

# Look alike/sound alike drugs: a literature review on causes and solutions

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**Abstract** *Background* The implementation of preventive measures of look-alike/sound-alike drugs incidents has given rise to a fundamental rule in Clinical Risk Management, but the problem is underestimated, endorsed by the absence or inadequate presence of specific uniformed procedures. In literature, there are few reviews about look-alike/sound-alike drugs. *Aim of the review* To collect and summarize best practice and significant technological solutions proposed by different disciplines involved in look-alike/sound-alike drugs limiting solution research. *Method* A PubMed (any date) and EMBASE (all years) search was conducted in January 2013 with look alike sound alike drug [look AND (sound/exp OR sound) AND alike AND (drug/exp OR drug)] as search term. Later, references were selected focusing on look-alike/sound-alike drugs original research describing incident, identifying health operator difficulty, testing any type of intervention against errors, reporting a qualitative or quantitative description of the look-alike/sound-alike drugs errors. *Results* Forty and ninety-four articles were identified by a PubMed and Embase search respectively, with search term and limits described above. Later, articles not respecting selection criteria or overlapping were eliminated. In the end, 14 references were considered, 10 being from PubMed and 4 from Embase. *Conclusion* Results show and confirm the multidisciplinary interest of the research on look-alike/

sound-alike drugs, and the difficulty to perform systematic review or metaanalysis for many clinical questions that have great relevance. This review has identified technology and management solutions that could effectively limit, or eliminate, look-alike/sound-alike drugs errors in hospital wards, or outside the hospital where the risk is more uncontrollable: however look-alike/sound-alike drugs therapy errors are not supported by reliable statistics but events reported in the literature can not be underestimated.

**Keywords** Drug names · Look alike/sound alike · Medication errors · Patient safety · Risk management

## Impacts on Practice

- All medical professional can prevent look-alike/sound-alike drugs incidents by applying very simple preventative measures.
- Clinical Pharmacist should consider and discuss look-alike/sound-alike drugs risks, especially when patients are discharged from hospital.
- Some professionals consider a look-alike/sound-alike drugs risk as “banal”, but it is a very complex problem to manage properly.

## Introduction

In 1973 Benjamin Teplitsky [1] published a list of look-alike or sound-alike drugs (LASA) names. This was the first of several alerts on confusion caused by LASA associated with therapy or dispensing errors.

Forty years since this alert, the implementation of preventative measures of LASA incidents has given rise to a

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fundamental rule in Clinical Risk Management. Nevertheless, today the problem is underestimated, endorsed by the absence or inadequate presence of specific uniformed procedures.

Quantitative estimates of LASA incidents are lacking [2]. There are some examples in literature, but they are not statistically relevant to improve a real quantification: for example Berman generically described errors due to LASA as common and responsible for thousands of deaths and millions of dollars in costs each year in USA: more than 25 % of all medication errors are attributed to name confusion, and 33 % due to packaging or labelling confusion [3].

Some studies analyzed the problem in a specific therapeutic area, as Basco et al., that tested a screening approach to detect 11 LASA paediatric drug pairs in outpatient prescriptions for patients who usually received one drug in a pair: on 1,420,091 prescriptions for 173,005 subjects there were 0.03 LASA errors for 1,000 prescriptions, and the rate of LASA paediatric drug errors appearing much lower [4].

Generally LASA drugs are correlated to dispensing errors, but more disciplines are involved in research solutions, as orthography, packaging, regulatory affairs and clinical management, because they could influence human factors and limit errors. Therefore solutions could be offered by observations in pharmaceutical care area, in technological area, in physiological analysis, in research of new design languages.

Literature offers several examples of this multidisciplinary attention, but there are few reviews that summarize results of current research about LASA.

### Aim of the review

The aim of this review is to collect and summarize best practice and significant technological solutions proposed by different disciplines involved in LASA limiting solution research.

