ORIGINAL ARTICLES AND REVIEWS

Frequency and trends of hospital discharges against medical advice (DAMA) in a large administrative database

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Abstract

Objective. The aim of this research was to characterize hospitalizations associated with discharges against medical advice (DAMA) in a large, population-based data system. Materials and methods. This was a retrospective cohort study on 11 436 500 hospital admissions. The hospital discharge records for residents of the Veneto region (north-east Italy) discharged from 2001 to 2012, from both public and accredited private hospitals, were considered. The DAMA rate was calculated by type of hospital admission, excluding patients who died. The time trend of the DAMA rate was charted from the average annual percent changes.

Results. During the period considered, 66 549 DAMA were recorded, amounting to an overall DAMA rate of 6.0% admissions. Analyzing the diagnostic categories, admissions for substance abuse (drugs or alcohol) and dependence coincided with the highest DAMA rate (83.5%), followed by poisoning (40.2%), psychiatric disorders (24.7 %), traumas (21.1%), HIV-related diseases (19.9%), burns (10.5%), and - for women - issues relating to pregnancy, childbirth and the postnatal period (11.2%). The DAMA rate dropped from 6.72 to 5.55 from 2000 to 2008, then remained stable.

Conclusion. The DAMA rate dropped slightly over the period considered. Several diagnostic categories are associated with a higher likelihood of patients leaving hospital against their doctor's advice.

Key words

- delivery of health care
- health care surveys
- hospital administration

INTRODUCTION

Policies for cost containment and quality improvement have recently turned their attention to hospital readmissions as the largest source of waste in healthcare systems [1]. When patients choose to leave the hospital before the physician treating them has recommended they do so, i.e. they are discharged against medical advice (DAMA), they are more likely to have to return, often for the same or related conditions [2, 3]. The readmission rates for cases of DAMA are 20% to 40% higher than for normally discharged patients [4]. The cases of DAMA in a sample of patients with CVD were found associated with a higher likelihood of hospital readmissions [5], for instance, and the same was true of DAMA for patients with conditions such as alcohol abuse, asthma, and complications of HIV [6].

Leaving hospital against the physician's advice may expose patients to the risk of their medical problem going inadequately treated [7]. Research has shown that such patients are at higher risk of adverse health outcomes in terms of both morbidity and mortality, with an adjusted relative

risk of 30-day mortality that may be as much as 10% higher than for conventionally-discharged patients [8]. Some characteristics have already been consistently found associated with DAMA, including a lower socio-economic class, male gender, younger age, no health insurance, and substance abuse [5]. It is clearly important to further analyze and better characterize the hospital admissions at greater risk of DAMA with a view to identifying cases at higher risk and possibly taking early action to prevent the related additional burden of morbidity, mortality, and healthcare costs. The aim of this study was to characterize hospitalizations associated with DAMA in a large population-based data system.

METHODS Materials

This was a retrospective cohort study on administrative data using the anonymous computerized database of hospital discharges in the Veneto Region (North-East Italy), an area with a population of about 4 500 000. This database is not publicly available.

The study area is divided into 7 provinces. There are 60 hospitals in all, with about 20 000 beds for acute patient care. All Veneto residents discharged alive after being admitted to public and accredited private hospitals between 1 January 2000 and 31 December 2012 were identified.

The study included both ordinary and day hospital admissions. Based on Italian legislation, a patient failing to attend a scheduled cycle of day hospital appointments should be considered as having resigned voluntarily[9].

Age, sex, citizenship and residence were established from the hospital discharge record for each episode of hospital care. Other aspects considered were: the type of hospital (private or public), the type of admission (for surgical or medical treatment), the type of stay (ordinary or day hospital), and the level of urgency (emergency or scheduled hospitalizations, counting admissions that started with a mandatory medical treatment and those identified as observation after intensive care as urgent. The length of each hospital stay was calculated from the date of admission to the date of discharge.

