

Original article

## [Translated article] Gender perspective in medication-related problems resulting in emergency department attendance involving high-alert medications

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### A B S T R A C T

**Objectives:** To characterize medication-related problems resulting in emergency department attendance involving high-alert medications, paying particular attention to sex-related differences in the type of the problem and medication associated with it.

**Methods:** Retrospective observational study (2021–2022) based on the medical history at discharge, including adult patients seeking emergency department due to medication-related problems as a primary or secondary diagnosis. Patient grouping was performed according to the class of medication implicated in the event, as defined by the reference list of high-alert drugs for chronic patients (HAMC list). Sociodemographic and clinical baseline variables were collected. To explore gender differences in the type of problem and drug involved, statistical analysis included binomial tests and binary logistic regression with odds ratio estimation.

**Results:** Among the 1,611 adult patients admitted to the emergency department with adverse events associated with a medication problem, 1,028 (64%) involved a high-alert medication. Women with moderate- and high-risk comorbidity showed a significant greater incidence of medication-related problems. Gender differences were particularly notable for events associated with loop diuretics (136 women [70%] vs 57 men [30%],  $p = 0.000$ ); antipsychotics (30 women [65%] vs 16 men [35%],  $p = 0.039$ ); opioids (37 women [73%] vs 11 men [27%],  $p = 0.000$ ) and digoxin (22 women [81%] vs 5 men [19%],  $p = 0.02$ ). Women showed a trend toward higher odds of experiencing unintentional drug poisoning (OR = 2.5; 95% CI: 0.786–8.356;  $p = 0.119$ ). In contrast, non-adherence to prescribed high-alert medications occurred with greater frequency in men (OR = 0.711, 95% CI: 0.473–1.070;  $p = 0.102$ ).

**Conclusions:** A considerable proportion of medication-related problems that lead to emergency room attendance involve high-risk medications, and the type of problem presented and the type of drug involved differ between sexes. Findings highlight that addressing gender differences, especially with regard to high-risk medicines, could be crucial in moving toward safer and more equitable healthcare.

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### Perspectiva de género en problemas asociados a medicamentos de alto riesgo atendidos en urgencias

### R E S U M E N

**Objetivo:** caracterizar los problemas relacionados con medicamentos de alto riesgo que causan consulta a urgencias, analizando las diferencias por género en el tipo de problema y medicamento asociado.

**Método:** estudio observacional retrospectivo (2021–2022) basado en la historia clínica al alta, incluyendo pacientes adultos que acudieron a urgencias por un problema relacionado con los medicamentos (diagnóstico

#### Palabras clave:

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Diferencias por sexo  
Equidad de género  
Gestión de riesgos

principal o secundario). Los medicamentos se clasificaron según la lista de referencia MARC de medicamentos de alto riesgo en pacientes crónicos. Se recopilaron variables sociodemográficas y clínicas basales. Para identificar diferencias de género en los tipos de problemas y medicamentos asociados, se analizó la información empleando pruebas binomiales y regresión logística, incluyendo la estimación de odds ratios.

**Resultados:** acudieron a urgencias 1.611 pacientes por un problema relacionado con los medicamentos, de los cuales 1.028 (64%) estaban asociados a un medicamento de alto riesgo. Las mujeres con enfermedades crónicas con riesgo moderado y alto presentaron una incidencia significativamente mayor. Se observaron diferencias significativas por género en el tipo de medicamento asociado: diuréticos del asa (136 mujeres [70%] frente a 57 hombres [30%],  $p = 0,000$ ); antipsicóticos (30 mujeres [65%] frente a 16 hombres [35%],  $p = 0,039$ ); opioides (37 mujeres [73%] frente a 11 hombres [27%],  $p = 0,000$ ) y digoxina (22 mujeres [81%] frente a 5 hombres [19%],  $p = 0,02$ ). Las mujeres mostraron una tendencia marginalmente significativa a una mayor frecuencia de intoxicación no intencionada por fármacos (OR = 2,5; IC 95%: 0,786–8,356;  $p = 0,119$ ). En cambio, los hombres mostraron una tendencia marginalmente significativa a presentar problemas asociados a una falta de adherencia (OR = 0,711; IC 95%: 0,473–1,070;  $p = 0,102$ ).

