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ORIGINAL ARTICLE

Negative results related to drugs required in hospitalisation

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KEYWORDS
Adverse effects;
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Negative results associated with medication

Abstract
Objective: To assess the prevalence of negative clinical outcomes associated with medication as a cause of hospital admission and to determine their characteristics (types, categories, avoidability, severity, and the drug groups involved). To determine possible risk factors related to the appearance of this problem.
Method: An observational study carried out over a 3 month period in a department of the university hospital, 163 patients were selected at random. The information obtained from the patient interview, the revision of clinical records and clinical sessions were used to then identify negative clinical outcomes using the Dader method.
Results: In 27 cases (16.6%; 95% confidence interval [CI], 1.6-23.0), negative clinical outcomes associated with medication were considered to be the main cause of hospital admission. The most frequent negative clinical outcomes associated with medication were untreated health problems, non-quantitative ineffectiveness, and quantitative safety problems respectively. The overall prevalence of preventable admissions due to negative clinical outcomes associated with medication was 88.9%; (95% CI, 71.9-96.1). With regards to severity, 74.1% (95% CI, 55.3-86.1) of the total admissions were moderate. The most common drugs implicated in hospital admissions were: antibacterial for systemic use, cardiovascular, and non steroidal anti-inflammatory agents. Apart from age, no other factors were found for hospital admissions due to negative results associated with medication.
Conclusions: Negative clinical outcomes associated with medication as cause of hospital admission are a prevalent problem and most of them are avoidable with pharmacotherapeutic follow-up.

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PALABRAS CLAVE
Efectos adversos;
Acontecimientos adversos por medicamentos;
Ingresos hospitalarios;
Resultados negativos asociados con medicamentos

Resultados negativos asociados con medicamentos como causa de ingreso hospitalario

Resumen
Objetivo: Estimar la prevalencia de resultados negativos asociados a medicamentos como causa de ingreso hospitalario y determinar sus características (dimensiones, tipos, evitabilidad, gravedad y grupos terapéuticos implicados). Buscar posibles factores asociados a la aparición de este problema.
Método: Estudio observacional transversal, durante 3 meses, en una unidad del hospital universitario, seleccionando al azar mediante el método de extracción de bolas de una urna a 163 pacientes.
La información obtenida de la entrevista con el paciente, de la revisión de historias clínicas y la procedente de las sesiones clínicas se empleaba para la identificación posterior de los resultados negativos asociados con medicamentos mediante el método Dáder.
Resultados: En 27 de los 163 pacientes estudiados (16,6 %; intervalo de confianza [IC] del 95 %, 1,6-23,0), el ingreso fue causado principalmente por un resultado negativo asociado con los medicamentos. Los pacientes ingresaron por problemas de salud no tratados, inefectividades no cuantitativas e inseguridades cuantitativas respectivamente. Un 88,9 % (IC del 95 %, 71,9-96,1) de los ingresos por resultados negativos asociados con medicamentos fueron evitables. En cuanto a la gravedad, el 74,1 % (IC del 95 %, 55,3-86,1) fueron moderados. Los principales grupos farmacológicos implicados en los ingresos fueron antiinfecciosos sistémicos, fármacos relacionados con el aparato cardiovascular y antiinfl amatorios no esteroideos. A excepción de la edad, no se encontraron factores asociados a la aparición de ingresos por resultados negativos asociados con medicamentos.
Conclusiones: Los ingresos por resultados negativos asociados con medicamentos son un problema de elevada prevalencia y la mayoría son evitables mediante seguimiento farmacoterapéutico.

Introduction

It is believed that negative results related to drugs (NRD) represent a significant public health problem. These problems are frequent, have serious consequences, are of increasing prevalence, and have a significant impact on healthcare, the economy, society, and even the media. In addition, many of them are preventable.[1]

There has been much research into this problem and prevalence varies depending on the type of study. Recent articles have cited the prevalence at around 14.7%.[2] However, the lack of definition and an agreed methodology for measuring this mean that the results vary significantly. Although there are quite a few publications on this subject,[3-6] the results of the studies differ and prevalence varies between 0.4% and 40%, mainly due to the methodology used.

Between 25% and 99% of admissions due to NRD are considered moderate or serious at hospital level.[7-11] Fortunately, despite the magnitude of the problem and its consequences, it has been calculated that approximately half of admissions due to NRMs are preventable.[12,13]

The therapeutic groups mainly affected by admissions due to NRD also vary depending on where the study was carried out. The hypothesis of this research is that NRMs are a frequent cause of hospital admissions and that the majority of these may be prevented with pharmacotherapeutic follow-up. Another hypothesis put forward in this study is that there are variables associated with the patient's characteristics, their habits and their pharmacological treatment that could be possible factors associated with the presence of NRD. If this hypothesis is confirmed, this would contribute to knowledge of NRD in this hospital and advance the development of appropriate strategies to prevent this.

