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ORIGINALS

Grading the potential safety risk of medications used in hospital care

Clasificación de los grupos de medicamentos según su nivel de riesgo en el ámbito hospitalario

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Abstract

Objective: The aim of this study was to stratify medications used in hospital care according to their potential risk.

Method: The RAND/UCLA Appropriateness Method was used. Anatomical Therapeutic Chemical subgroups were classified according to their potential risk. A literature search, bulletins, and alerts issued by patient safety organizations were used to identify the potential safety risk of these subgroups. Nine experts in patient/medication safety were selected to score the subgroups for their appropriateness in the classification. Two evaluation rounds were conducted: the first by email and the second by a panel meeting.

Results: A total of 298 Anatomical Therapeutic Chemical subgroups were evaluated. They were classified into three scenarios (low, medium, and high risk). In the first round, 266 subgroups were classified as *appropriate* to the assigned scenario, 32 were classified as *uncertain*, and none were classified as *inappropriate*. In the second round, all subgroups were classified as *appropriate*. The most frequent subgroups in the low-risk scenario belonged to group A "Alimentary tract and metabolism" (44%); the most frequent in the medium-risk scenario belonged to group J "Antiinfectives for systemic use" (32%); and the most frequent in the high-risk scenario belonged to group L "Antineoplastic and immunomodulating agents" (29%) and group N "Nervous system" (26%).

KEY WORDS
Risk assessment; Risk management; Medication errors; Hospital; RAND/UCLA Appropriateness Method.

Resumen

Objetivo: Estratificar los medicamentos utilizados en el ámbito hospitalario según el riesgo de provocar daño al paciente.

Método: Se utilizó la metodología RAND/UCLA para clasificar los subgrupos terapéuticos del código Anatómica, Terapéutica, Química según el riesgo de provocar daño al paciente. Para ello se realizó una revisión de la evidencia disponible en publicaciones, boletines y alertas de organismos de seguridad del paciente. A continuación se seleccionaron nueve expertos en seguridad del paciente/medicamento para evaluar la clasificación de los subgrupos terapéuticos: una primera ronda de evaluación por vía telemática y una segunda ronda en una reunión presencial en la que se presentaron y discutieron los resultados de la primera.

Resultados: Se evaluaron 298 subgrupos terapéuticos. Se clasificaron en tres escenarios (riesgo bajo, medio y alto). En la primera ronda se clasificaron 266 subgrupos como *adecuados* al escenario asignado, 32 subgrupos fueron clasificados como *inciertos* y ninguno fue clasificado como *inapropiado*. En la segunda ronda, todos los subgrupos fueron clasificados como *adecuados*. Los subgrupos más frecuentes en el escenario de riesgo bajo pertenecieron al Grupo A: "Tracto alimentario y metabolismo" (44%), en el de riesgo medio al Grupo J: "Antiinfecciosos para uso sistémico" (32%), y en el de riesgo alto al Grupo L: "Agentes antineoplásicos e inmunomoduladores" (29%) y al Grupo N: "Sistema nervioso" (26%).

PALABRAS CLAVE
Gestión del riesgo; Evaluación del riesgo; Errores de medicación; Hospital; Método RAND/UCLA.

Conclusions: Based on the RAND/UCLA appropriateness method, Anatomical Therapeutic Chemical subgroups used in hospital care were classified according to their potential risk (low, medium, or high). These lists can be incorporated into a risk-scoring tool for future patient/medication safety studies.

Conclusiones: La metodología RAND/UCLA ha permitido estratificar los subgrupos utilizados en el ámbito hospitalario según el riesgo potencial de provocar daño al paciente. Esta estratificación puede servir como herramienta para futuros estudios de seguridad en la utilización de medicamentos.

Introduction

Medication errors (ME) are important contributors to patient morbidity and mortality, and are associated with inadequate patient safety measures[1]. The severity of an ME can be graded according to its impact on the patient and/or its potential future risk to patients and the healthcare organization. This approach has the advantage that it can classify and analyse the severity of MEs that pass unnoticed because they have no effect on the patient. Moreover, this type of assessment is useful for prioritizing cases that require special monitoring, analysis, or urgent solutions[2].