**Conclusiones:** una elevada proporción de los problemas relacionados con medicamentos que motivan consultas en urgencias está asociada a medicamentos de alto riesgo y, además, existen diferencias significativas por género en el tipo de problema presentado y el tipo de fármaco implicado. Abordar las diferencias de género en este ámbito, especialmente respecto a medicamentos de alto riesgo, podría ser determinante para avanzar hacia una atención sanitaria más segura y equitativa.

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## Introduction

Medication-related problems (MRPs) are considered a public health priority and pose a major challenge to patient safety, particularly in patients with multiple chronic diseases.<sup>1</sup> Numerous studies show that MRPs are highly preventable and are associated with multimorbidity, polypharmacy, inappropriate prescribing, duplication, and interactions.<sup>2,3</sup> Published data indicate that approximately 10% of emergency department (ED) visits are associated with preventable MRPs,<sup>4</sup> a figure similar to that recorded in other settings.<sup>5</sup>

In 2017, the World Health Organisation launched its third Global Patient Safety Challenge, with the goal of reducing severe avoidable medication-related harm by 50% over 5 years. The strategy for improvement actions addresses 3 priority areas: inappropriate polypharmacy, transitions of care, and high-risk medicines.<sup>6</sup> Within this framework, hospital pharmacy services play a key role in reducing medication errors and ensuring greater safety in the administration of medicines.

High-risk medicines carry a significant risk of causing severe or fatal harm in the event of an error. Lists adapted to different healthcare settings have been established to prioritise interventions according to the care setting. The high-risk medicines for chronic patients (MARC) list was developed in Spain specifically for such patients.<sup>7</sup>

Although research on MRPs leading to ED visits has advanced, sex differences in this area remain largely unexplored. Women have a greater risk of adverse effects and often receive higher doses, whereas men are more likely to underuse necessary medications.<sup>8</sup> These disparities can have more serious clinical consequences when high-risk medications are involved. Furthermore, many high-risk medications have a narrow therapeutic margin or specific contraindications. In the case of renal clearance disorders, biological differences between sexes increase the incidence and severity of MRPs.<sup>9</sup> A sex-based analysis and characterisation of the types of MRP leading to ED visits involving MARC-list medications are essential to guide preventive strategies in chronic patients, as identifying differences between women and men would enable the development of safer and more equitable medication use strategies.

The objective of this study was to characterise the problems associated with high-risk medications leading to ED visits in a high-complexity tertiary hospital in Catalonia (Spain), and to analyse sex differences in relation to the type of MRPs and medications involved.

## Methods

### Study design and scope

An observational retrospective study using existing electronic clinical records was conducted between 1 January 2021 and 31 December 2022. The study was conducted in the ED of a high-complexity tertiary hospital in Catalonia, where the ED has implemented a Frailty Care Programme designed to improve continuity of care, medication reconciliation, and pharmacological follow-up of vulnerable patients.<sup>10</sup> Since 2021, the secondary prevention “Código Medicamento” programme has also been implemented in this ED to identify and reduce MRPs in frail polymedicated patients.<sup>11</sup>

### Study population

**Inclusion criteria:** patients aged 18 years or older presenting to the ED with an MRP recorded as the primary or secondary diagnosis and an ED stay of at least 12 h.

**Exclusion criteria:** patients presenting to the ED after ingesting medications with suicidal intent and those considered to be in the terminal phase, with an estimated life expectancy of less than 30 days as determined by the emergency physician. These criteria are the same as those defined in the “Código Medicamento” programme.

The entire database of the “Código Medicamento” programme was used to select the study population, without applying additional exclusion criteria.

