Redesign of a clinical decision support system for a drug - drug interaction alert.

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Abstract. The clinical decision support systems (CDSS) in general and those related to prescription systems in particular have the potential to reduce and prevent morbidity and mortality associated with adverse events and improve the quality of patient care. Most electronic health records (EHR) has CDSS used as support for clinical decision making. In the context of electronic prescribing systems, knowledge databases necessary for the implementation of systems alerting for drug - drug interactions are not adapted to local contexts of use, generating a high rate of false positives and producing "alert fatigue". Redesigned of the notification system for drug interactions in areas like structuring a knowledge database of drugs, modification and validation of a knowledge database on drug - drug interactions, generating case studies and frequency of interactions at the local level and redesigning of the alert interface could be beneficial. Create a CDSS for making decisions about drug - drug interaction is a complex process that requires supportive evidence, structured databases, good interface design and trained staff to adapt the evidence to the healthcare context of a health institution.

Keywords. Clinical decision support system, Drug-drug interaction system, Electronic health record

1. Introduction

Decrease medical errors, improve health processes and ensure high quality health care for patients has been the focus of constant concern of all members of the health care team. In this context arise computerized support systems (CDSS) in response to the need to improve the process of clinical care (1). The CDSS in general and those related to prescription systems in particular have the potential to reduce and prevent morbidity and mortality associated with adverse events and improve the quality of patient care (2). Most electronic health records (EHR) has CDSS used as support for clinical decision making. In the context of electronic prescribing systems, knowledge databases necessary for the implementation of systems alerting for drug - drug interactions use commercial knowledge databases, usually created in the United States and in English language. These databases are not adapted to local contexts of use, generating a high rate of false positives and producing "alert fatigue" (3–5), situations in which the user, after receiving numerous warnings, with no real clinical impact , ignore and / or dismiss this advise, even though in some cases have medical relevance. To solve this problem, the databases of the CDSS should take into account the context of clinical use, the health system and the clinical evidence.

Although the benefits of CDSS are known, it is not uncommon to find reports indicating a high rate of omission of these alerts on grounds ranging, as previously discussed, since the inadequate content of the knowledge database of such systems and the lack of clinical significance of the recommendations to the poor design of human-computer interfaces (6,7) therefore, all references to improve these aspects result in improved safety for patients (8).

Interactions among drugs administered to a patient, occur when a drug causes changes in metabolism of the other, a phenomenon known as drug-drug interactions (DDI) (9). These DDI can cause unwanted adverse events in the patient and the severity of symptoms can vary from

negligible to potentially lethal. The occurrence of DDI is associated with increased morbidity and mortality (10,11), with prolonged hospitalization (12) and high health care costs (6). The increasing use of new pharmacological agents (7), the clinical context of the patient (8) increasingly complex and other factors such as prolonged hospitalization, makes identifying these DDI is beneficial and at the same time increasingly difficult (13).

El Hospital Italiano de Buenos Aires (HIBA) developed and implemented an electronic health record (EHR) with a notified drug interactions system (14), but in first instance the rate of cancellation of alerts presented was high. The decision was then to redesign the system components for notify drug interactions, consistent with the recommendations in the literature and using techniques of user centered design (UCD). First we worked on the first phase of debugging the knowledge database and the categorization of its recommendations (4) and an analysis of the cases was conducted to determine the local occurrence and to then, move forward in redesigning alerts with techniques based on user-centered design (UCD).

The redesigned of the notification system for drug interactions was organized in the following steps:

- Structuring a knowledge database of drugs
- Modification and validation of a knowledge database on drug - drug interactions
- Case studies and frequency of interactions at the local level
- Redesign of the alert interface