### Method

A PubMed (any date) and EMBASE (all years) search was conducted on 23th January 2013 with *look alike sound alike drug* [look AND (sound/exp OR sound) AND alike AND (drug/exp OR drug)] as search term.

Later, references were selected focusing on LASA original research describing incident, identifying health operator difficulty, testing any type of intervention against errors, reporting a qualitative or quantitative description of LASA errors. Reviews, original research considering

LASA secondary to other topics, reports on general procedures of Clinical Risk Management, pieces containing opinions or lists of LASA were excluded.

Assuming the heterogeneity of the research on LASA, with different multidisciplinary outcomes and the real difficulty to have sufficient data on specific outcomes to perform a systematic review or a meta-analysis [2], it was designed a specific methodology to make a narrative review of the articles collected: this method is schematized in Fig. 1. Considering Reason theory on “person” approach and “system” approach of the errors in medicine [5], references were pooled into two groups. In one group, “person group”, are grouped references studying and analyzing health operators and patients connections with LASA, describing setting, drugs involved, incident or problem signalled, effect on patient, intervention or proposal to solve problem. References of the other group, “system group”, consider non direct human factors influencing or favouring LASA criticality in a sanitary setting, and intervention or proposal to solve problems.

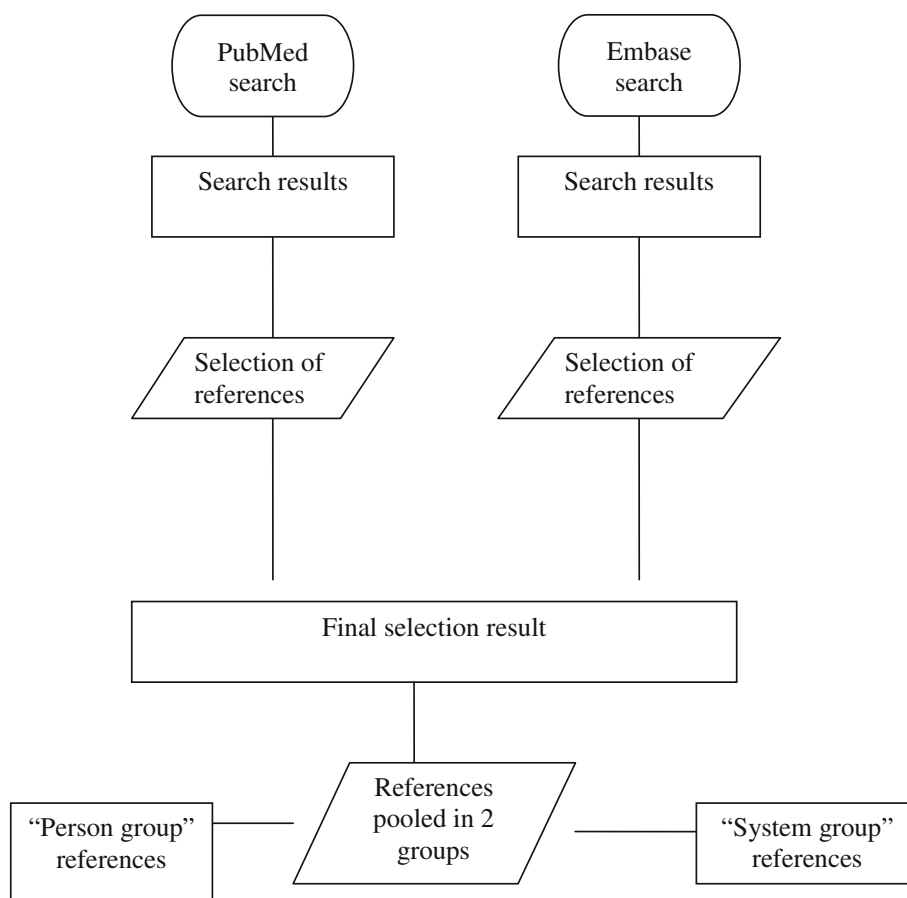
### Results

Forty and ninety-four articles were identified by a PubMed and Embase search respectively, with search term and limits described above. Later, articles not respecting selection criteria were eliminated. As schematized in Fig. 2, 14 references were considered, 10 from PubMed and 4 from Embase. None of references appear in both databases. The heterogeneity of the study objects and results confirm of the difficulty to perform a classic systematic review or meta-analysis. Consequently, the model proposed for a narrative review was applied: six studies were included in “person group”; eight in “system group”.