### Variables

The following outcome variables were collected:

- Reason for visit:** defined as the diagnosis associated with the MRP and recorded according to the International Classification of Diseases as an ICD-10 code, as this system is used in the hospital to identify MRPs.<sup>12</sup>
- Type of MRP:** classified by the Third Granada Consensus<sup>13</sup> into the following categories:

#### a. Need

- Untreated health problem: the patient has a health problem associated with not receiving the medication that is needed.

- Effect of unnecessary medication: the patient has a health problem associated with receiving a medication that is not needed.
- b. *Effectiveness*
- Non-quantitative ineffectiveness: the patient has a health problem associated with the non-quantitative ineffectiveness of the medication.
  - Quantitative ineffectiveness: the patient has a health problem associated with the quantitative ineffectiveness of the medication.
- c. *Safety*
- Non-quantitative safety issue: the patient has a health problem associated with the medication itself, resulting in an adverse drug reaction (ADR).
  - Quantitative safety issue: the patient has a health problem associated with a dose, dosing schedule, or duration that exceeds what is therapeutically necessary.
3. **Medication associated with the MRP:** defined as the medication that caused the ED visit, assigned to one of 18 groups according to the MARC list<sup>7</sup>:
- a. Fourteen therapeutic groups: antiplatelet agents, oral anticoagulants, narrow-therapeutic-index antiepileptics, nonsteroidal anti-inflammatory drugs, antipsychotics, benzodiazepines and analogues,  $\beta$ -adrenergic blockers, oral cytostatics, long-term corticosteroids, loop diuretics, oral hypoglycaemic agents, immunosuppressants, insulins, and opioids.
  - b. Four specific medications: amiodarone, digoxin, spironolactone/epirenone, and oral methotrexate (non-oncological use).

The following sociodemographic and clinical variables were collected: age; sex (binary variable: female/male); social support; dependency and dementia; number of medications taken; presence of chronic diseases most frequently associated with ED revisits<sup>14,15</sup> (hypertension, diabetes mellitus, atrial fibrillation, ischemic heart disease, chronic kidney disease, stroke, chronic obstructive pulmonary disease, and oncological diagnosis); and adjusted morbidity group (AMG) using the scale provided by the Catalan Department of Health.<sup>16</sup>

The study cohort was grouped based on 2 key aspects: multimorbidity and complexity. Using these data, patients were categorised into 4 groups (AMG 1: low risk, AMG 2: medium risk, AMG 3: moderate risk, and AMG 4: high risk). The groups are associated with the risk of ED visits, hospital admission, and mortality. The higher the AMG, the greater the risks described for patients within that category.<sup>17</sup>

*Data collection*

Hospital pharmacists with clinical experience in the ED identified MRPs by reviewing discharge reports retrospectively, using ICD-10 codes linked to alert diagnoses. For coding purposes, we recorded a single diagnosis representing the main clinical problem associated with the MRP, as determined by the emergency physician. In cases where causality was uncertain, the “Código Medicamento” committee was consulted to resolve the discrepancy by consensus.

*Statistical analysis*

Qualitative variables are expressed as absolute frequencies and percentages, and quantitative variables are expressed as descriptive statistics (means and standard deviations). Comparisons of proportions were analysed using binomial tests and the chi-squared test. Associations were analysed using binary logistic regression, including those between the type of MRP associated with MARC medication and sex.

A descriptive analysis was conducted on the demographic distribution of the sample by sex, taking into account the proportion of women and men in each age group according to data from the Catalan Institute of Statistics.<sup>18</sup> Age groups were analysed both as a whole and by specific age subgroups. Given that the average life expectancy in Catalonia is 83.96 years and the proportion of the female population attending EDs for MRPs increases with age, the population was stratified into the following subgroups: less than 75 years, 75 to 84 years, and more than 85 years. This stratification allows a more accurate assessment of potential statistical differences between sexes by age subgroup.

The analysis of MRP distribution by drug type and sex was stratified using the Catalan Department of Health AMG scale. This scale forms part of the official clinical risk stratification system used by the Catalan Health Service (CatSalut) to classify the population according to morbidity, complexity, and health risk.