The National Patient Safety Agency (NPSA) designed a risk matrix for grading MEs according to their potential future risk to patients and the healthcare organization. This matrix has two categories: *likelihood of recurrence*; and *most likely consequences*. However, details were not provided on the criteria by which a specific type of ME is classified according to its likelihood of recurrence and consequences[3]. Thus, the lack of definition allows room for subjectivity and researchers will interpret the risk matrix according to their knowledge and expertise[4].

Subjectivity can be reduced by standardizing the classification of the potential risk of an ME. In a previous article, we adapted the NPSA risk matrix to medication errors in medication administration records (ME-MAR). The definition of each grade of the *likelihood of ME-MAR recurrence* was based on the incidence of ME-MAR in our hospital, and that of the *most likely consequences* was based on the type of ME-MAR and the medication involved. We found that this adaptation was reliable. However, during this process, the degree of agreement differed according to the medication involved in the error. The highest degree of agreement was achieved on high-risk medications[5].

All medications can cause adverse events if they are incorrectly used. Nonetheless, certain medications are more dangerous than others and can have very severe or even catastrophic effects on patient health[6]. The Institute of Safe Medication Practices (ISMP) has provided a list of high-risk medications in hospitals[7,8]. However, lists of low- and medium-risk medications are not available. The hospital pharmacotherapeutic guide (HPG) not only includes high-risk medications but also unclassified medications, which may range from low to high risk. Therefore, the aim of the present study was to stratify medications in the HPG according to their potential risk.

Methods

The study was conducted between October 2015 and March 2016 in a 947-bed teaching hospital. The RAND/UCLA Appropriateness Method (RAM)[9,10] was used to stratify medications in the HPG according to their potential risk. The medications included in the HPG are classified according to the Anatomical Therapeutic Chemical (ATC) classification system[11] , and so the medications were evaluated per ATC subgroup.

The first step in the RAM was to identify scenarios, which were subsequently assessed by an expert panel in 2 consecutive rounds.

Information search and development of scenarios

In order to develop the scenarios (i.e., the stratification of the ATC subgroups according their potential risk), we conducted a review of MedLine publications (October 2005 to October 2015) on medications and their potential risk to inpatients. The search was restricted to the English and Spanish languages (see search strategy in Table 1). We selected studies that stratify medication risk or those that meet the following criteria: a) contain information on incidents caused by the clinical use of medications; b) report the number or percentage of incidents associated with each different medication /medication class, or provide sufficient information to calculate the number or percentage; and c) report the severity or the potential risk of these incidents.

This information was supplemented by searching the websites of safety organizations for bulletins and alerts referring to severe MEs[12-15], by consulting recent drug information[16, 17], and by reviewing high-alert medications lists published for hospitals by the ISMP [8].

Expert panel selection

The panel was selected according to the following criteria: a) expertise in medication and patient safety and management; b) expertise in medication use process (physicians, pharmacists, and nurses).

The panel comprised 9 experts: 3 physicians (a geriatrician, an internist, and a pharmacologist); 3 hospital pharmacists with clinical experience in geriatrics, paediatrics and rheumatology, and intensive medicine, respectively; and 3 nurses (the inpatient care chief nurse, the emergency department nurse manager, and the traumatology department nurse manager).

Expert panel evaluation

The experts participated in two consecutive evaluation rounds. In the first round, they received the following documents by email: the identified scenarios, the evidence-based summary, the definitions of terms, and instructions for rating.

The experts were asked to assess the appropriateness of the ATC subgroup to the assigned scenario. Their appropriateness was rated on a

Table 1. Search strategy used to search MedLine

SEARCH TERMS	
NO MESH: Medication/drug Medication error/drug error /adverse event/adverse reaction/incident Stratification/classification/list/scoring method Potential Risk/harm/severity High-risk drugs/ high-alert medication/risk profile Hospital	**MESH:** Risk management Drug-related side effects and adverse reactions Medication errors Hospital

Search strategy:
#1 «(medication OR drug) AND (medication error OR drug error OR adverse event or adverse reaction or incident) AND (stratification OR classification OR list OR scoring method) AND ((potential AND (risk OR harm OR severity)) OR high-risk drugs OR high-alert medication OR risk profile) AND hospital» [All fields]
#2 ((medication errors [MeSH Terms]) OR ("Drug-Related Side Effects and Adverse Reactions"[Mesh])) AND (risk management [MeSH Terms]) AND (hospital [MeSH Terms])
#1 OR #2

9-point scale, where 1 indicated "completely inappropriate" and 9 indicated "completely appropriate". Agreement was defined as no more than 2 panel members rating the indicator as being outside the same 3-point region as the observed median (i.e., 1–3, 4–6, 7–9). The median panel rating and interquartile range were calculated. Any median ratings that fell exactly between the 3-point boundaries (3.5 and 6.5) were included in the higher appropriateness category.