2. Setting

El Hospital Italiano de Buenos Aires (HIBA) is a university hospital of high complexity founded in 1853 belongs to a nonprofit health network including a second hospital, 25 outpatient centers and 150 private clinics distributed in the city of Buenos Aires. The infrastructure is complete with 750 inpatient beds, 200 of which are for critical care, a home care service and 41 operating rooms. A team of 2800 doctors, 3000 agents of the health team and 1900 persons for administrative tasks and management process work at the hospital. Approximately 45,000 discharges per year, 3 million annual visits and 45,000 surgical procedures were performed. Since 1998 has been gradually implemented a Health Information System (HIS) development "in house" that handles the medical and administrative information from capture to analysis. It includes a unique problem-oriented and patient-centered health record, known by the name of ITALICA (14). EHR allows documentation of care in areas including: outpatient, inpatient, emergency and home care. ITALICA allows the request of complementary studies, drug prescriptions and results display that includes a PACS (Picture archiving and communication system). Since the implementation of the EHR, a Terminology Server for vocabulary representation was created. The Terminology Server allows linking free text entered by the health team in the EHR and references it with SNOMED CT, plus the ability to associate them with different classifications, such as ICD-9-CM, ICD10, ICPC, LOINC, among others. In 2006 the HIBA start the Personal Health Portal Project (PHR). The PHR is linked to ITALICA, which provides services and unified access to multiple data applications, allowing the patients see their health data stored in the health network, and allow them to interact or consult their medical or administrative information.

3. Redesign process

3.1. Structuring a knowledge database of drugs

In order to integrate scientific knowledge with the clinical decision support systems the hospital decided to start its e-prescribing project, progress on both the development of its own CPOE, and will develop a structured knowledge database on drugs and serve substrate for the creation of support systems. From this decision created a group comprised of physicians, pharmacists, and students of medicine and pharmacology that dealt with several databases of national and international information and created a data structure that allow the storage of structured and coded information. The uploaded data are referenced to SNOMED CT, the same standard terminology that the health information contained in patient clinical data repository.

This process enables the creation of CDSS, and the use of international standards facilitates the decision system creation process, EHR integration and implementation.

The knowledge database of drugs, in addition to basic drug information contains also commercial information like products´ names and presentations, and also, has information on the interaction of the drug with other active ingredients.

This database that fed in a first instance to the notification system of interactions was based on international knowledge database, so its lack of contextualization to local realities generated false positives causing alert fatigue. It was then decided to modify and validate this knowledge database on DDI and also make taxonomy of recommendations for actions to be taken by professionals, with the aim of providing the warning message to perform a specific action.

3.2. Modification and validation of a knowledge database on drug - drug interactions

In the electronic prescribing module the Notify System for Drug Interactions, worked at the beginning using a commercial database, Evaluations of Drug Interactions (EDI) (4,15) of the company First Data Bank. The database uses the terminology of Table 1 for the categorization of risk of each interaction.

Table 1 Terminology used in Evaluations of Drug Interactions (EDI) - First Data Bank

Code	Category	Description
I	*High clinical significance*	DDI that have great potential to harm the patient, are predictable or occur frequently and are well documented
II	*Moderate clinical significance*	DDI who have a moderate potential to harm the patient, are less predictable or occur infrequently, or lack of complete documentation
III	*Low clinical significance*	DDI who have a low potential to harm the patient, have a varied predictability or occur infrequently,

		or has poor documentation
IV	*No clinical significance*	Although these DDI can occur, the documentation is based on unproven theoretical foundations or effect resulting from the interaction is not clinically significant and / or any adverse event is not expected

To avoid false positives and alert fatigue evidenced in the literature we asked pharmacologists at the Clinical Pharmacology Section of HIBA to review and validate the DDI that are the basis of system.

Work were organized in two phases: In the first, we worked with DDI level I of EDI, which were evaluated between two pharmacologists physicians, determining each other, which ones, according to the literature, the health care setting and prevalence, were relevant. In the second phase, the remaining levels (II, III and IV) were distributed between two other pharmacologists. In the absence of agreement on an interaction, the level was assigned by the intervention of a third pharmacologist to arrive at a consensus.

We decided then to re-classify interactions using a standardized layering system of interactions with the knowledge database Lexicomp® (16). For the re-classification of the clinical significance of DDI by severity, likelihood of occurrence in our environment and level of care (outpatient, critical or noncritical hospitalization), two pharmacologists evaluated according to clinical criteria, scientific evidence in the literature and using standardized tools(Lexicomp®) (Table 2) each of the interactions after the first purification step and assigned the corresponding risk. If there is a disparity between the two, a third pharmacologist evaluated the same and defined.