A p-value of <0.05 was used as a cutoff for statistical significance.

*Ethical considerations*

The protocol was reviewed and approved by the hospital's Clinical Research Ethics Committee (CEIC) (code IIBSP-COD-2022-40).

**Results**

The sample comprised 1611 adult patients (926 women and 685 men), who attended the ED with an MRP as their primary or secondary diagnosis. Table 1 shows the baseline sociodemographic and clinical characteristics by sex.

Of the total patients, 1028 (64%) had an MRP associated with a MARC medication: 580 women (63% of all women in the sample) and 448 men (65% of all men in the sample). Women had a higher frequency

**Table 1**  
 Baseline sociodemographic and clinical characteristics by sex.

Baseline sociodemographic and clinical variables	Total patients (n = 1611)		p
	Women n = 926 (%)	Men n = 685 (%)	
Sex	926 (57)	685 (43)	<0.001
Age, y			
<75	225 (46)	260 (54)	0.680
≥75 to <85	272 (56)	217 (44)	0.011
≥85	429 (67)	208 (33)	<0.001
Number of drugs at admission	8.92 (4.13)	8.48 (4.50)	0.041
<i>Chronic diseases</i>			
Hypertension	720 (59)	503 (41)	<0.001
Diabetes mellitus	257 (49)	263 (51)	0.826
Atrial fibrillation	337 (59)	230 (41)	<0.001
Ischemic heart disease	130 (45)	160 (55)	0.089
Chronic renal failure	214 (58)	158 (42)	0.004
Stroke	133 (58)	95 (42)	0.015
Chronic obstructive pulmonary disease	68 (39)	106 (61)	0.005
Cancer diagnosis	66 (43)	89 (57)	0.076
<i>Adjusted morbidity group</i>			
Adjusted morbidity group 1	17 (47)	19 (53)	0.868
Adjusted morbidity group 2	67 (43)	89 (57)	0.093
Adjusted morbidity group 3	225 (61)	143 (39)	<0.001
Adjusted morbidity group 4	561 (58)	399 (42)	<0.001
<i>Social support</i>			
Partner	80 (40)	122 (60)	0.004
Other family member	291 (64)	167 (36)	<0.001
Part-time carer	81 (74)	28 (26)	<0.001
24-h residence/support	173 (70)	74 (30)	<0.001
No social support	45 (45)	54 (55)	0.422
<i>Functional dependence</i>			
No	302 (50)	300 (50)	0.968
Mild	298 (62)	183 (38)	<0.001
Moderate/severe	289 (65)	157 (35)	<0.001
<i>Dementia</i>	222 (53)	148 (65)	0.022

of MRPs associated with loop diuretics than men (136 [70%] vs 57 [30%],  $p = .000$ ), antipsychotics (30 [65%] vs 16 [35%],  $p = .039$ ), opioids (37 [73%] vs 11 [27%],  $p = .000$ ), and digoxin (22 [81%] vs 5 [19%],  $p = .02$ ). The age-stratified analysis showed that men under 75 years had a higher frequency of MRPs associated with insulin (11 women [30%] vs 26 men [70%],  $p = 0.014$ ) and oral hypoglycaemic agents (5 women [24%] vs 16 men [76%],  $p = 0.016$ ). Table 2 shows the overall distribution of MRPs by sex and drug type, and the supplementary material details the age-stratified analysis.

The comorbidity level analysis showed that the proportion of women who experienced MRPs was significantly higher in the moderate- and high-risk groups (AMG 3 and 4) than in the lower-risk groups (AMG 1 and 2). In these higher-risk categories, a statistically significant association was found between female sex and a higher frequency of MRPs associated with loop diuretics (AMG 3: 31 women [72%] vs 12 men [28%],  $p = 0.004$ ; AMG 4: 91 women [71%] vs 38 men [29%],  $p < 0.001$ ), digoxin (AMG 4: 19 women [79%] vs 5 men [21%],  $p = 0.004$ ), and opioids (AMG 4: 24 women [80%] vs 6 men [20%],  $p = 0.001$ ). Non-significant trends were observed in the AMG 3 group for digoxin (2 women [100%] vs 0 men,  $p = 0.5$ ) and opioids (6 women [86%] vs 1 man [14%],  $p = 0.125$ ). Fig. 1 shows the distribution of MRPs by drug type in AMG 3 and AMG 4. The supplementary material shows the distribution of MRPs by drug type and sex in all AMGs.