Certain diagnosis-related groups (DRGs) identified in the literature as being associated with DAMA were derived from the hospital discharge records [10-13], such as psychiatric disorders (DRG 424-432), HIV-related conditions (488-490), and substance, drugs and/or alcohol abuse or addiction (433-437). Other DRGs were also found associated with DAMA, including trauma (9, 27-33, 72, 83, 84, 235-237, 250-255, 280-282, 439-446, 454, 455, 485-487), burns (505, 507-511), poisoning (449-451), infectious diseases (21, 44, 67-71, 79-81, 89-91, 126, 238, 242, 320-322, 417-423, 560, 561, 575, 576, 578, 579), neoplastic diseases (10, 11, 64, 82, 146, 147, 172, 173, 199, 203, 239, 257-260, 274, 275, 303, 318, 319, 338, 344, 346, 347, 353-357, 363, 366, 367, 401-404, 406-414, 465, 473, 492), and pregnancy, childbirth and puerperium (370-384).

Statistical methods

A suitable descriptive analysis was run to calculate the distribution of absolute and relative frequencies for categorical variables, and the average for quantitative variables. To quantify DAMA rates, the indicator used was as proposed by the Association of Maryland Hospitals & Health Systems in the context of the Quality Indicator Project, *i.e.* n. DAMA/1000 total admissions [14, 15]. Patients who died were not considered for the purposes of calculating the indicator.

Significant trends over the years considered were assessed as average annual percent changes (AAPC), a summary measure of a trend over a given fixed interval. This is computed as a weighted average of the annual percent change (APC) emerging from the join-point model, using weights equating to the length of the APC interval [16]. If the confidence interval for the AAPC contains a zero, then there is no evidence to justify rejecting the null hypothesis that the true AAPC is zero at the significance level of α ; if not, then we can reject the null hypothesis in favor of the alternative hypothesis, *i.e.* that the true AAPC is different from zero. A bivariate logistic regression model was applied to verify any association between the characteristics of hospitalization and the outcome (DAMA).

Ethical issues

The study was conducted on data routinely collected by the health services in anonymized records with no chance of individuals being identified. The data analysis was performed on aggregated data. The data in the Local Health Authority registries are recorded with the patient's consent and can be used as aggregated data for scientific studies without further authorization (*Garante per la protezione dei dati personali*, Resolution of 1 March 2012, n. 85). The study complies with the Declaration of Helsinki and with the Italian Decree n. 196/2003 on the protection of personal data.

RESULTS

During the period considered (2000-2012) there were 11 436 500 hospital admissions in the Veneto region, 73.2% of them ordinary admissions (8 366 140), corresponding to 72 048 448 days spent in hospital and an average stay lasting 8.61 days; and 3 070 360 day hospital cycle with an average of 2.96 accesses for a total of 9 073 327 days of admissions. During this period, 66 549 cases of DAMA were identified, amounting to a DAMA rate of 5.8 per 1000 hospital admissions.

Procedural characteristics of admissions

In 93% of cases (61,747 episodes), the DAMA were related to ordinary hospital admissions, pointing to a protective effect of the day hospital solution (OR: 0.2; 95% CI: 0.20 to 0.21, p < 0.000), with a DAMA rate of 1.6‰ for day hospital admissions as opposed to 7.7‰ for ordinary hospital admissions (Table 1). Otherwise, the cases of DAMA after ordinary admissions coincided with shorter hospital stays (4.54 ν s 8.64 days for non-DAMA-related ordinary hospital admissions, p < 0.05), while the day hospital cycles that ended with a DAMA coincided with a higher number of accesses (3.72 ν s 2.95, p < 0.05) than those that did not.

A feature proving an important risk factor for DAMA concerned emergency admissions (with a DAMA rate of 11.6% vs. 2.2% for scheduled admissions, OR: 2.51, 95% CI: 2.47-2.56). On the other hand, a factor protecting against DAMA (especially in males) was a surgical as opposed to a medical DRG (OR: 0.17, 95% CI: 0.16-0.17). Finally a higher risk of DAMA was associated with admissions to accredited private hospitals (OR: 1.17, 95% CI: 1.15-1.19, p < 0.000), representing 18% of total admission produced in the period considered, particularly as regards males (1.27‰ vs 0.97‰, OR: 1.36, 95% CI: 1.31-1.41, p < 0.000) (*Table 1*).