ATC subgroups with a median rating in the top third of the scale (7-9) without disagreement were classified as *appropriate*, those with intermediate median ratings (4-6) or any median with disagreement were classified as *uncertain*, and those with median ratings in the bottom third (1-3) without disagreement were classified as *inappropriate*.

The second round comprised a face-to-face meeting during which the results of the first round were presented. Each panel member received an individualized evaluation questionnaire with the panellist's own rating from round one, the overall panel median rating from round one, and the anonymised frequency distribution of the ratings for purposes of comparison. During the meeting, the moderator introduced the ATC subgroups that had been classified as *inappropriate* or *uncertain* during round one. The experts discussed each of these ATC subgroups with the option of changing the assigned scenario. Changes were made by panel consensus. Finally, the members individually and anonymously re-evaluated the ATC subgroups. The results obtained from the second round were analysed and classified using the same methods as those used in the first round.

Results

Review of information and definition of scenarios

A total of 593 articles were reviewed, of which 38 were initially selected based on the title and abstract screening. After reviewing the full text of the articles, 19 were finally selected. The main reasons for exclusion were not reporting the number or percentage of incidents associated with each medication (n = 8), not reporting the severity or the potential risk of the incidents associated with each medication /medication class (n = 7), or not including in-hospital events (n = 4).

The scenarios comprised three lists: low-risk (*scenario 1*), medium-risk (*scenario 2*), and high-risk medications (*scenario 3*). The *low-risk list* contained the ATC subgroups unlikely to cause patient discomfort or clinical deterioration; *medium-risk list* contained the ATC subgroups with the potential to cause moderate discomfort or clinical deterioration; and *high-risk list* contained the ATC subgroups with the potential to cause severe discomfort or clinical deterioration.

The literature review and web search yielded 47 subgroups that were classified as *low-risk*, 136 subgroups as *medium-risk*, and 115 subgroups as *high-risk*.

Results of the evaluation rounds

A total of 298 ATC groups were evaluated and rated. Sixty-one (21%) of the ATC subgroups included in the HPG were classified as *low-risk*, 126 (42%) as *medium-risk*, and 111 (37%) as *high-risk*. The most frequent ATC subgroups in the *low-risk list* belonged to group A "Alimentary tract and metabolism" (44%, n = 27), the most frequent in the *medium-risk list* belonged to group J "Antiinfectives for systemic use" (32%, n = 40), and the most frequent in the *high-risk list* belonged to groups L "Antineoplastic and immunomodulating agents" (29%, n = 32) and N "Nervous system" (26%, n = 29) (see Figure 1).

Nine experts were selected to serve on the panel. All 9 completed the first round and 8 completed the second.

In the first round, 266 ATC subgroups were classified as *appropriate*, 32 were classified as *uncertain*, and none were classified as *inappropriate*. In the second round, the experts met face-to-face to re-evaluate the ATC subgroups classified as *uncertain*. After discussion, 12 subgroups remained in the same class, whereas 20 subgroups changed class by consensus (Table 2). The final rating panel classified all subgroups as *appropriate*.