Analysis of the association between MRPs and MARC medications by sex showed that the probability of experiencing a safety problem increased 5-fold for both men and women when a quantitative safety problem occurred and the drug was included in the MARC list (men: odds ratio [OR] = 4.9; 95% confidence interval [95% CI]: 3.21–7.34; women: OR = 5.3; 95% CI: 3.60–7.77). In addition, the probability of experiencing a non-quantitative safety issue increased 2.5-fold for both men and women when an ADR involving a MARC medication occurred (men: OR = 2.5; 95% CI: 1.85–3.35; women: OR = 2.7; 95% CI: 2.12–3.52).

Analysis of the relationship between the reason for consultation, the drug type associated with the MRP, and sex showed that women were more likely to experience unintentional drug poisoning, although this difference was not statistically significant (OR = 2.5; 95% CI: 0.79–8.36,  $p = .119$ ). Men were 1.41 times more likely to experience problems associated with nonadherence when a MARC medication was involved, although this difference was not statistically significant (OR: 0.711, 95% CI: 0.473–1070,  $p = 0.102$ ). All cases of hypokalaemia

occurred in the MARC medication group. The proportion of hyponatraemia increased 20-fold in men (OR = 20.0; 95% CI: 2.68–149.0) and 7-fold in women (OR = 7.1; 95% CI: 3.54–14.29) when a MARC medication was involved. Table 3 shows the relationship between MARC medications and sex according to the type of MRP and the reason for consultation.

## Discussion

The results show that high-risk medicines are involved in a high proportion of MRPs, leading to ED visits. This finding is in line with those of previous studies, suggesting that a high proportion of preventable adverse drug events are caused by these drugs.<sup>19</sup> The value of this study lies in being, to the best of our knowledge, the first to provide a sex-based analysis of MRPs associated with MARC medications leading to ED visits. These MRPs include not only ADRs but also negative outcomes related to therapeutic effectiveness and treatment necessity.

Medication-related problems associated with loop diuretics, digoxin, opioids, and antipsychotics showed significant sex differences, with women being more frequently affected across all age groups. These results support the development of specific recommendations tailored to different healthcare settings and a sex-based approach to safe medication management.<sup>7</sup>

Notably, the study shows that dosing-related MRPs were observed more frequently in women and that, when a high-risk medication was involved, the clinical consequences significantly differed between women and men. Furthermore, unintentional drug poisoning was observed more frequently in women; however, this difference was not statistically significant. Although pharmacokinetic differences influencing women's drug metabolism and pharmacologic response are well documented,<sup>20</sup> sex-adjusted dosing is often underutilised when aiming to reduce the risk of MRPs, particularly for high-risk medications.<sup>21,22</sup> This study confirms previous evidence that women experience ADRs more frequently than men.<sup>23</sup>

Additionally, the results show that both male and female patients who used a MARC medication at doses higher than recommended were 5 times more likely to have an MRP. These findings provide a new perspective by highlighting that the inappropriate use of MARC medications increases the risk of MRPs in both men and women.