#### “Person group”

An overview of the included studies in this group, is presented in Table 1. Thuoy et al. [6] described that in an Emergency Department, a patient died after receiving 10 mg hydromorphone, tablet, instead of the 10 mg of morphine, tablet, which was prescribed. A nurse made this error for the look-alike packaging of the two drugs, produced by the same manufacturer. The patient was discharged shortly after the drug was administered, and without reassessment. On the way home, the patient experienced respiratory arrest and could not be revived. They considered that Emergency Departments is the prime locations for mix-ups with look-alike and sound-alike drug names and packaging. Frequent verbal orders, crowded storage spaces, and the need for rapid administration of medications could contribute to errors, and opioids, lipid-

**Fig. 1** Flow chart on specific methodology designed to review the articles collected. Considering the real difficulty to have sufficient data on specific outcomes to perform any sort of systematic review or meta-analysis, references were pooled into two groups: “person group”, studying and analyzing a connection of health operators and patients with LASA, and “system group”, considering non direct human factors influencing LASA criticality

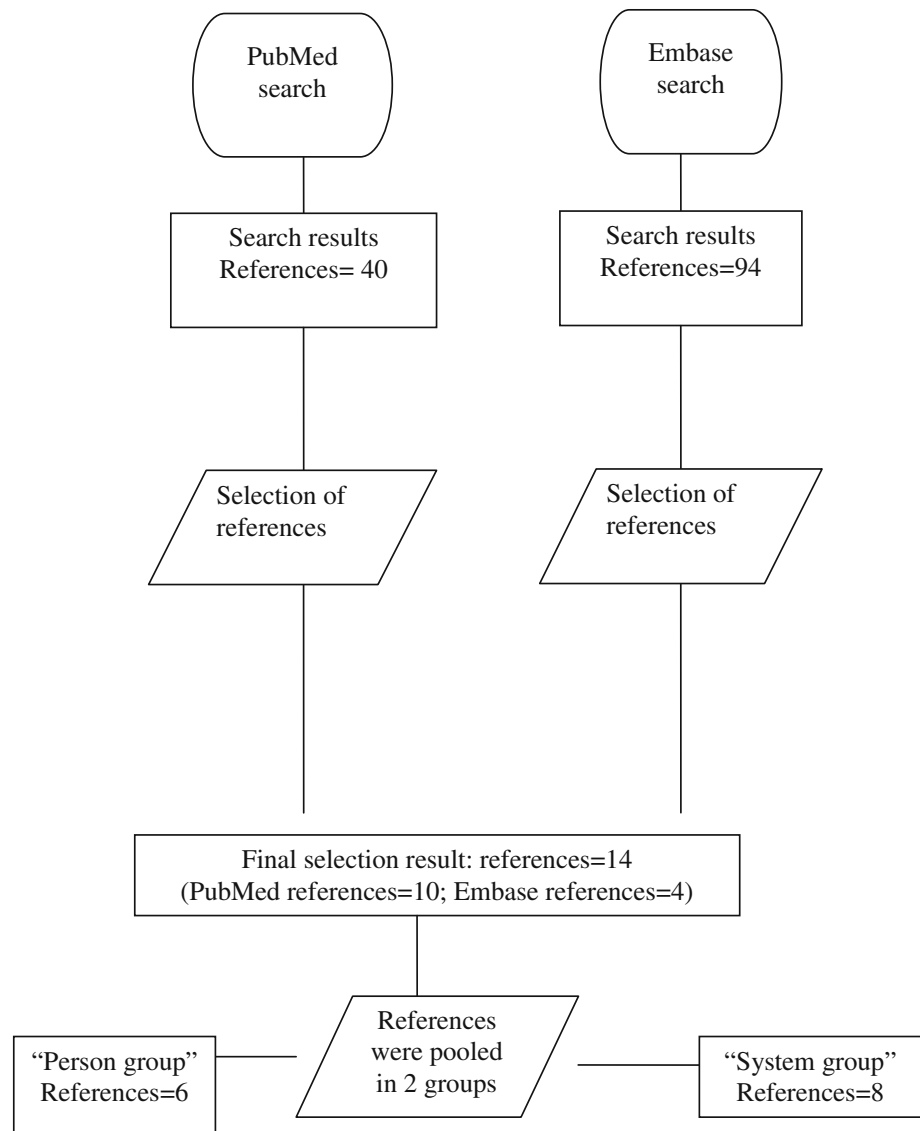


based products, and newer insulin mixtures are the drug classes in which medication names are commonly confused.

Cohen et al. [7] described a patient, who had black stools and tongue, relapsed from orthopaedic surgery with a prescription of *Maalox Total Stomach Relief*<sup>®</sup>, an “over the counter” drug containing aluminium-magnesium hydroxide and simethicone, for nausea and upset stomach. This event was manifested because he took *Maalox*<sup>®</sup>, containing bismuth subsalicylate which can cause black stools and tongue: the patient was confused by the products packages, that were similar, in white plastic containers, same size and shape, and the name *Maalox*<sup>®</sup> was highlighted on the front label panel of each product, with minimal differentiations. Sauberan et al. [8] studied five events in a paediatric ward. Three resulted as near misses events, with the potential to cause harm; two reached the patients but did not cause harm. The medication mix-ups involved adult and neonatal phytomenadione injectable emulsion, sodium citrate injection and vancomycin-heparin combination injection, adult Tetanus-Diphtheria-Acellular Pertussis vaccines and infant Diphtheria-Tetanus-Acellular Pertussis [DTaP] vaccines, *Haemophilus B* and DTaP vaccines, and cisatracurium and vecuronium. These errors