Table 2. Lexicomp® terminology.

Severity	Action	Description
A	*Unknown interaction*	The data have not demonstrated pharmacodynamic or pharmacokinetic interactions between agents
B	*Not action required*	The data demonstrate that the specified agents may interact with each other, but there is little or no evidence of clinical interest resulting from concomitant use
C	*Monitoring*	The data demonstrate that the specified agents may interact with each other in a clinically meaningful way. The benefits of concomitant use of these two medications usually outweigh the risks. An appropriate monitoring plan should be implemented to identify potential negative effects. Adjustments may be necessary dose of one or both agents in

		a minority of patients
D	*Consider modification of treatment*	The data demonstrate that the two drugs can interact with others in a clinically significant way. A specific patient assessment should be conducted to determine whether the benefits of the combined therapy outweigh the risks. Specific actions to be taken in order to obtain the benefits and / or minimize the toxicity resulting from concurrent use of agents. These actions may include aggressive monitoring, empirical dose changes, the choice of alternative agents
X	*Avoid combination*	The data demonstrate that the specified agents may interact with others in a clinically significant way. The risks associated with the concomitant use of these agents usually outweigh the benefits. These agents are generally considered contraindicated.

So the categories I, II, III and IV of the first stage be re analyzed and reclassified using the nomenclature A, B, C, D and X of Lexicomp®.

As a first step before starting the analysis of interactions, DDI drugs not available in Argentina were eliminated. So from the total of 4148 DDI (768 level I, 1736 level II, 1591 level III and 53 level IV) were discarded in the first instance 381 cases, since this drugs are not available or authorized for use in the country.

For the remaining 3767 pairs of drugs, that generated some interaction, the evaluation task was performed by two clinical pharmacologists. Of the 3767 interactions evaluated the degree of agreement between the two observers was very good. However in cases where there was disagreement, a third pharmacologist evaluated all cases where there had been no match for defining risk. The final database included 3767 DDI re-categorized as level I (437), level II (1713), level III (1563), level IV (54).

In the second stage, the DDI classified as Level I and II (2150) were reclassified to level X or D 683 (548 X and 135 D). This process bases debug and modify the value of risk of several pairs of drugs, which meant a reduction of 69% of interactions with important clinical significance. For this stage the strength of agreement was also good, and discrepancies were defined by a third pharmacologist.

Validation of pharmacological databases for use in a CDSS integrated into an EHR from commercial databases is a complex but necessary process. Adapting to health care settings and the local reality of the health system will impact the alerts that interrupt clinical workflow and acceptance of electronic prescribing alerts. The 69% reduction in the number of possible DDI would alert a possible interaction during the medical procedure not only impacts the quality of alerts, but on the quality of information for the physician and patient. At the same time reduces the possibility of false positives with consequent alert fatigue.

In this paper the concordance between observers was very good, which adds an extra value to the validation process of the knowledge databases. The way on observers classified the DDI was based on the pharmacological and pharmacokinetic potential changes of DDI, and accordingly the clinical consequences. The database Lexicomp® better fits this model, so we took the decision to use it for the award of levels D and X.

The lack of primary literature to evaluate commercial databases hinders its applicability in a particular scenario. The DDI databases vary by country and its laws, the users, the characteristics of the patient population, funding and technology infrastructure.

3.3. Modification and validation of a knowledge database on drug - drug interactions

In order to select cases of real and representative of the different levels of care in our network, was carried out a work to analyze the frequency of potential drug-drug interactions in pharmacological indications of the different levels of care and analyzed the characteristics of the most clinically significant. The study population in order to cover the widest possible spectrum of care processes implied two care models of drug prescriptions, episodic and longitudinal (outpatient). The episodic model looked pharmacological requirements of the care received by patients in both the central emergency and inpatient episodes; the instructions given in this care model are updated by the attending physician daily. The longitudinal model considered pharmacological prescriptions made by professionals in outpatient visits, these particulars are updated as needed in the patient's medication list in the EHR.