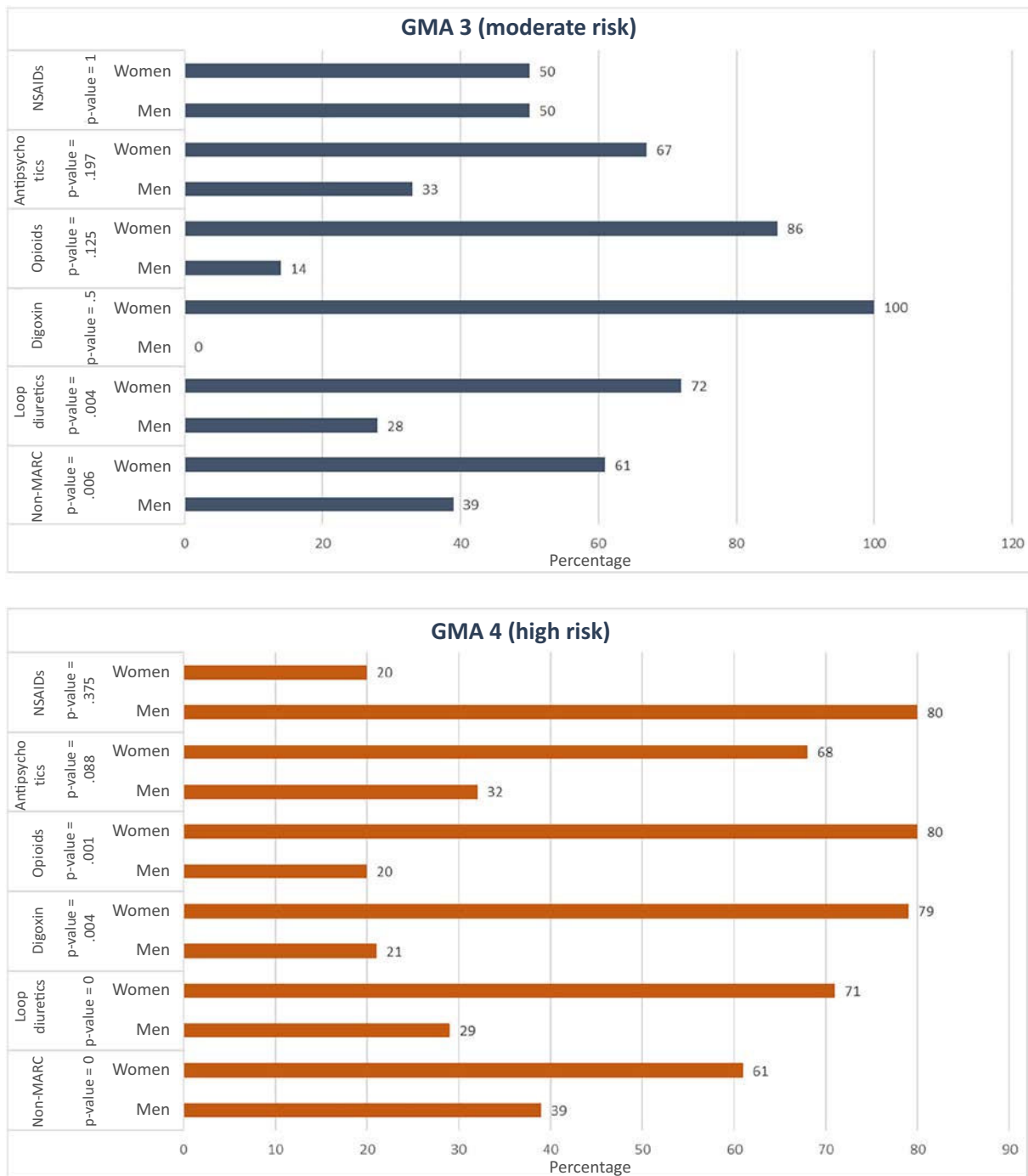
Nonadherence to therapy remains a key factor contributing to ED visits for MRPs. Three out of 5 patients in the sample were women who were nonadherent to therapy. However, analysis of the relationship between medication type and sex showed that men had a 1.4-fold higher risk of ED visits due to non-adherence, although this difference was not statistically significant. This finding may be related to sex differences in the management of chronic diseases, including type 2 diabetes. Men tend to rely mainly on support from their partner for health-related matters, whereas women tend to be more actively engaged in managing their own health or to draw on broader social networks, which may promote better adherence to therapy.<sup>24</sup>