Due to the morbi-mortality associated with admissions due to NRD, the variability observed in the reviewed literature, but, in particular, the fact that it is thought that a high percentage of these are preventable, the main objectives of this study were to establish the prevalence and characteristics of the negative results associated with pharmacotherapy that cause hospital admissions.

Method

An observational transversal study with an analytical component carried out from July 1, 2004 to September 30, 2004 in the High Resolution Unit (HRU) at the Hospital Universitario Marqués de Valdecilla in Santander, which is a third level hospital.

The chosen unit is: *a)* for short stays; *b)* for rapid intervention for patients whose prognosis largely depends on early treatment; and *c)* for intermediary care to provide continuity in care between the emergency department and hospitalisation departments for patients who are in a serious

condition, are unstable or who require semi-intensive follow-up and monitoring. The criterion for inclusion of patients was admission to the HRU during the study period. Exclusion criteria included the following: acute voluntary intoxication, patients admitted to the unit on 2 or more occasions, and patients whose clinical or mental condition prevented the collection of the necessary information for their assessment and for whom there was no one capable of responding to the questionnaire.

Based on the literature consulted, a prevalence of 12% was taken as the reference value. To estimate the prevalence with risk α=.05%, and precision of (5%), using the formula (1), a sample size of 163 patients was calculated. Since a possible 3% loss was predicted, the sample size increased to 168 patients.

$$n = \frac{Z^2\alpha\, p(1-p)}{i^2}$$

where n: sample size; Zα: 1.96 (value Z of normal distribution for an error α=.05); *P*: estimated proportion .12; i: estimation precision (5%).

The patient was interviewed using a questionnaire designed and validated for detecting NRD in the emergency department.[14] This is outlined in Appendix 1. Furthermore, additional information was obtained from the clinical history and clinical sessions. This information was assessed using the Dader method to identify possible suspected cases of admission due to NRM.[15]

Every working day on which a clinical session was held, the total number of patients admitted the day before was established using the nurse's admissions register. The average number of admissions into the unit during the study period was 6 patients a day. In the time available, it was only possible to interview 5 patients a day and therefore if less than 5 patients were admitted, all were interviewed.

If more than 5 were admitted, the patients were selected at random by picking a total of 5 balls from a box containing the total patients admitted. Therefore, 168 patients were selected from the 550 patients that were admitted during the study period.

The suspected cases of NRD detected using the Dader method were discussed with the doctor in charge of the unit. In the event of a discrepancy, the doctor's opinion always prevailed.

To give greater depth to the research into the contribution of NRD to patient admission, 2 groups were established: *a)* NRD as the reason for admission (NRDr), which included all those cases in which NRD was the reason for the patient's admission to hospital regardless of the existence or not of associated factors, and *b)* NRD contributing to admission (NRDc), which included all those cases in which NRD was present at the time the patient was admitted, and which contributed to this to some extent, but was not the main reason for admission. No specific tool for the definition of NRD was found in the literature to assess this aspect and therefore a tool was created and is detailed in Figure 1. This was used to assess the contribution of NRD to admission, once NRD had been identified and confirmed. This tool did not replace or modify the Dader method, rather it was used as a supplementary tool to assess whether the NRD was the direct reason or contributed to the patient's admission. The tool is based on the 5 criteria used in the SEFV (Spanish Pharmacovigilance System) to assess the causality of the appearance of adverse reactions (literature, chronology, evolution, re-appearance, existence of an alternative cause). A question adapted to the definition of NRD was established for each of these criteria, taking into account that negative effects on health resulting from the necessity, efficacy, and security of drugs were assessed, not just security. In addition, the re-appearance criterion took into account whether there were any analytical tests to explain the problem, and therefore these data are relevant for confirming the degree to which NRD contributed to the patient's admission. For the last criterion, which is the existence of an alternative cause, it was specified whether there was no other alternative cause that directly justified the patient's admission (decompensating factors of the disease, worsening of the disease, etc), which enabled the distinction between NRDr and NRDc. Just with the SEFV algorithm, greatest importance was placed on the latter aspect when establishing the degree to which NRD contributed to the hospital admission. The criteria used in the study to determine the degree to which the NRD identified could have been prevented corresponded to the questionnaire designed by Baena et al,[16] which is included in Appendix 2.

To establish the prevalence of hospital admissions due to negative results related to drugs, and the other characteristics of NRD, dependant NRDr and NRDc variables were taken.

In the analysis of the factors associated, only NRMs which were the direct reason for the patient's admission were included. The independent variable was pharmacotherapy. To find possible factors associated with admissions due to NRD, variables such as the following were taken into account in the assessment: *a)* age; *b)* sex; *c)* number of drugs; *d)* self-medication; *e)* number of prescribers; *f)* smoking habit; *g)* education level; *h)* consumption of drugs with a narrow therapeutic margin; *i)* complex medication; *k)* allergies; *l)* underlying disease; *m)* alcohol consumption; *n)* medicinal plants; and *o)* co-morbidity.