In both models of care, when a new drug indication was registered by a professional in the EHR, new drugs and preexisting indicated were combined and then contrasted with the knowledge base in the system in order to reach for potential DDI. The pair combinations of drugs that showed a positive result, after being processed with the System were considered for analysis. Both the longitudinal model and the episodic one was recorded only the first occurrence of the pair of drugs that generated a potential DDI, discarding subsequent repetitions during the same episode.

Data Analysis: A descriptive cross-sectional study in which two types of units of analysis were considered was performed: the only positive combinations, by patient or episode, in the year of study, in order to determine their impact; and on the other hand, patients who met the inclusion criteria in order to know how many of them could potentially suffer at least one DDI. Data are presented as mean and standard deviation (SD). In order to obtain the frequency of occurrence of DDI by the severity of the clinical cases seen in the episodic care model, the requirements were grouped into critical episodic (those made in critical care units in hospital and emergency center) and episodic not critical (the rest). The characteristics of the DDI were analyzed according to the amount of co-prescription drugs, their potential clinical significance (severity of the interaction) and taxonomy of recommendations (actions) contained in the knowledge database. Of these groups the serious severity selected and recommending an action to avoid the absolute torque joint use drug, and that this subset includes active and intrusive process alerts prescriptive. In this last subgroup of the prescribing professional specialties analyzed and the routes of administration.

Between March 2011 and February 2012 on the episodic model of care drug prescriptions, 1,587,167 drug combinations were generated, showing 19,162 potential DDI. From a total of

36,013 patients treated in this model of care, 6,338 had at least one DDI, with an annual incidence of 17.6 per 100 patients with DDI patients seen. While in ambulatory model drug combinations were 4,084,043 observed potential DDI in 29,251 opportunities. From a total of 55,119 patients treated in the longitudinal model, 15,267 had at least one DDI, with an annual incidence of 27.7 per 100 patients with DDI patients.

Once made in analysis of frequency of occurrence of potential DDI model episodic attention was divided into episodic critics (those made in the critical care units of hospital and emergency center) and episodic non-critical (the rest) in order to obtain different combinations grouped by positive indirect appearance in the complexity of the clinical cases. First the amount of drugs administered simultaneously (co-prescribed) when generating the DDI, divided by the different levels of care, showing a maximum of 5 to 10 concurrent drugs prescribed, mean were analyzed in the critical sectors of 11.76 (SD 4.70), in non-critical of 11.68 (SD 4.63), and outpatient 11.19 (SD 8.51).

In a previous study, the first phase of debugging the knowledge database for the Interactions System contemplated removing multiple interactions considered irrelevant, by classifying the remaining clinical significance (severity) in beneficial, mild, moderate and severe interactions. In this study, positive combinations tested were grouped according to this classification. Of the 48,413 total observed potential DDI, 3,180 were severe (6.6%), of which 167 were in the episodes grouped as critical, 1,694 in non critical and 1,319 in the outpatient setting.

In previous work, taxonomy of recommendations for actions to be taken by the practitioner, in order to deliver the message of the alert a specific action to perform will also drew up and that acceptance of that action is accounted for as a cancellation alert. In applying this taxonomy to the knowledge database, each DDI could have more than one recommendation. The recommendation "Avoid combination" was the only one considered in the EHR as an active and intrusive (regardless of severity) alert. As with severity, in this paper, the DDI potential observed were grouped according to the model of care and according to the above taxonomy, being 301 potential DDI avoid combination, not positive combinations in critical incidents, 23 in non-critical and 278 in the outpatient setting.

In order to create representative clinical cases of our clinical reality for the user-centered redesign of alerts, and to focus the second treatment stage in our database for interactions, we select the most frequent potential DDI in our subgroup represented by the DDI of "high" severity (no matter what action or actions recommended in the taxonomy) and those recommending action "Avoid combination" (no matter how severe they had). Subsequently those with both attributes were considered only once (subtracted from the total) for the net number of potential DDI that would have been presented to professionals and active and intrusive alerts. In this subgroup analysis of a net total of 3,356 positive combinations, 167 episodes were classified as critical, 1,709 as non critic and 1,480 in the outpatient setting were found.