This study has several limitations. Firstly, the integrated medical record system of Catalonia does not collect variables related to sex roles, such as domestic and family responsibilities, or potential sex biases in clinical care. Similarly, no data were collected on educational and income levels, which have been identified as common risk factors for MRPs associated with poor therapeutic adherence. Secondly, no data were collected on the frequency of use of health services, although we believe that this may have had little influence on the results, even though men consult health services less often and tend to seek help later than women.<sup>25</sup> Thirdly, the methodology used, which included patients only during a limited period of the day and within working hours, did not comply with the guidelines required for conducting a prevalence analysis. Fourthly, information bias may have been introduced because the medication code database does not include over-the-counter medicines, patients who attended the emergency department after consuming medicines in a suicide attempt, or those in the terminal phase

**Table 2**  
Distribution of MRPs by sex and drug type across all age groups.

Type of medication	Women n (%)	Men n (%)	<i>p</i>
Non-MARC	346 (59)	237 (41)	0.000
MARC	580 (56)	448 (44)	0.000
Oral anticoagulants	136 (52)	126 (48)	n.s.
Loop diuretics	136 (70)	57 (30)	0.000
Adrenergic $\beta$ -blockers	54 (55)	44 (45)	n.s.
Opioids	37 (73)	11 (27)	0.000
Antiplatelet agents	34 (46)	40 (54)	n.s.
Insulins	33 (42)	46 (58)	n.s.
Antipsychotics	30 (65)	16 (35)	0.039
Narrow-therapeutic-index antiepileptics	29 (46)	34 (54)	n.s.
Oral hypoglycaemic agents	26 (47)	29 (53)	n.s.
Digoxin	22 (81)	5 (19)	0.002
Benzodiazepines and analogues	11 (69)	5 (31)	n.s.
Oral cytostatics	10 (71)	4 (29)	n.s.
Long-term corticosteroids	10 (44)	13 (56)	n.s.
Non-steroidal anti-inflammatory drugs	9 (43)	12 (57)	n.s.
Immunosuppressants	2 (40)	3 (60)	n.s.
Amiodarone	1 (25)	3 (75)	n.s.

MARC, drug included in the MARC (high-risk drugs for chronic patients) list; Non-MARC, drug not included in the MARC list; MRP, medication-related problem; n.s., non-significant ( $p > 0.05$ ).



**Figure 1.** Distribution of MRPs by drug type and sex in moderate- (AMG 3) and high-comorbidity (AMG 4) risk groups. NSAIDs, non-steroidal anti-inflammatory drugs; AMG, adjusted morbidity group; Non-MARC, drug not included in the MARC list; MRP, medication-related problem.

with an estimated life expectancy of less than 30 days, according to the emergency physician's judgement. The limited number of cases included for some of the MARC medications prevented a specific multivariate analysis to confirm sex differences for each drug, highlighting an important issue to address in future studies. Finally, we did not conduct an epidemiological analysis to assess the relationship between the MRPs observed in the ED and those expected based on the use of the same drugs in the general Catalan population.

In conclusion, this study highlights the need for the structured integration of the sex-based perspective into prescribing and pharmacotherapeutic follow-up protocols, staff training programmes, and educational materials for patients. This approach is of particular

relevance to patients with multimorbidity and polypharmacy, who are more likely to experience adverse events with high-risk medications. Future research should investigate the factors contributing to the discrepancies observed between women and men to improve understanding of sex disparities in medication safety.

**Contribution to the scientific literature**

This study identifies sex-based differences in problems associated with high-risk medicines treated in emergency departments and provides evidence of the need to incorporate a sex-based perspective into patient safety.

**Table 3**

High-risk medications for chronic patients by sex according to the reason for consultation and the type of medication-related problem.