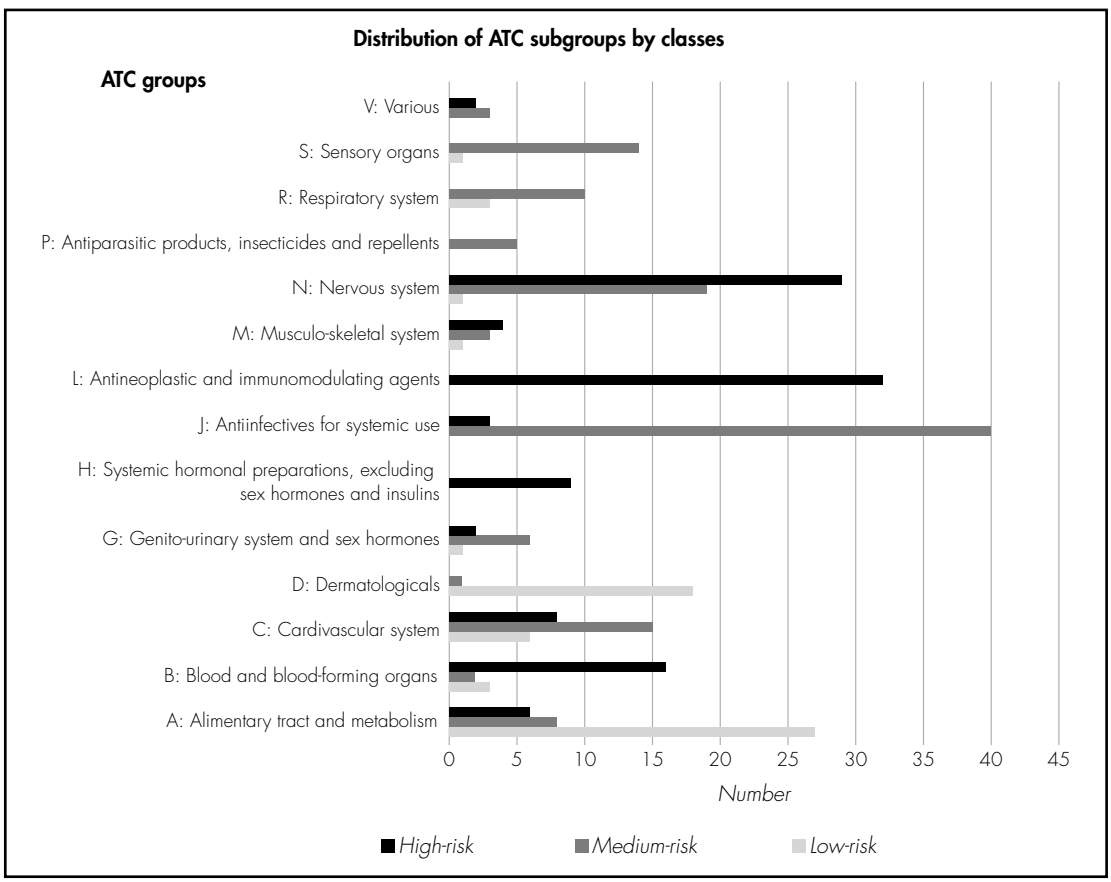

Figure 1. *Distribution of ATC subgroups by medication class.*

Table 2. ATC subgroups classified as *uncertain* in the first round and changes after the second round

Scenario: Round 1	ATC subgroups	Scenario: Round 2
	A12CC Magnesium	*Class 1*
1 (low-risk)	A12CX Other mineral products	*Class 1*
	A12BA Potassium	*Class 2*
	A01AB Antiinfectives and antiseptics for local oral treatment	*Class 1*
	C10AA HMG CoA reductase inhibitors	*Class 1*
	C10AB Fibrates	*Class 1*
	C10AC Bile acid sequestrants	*Class 1*
	D01AC Imidazole and triazole derivatives	*Class 1*
	D05AA Tars	*Class 1*
	D05AX Other antipsoriatics for topical use	*Class 1*
	D06AX Other antibiotics for topical use	*Class 1*
	D06BB Antivirals	*Class 1*
	D07AB Corticosteroids, moderately potent (group II)	*Class 1*
	D07AC Corticosteroids, potent (group III)	*Class 1*
	D07CC Corticosteroids, potent, combinations with antibiotics	*Class 1*
2 (medium-risk)	D09 MEDICATED DRESSINGS	*Class 1*
	D11 OTHER DERMATOLOGICAL PREPARATIONS	*Class 1*
	M04AA Preparations inhibiting uric acid production	*Class 1*
	C02CA Alpha-adrenoreceptor antagonists	*Class 2*
	C02KX Other antihypertensives	*Class 2*
	D06BA Sulfonamides	*Class 2*
	J05AB Nucleosides and nucleotides excl. reverse transcriptase inhibitors	*Class 2*
	J05AD Phosphonic acid derivatives	*Class 2*
	M05BA Bisphosphonates	*Class 2*
	M01A ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS, NON-STEROIDS	*Class 2*
	M04AC Preparations with no effect on uric acid metabolism	*Class 2*
	N02BA Salicylic acid and derivatives	*Class 2*
	N02BB Pyrazolones	*Class 2*
	N04AA Tertiary amines	*Class 2*
	N04BA Dopa and dopa derivatives	*Class 2*
3 (high-risk)	N04BC Dopamine agonists	*Class 2*
	N04BX Other dopaminergic agents	*Class 2*

Table 3 shows the final lists of ATC subgroups according to their potential risk.