When the characteristics of this subgroup were analyzed by specialty doctor who performed the indication can see that cardiology and internal medicine are the specialties most exposed to positive combinations. Because the route of drug administration is a consideration to avoid false positive alerts we were analyzed which route was frequently prescribed in the potentially active alerts, resulting intravenous and oral routes the most frequently used.

3.4. Redesign of the alert interface

For the redesigned interfaces alert, a team consisting of 3 doctors and 2 computer usability specialists work in the process of designing user-centered interfaces for the development of a new support system for warning drug - drug interactions at the time of prescription. The project was raised in iterative steps.

In total, in the three stages, 24 doctors participated (Table 1).

Data	Value
Sex	male 58%
Age (mean in years)	33
Years of graduated (mean)	9
Years of experience using the EHR (mean)	7
Setting	outpatient 37%
	inpatient 25% (20% non intensive care - 5% intensive care)
	Both 38%

TABLA 1: Users profile

STEP 1: INDAGATION

This first stage consisted of observations and contextual interviews to physicians who perform both electronic prescriptions in the outpatient setting and inpatient areas. In these interviews, semi structured questionnaires dealing topics and scenarios concerning the processes of drug prescribing in situations where drug interactions are presented were performed. From the analysis of these interviews were generating low-fidelity prototypes, in order to confront the ideas that emerged from these interviews with the design of interfaces for interaction with medical drug – drug interaction alerts.

Profile of participants: at this stage physicians working in ambulatory care, inpatient in critical and not critical areas participated in the study. The minimum required experience was 4 years of use of our EHR, trying to select participants with experience in the prescription process that could convey their knowledge in the field (know how). At this stage a semi-structured questionnaire to guide the user towards dynamic test cases, basing these on real clinical cases were created using the case study as the incidence of possible interactions in relation to the history of prescriptions presented (17).

6 doctors participated in the first stage, the interviews in this stage were the basis for structuring the prototypes. Emerges from these interviews that the DDI is a common concern among physicians and the tools that support these issues would be useful in this instance. From this concept, several participants took pertinent comments that have agreement with those published in the literature, such as the difficulty of finding good resources for detecting interactions, poor interface design, the amount false positive, and alert fatigue that this causes. We took what was expressed by users referring to past experiences to the structuring of the prototypes that will be used in the following steps. They also expressed the need for convenience or alerts provide information and guidance concerning the conduct to follow.

STEP 2: PARTICIPATORY DESIGN:

From the previous stage and on the basis of low-fidelity prototypes stage participatory design was performed, where the participating physicians, through their opinions arising from the interaction with the first prototypes were guiding the development of a new prototype closest to the user feedback. Were performed in this instance 2 cycles of prototyping and testing. At this stage the focus was qualitative, seeking saturation domain. The opinions and thoughts of physicians were obtained and recorded from the Think Aloud technique (18). The experiments were recorded on a mobile usability lab, and tests were carried out mainly in the workplace participants. Participants in this stage different users of the above but with a similar profile. The script used in the test was also based on real cases. At this stage, two prototypes were used, the 1st made in Balsamiq (19) was printed on paper and showed to the users, the 2nd done in Balsamiq was exported and used in order to reproduce the prescription process as closely as possible.

At this stage, a different medical group as above, from participatory design techniques, generated, along with the team carrying out this study, a design of the interfaces to be used when facing a DDI alert.

The results at this stage were analyzed by non-stringent qualitative techniques, in order to analyze the results and semi structures the results. The opinions given at this stage were: alerts were generally well received, were highly valued the ability to take actions from the same alert, without interrupting the workflow and restart the prescription process. Recommended actions that are integrated as operations were received as a great advantage. On this workflow, this was the most complex to elaborate on the design of interfaces. Among the negatives, navigating the various options offered by an alert, were complex. These results were considered for the redesign and re testing of prototypes, until they were considered adequate by users. Comments from users about the relevance of an alert appears or were not assessed and taken into account for debugging knowledge databases and developing test cases. Perhaps the main result of this stage was to understand, from the views of users, the interface should be action-oriented, and not just information. In other words, the user wanted to see not only the data, but perform the recommended action from the same screen.