The seriousness of the NRMs was classified according to the criteria described by the US Food and Drug Administration, which classifies these as follows: *a)* minor, which refers to those that do not require treatment or longer hospital stay; *b)* moderate, those that require changes in the pharmacotherapy, although the drug which was the cause of the NRD is not always suspended; *c)* serious, those that are life-threatening, require suspension of the therapeutic agent that caused the NRD, and specific treatment; and *d)* lethal, those that, directly or indirectly, cause the patient's death.

The data obtained to identify and assess the NRMs were stored in a valid database for processing with SPSS packages (version 12.0 for Windows) and S-PLUS 6.0.

The statistical analysis of a qualitative variable was performed by calculating frequencies, based on the recommended Wilson formula. The statistical analysis of a quantitative variable was performed by calculating the average and its standard deviation. When 2 qualitative variables were compared, the χ^2 or Fischer test were used and, if one variable was qualitative and the other quantitative these were compared using the Student *t* test.

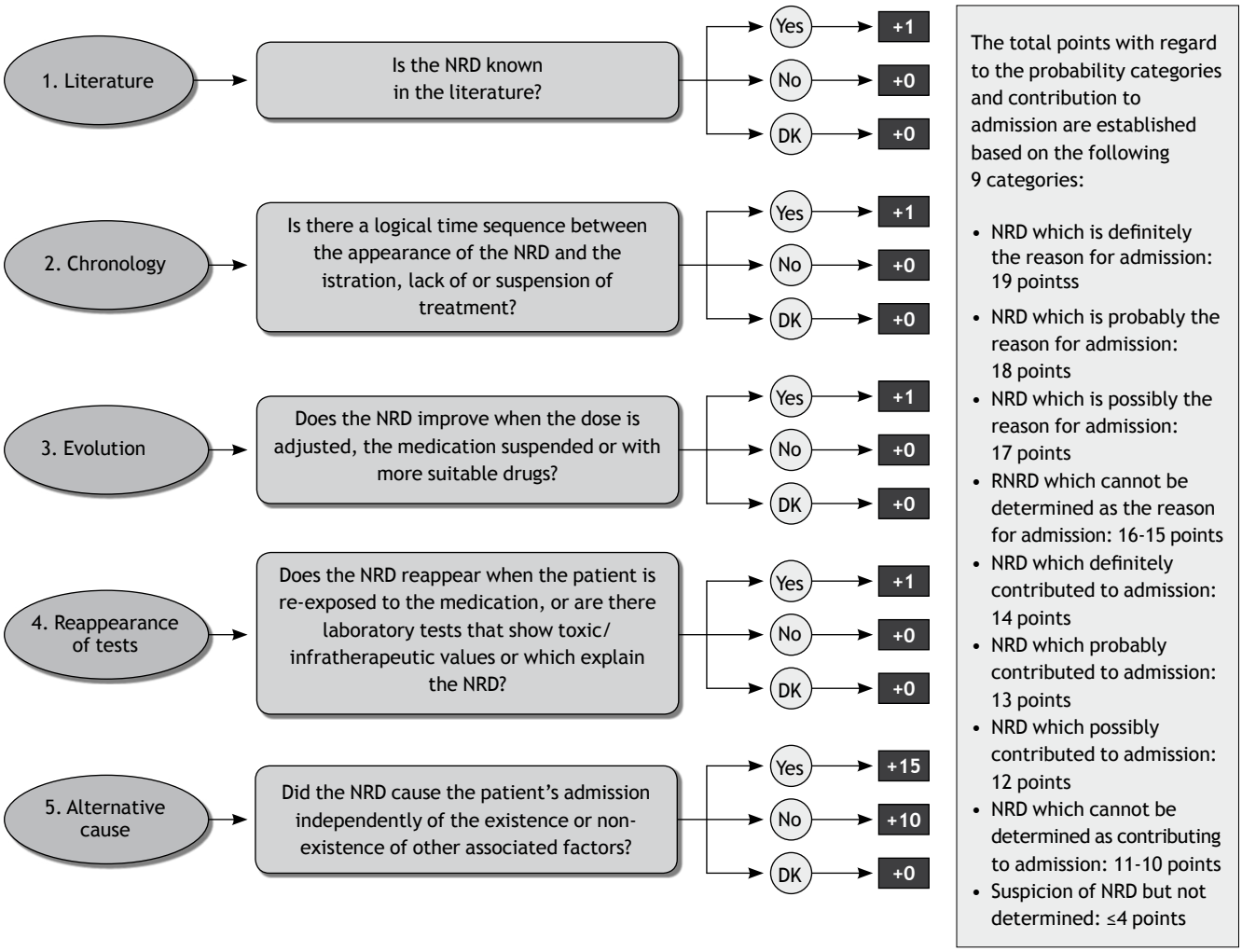

Figure 1 Algorithm to evaluate the degree of contribution of the negative results associated with medicines (NRD) to the revenue.

If the qualitative variable had more than 2 categories, ANOVA was used. Multivariant analysis was also performed using logistic regression. Statistical significance was considered when *P* was <.05.