Discussion

To the best of our knowledge, this is the first study to stratify medications used in hospital care according to their potential risk (low to high-risk). The RAM was used to classify the ATC subgroups included in the HPG into low, medium, and high potential risk. In the first evaluation round, 32 groups were classified as *uncertain*. Because the potential risk of a medication is driven by the clinical characteristics of the patient[18], the majority of the disagreements between experts could have been due to their experience in attending and treating different types of patients. However, we believe that the final results were enriched by the different criteria applied by the experts.

Some subgroups classified as *uncertain* were subject to further discussion. These subgroups included some dermatological subgroups, some subgroups which belong to group C10 "Lipid-modifying agents", and some anti-Parkinson drug subgroups. The dermatological subgroups were finally reclassified as *low-risk*. This classification is consistent with those reported by other studies that consider this group to have no association with patient harm[19, 20]. The subgroups that belong to group C10 "Lipid-modifying agents" were also reclassified as *low-risk*. The expert panel considered that the potential risk for inpatients was low. Authors such as Saeder *et al.*[21] have also classified fibrates as low risk. The anti-Parkinson drug subgroups were reclassified as *medium-risk*, although the nervous system group is associated with severe adverse events[22]. According to the clinical experience of the experts, severe adverse events are uncommon with anti-Parkinson drugs. This reclassification is consistent with the high-alert medication list for patients with chronic disease, which excluded anti-Parkinson drugs (see Otero *et al.*[23]).

The methodology used in this study has some limitations. Firstly, although the RAM has objective characteristics, it also has subjective ones because it measures opinions[24]. However, this method has advantages over other methods used to reach consensus, because it uses confidential ratings and group discussion. It has good reproducibility and is considered to be a rigorous method that can be used whenever a combination of scientific evidence and expert opinion is required[9,23,25]. Secondly, the results of the RAM always depend on the composition of the expert panel[9]. The RAM panel included physicians and nurses from different medical specialities, and pharmacists with different types of clinical expertise. Thus, several fields were covered by experts with deep knowledge of all medications assessed in this study.