depending by weaknesses in the system of neonatal medication storage: through a collaborative approach of the operators, that was involved a reorganization using a differently coloured labelling scheme for products nearly identical, changing the infant vaccine order and storage. Likewise Mc Coy reported a 69-year-old woman admitted to the oncology unit for correction of electrolyte imbalances, who was mistakenly administered Primacor<sup>®</sup> (milrinone) instead of potassium chloride, reflecting a look-alike packaging medication error [9]. Later, the medical center developed and implemented process changes, including moving and reorganizing shelf storage bins, enhancing labeling for intravenous medications with similar packaging, tracking and responding to automated dispensing cabinet-filling errors, and revising processes for selecting and maintaining the list of look-alike, sound-alike medications to include the “real time” review of new medications added to the formulary and changes in packaging resulting from contract changes or drug shortages. Approaching pharmacy staff, Acciarri et al. [10] studied the absence of LASA alert measures in the supply chain from pharmacy to wards. Analyzing the Anatomical Therapeutic Chemical Classification System (ATC) groups with high risk of LASA, a table for operators was created,

**Fig. 2** Flow chart on results of the review method applied. 14 references were considered: 10 being from PubMed and 4 from Embase. Six studies were included in “person group”; eight in “system group”



pointing out LASA, consequences of confusion and strategy to avoid them. Furthermore, security symbols and special labels were put on packaging of high-risk drugs. In the hospital supply chain, Joshi et al. [11] analyzed difficulties encountered by nursing staff and LASA medications errors associated with electronically ordered drugs to the pharmacy. Identical brand names with the same generic name had the highest occurrence at 84.01 %; the lowest occurrence, 4.51 %, had sound alike drugs with the same generic name only. As a solution, it was suggested to write the generic name of the prescribed drug in brackets along with the brand name.