As with the majority of studies, there are limitations. There was the possibility of bias in the information provided by the patient. In this instance, bias would mean that the prevalence found was underestimated and therefore the problem which we are trying to quantify would be even greater. An attempt was made to reduce the interviewer's bias by using only one interviewer, one structured and validated questionnaire, and carrying out one pilot phase. Finally, the prevalence of the problem could be overestimated and therefore this was minimised by assessing the NRMs in conjunction with the doctor.

Results

Description of the population

Table 1 presents the demographic characteristics of the 163 patients included in the study. Of the 163 people studied, 53 presented an NRD at the time of admission, that is, 32.5% (95% confidence interval [CI], 25.8-40.0) of the population

Table 1 Demographic characteristics of the population included in the study

Average age	64.6 (18.1)
Females	49.1%
Males	50.9%
Average number of drugs taken	4 (3.0)
Proportion of patients with arterial hypertension	46.6%
Proportion of patients with diabetes	19.6%
Proportion of patients with COPD or asthma	12.9%
Proportion of patients with kidney disease	9.8%
Proportion of patients without underlying disease	36.8%
Patients admitted for circulatory disease	39.3%
Patients admitted for respiratory disease	19.0%
Patients admitted for digestive problems	15.3%
Admissions due to poorly defined symptoms/signs	10.4%
Admissions due to mental health issues	3.7%
Admissions due to genitourinary problems	3.1%
Admissions due to infectious diseases	1.8%
Admissions due to intoxication	0.6%
Admissions due to osteoarticular problems	0.6%

COPD indicates chronic obstructive pulmonary disease.

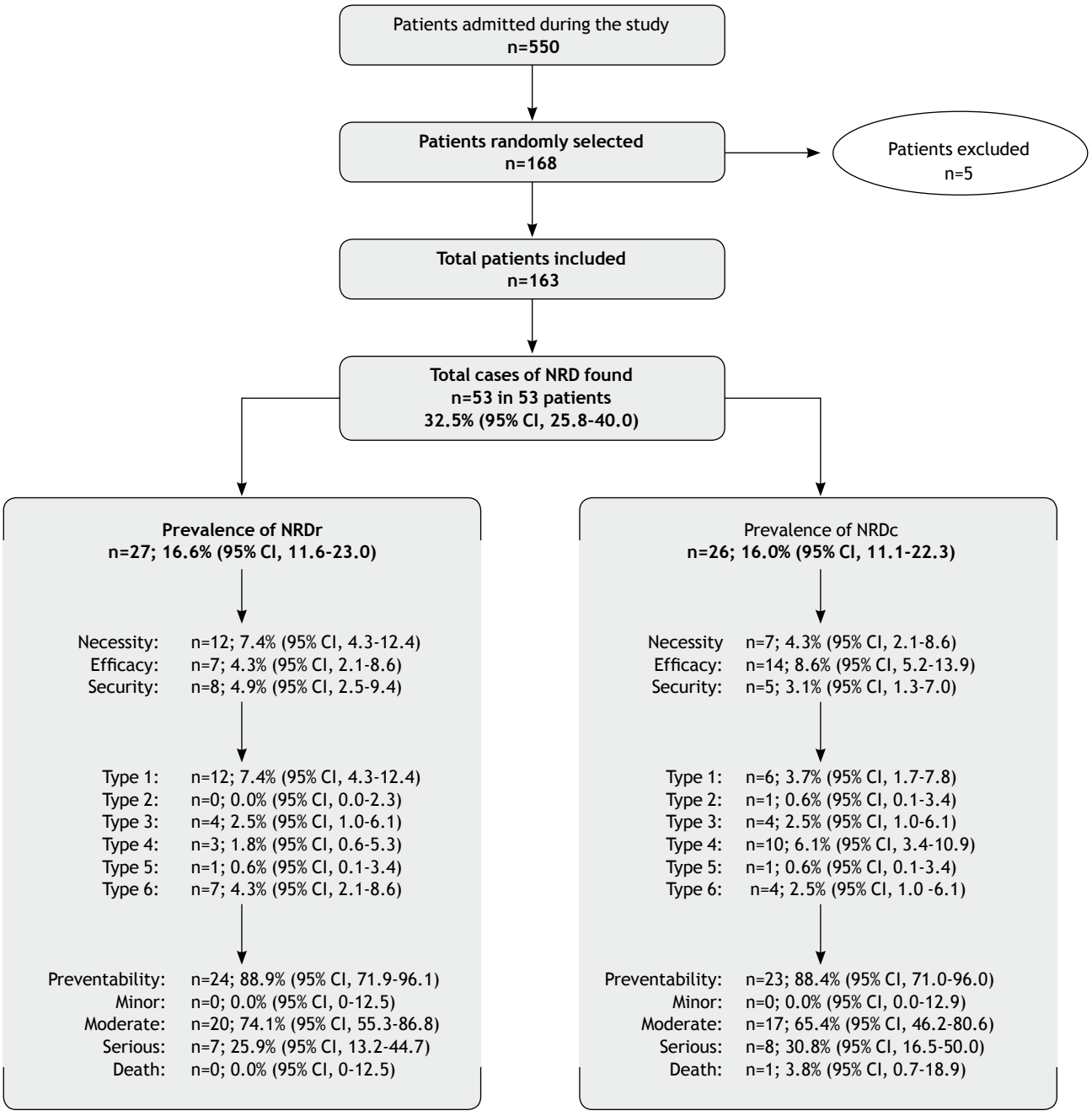

Figure 2 Prevalence and characteristics of the negative results related to drugs (NRD) that were found. CI indicates confidence interval; NRDc, NRD contributing to the admission; NRDr, NRD which were the reason for admission.