Table 3. Final lists of ATC subgroups according to their potential safety risk

Low-risk subgroups	Medium-risk subgroups	High-risk subgroups
A01AB Antiinfectives and antiseptics for local oral treatment	A03F PROPULSIVES	A03BA Belladonna alkaloids, tertiary amines
A02A ANTACIDS	A04AA Serotonin (5HT3) antagonists	A03BB Belladonna alkaloids, semisynthetic, quaternary ammonium compounds
A02BA H2-receptor antagonists	A04AD Other antiemetics	A10A INSULINS AND ANALOGUES
A02BC Proton pump inhibitors	A07AA Antibiotics	A10BA Biguanides
A02BX Other drugs for peptic ulcer and gastro-oesophageal reflux disease	A07DA Antipropulsives	A10BB Sulfonamides, urea derivatives
A03AX Other drugs for functional gastrointestinal disorders	A07EA Corticosteroids acting locally	A10BF Alpha glucosidase inhibitors
A05AA Bile acid preparations	A07EC Aminosalicylic acid and similar agents	B01AA Vitamin K antagonists
A06AA Softeners, emollients	A12BA Potassium	B01AB Heparin group
A06AB Contact laxatives	B02BC Local hemostatics	B01AC Platelet aggregation inhibitors excl. heparin
A06AC Bulk-forming laxatives	B03XA Other antianemic preparations	B01AD Enzymes
A06AD Osmotically acting laxatives	C02CA Alpha-adrenoreceptor antagonists	B01AE Direct thrombin inhibitors
A06AG Enemas	C02KX Other antihypertensives	B01AX Other antithrombotic agents
A07CA Oral rehydration salt formulations	C03AA Thiazides, plain	B02AA Amino acids
A09AA Enzyme preparations	C03BA Sulfonamides, plain	B02AB Proteinase inhibitors
A11AA Multivitamins with minerals	C03CA Sulfonamides, plain	B02BA Vitamin K
A11BA Multivitamins, plain	C03DA Aldosterone antagonists	B02BD Blood coagulation factors
A11CA Vitamin A, plain	C03EA Low-ceiling diuretics and potassium-sparing agents	B05AA Blood substitutes and plasma protein fractions
A11CC Vitamin D and analogues	C07AA Beta blocking agents, non-selective	B05BA Solutions for parenteral nutrition
A11DA Vitamin B1, plain	C07AB Beta blocking agents, selective	B05BB Solutions affecting the electrolyte balance
A11DB Vitamin B1 in combination with vitamin B6 and/or vitamin B1	C07AG Alpha and beta blocking agents	B05BC Solutions producing osmotic diuresis
A11GA Ascorbic acid (vitamin C), plain	C08CA Dihydropyridine derivatives	B05X I.V. SOLUTION ADDITIVES
A11HA Other plain vitamin preparations	C08DA Phenylalkylamine derivatives	B06AB Other hem products
A11JA Combinations of vitamins	C08DB Benzothiazepine derivatives	C01A CARDIAC GLYCOSIDES
A12AA Calcium	C09A ACE INHIBITORS, PLAIN	C01B ANTIARRHYTHMICS, CLASS I AND III
A12AX Calcium, combinations with vitamin D and/or other drugs	C09C ANGIOTENSIN II ANTAGONISTS, PLAIN	C01CA Adrenergic and dopaminergic agents
A12CC Magnesium	D06BA Sulfonamides	C01CE Phosphodiesterase inhibitors
A12CX Other mineral products	G03A HORMONAL CONTRACEPTIVES FOR SYSTEMIC USE	C01CX Other cardiac stimulants
B03A IRON PREPARATIONS	G03H ANTIANDROGENS	C01D VASODILATORS USED IN CARDIAC DISEASES
B03BA Vitamin B12 (cyanocobalamin and analogues)	G03X OTHER SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	C01EA Prostaglandins
B03BB Folic acid and derivatives	G04BD Drugs for urinary frequency and incontinence	C01EB Other cardiac preparations
C04A PERIPHERAL VASODILATORS	G04BE Drugs used in erectile dysfunction	G02A OXYTOCICS
C05AA Corticosteroids	G04CB Testosterone-5-alpha reductase inhibitors	G02CB Prolactine inhibitors
C05BA Heparins or heparinoids for topical use	J01AA Tetracyclines	H01A ANTERIOR PITUITARY LOBE HORMONES AND ANALOGUES
C10AA HMG CoA reductase inhibitors	J01CA Penicillins with extended spectrum	H01B POSTERIOR PITUITARY LOBE HORMONES
C10AB Fibrates	J01CE Beta-lactamase sensitive penicillins	H01C HYPOTHALAMIC HORMONES
C10AC Bile acid sequestrants	J01CF Beta-lactamase resistant penicillins	H02A CORTICOSTEROIDS FOR SYSTEMIC USE, PLAIN

Table 3 *(cont.)*. Final lists of ATC subgroups according to their potential safety risk