#### “System group”

Automated measures of similarities between medication names were, for the first time, proposed by Lambert [12].

This was based on three automated quantitative measures, bigram and trigram similarity, and Levenshtein distance. On the basis of the three similarity measures, three parallel and unmatched case-control tests for predicting confusion, based on orthographic similarity as risk factor for medication errors, were developed and evaluated. The test correctly identified 91 % of pairs, errors or controls, with a sensitivity of 84 % and a specificity of 99 %.

In another study, Lambert evaluated other tests using twenty-two computerized measures of orthographic similarity, distance, and phonetic similarity, to compute similarity/distance scores for  $n = 1,127$  cases and  $n = 1,127$  controls [13]. Cases had significantly higher similarity scores than controls. Every measure of similarity proved to be a significant risk factor for error. There was a significant increasing trend in the odds-ratio as a function of similarity. A three-predictor logistic regression model had cross-

**Table 1** “Person group” references

| “Person”                  | Reference        | Setting                  | Drugs involved   | Incident and/or problem signalled  | Effect on patient       | Intervention or proposal to solve problem   | Results  |
|---------------------------|------------------|--------------------------|--|--|-------------------------|---|--|
| Nursing operator, patient | Thuoy et al. [6] | Emergency department     | Hydromorphone (A); morphine (B)  | Nurse administered A instead of B<br>Look alike packaging                                    | Death                   | Strategies reducing LASA mix-ups with high-alert medications, and considering: verbal orders, storage, rapid drug administration<br>Strategies considering patients, who take numerous prescription medications | Verbal orders: “read back” the order, spelling the name aloud<br>Storage: do not store look-alike medications side-by side or alphabetically<br>Reminders and alerts: find out about placing alerts for LASA products<br>Differentiate: apply “name alert” labels to look-alike products. Use tactile clues, bright colored highlighters to draw out names. Use “tall man” lettering<br>Patients: upon discharge, provide them with written information about their drugs, including the brand and generic names |
| Patient, Physician        | Cohen et al. [7] | Orthopaedic surgery ward | <i>Maalox Total Stomach Relief</i> ® (C) (aluminum-magnesium hydroxide and simethicone); <i>Maalox</i> ® (D) (bismuth subsalicylate) | Patient took C instead of D<br>Look alike packaging<br>Physician prescribed D without detail | Black stools and tongue | Alert practitioners about brand-name extensions with <i>Maalox</i> ®, especially since hospitals will need to purchase the products in look-alike bulk bottles  | Patients should be warned about brand name extensions and advised to check the active ingredients before purchase  |
| Nursing operator, patient | Mc Coy [9]       | Oncology unit            | Primacor® (milrinone) (E); potassium chloride (F)  | E administered instead of F for correction of electrolyte imbalances<br>Look alike packaging | Adverse event           | Development and implement control systems limiting errors in drugs dispensing process   | Reorganization of shelf storage bins<br>Special label for intravenous medications with similar packaging<br>Tracking of automated dispensing cabinet-filling errors<br>Revising processes for selecting and maintaining the list of look-alike, sound- alike medications<br>Review of new medications added to the formulary and changes in packaging resulting from contract changes or drug shortages  |