admitted had this problem. Of these 53 people, in 27 the NRD was the main cause (NRDr) of admittance and in 26 the NRD contributed to admittance (NRDc), that is, 16.6% (95% CI, 11.6-23.0) and 16.0% (95% CI, 11.1-22.3) respectively.

Of the 27 cases of NRDr found, 15 (55.6%; 95% CI, 37.3-72.4) were definitely the main cause of admittance, 10 were probable (37.0%; 95% CI, 21.5-55.8), and 2 were possible (7.4%; 95% CI, 2.1-23.4).

Figure 2 shows the characteristics of the NRMs found (dimensions, types, preventability, and severity).

The main therapeutic groups involved in the cases of NRDr were those used for cardiovascular related diseases (nitroglycerine, furosemide, digoxin, diltiazem, and quinapril) and those used for infectious diseases (Figure 3).

Associated factors

Bivariant analysis

Table 2 shows the results of the bivariant statistical analysis. When the different variables were analysed as possible factors associated with the appearance of NRD, a statistically significant association was only found for the

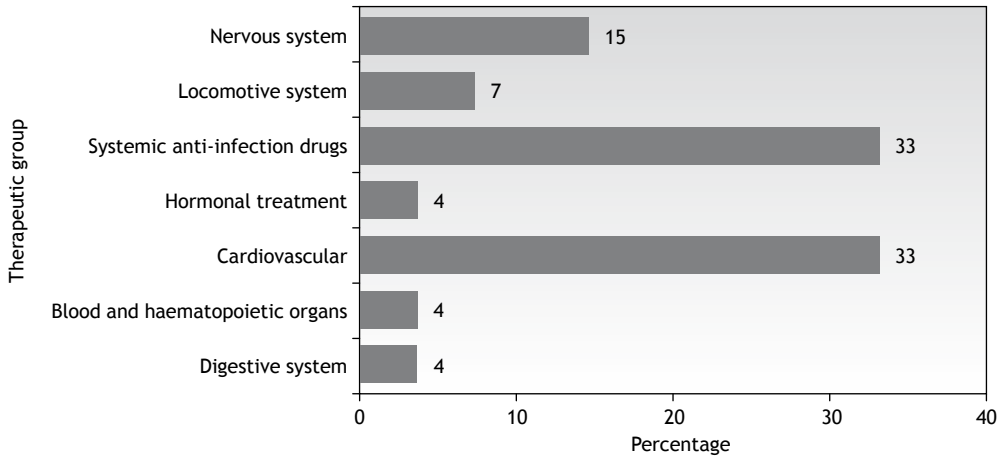

Figure 3 Therapeutic groups linked with the negative results related to drugs (NRD) which were the reason for admission.

Table 2 Results of the bivariant statistical analysis

Variables studied	Categories	Yes NRD, % or SD (95% CI)	*P*
Sex	Male	19.3 (12.2-29.0)	.402
	Female	13.8 (7.9-23.0)	
Age	Continuous	55.9 (18.2) years (48.7-63.1)	.010
Number of drugs	Continuous	4.1 (3.30 drugs (2.8-5.4)	.567
UD	Having UD	12.6 (7.5-20.4)	.085
	Not having UD	23.3 (14.4-35.4)	
Comorbidity	Yes	7.4 (2.1-23.4)	.161
	No	18.4 (12.8-25.7)	
Educational level	No studies	10.0 (4.9-19.2)	.050
	Secondary education graduate	21.3 (12.9-33.1)	.207
	Three-year graduate (university level)	30.4 (15.6-50.9)	.054
	Five-year graduate (university level)	0.0 (0.0-29.9)	.169
Smoking habit	Smoker	26.3 (15.0-42.0)	.081
	Non-smoker	13.6 (8.7-20.7)	
MNTM	Taking MNTM	14.6 (7.2-27.2)	.818
	Not taking MNTM	17.4 (11.5-25.3)	
Self-medication	Yes	14.3 (5.0-34.6)	1.000
	No	16.9 (11.6-23.9)	
Number of prescribers	0-2 prescribers	17.0 (11.7-24.1)	.532
	≥3 prescribers	13.6 (4.7-33.3)	
Phytotherapy	Yes	10.0 (4.3-21.4)	.172
	No	19.5 (13.2-27.7)	
Alcohol	Yes	15.6 (7.7-28.8)	1.000
	No	16.9 (11.2-24.7)	
CM	Taking CM	5.3 (1.5-17.3)	.044
	Not taking CM	20.0 (13.9-27.9)	

CI indicates confidence interval; CM, complex medication; MNTM, medications of narrow therapeutic margin; SD, standard deviation; UD, underlying disease.

