html format, as each one prefers. Now, The WEB system only saves the results of the number of alerts and types of alerts detected; if you wanted for making a big data could save the results of the affected drugs, and could be used by EAHP for research. It is not intended for analysis with economic interests by the industry.

5.- FUTURE DEVELOPMENT

ALTOMEDICAMENTOS® needs to improve their configuration. Future improvement will cover the relationship between drugs and analytical results: sodium, potassium, hemoglobin, eosinophils, neutrophils, platelets. This requires assessing the feasibility of integration between laboratory software of the various centers and ALTOMEDICAMENTOS®, as well as the clinical study of laboratory abnormalities caused by drugs in patients.

The process will continue obtaining the analytical results of patients and analyze them based on their treatment, for which the system applies specific algorithms that we have developed to study the interaction between analytical and pharmacological treatments. The result of these algorithms decision (to suspend a certain drug, dose reduction, review the patient's condition) will be analyzed to assess the final implementation of this new part of the project.

Additionally, ALTOMEDICAMENTOS® offers the opportunity to create Big Data Word with the analysis of millions of errors and drug related problems detected.

This could be negotiated between EAHP and altomedicamentos.

6. ACHIEVEMENTS AND PRIZES

6.1 ACHIEVEMENTS:

ALTOMEDICAMENTOS® (www.altomedicamentos.es) was presented through the mailing list of SEFH (Spanish Society of Hospital Pharmacy) in April 2015. This project was presented after being supported as a good professional activity by the Spanish Board, more than 70 hospitals were interested in performing virtual assisted validation and 50 of them (public and private, from 12 Spanish regions, with different computer programs and levels of care) performed assisted validation. The project is running for the last 21,5 months.

Hospitals as: H Clinic Madrid, H La Paz, H La Princesa, H National Paraplegics, H Avila, H Miguel Servet, H Alcazar de San Juan, H Bellvitge, H October 12, H Alcorcón, H San Jorge Huesca, are working with ALTOMEDICAMENTOS®.

Last review report of the use of the validation tool coming from March 15, 2015 to December 31, 2016, showed that 6,332,392 prescriptions were analyzed corresponding to more than 300,000 patients from 50 hospitals and detected 130,604 alerts (2.06%) and 824,933 (13,03%) reviews for minor problems.

Alerts: 130,604 (2.06%)

	Number	%
Dose	68.760	1,09
Renal failure fictional	5.142	0,08
Real Renal failure	6.711	0,11
Interaction	20.004	0,32
Duplicities	29.987	0,47

Reviews: 824,933 (13,03%)

	Number	%
Dose	67.571	1,07
Days	422.713	6,68
Renal failure fictional	21.021	0,33
Real Renal failure	26.210	0,41
Enteral administration	20.795	0,33
Administration route	78.239	1,24
Active ingredients route	91.538	1,45
Minimal Dose	36.643	0,58
Interaction	17047	0,27
Hepatic failure	26109	0,41

Renal failure fictional: In these cases the Cr value of the patient was not introduced in the program, reason why the CrCr was estimated in function of the age. Administration route: problems with the drug marketed and the route of administration. Active ingredients route: problems with the Active ingredients and the route of administration.

6.2 PRIZES OF OUR SYSTEMS:

2015-2017:

- First Spanish Society of Hospital Pharmacy SEFH-VIFOR quality and safety in the use of drugs Pharmacy Services award 2015: €9,000

- First prize for the best project for Improvement of Quality Management in the Second Edition of the Awards of the Madrid Association of Healthcare Quality 2016: € 300
- Hospital Pharmacy Award J.R. Ferrándiz 2016. Spanish Hospital Pharmacy Foundation: € 5000
- Prize in the 14th edition of the Professor Barea Awards 2016 in the category Innovation, Development and New Technologies.
- Finalist in Best in Class 2016 Awards in the category e-health.
- Finalist in Ad Qualitatem 2017 Awards in the category e-health.

7. BUDGET

7.1- Data Base and software traducing: 13.000€

7.2- Educational program: 4.500€

7.3- Incorporation of code of drug/hospital: 1.000€/per country, (we need the official code of each drug, the ATC code, description, dose, pharmaceutical form, and the equivalent of "Virtual Medicinal Product" (VMP) (active principles, dosage, unit of dosage and simplified pharmaceutical form, based in the terminology Snomed-CT used to define each medicine).

8.-TIMELINE

February-July 2017: Commissioning of the system in English and incorporation of code of drug/hospital.

September 2017: Start of the system in the hospitals of the rest of Europe that want to use it.

December 2017: Report on use in European hospitals.

9. FINAL CONSIDERATION

Linkage between EAHP project/mission/purpose and the proposed project

EAHP represents and develops the hospital pharmacy profession within Europe in order to ensure the continuous improvement of care and outcomes for patients in the hospital setting, making the difference in medication. This is achieved through science, research, education, practice, as well as sharing best-practice and responsibility with

other healthcare professionals. These goals are performed promoting the best and safest use of medicines and medical devices for the benefit of patients in Europe, creating a platform for the education and training of hospital pharmacists to a level of specialisation and maintaining continuing professional development (CPD)

Our work pathways are changing and it appears a clear need for professional tasks integration with intelligent machines for improving outcomes, as it is happening now to other professions according to the white house report of December 2016. <https://www.whitehouse.gov/sites/whitehouse.gov/files/documents/Artificial-Intelligence-Automation-Economy.PDF>.