Low-risk subgroups	Medium-risk subgroups	High-risk subgroups
D01AC Imidazole and triazole derivatives	J01CR Combinations of penicillins, incl. beta-lactamase inhibitors	H03A THYROID PREPARATIONS
D02AB Zinc products	J01DB First-generation cephalosporins	H03B ANTITHYROID PREPARATIONS
D02AC Soft paraffin and fat products	J01DC Second-generation cephalosporins	H04A GLYCOGENOLYTIC HORMONES
D03BA Proteolytic enzymes	J01DD Third-generation cephalosporins	H05BA Calcitonins
D05AA Tars	J01DE Fourth-generation cephalosporins	H05BX Other anti-parathyroid agents
D05AX Other antipsoriatics for topical use	J01DF Monobactams	J06AA Immune sera
D06AX Other antibiotics for topical use	J01DH Carbapenems	J06BA Immunoglobulins, normal human
D06BB Antivirals	J01EC Intermediate-acting sulfonamides	J06BB Specific immunoglobulins
D07AB Corticosteroids, moderately potent (group II)	J01EE Combinations of sulfonamides and trimethoprim, incl. derivatives	L01AA Nitrogen mustard analogues
D07AC Corticosteroids, potent (group III)	J01FA Macrolides	L01AB Alkyl sulfonates
D07CC Corticosteroids, potent, combinations with antibiotics	J01FF Lincosamides	L01AC Ethylene imines
D08AC Biguanides and amidines	J01GA Streptomycins	L01AD Nitrosoureas
D08AF Nitrofuran derivatives	J01GB Other aminoglycosides	L01AX Other alkylating agents
D08AG Iodine products	J01MA Fluoroquinolones	L01BA Folic acid analogues
D08AJ Quaternary ammonium compounds	J01XA Glycopeptide antibacterials	L01BB Purine analogues
D08AL Silver compounds	J01XB Polymyxins	L01BC Pyrimidine analogues
D09 MEDICATED DRESSINGS	J01XD Imidazole derivatives	L01CA Vinca alkaloids and analogues
D11 OTHER DERMATOLOGICAL PREPARATIONS	J01XE Nitrofuran derivatives	L01CB Podophyllotoxin derivatives
G01AX Other antiinfectives and antiseptics	J01XX Other antibacterials	L01CD Taxanes
M04AA Preparations inhibiting uric acid production	J02AA Antibiotics	L01CX Other plant alkaloids and natural products
N02BE Anilides	J02AB Imidazole derivatives	L01DA Actinomycines
R01AA Sympathomimetics, plain	J02AC Triazole derivatives	L01DB Anthracyclines and related substances
R01AD Corticosteroids	J02AX Other antimycotics for systemic use	L01DC Other cytotoxic antibiotics
R05CB Mucolytics	J04AB Antibiotics	L01XA Platinum compounds
S01XA Other ophthalmologicals	J04AC Hydrazides	L01XB Methylhydrazines
	J04AK Other drugs for treatment of tuberculosis	L01XC Monoclonal antibodies
	J04AM Combinations of drugs for treatment of tuberculosis	L01XE Protein kinase inhibitors
	J05AB Nucleosides and nucleotides excl. reverse transcriptase inhibitors	L01XX Other antineoplastic agents
	J05AC Cyclic amines	L02AB Progestogens
	J05AD Phosphonic acid derivatives	L02AE Gonadotropin releasing hormone analogues
	J05AE Protease inhibitors	L02BA Anti-estrogens
	J05AF Nucleoside and nucleotide reverse transcriptase inhibitors	L02BB Anti-androgens
	J05AG Non-nucleoside reverse transcriptase inhibitors	L02BG Aromatase inhibitors
	J05AH Neuraminidase inhibitors	L02BX Other hormone antagonists and related agents
	J05AR Antivirals for treatment of HIV infections, combinations	L03AA Colony stimulating factors
	J05AX Other antivirals	L03AB Interferons
	M01A ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS, NON-STEROIDS	L03AC Interleukins
	M04AC Preparations with no effect on uric acid metabolism	L03AX Other immunostimulants
	M05BA Bisphosphonates	L04A IMMUNOSUPPRESSANTS

Table 3 *(cont.)*. Final lists of ATC subgroups according to their potential safety risk