Table 3 Variables included in the multivariant statistical analysis

	B	SE	Wald	DF	Sig	OR
Age	−0.019	0.015	1.619	1	0.203	0.981
Underlying disease	−0.110	0.535	0.042	1	0.837	0.896
Smoking habit	−0.264	0.519	0.258	1	0.611	0.768
Educational level	0.299	0.553	0.293	1	0.589	1.349
Comorbidity	0.339	0.840	0.163	1	0.686	1.404
CM	1.249	0.797	2.453	1	0.117	3.486
Phytotherapy	0.426	0.572	0.554	1	0.457	1.531
Constant	−2.079	1.623	1.642	1	0.200	0.125

B indicates coefficient; CM, complex medication; DF, degree of freedom; OR, odds ratio; SE, standard error; Sig, significance of coefficient B; Wald, statistical significance test.

age variable and the consumption of complex medication, which, in the bivariant analysis, acted as a protective factor for admission due to NRD.

Multivariant analysis

This was studied using a binary logistic regression model. The analysis included all the variables with a degree of significance less than 0.2 ($P<.2$) in the bivariant analysis: age, having an underlying disease, smoking habit, education, comorbidity, using complex medication, and the consumption of medicinal plants (Table 3). After eliminating the non-significant variables, only age remained, with a degree of significance of $P=.008$, which is similar to that presented in the bivariant analysis.

Discussion

The hypothesis that negative results related to drugs affect a large part of the population admitted into a high resolution hospital unit was confirmed. This percentage is explained by the type of patients who attend the unit (the elderly, polymedicated, pluri-pathological, acutely ill, etc), the characteristics of the service and the speciality of the doctors attending (emergency doctors or an internist).

In publications that used the interview as a detection method and performed these in observation units (short stay or internal medicine), the range of admissions due to NRD varied between 14% and 46%.[2,17] This interval positions the prevalence of 16.6% found in the present article within the range of results found in other articles.

Looking now at the results for prevalence relating to NRMs that contributed to the patient's admission, but where there was an alternative cause explaining their admission, it was found that 16.0% of people were admitted for this problem. There are very few studies that take this aspect into account and, in general, the prevalence found is very low, most likely due to the methodology used.[11,18]

With regard to aspects relating to cases of NRDr, patients were admitted for problems relating to necessity, security, and efficacy, respectively. In terms of type, the patients were mainly admitted for untreated health problems, non-quantitative infectivities, and quantitative insecurities, respectively.

The greater prevalence of untreated health problems can be explained by the use of the clinical interview as the identification method, which facilitates the detection of a greater number of this type of NRD. In addition, this may also be due to the fact that it is common to have a delay in the diagnosis of diseases.

This result coincides fully with the types found in the research performed by Baena et al,[19] although in this case quantitative insecurities exceeded untreated health problems, probably due to differences in the environments.

There are other studies whose results do not coincide with those of this study.[8,17,20] However, they did not use the same classification for the types of NRD or the research was carried out in a different environment.

On studying the severity, it was observed that 74% of the cases of NRD were moderate, while the remaining 26% were considered serious. No cases of minor NRD were found, nor any cases of death.

This supports the results of other articles.[8,10,11,17] Cases of NRDr in this environment are mainly moderate. Just as the most serious patients are in hospital, cases of NRD causing the hospital admission were also serious.[21] The prevalence of moderate NRMs is greater than that of serious NRMs. This is most likely due to the fact that the more serious cases are in intensive care units.

A total of 89% of cases of NRD could have been prevented with pharmacotherapeutic follow-up. The greatest prevalence of NRMs which could have been prevented was among patients who were admitted for problems of necessity.

The preventability interval for admissions due to NRD found in the literature ranges from 40% to 97%,[10,22,23] and therefore the preventability of 89% which was found in this study is within the range presented in the published literature.

This high level of preventability is explained by the prevalence of admissions due to untreated health problems and the fact that, although a specific algorithm was used, this aspect was measured by one single researcher.

The main therapeutic groups involved in the admissions directly resulting from NRD were: antibiotics and cardiovascular drugs, drugs related to the nervous system, and non-steroidal anti-inflammatories. The result found coincides with the majority of publications.[3,10,24,25] The fact that cardiovascular related diseases is one of the most commonly treated problems in the selected unit could explain why this pharmacological group is involved in a high percentage of admissions due to NRD. Antibiotics and non-steroidal anti-inflammatories are due to the percentage of patients admitted with respiratory and digestive problems.