Table 1 continued

| “Person”                  | Reference            | Setting           | Drugs involved  | Incident and/or problem signalled   | Effect on patient  | Intervention or proposal to solve problem  | Results   |
|---------------------------|----------------------|-------------------|---|---|--|--|---|
| Nursing operator, patient | Sauberan et al. [8]  | Pediatric ward    | Neonatal phytonadione injectable emulsion (G);<br>Adult phytonadione injectable emulsion (H);<br>Sodium citrate injection (I);<br>vancomycin-heparin combination injection (J);<br>adult tetanus-diphtheria-acellular pertussis (K);<br>infant diphtheria-tetanus-acellular pertussis [DTaP] vaccines (L);<br>haemophilus B(M);<br>cisatracurium (N);<br>vecuronium (O) | Medication mix-ups administration involved:<br>G instead of H;<br>I instead of J;<br>K instead of L;<br>L instead of M;<br>N instead of O<br>Look alike packaging | Three resulted in near misses with the potential to cause harm<br><br>Two errors reached the patients but did not cause harm | Resolution of problems in the system of neonatal medication storage, labelling, delivery, knowledge, and administration with a collaborative approach of operators | Coloured labelling scheme for products nearly identical;<br>Changing the infant vaccine order and storage<br><br>Instituting centralized and decentralized pharmacist review of pharmacy technician automated dispensing cabinet-filling activities |
| Pharmacy operators        | Acciarri et al. [10] | Hospital pharmacy | Drugs of local Health Service lists   | Operators denounced absence of LASA alert measures in the supply chain from pharmacy to wards   | /  | Resolution of problems in the system of medication storage, labelling, delivery, knowledge, with a collaborative approach of operators                             | A table edited for operators, pointing out LASA drugs<br><br>Security symbols, special labels, to put on risk drugs packaging   |
| Health operators          | Joshi et al. [11]    | Hospital wards    | Drugs of local health service lists   | High frequency of LASA errors associated at electronically drug orders to the pharmacy  | /  | Legal steps to stop the marketing of those brand names with intentional look alike and sound alike names<br><br>Local measures                                     | Local measures: write the generic name of the prescribed drug in brackets along with the brand name   |

validated sensitivity of 93.7 %, specificity of 95.9 % and accuracy of 94.8 %.

Kovacic et al. experienced the Levenshtein Distance and Bigram Similarity algorithms, same first and last letters, and Lexi-CompR on-line alerts to review the outpatient oncology formulary to identify potential LASA generic drug name pairs. Results indicated there are more potential LASA generic drug name pairs in the oncology formulary than are published in the literature. The risk detection methods used in this study identified unique and common LASA drug pairs. The Bigram Similarity algorithm identified 186 LASA drug pairs from 3,320 possible pairs. The Levenshtein Distance algorithm, same first and last letters, and Lexi-CompR methods identified 42, 75, and 38 LASA drug pairs, respectively. Five generic LASA drug pairs were identified in common by all four of the risk determination methods [14]. Similarly Phatak et al. [15] estimated frequencies of potential errors involving similarly named drugs using a retrospective claims database, and measured the association between frequencies of potential errors with the edit distance and normalized edit distance. 300 drug pairs studied, 106 [35.33 %] were involved in at least one potential error. A total of 1,138 dispensing episodes satisfied the criteria for potential errors. Frequencies of potential errors for drug pairs were negatively associated with edit distance, and normalized edit distance.

Kondrak and Dorr developed a test, named ALINE, which represented several experiences detecting drug-name confusions produced by high phonetic similarity. The method was based on phonetic transcription of the two names, which could reveal a sound-alike similarity that was not apparent in their orthographic form [16]. Gabriele categorized the typographic elements that shape visual communication and design materials, such as, content, composition/layout, typography, colour and visuals [17]. These aspects were especially analyzed in a test for 11 acute care hospital nurses, based on a design selected on the basis of the legibility and the capacity to create emphasis. The typographic variations consisted of, in the least extreme, a change from lowercase to uppercase characters; in intermediate, a contrast in character weight from standard to boldface (lowercase) characters; the most extreme, a contrast of black characters to white characters on a solid black rectangle. In the test, nurses read the pair “hydroxyzine- hydralazine”, presented in three lists of seven graphic combinations, according to the previous design criteria. Subsequently, in a second test, participants were asked to give their opinion regarding the ease in differentiating between drug names within a label context. Participants recognized more names with the use of uppercase characters than with boldface characters. However, as expected by Gabriele, white characters on the