Low-risk subgroups	Medium-risk subgroups	High-risk subgroups
	N02BA Salicylic acid and derivatives	L04AX Other immunosuppressants
	N02BB Pyrazolones	M03AB Choline derivatives
	N02CC Selective serotonin (5HT1) agonists	M03AC Other quaternary ammonium compounds
	N04AA Tertiary amines	M03AX Other muscle relaxants, peripherally acting agents
	N04BA Dopa and dopa derivatives	M03BX Other centrally acting agents
	N04BC Dopamine agonists	N01AB Halogenated hydrocarbons
	N04BX Other dopaminergic agents	N01AF Barbiturates, plain
	N05BA Benzodiazepine derivatives	N01AH Opioid anesthetics
	N05BB Diphenylmethane derivatives	N01AX Other general anesthetics
	N05CD Benzodiazepine derivatives	N01BA Esters of aminobenzoic acid
	N05CF Benzodiazepine related drugs	N01BB Amides
	N05CM Other hypnotics and sedatives	N01BX Other local anesthetics
	N06AA Non-selective monoamine reuptake inhibitors	N02AA Natural opium alkaloids
	N06AB Selective serotonin reuptake inhibitors	N02AB Phenylpiperidine derivatives
	N06AX Other antidepressants	N02AE Oripavine derivatives
	N06BA Centrally acting sympathomimetics	N02AX Other opioids
	N06BX Other psychostimulants and nootropics	N03AA Barbiturates and derivatives
	N06D ANTI-DEMENTIA DRUGS	N03AB Hydantoin derivatives
	N06DX Other anti-dementia drugs	N03AD Succinimide derivatives
	P01BB Biguanides	N03AE Benzodiazepine derivatives
	P01BD Diaminopyrimidines	N03AF Carboxamide derivatives
	P01CB Antimony compounds	N03AG Fatty acid derivatives
	P01CX Other agents against leishmaniasis and trypanosomiasis	N03AX Other antiepileptics
	P02CA Benzimidazole derivatives	N05AA Phenothiazines with aliphatic side-chain
	R03AC Selective beta-2-adrenoreceptor agonists	N05AD Butyrophenone derivatives
	R03AK Adrenergics and other drugs for obstructive airway diseases	N05AE Indole derivatives
	R03BA Glucocorticoids	N05AH Diazepines, oxazepines, thiazepines and oxepines
	R03BB Anticholinergics	N05AL Benzamides
	R03CC Selective beta-2-adrenoreceptor agonists	N05AN Lithium
	R03DA Xanthines	N05AX Other antipsychotics
	R05DA Opium alkaloids and derivatives	N07AA Anticholinesterases
	R06AB Substituted alkylamines	N07BB Drugs used in alcohol dependence
	R06AD Phenothiazine derivatives	N07BC Drugs used in opioid dependence
	R06AX Other antihistamines for systemic use	N07XX Other nervous system drugs
	S01AA Antibiotics	V03AB Antidotes
	S01AD Antivirals	V08A X-RAY CONTRAST MEDIA, IODINATED
	S01AE Fluoroquinolones	
	S01BA Corticosteroids, plain	
	S01BC Antiinflammatory agents, non-steroids	
	S01CA Corticosteroids and antiinfectives in combination	
	S01EA Sympathomimetics in glaucoma therapy	

Table 3 *(cont.)*. Final lists of ATC subgroups according to their potential safety risk

Low-risk subgroups	Medium-risk subgroups	High-risk subgroups
	S01EB Parasympathomimetics	
	S01EC Carbonic anhydrase inhibitors	
	S01ED Beta blocking agents	
	S01EE Prostaglandin analogues	
	S01FA Anticholinergics	
	S01FB Sympathomimetics excl. antiglaucoma preparations	
	S01HA Local anesthetics	
	V03AC Iron chelating agents	
	V03AE Drugs for treatment of hyperkalemia and hyperphosphatemia	
	V03AF Detoxifying agents for antineoplastic treatment	

The lists that were created provide an objective measure that could be used during routine data collection of MEs in order to reduce subjectivity and provide a standard by which the severity of an ME can be assessed and measured. These medication lists could be a useful tool for future patient/medication safety studies, leading to better prevention measures and the improved management of follow-up activities after the detection of an ME.

Ideally, these lists could be integrated into an electronic tool to facilitate resource allocation for patients at high risk of severe MEs. It is relevant to individualize the risk assessment for each patient undergoing drug therapy[21,26]. Given that resources are limited, the same intervention is currently provided to all patients in our hospital, even though they may receive medications with a higher risk of adverse events. The integration of these lists into an electronic tool would assist in patient stratification.

A RAM was used to classify ATC subgroups by their potential risk (low, medium, or high). The main contribution of this study is to make these reference lists available. These lists can be integrated into a risk-scoring tool for future patient/medication safety studies.

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Conflict of interests

No conflict of interests.

Contribution to scientific literature

All medications can cause adverse events if they are incorrectly used. Nonetheless, certain medications are more dangerous than others. A list of high-risk medications has been published, but lists of low- and medium-risk medications are not available. This study is the first to classify medications used in hospital settings according to their potential risk. This classification is of relevance to future patient/medication safety studies and for patient resource allocation according to treatment.

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