Factors associated with cases of NRDr

There are no statistically significant differences in terms of sex. This result coincides with the majority of research projects.[9,26] Some studies found that the female sex had a greater risk of admission due to NRM,[20,27] although a multivariant analysis was not performed.

Contrary to what was found in the literature, there was greater prevalence of NRD in individuals under 60. This may

be due to the fact that in the majority of young people NRD itself was the cause of admission or the environment in which the research was carried out. This finding is new and no article has been found that shows that admissions due to NRD are more frequent in the adult population. Different studies associate admissions due to NRD with the adult population,[19,28] and others did not find any association with this factor.[29] On comparing this study with those that did find an association for this variable, it was observed that these were performed in different environments and did not use the same definition for NRD as that taken into account in this research.

It was found that there were no statistically significant differences between the number of drugs that the patient took and the probability of the appearance of NRD. This result does not coincide with what has been published.[26,28,29] This may be because the majority of patients in the selected unit were polymedicated.

None of the remaining variables, such as the presence of diseases, level of education, self-medication, consumption of drugs with strict therapeutic margins, complex drugs, alcohol, medicinal plants, and the number of prescribers were associated with the appearance of NRD. As commented in previous paragraphs, the patients' diseases treated in these intermediate care units, as well as the functioning and specific characteristics of this department may explain the results. In addition, another explanation is that the majority of patients have a carer who pays more attention to their health and the drugs they take.

Finally, with regard to the presence of associated factors, and in accordance with the results found in this research, the following reflection or hypothesis may be drawn: with the exception of age, if there is no statistically significant association between the other variables related to the patients' characteristics and their pharmacotherapy, what may be relevant is the patient's attitude towards their health and pharmacological treatment and importance must be given to the type of disease they have and the number of drugs they take.

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Appendix 1 Questionnaire for detecting negative results associated with drugs

QUESTIONNAIRE NO. _____ INTERVIEW DATE ___/___/___ TIME ___:___

1(*). Date of admission to HRU ___/___/___
Date of discharge from HRU ___/___/___

2(*). Was the patient admitted to other hospital departments? Yes ☐ No ☐ DK ☐
(To be completed by the interviewer)

3. Clinical history number: _____
(To be completed by the interviewer)

CLINICAL HISTORY

3. Reason for admission (outline the symptoms described by the patient, family member, friend)

	SYMPTOMS
1	
2	
3	
4	
5	
6	
7	
8	
9	

4. Underlying diseases (outline the diseases described by the patient, family member, friend…)

	ICD-9

5. Medical diagnosis: (do not complete during the interview. Note the medical diagnosis later, from the emergency department file)

	ICD-9

PHARMACOTHERAPEUTIC HISTORY

6. Are you taking any drug? Sí ☐ No ☐ NS ☐

7(*). Do you know if you are allergic to any drug? Yes ☐ No ☐ DK ☐

DRUG

Other allergies? Yes ☐ No ☐ DK ☐

Please tick: ☐ Food ☐ Environmental ☐ Plants ☐ Animals

8. How long have you been having the symptoms that you described to the doctor? ___/___/___

More than one week ☐ Less than one week ☐

IF YOU ARE NOT TAKING DRUGS, GO TO QUESTION NO. 27

PHARMACOTHERAPEUTIC ASSESSMENT

9. Which drugs are you taking?

INN		
And in relation to these drugs…		
10. Can you tell me how much? (dose)	Yes ☐ No ☐ NK ☐ GM ☐	Yes ☐ No ☐ NK ☐ GM ☐
11. When do you take it? (dosage)	Morning ☐ Midday ☐ Afternoon ☐ Night ☐	Morning ☐ Midday ☐ Afternoon ☐ Night ☐
12. How to do you take it? (way)	Oral ☐ IIntravenous ☐ Other ☐	Oral ☐ Intravenous ☐ Other ☐
13(*). At what time do you have breakfast, lunch, and dinner?	__:__ __:__ __:__	__:__ __:__ __:__
14(*). At what time do you take this medication?	__:__ __:__ __:__	__:__ __:__ __:__
15(*). How long have you been taking this medication? (Approximate)	___/___/___	___/___/___
16. Do you take it every day or are there rest periods?	Continuous ☐ Intermittent ☐	Continuous ☐ Intermittent ☐
17(*). Did you take the medication yesterday as instructed by the doctor?	Yes ☐ No ☐ DK/DA ☐	Yes ☐ No ☐ DK/DA ☐
18(*). And the day before?	Yes ☐ No ☐ DK/DA ☐	Yes ☐ No ☐ DK/DA ☐
19(*). And did you take it as instructed during the last 5 days?	Yes ☐ No ☐ DK/DA ☐	Yes ☐ No ☐ DK/DA ☐

PHARMACOTHERAPEUTIC ASSESSMENT (Cont.)

So, we agree that you are taking this medication now, aren't you?