black rectangle seemed to be most helpful in differentiating names and participants perceived that differentiating the name with uppercase characters did not make the names distinctive enough. All opinions were split evenly on the versions that used the boldface characters and those that used white characters on a black rectangle. In terms of effectiveness to differentiate look-alike/sound-alike drug names, this study indicated that the stronger degree of contrast provided by “tallman letters,” specifically, white text on a black rectangle, might help to make names more recognizable. To further support the use of tallman letters, in order to reduce errors, three experiments were made by Filik et al. [18]. He evaluated the proposal that highlighting sections of drug names using uppercase tallman lettering and/or colour may reduce the confusability of similar drug names. In Experiments 1 and 2, participants time to decide similar name pairs were the same or two different names was measured. Experiment 3 was a recognition memory task. Results from Experiments 1 and 2 showed that highlighting sections of words using tallman lettering can make similar names easier to distinguish if participants are aware of the intervention purpose. Results from Experiment 3 suggested that tallman lettering and/or colour does not make names less confusing in memory but may increase lecture attention. An example of successful implementation of the “tallman” letters, into the medication selection process in a hospital network (3 hospitals, 7 dispensaries and 40 ward medication storage areas), as a safety action to minimise the risk of selecting the wrong medication, was reported by Van de Vreede et al. [19]. The implementation consisted of three steps: a short LASA list was piloted in the inpatient dispensary for 6 months; a comprehensive LASA list was developed that consisted of 51 items to distinguish between generic names ( $n = 41$ ), brand names ( $n = 6$ ) and generic and brand name combinations ( $n = 4$ ); tallman letters were included into the pharmacy dispensing software of the hospital network. Table 2 resumes the most important features of “system group” studies.

## Discussion

Results show and confirm the multidisciplinary interest on LASA, and the difficulty to perform systematic review or meta-analysis for the various outcome measured in references considered.

The approach to the “person” has insufficient evidence to describe incidents from LASA in quantitative and qualitative terms, which contribute a complete statistical description of the problem. This confirmed that the true incidence of LASA errors is difficult to obtain due to poor reporting, differences in definitions of medication errors,



**Table 2** “System group” references

| “System”                 | Reference             | Setting              | LASA criticality observed   | Intervention or proposal to solve problem  | Results   |
|--------------------------|-----------------------|----------------------|---|--|---|
| Orthography of drug name | Lambert [12]          | Health structure     | Few procedures existing to ensure the safety of new drug nomenclature or to identify confusingly similar names from within existing databases | Evaluation of technological LASA alerts based on 3 orthographic similarity measures: Bigram similarity, trigram similarity, Levenshtein distance   | Tests correctly identified 91 % of LASA pairs, with a sensitivity of 84 % and a specificity of 99 %   |
| Orthography of drug name | Lambert [13]          | Health structure     | The high rate of name-confusion errors might be reduced; new and confusing names were not allowed on the market                               | Evaluation of technological LASA alerts based on 22 computerized measures of orthographic similarity, distance, and phonetic similarity  | Tests showed main rates sensitivity of 93.7 %, specificity of 95.9 % and accuracy of 94.8 %   |
| Orthography of drug name | Kovacic et al. [14]   | Oncology hospital    | Medication errors with oncology LASA  | Evaluation of technological alerts based on orthographic similarity measures: the Levenshtein Distance and Bigram Similarity algorithms, same first and last letters, and Lexi-Comp[R] on-line alerts  | From a list of 3,320 pairs: the Bigram Similarity algorithm identified 186 LASA pairs; the Levenshtein Distance algorithm, same first and last letters, and Lexi-Comp[R] methods identified 42, 75, and 38 LASA pairs, respectively   |
| Orthography of drug name | Phatak et al. [15]    | Health local service | Frequencies of potential errors involving similarly named drugs   | Test of technological alerts based on orthographic similarity measures: frequencies measures of potential errors with the edit distance and normalized edit distance   | 300 drug pairs studied, 106 [35.33 %] were involved in at least one potential error. A total of 1,138 dispensing episodes satisfied the criteria for potential errors   |
| Orthography of drug name | Kondrak and Dorr [16] | Health services      | Drug-name confusions produced by high phonetic similarity   | Development of a test, named ALINE   | Test could reveal a sound-alike similarity that was not apparent in their orthographic form   |
| Packaging aspects        | Gabriele [17]         | Acute care hospital  | Typographic and visual elements increase LASA errors  | Test of typographic label variations consisted in: the least extreme, a contrast in case - a change from lowercase characters to uppercase characters; a middle ground, a contrast in weight - a change from medium-weight characters to boldface [lowercase] characters; the most extreme, a contrast - a change from black characters to white characters on a solid black rectangle | Operators recognized more names with the use of uppercase characters than with boldface characters<br>White characters on the black rectangle seem to be most helpful in differentiating names<br>Names with uppercase characters did not make the names distinctive enough |
| Orthography of drug name | Filik et al. [18]     | Health organization  | Visual confusability of similar drug names  | Highlighting sections of drug names using uppercase “tallman” lettering and/or colour may reduce the confusability of similar drug names   | Highlighting sections of words using tall man lettering can make similar names easier<br>“Tallman” lettering and/or colour does not make names less confusable in memory  |
| Orthography of drug name | Van de Vreede [19]    | Hospital             | General errors associated with LASA   | Implementation of “Tallman” letters into the medication selection process in the hospital network  | Tallman letters were included into the pharmacy dispensing software, improving safety by minimising the risk of selecting the wrong medication  |