STEP 3: USABILITY TEST

High fidelity prototype was created in Axure (20) for testing usability, which was presented as a functional prototype to different users of the participants in previous stages. In turn, this instance is used for measuring EFFECTIVENESS (understood from two variables, the first referring to the course pursued, i.e., if they ignore the warning or take into account, being the effective design if the alert is taken into account and the recommendations are followed. The other endpoint is whether they can complete the process of prescribing) and SATISFACTION (which was assessed using a questionnaire SUS -. system usability scale (21)).

EFFECTIVENESS: the first variable, understood as the course pursued, i.e., if they ignore the warning or take into account, showed the following results: of the 24 participating physicians, 11 physicians ignored the warning (45.8%) and 13 (54.2%) agreed.
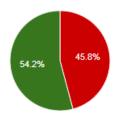
Figure 2: effectiveness of the alert acceptance

The other measure of effectiveness is whether it can finish the prescription process, in which the following results were evident: 13 (52.17%) physicians completed the task without difficulty, 10 (43.48%) completed the activity with questions, 1 (4.35%) with some errors and there were no serious errors that can´t allow to complete the action.
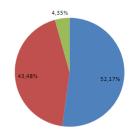

Figure 3: effectiveness of alert process

The number of errors was also measured during the process and are shown below: no error 82,6%, small mistakes 13%, severe mistake 4,4%
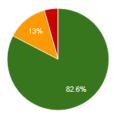

Figure 4: Errors

SATISFACTION, which was evaluated from a SUS questionnaire, yielded an average value per participant of 77.90 on a scale of 0 to 100 that indicates a value more than adequate, this equals a percentile of 83%, which means in other words, that the acceptance rate of the system is above 80%.

4. Discussion

Structure, validate and adapt the knowledge databases that served as a substrate for the development of this system resulted extremely difficult, in the same way, the creation of clinical cases also resulted complex, as they refer to rare problems that doctors do not handle usually,

what is presented as one of the challenges for the design framework, in this sense, the use of DDI alert systems is not easy for training because due to their low prevalence, it may be a long time from training until the appearance of the case, so the challenge is that these interfaces should be as intuitive as possible (having a short or fast learning curved), then there lies the benefit of investing time and resources in the participatory design of this type of support systems.

As for the interface design process, the parameters in the studies were more than satisfactory. From the detailed analysis of the metrics considered in the later stages, both the values of effectiveness, and satisfaction were improved to achieve the final prototype that will be used in the last stage. With respect to satisfaction, it is interesting to note that in comparison with the literature, where these types of systems have yielded no positive values, percentile values greater than 80% shows the importance of involving users in the design of the system. With regard to the acceptance of the recommendations, although a percentage above 50% is generally low impact, this performance is more than acceptable in this particular topic, where similar studies have thrown alerts omission rate much higher.

Getting doctors to participate in the test was not easy, however the number of participants was appropriate as many users as needed were interviewed to obtain saturation.

Future lines: the final stage will be held by the final prototype, with which laboratory test will be performed from cases generated from the actual incidence based on the frequency of cases recovered in pre analysis.

Limitations: This study was conducted at a single center, with doctors trained in the same institution, so that the processes for incorporating external validation must be done elsewhere. On the other hand, the correlation between the clinical case and physician specialty was not always desired by both, some physicians may face situations not common practice, so the behavior is not taken from the knowledge of field, but influence by the alert itself, which tends to select "suspend" rather than harm.

5. Conclusion

Create a CDSS for making decisions about drug - drug interaction is a complex process that requires supportive evidence, structured databases, good interface design and trained staff to adapt the evidence to the healthcare context of a health institution.

6. Bibliography

1.   Greenes RA. Clinical Decision Support: The Road Ahead. Academic Press; 2011. 600 p.

2.   Bates DW, Kuperman GJ, Wang S, Gandhi T, Kittler A, Volk L, et al. Ten Commandments for Effective Clinical Decision Support: Making the Practice of Evidence-based Medicine a Reality. J Am Med Informatics Assoc JAMIA. 2003;10(6):523–30.