20. Who prescribed this medication?	GM ☐ C ☐ Ph ☐ SM ☐	GM ☐ C ☐ Ph ☐ SM ☐
21. Can you tell me what it was prescribed for/what you use it for?		
22. Do you know until when you must take the medication? (Approx.)	Days ☐ Weeks ☐ Months ☐ Years ☐ Always ☐ DK/DA ☐	Days ☐ Weeks ☐ Months ☐ Years ☐ Always ☐ DK/DA ☐
23(*). How do you find this medication?	Very bad ☐ Bad ☐ OK ☐ Good ☐ Very good ☐	Very bad ☐ Bad ☐ OK ☐ Good ☐ Very good ☐
24. Is the medication included in the list of drugs with narrow therapeutic margin? (To be completed by the interviewer)	Yes ☐ No ☐ ➔Go to question 27	Yes ☐ No ☐ ➔Go to question 27
25. Are regular blood samples taken to control the medication?	Yes ☐ No ☐ DK/DA ☐	Yes ☐ No ☐ DK/DA ☐

26. Number of drugs you are currently taking: _____
(To be completed by the researcher)

27. Are you taking any medicinal plants?
Yes ☐ No ☐ Go to question 32

28. What plant are you taking? _____

29(*). Can you tell me how much? (Dose)
Yes ☐ No ☐ DK/DA ☐

30. How often do you take this? Continuously ☐ Intermittently ☐
Morning ☐ Midday ☐ Afternoon ☐ Night ☐

31(*). How long have you been taking this plant? ___/___/___

32(*). Do you smoke? Yes ☐ Continuously ☐ Number of cigarettes/day:_____
Intermittently ☐
No ☐ DK/DA ☐

33(*). Do you drink alcohol? Yes ☐ Continuously ☐ Grams of ethanol/day:_____
Intermittently ☐
No ☐ DK/DA ☐

34. Have you had any drink, beer or similar during the period in which you have had these symptoms?
Yes ☐ No ☐ DK/DA ☐

DEMOGRAPHIC DATA

35(*). Sex: Female ☐ ➔ **36.** Are you pregnant? Yes ☐ No ☐ DK/DA ☐
Are you breastfeeding Yes ☐ No ☐ DK/DA ☐
Male ☐

37(*). Date of birth: ___/___/___

38(*). Which is your educational level?
☐ I have not studied
☐ Basic
☐ Professional training (level 2) / Three-year university graduate
☐ Five-year university graduate
☐ Doctorate and above

In the event that the patient does not remember something about the drugs they are taking, ask them: would you mind giving us a contact telephone number so we can ask you the questions you do not remember regarding your medication?

Contact telephone:

39(*). Where do you live?: _____

☐ Santander (capital)
☐ Province of Cantabria
☐ Other provinces

40. Who has responded? Patient ☐ Family member ☐ Carer ☐

41. End time: __:__

42(*). Have you ever been admitted to this unit before?
Yes ☐ ➔ **43.** When? __/__/__
No ☐

COMMENTS:

_____
_____
_____
_____
_____

END OF QUESTIONNAIRE

Note: The questions marked with an asterisk (*) have been modified with respect to the Baena questionnaire to adapt them to the scope of this study and/or obtain more information on those questions considered relevant to identifying NRD.estudio y/o obtener más información sobre aquellas cuestiones que se consideraron relevantes para la identificación de PRM.

C indicates vonsultant; GM, general medicine doctor; HRU, high resolution hospital unit; ICD-9, International Classification of Disease; INN, International Non-property Name for drugs recommended by the WHO; Ph, pharmacist; DK/DA, don't know/don't answer; SM, self-medication.

Appendix 2 Baena criteria to determine the degree of preventability of the negative results related to drugs (NRD)

1. Has the patient's problem developed over a period of time which is sufficient to receive treatment and yet the necessary drugs have still not been prescribed or indicated?
2. The patient's health problem is a result of having taken drugs which are not necessary?
3. The health problem presented is the result of prolonged inefficiency, despite having been treated with the recommended therapeutic doses for the clinical condition?
4. The patient's health problem is a result of a drug interaction?
5. The patient's health problem is the result of having taken the incorrect dose of medication (high or low) due to patient's non-compliance?
6. The patient's health problem is the result of having been prescribed the incorrect dose (high or low) for their age, body mass index or clinical condition?
7. The patient's health problem is the result of a length of treatment that differs from that recommended for their clinical condition (longer or shorter)?
8. The patient's health problem is a result of incorrect self-medication?
9. The patient's health problem is the result of an error in the administration of the drug by the patient?
10. The patient's health problem is the result of having taken a drug (either with a narrow therapeutic margin or foreseeable adverse effects) that requires follow-up and/or laboratory controls which were not carried out?
11. The patient's health problem is the result of having taken drugs which are contraindicated for their characteristics or underlying disease?
12. The patient's health problem is the result of an adverse reaction which had previously manifested in the patient?
13. The patient's health problem is the result of not having taken prophylactic treatment to prevent an adverse reaction, when they meet criteria for this?

*Thirteen questions to each NRD.
An affirmative answer to one or more of these questions implies that the NRD is preventable.
More than one affirmative answer does not imply greater preventability.