lack of time, fear of litigation, inability to determine causality, reluctance to admit error and cost [20]. LASA error could be identified as latent failures in the system, and also as “slips” [21], for their nature is unconscious and unplanned: the people who make them do not intend or choose to do so [21]. Slips are not easily preventable, and they are caused by wrong decisions based upon insufficient or inaccurate information.

Works of “*Person group*” reflect this opinion. Authors do not condemn health operators involved in errors, but evidencing the responsibility of “*Trade dress*”, the concept that underlies labelling and packaging issues for the drug industry, ignoring human factors, concepts of simplicity, standardization, differentiation, lack of duplication, and unambiguous communication, relevant to the medication-use process [22]. Defining effective solutions with the operators and according to their needs, is a proven approach. LASA error is a “slip” to prevent actions built on the weaknesses of the operator.

However the confusion in identification is committed also by patient: it is easier to detect incidents in hospital, but the risk of confusion remains also outside, especially for “over the counter” drugs which, in some countries, are offered for sale without the presence of pharmacist. In orthographic confusion, technology offers 22 detection methods of the orthographic similarity [16], whose prototypes were successfully detected in highly precise signaling of LASA pairs into lists of drugs more or less complex. When this technological approach cannot be supported, simpler measures of specific signaling can be effective, notifying to operator the risk of similarity graphics or literal, during storage. The use of graphics in “tallman” style stimulates the health care worker to increase the threshold of attention to differentiate well nomenclature similar, compared to other solutions, such as the quadrature of colored individual letters. There are not any national or international standards that unify these technological solutions but there are some initiatives by local health services. Absence of these standards is also associated with the lack of valid regulatory requirements that limit the confusion in the allocation of names and graphics to pharmaceutical products [15].

## Conclusion

Today the real difficulty remains to have sufficient data on specific outcomes and perform a classic systematic review or meta-analysis on LASA errors. References on this topic could be revised through an alternative model of literature analysis. LASA therapy errors are not supported by reliable statistics but events reported in the literature should not be underestimated. Research has identified technology and

management solutions that could effectively limit, or eliminate, LASA errors in hospital wards, or outside the hospital where the risk is more uncontrollable. To apply this solution, it is more advisable to introduce uniform standards in national or international regulatory legislation, which will implement this solution.

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**Conflicts of interest** The authors have no conflicts of interest to declare.

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