3.   Van der Sijs H, Aarts J, Vulto A, Berg M. Overriding of drug safety alerts in computerized physician order entry. J Am Med Informatics Assoc JAMIA. 2006 Apr;13(2):138–47.

4.   Luna D, Otero V, Canosa D, Montenegro S, Otero P, de Quirós FGB. Analysis and redesign of a knowledge database for a drug-drug interactions alert system. Stud Health Technol Inform. 2007;129(Pt 2):885–9.

5.   Luna, D., Gonzalez Bernaldo de Quiros, F., Martinez, M., Gambarte, M. L., Morchón, A. ¿Porque se ignoran los alertas sobre interacciones farmacológicas? Buenos Aires; 2004.

6.   Bates DW, Spell N, Cullen DJ, Burdick E, Laird N, Petersen LA, et al. The costs of adverse drug events in hospitalized patients. Adverse Drug Events Prevention Study Group. JAMA J Am Med Assoc. 1997 Jan 22;277(4):307–11.

7.   Seymour RM, Routledge PA. Important drug-drug interactions in the elderly. Drugs Aging. 1998 Jun;12(6):485–94.

8.   Hartholt KA, van der Velde N, Looman CWN, Panneman MJM, van Beeck EF, Patka P, et al. Adverse Drug Reactions Related Hospital Admissions in Persons Aged 60 Years and over, The Netherlands, 1981–2007: Less Rapid Increase, Different Drugs. PLoS ONE. 2010 Nov 12;5(11):e13977.

9.   Kuperman GJ, Bobb A, Payne TH, Avery AJ, Gandhi TK, Burns G, et al. Medication-related clinical decision support in computerized provider order entry systems: a review. J Am Med Informatics Assoc JAMIA. 2007 Feb;14(1):29–40.

10. Phillips DP, Christenfeld N, Glynn LM. Increase in US medication-error deaths between 1983 and 1993. Lancet. 1998 Feb 28;351(9103):643–4.

11. Classen DC, Pestotnik SL, Evans RS, Lloyd JF, Burke JP. Adverse drug events in hospitalized patients. Excess length of stay, extra costs, and attributable mortality. JAMA J Am Med Assoc. 1997 Jan 22;277(4):301–6.

12. Fanikos J, Cina JL, Baroletti S, Fiumara K, Matta L, Goldhaber SZ. Adverse Drug Events in Hospitalized Cardiac Patients. Am J Cardiol. 2007 Nov 1;100(9):1465–9.

13. Glassman, P. A., Simon, B., Belperio, P., & Lanto, A. Improving recognition of drug interactions: benefits and barriers to using automated drug alerts. Med Care. 2002;40(12):1161–71.

14. Fernán González Bernaldo de Quirós, Daniel Luna, Analía Baum, Fernando Plazzotta, Carlos Otero, Sonia Benítez. Incorporación de tecnologías de la información y de las comunicaciones en el Hospital Italiano de Buenos Aires. CEPAL;

15. First Data Bank - Evaluation of Drug Interactions | EDI [Internet]. Available from: http://www.fdbhealth.com/fdb-medknowledge-clinical-modules/drug-drug-interaction/

16. Lexicomp [Internet]. Available from: http://www.lexi.com/

17. Daniel Luna MD. MSc cand. PhD cand, Martín Waldhorn MD, , Lic. Adriana Ianicelli1, Marcelo, Risk Ing. MBA MSc PhD3, y Fernán González Bernaldo de Quirós MD MSc FACMI. Drug-drug interaction in a healthcare network of Argentina: frequency and characteristics. Brasil; 2012.

18. Jaspers MWM, Steen T, van den Bos C, Geenen M. The think aloud method: a guide to user interface design. Int J Med Inf. 2004 Nov;73(11-12):781–95.

19. Balsamic. Available from: https://balsamiq.com/

20. Axure. Available from: http://www.axure.com/

21. P. W. Jordan, B. Thomas, B. A. Weerdmeester, & A. L. McClelland. SUS: a "quick and dirty" usability scale. SUS: a "quick and dirty" usability scale.

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