Socio-demographic characteristics of patients

The DAMA rate was higher for males than for females se (6.3‰ vs 5.7‰, OR:1.10, 95% CI: 1.08-1.11, p < 0.000). The distribution by age of patients who were DAMA showed that the overall DAMA rate was highest for the 15-to 24-year-olds (13.1‰), but when the analysis was stratified by gender, this age group continued to coincide with the highest rate for females (15.2‰), while for males the 25- to 44-year-old age group had the highest DAMA rate (12.5‰) (Table 2).

Not being a citizen of the European Union emerged as a risk factor for DAMA in both genders (OR: 2.64, 95% CI: 2.58-2.70, p < 0.000). So did place of residence outside Italy, which was associated with a more than 10-fold higher likelihood of DAMA (OR: 10.78; 95% CI: 10.47-11.09, p < 0.000), the rate being 54.2 ‰, and was much the same in both sexes. Place of residence outside the region (the Veneto in our study) was another risk factor (OR: 1.54, 95% CI: 1.51-1.58, p < 0.000), and for citizens of the Veneto Region, place of residence outside the province where the hospital was located was a risk factor too (OR: 1.07, 95% CI: 1.04-1.10, p < 0.000). Finally, analyzing the cases of DAMA among citizens hospitalized in their province of residence revealed that even being hospitalized in a different local health unit from one's own denoted an additional risk (OR: 1.15, 95% CI: 1.3-1.17, p < 0.000), and this phenomenon was especially true for women (OR: 1.22, 95% CI: 1.18-1.26, p < 0.000) (*Table 2*).

Diagnostic categories on admission

Analyzing the diagnostic categories, the odds of admissions ending with a DAMA were highest for clinical conditions associated to substance, drug, or alcohol abuse or dependence, for which the rate was 83.5% (OR: 23.94; 95% CI: 22.99-24.92; p < 0.000). Higher odds of DAMA also emerged for cases of poisoning, with a rate of 40.2% (OR: 11.01; 95% CI: 10.17-11.9, p < 0.000), and psychiatric disorders, with a rate of 24.7% (OR: 6.65, 95% CI: 6.48-6.83), and this latter category accounted for about 10% of all cases of DAMA. The analysis showed that other clinical conditions associated with DAMA are traumas (OR: 5.66, 95% CI: 5.49-5.83, p < 0.000), and HIV-related diseases (OR: 5.34, 95% CI: 4.66-6.10, p < 0.000). Burns were involved in less than 1% of cases of DAMA, with a rate of 10.5% (OR: 2.79; 95% CI: 1.96-3.58; p < 0.001), while infectious diseases were associated with a DAMA rate of 7.9 % (OR: 2.10, 95% CI: 2.02 to 2.18, p < 0.000). Clinical conditions associated with neoplastic disease were definitely unlikely to end in DAMA, with a rate that was only half the figure for all other clinical conditions (OR: 0.82, 95% CI: 0.79 to 0.85, p < 0.000).

Finally, analyzing DAMA after admissions for clinical conditions related to pregnancy, childbirth and the postnatal period (MDC 14), and considering only females aged between 15 and 45 years, there were or 10 143 cases of DAMA, corresponding to 30% of all cases of DAMA involving the female gender in our sample population, and amounting to a rate of 11.2% (Table 3).

Time trend analysis of DAMA

The time trend analysis on the DAMA phenomenon (Figure 1) for the years from 2000 to 2012 identified a rate for ordinary admissions that decreased slightly but significantly over the years from 2000 2007, from 7.96‰ (in 2000) to 7.27‰ (in 2007); for day hospital admissions, there was a slight but significant drop in the DAMA rate from 2000 to 2008, from 2.86‰ (in 2000) to 1.11‰ (in 2008).