This project refers to pharmacist validations prescription process, and offers a way for helping us make our own decisions about reducing drug related problems at hospital level.

Regarding: The dissemination of the project results via one of the below methods and the cost of attendance to any of the below events should be included in the project budget: Its possible to present this project at academy seminars or at the congress: posters, oral presentations... EAHP can choose the more opportune of the two options.

PRACTICAL TOPICS

MODE OF APPLICATION: Hospitals would request the EAHP, or to whom it was established, to request an intelligent evaluation of the treatments with altomedicamentos®.

PAYMENT: The economic gain is not initially established as the main purpose of the project. While depending on how it is determined by EAHP and Altomedicamentos®, hospitals could pay an amount for use, especially due to the high cost of updating and maintaining the project. The annual cost for each hospital should never exceed 1,000 € / year, so that hospitals can be integrated into smart systems without economic problems.

Analysis result report and how to perform the interventions: The result of the analysis would be in excel and html. In this way it is easy to copy and paste into the intervention program that each European hospital uses. This way is easier and quicker to work and carry out the intervention

INSTRUCTIONS

Video of the new system Alto_Med

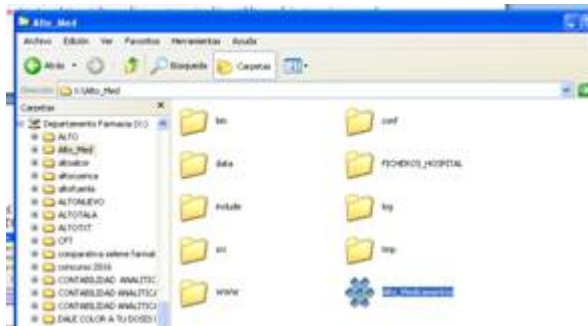
<https://www.youtube.com/watch?v=MRUWmqBOlaI>

o https://altomedicamentos.es/archivos/Altomed_instrucciones.mp4

Steps:

- 1) Get the census (censo.txt) and treatment (localiza.txt) listings.
- 2) In the directory where we have installed the program Alto_Med we click the hexagon

ALTOMEDICAMENTOS. 



This will create a virtual network on your computer.



(In the central part will appear texts in green: 2 Running, 1 Running, 3 Running). If it is in Red it does not work, and you must save Alto_Med on the hard disk of your computer, and not in the Pharmacy Network.

- 3) In Chrome or Firefox you type up localhost (where you type www.)

- 4) You already do the Altomed process: Step 1 Press TTO by FILES
- 5) Already creates TTO.txt
- 6) Step 2 upload to internet: put keys and upload (select TTO.txt file)
- 7) Press excel on the Web to download Results, you must call download it, replaces the previous one, and the format must be excel xls (it usually goes out by default) and we must save it in the file directory HOSPITAL within the ALTOMED program.
- 8) Step 3 Process result
- 9) Step 4 List by beds or by alerts. In excel o html. You save it by adding the date to the list name.

In FEW MINUTES the whole hospital is analyzed

DATA REQUIRED BY ALTOMEDICAMENTOS®:

LOCALIZA.TXT

Ncama / numberhc / cod_via / dose / cod_pauta / compute_0012 / dose / code / cod_practivo / unidad_med / des_farma / name

Fields instead of / must be separated by tabs.

The cod_practivo is the code of active principle, if it did not have, it should "A", so that it is not empty.

The name is the active ingredient

Cod_via is the abbreviation of the way of administration.

Compute_0012 are the treatment days.

Code is the national code or the code of the article. Or could be your own code (that will be transform by other excel cn.xls for transforming it in a code recognized by ALTOMEDICAMENTOS) (No hospital needs to change the codes it uses).

Unit_med: is the unit of measurement mg, g, ...

The first "dose" in units: 2 tablets.

The second "dose" in mg, g, meq, ml, ...: 150.

Important or each line of administration, ie for a 500mg amoxicillin every 8h will be 3 lines of administration of 1 tablet of amoxicillin and 500mg; Or could be 1 single line but in doses will be 3 tablets and 1500mg.

CENSO.TXT with:

Numberhc / ncama / service / lastname1 / lastname2 / name / sex / birthdata

Fields instead of / must be separated by tabs.

The data will be anonymised, and uploaded to the internet anonymised. The results of the internet will later be deanonymized in their own computer, to show only in his computer the bed, the patient's name and his medical history number. The system remembers the old alerts and especially in yellow indicates the new ones. This way the pharmacist will focus on the new alerts of today.

European Association of Hospital Pharmacists
Rue Abbé Cypers, 3
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Belgium

Madrid, 12nd January

Subject: Support ALTOMEDICAMENTOS® Project

To whom it may concern,

The Spanish Association of Hospital Pharmacists supports the project named ALTOMEDICAMENTOS®

At present, no European intelligent system is available to review the prescriptions and to analyze the clinical relevance of each error detected in the treatment of hospitalized patients. The system Altomedicamentos® also allows to work in network and then the Spanish Association of Hospital Pharmacists thinks that this initiative is very important for hospital pharmacists in benefit of our patients.

In this area, Dr. David García Marco has been working for several years achieving important improvements. We think his knowledge and wide experience environment will contribute to the future of the European Hospital Pharmacists.



Montserrat Pérez Encinas
Secretary SEFH