	Women n (%)	Men n (%)	MARC medication for women MARC/No-MARC (95% CI, p)	Odds ratio for men MARC/No-MARC (95% CI, p)	Odds ratio for women/men (95% CI, p)
<i>Type of MRP</i>					
Untreated health problem	87 (40)	80 (49)	0.669 (95% CI: 0.510–0.878, p = 0.004)	0.941 (95% CI: 0.694–1277, p = 0.697)	0.711 (95% CI: 0.473–1070, p = 0.102)
Effect of unnecessary medication	27 (69)	21 (64)	2.25 (95% CI: 1140–4441, p = 0.019)	1.75 (95% CI: 0.861–3557, p = 0.122)	1286 (95% CI: 0.481–3435, p = 0.616)
Non-quantitative ineffectiveness	11 (61)	15 (79)	1571 (95% CI: 0.609–4054, p = 0.350)	3.75 (95% CI: 1245–11,299, p = 0.019)	0.419 (95% CI: 0.098–1794, p = 0.241)
Quantitative ineffectiveness	67 (44)	49 (50)	0.798 (95% CI: 0.579–1100, p = 0.167)	1021 (95% CI: 0.686–1520, p = 0.919)	0.781 (95% CI: 0.469–1303, p = 0.344)
Non-quantitative safety issue	224 (73)	152 (71)	2732 (95% CI: 2121–3518, p = 0.000)	2492 (95% CI: 1851–3354, p = 0.000)	1096 (95% CI: 0.742–1619, p = 0.644)
Quantitative safety issue	164 (84)	131 (83)	5.29 (95% CI: 3604–7766, p = 0.000)	4.85 (95% CI: 3.2–7342, p = 0.000)	1.09 (95% CI: 0.620–1918, p = 0.764)
<i>Reason for consultation</i>					
Hypertension	2 (17)	1 (12)	0.200 (95% CI: 0.044–0.913, p = 0.038)	0.143 (95% CI: 0.018–1161, p = 0.069)	1.4 (95% CI: 0.105–18.615, p = 0.799)
Hyponatraemia	64 (88)	20 (95)	7111 (95% CI: 3539–14.288, p = 0.000)	20 (95% CI: 2685–149,000, p = 0.003)	0.356 (95% CI: 0.042–2980, p = 0.340)
Hypokalaemia	31 (100)	9 (100)	n/a	n/a	n/a
Gastrointestinal disorders	33 (23)	12 (16)	0.297 (95% CI: 0.202–0.438, p = 0.000)	0.188 (95% CI: 0.101–0.347, p = 0.000)	1586 (95% CI: 0.765–3286, p = 0.215)
Unintentional drug poisoning	14 (67)	41 (84)	5.12 (95% CI: 2403–10,932, p = 0.000)	2.01 (95% CI: 0.807–4955, p = 0.134)	2563 (95% CI: 0.786–8356, p = 0.119)

MARC, medication included in the MARC (high-risk medications for chronic patients) list; MRP, medication-related problem.

The findings support the development of safe medication strategies that integrate a sex-based approach in clinical and hospital practice, particularly for high-risk medicines.

### Ethical responsibilities

All authors have fulfilled all the responsibilities established by the International Committee of Journal Editors. In the event of publication, the authors exclusively assign the rights of reproduction, distribution, translation, and public communication of this work, by any means or medium, to *Farmacia Hospitalaria* and, by extension, to the Spanish Society of Hospital Pharmacy (SEFH).

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### Declaration on the use of generative artificial intelligence

None declared. The authors took full responsibility for the published content.

### Conflict of interest

None declared.

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### CRediT Author contribution statement

**Concepción Marín de la Bárcena:** Writing – review & editing, Writing – original draft, Visualisation, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Jesús Ruiz Ramos:** Writing – review & editing, Visualisation, Validation, Supervision, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Mireia Puig Campmany:** Writing – review & editing, Validation, Supervision, Methodology, Conceptualization. **María José Otero:** Writing – review & editing, Visualisation, Validation, Supervision, Methodology. **Ana Juanes Borrego:** Writing – review & editing, Visualisation, Validation, Supervision, Project administration, Methodology, Conceptualization.

### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.farma.2026.03.005>.

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