DISCUSSION

This analysis conducted on a large population-based data system identified an overall DAMA rate of 6.0%

and, for ordinary hospital admissions after which patients were discharged alive, the rate was 7.7‰. This proportion decreased significantly during the earlier part of the period analyzed.

The DAMA rate emerging for ordinary hospitalizations (7.7‰) was lower than reported in other recent studies (1.1-1.2%) [17, 18], but higher than in a previous, dated, Italian study [19]. This lower rate could be due primarily to the fact that previous analyses only considered admissions involving people over 19 years old, in fact the admission in younger age resulted less frequently in DAMA. Another explanation concerns the fact that, unlike the situation in the USA, financial considerations are unlikely to prompt cases of DAMA in Italy, where the health services are covered by general taxation and patients are charged nothing for their hospital stays.

Although patients may leave the hospital for various reasons, including family emergencies or other familyrelated needs [18] (which could at least partially explain the higher DAMA rate for patients hospitalized far from home), or their own opinions about their state of health, the DAMA rate could be considered as a quality indicator because it provides a measure of problems in the relationship between doctor and patient [20], the latter's dissatisfaction with their treatment, or divergences of opinion about the patient's condition, and it usually gives rise to a worse clinical outcome, and an unnecessary additional financial burden [21]. The fact that the DAMA rate seems to be higher for admissions to accredited private hospitals than for public hospitals is reassuring regarding the quality of the Region's public health system. Though this finding in our data could also be due to particular organizational features for example the fact that our sample included no private pediatric clinics, which tend to have much lower DAMA rates or more simply to different diagnostic categories-mix among structures. Our analysis of the DAMA rates by diagnostic category revealed an important issue, however, i.e. a remarkably high DAMA rate by comparison with other countries [17, 22]. This finding could be the sign of a crisis in the doctor-patient relationship prompting cases of DAMA discharge, due physicians adopting an excessively defen-

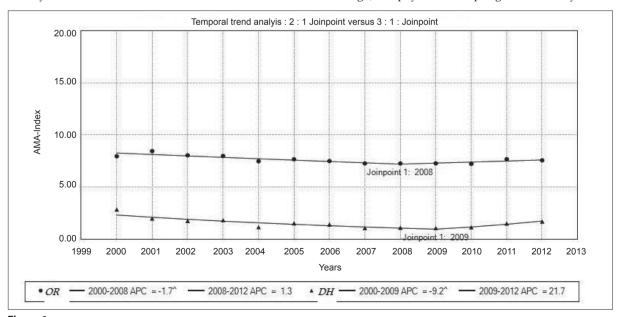


Figure 1
Time trend analysis results: OR = DAMA index for ordinary admission, DH = DAMA index for cycle of day hospital. ^ Annual percent change (APC) is statically significant from zero at alpha = 0.05.

Table 1 Distribution of DAMA: distribution of absolute and relative number, index for DAMA, odd ratio with confidence interval (CI) 95%, stratified for sex

	Female			Male								Total			
	n.	%	t* 1000	OR	CI 95%	n.	%	t* 1000	OR	CI 95%	n.	%	t* 1000	OR	CI 95%
Procedural characteristics	of adm	ission	S												
Public hospital	28 330	83%	5.8	1		26 178	81%	6.0	1		54 508	82%	5.9	1	
Private hospital	5747	17%	5.6	0.97	0.94-1.00	62 94	19%	7.6	1.27	1.23-1.30	12 041	18%	6.5	1.17	1.15-1.19
DRG not surgery	29 026	85%	8.6	1		30 125	93%	10.1	1		59 151	89%	9.3	1	
DRG surgery	5051	15%	2.0	0.23	0.22-0.23	2347	7%	1.1	0.11	0.10-0.11	7398	11%	1.6	0.17	0.16-0.17
Ordinary admission	31 229	92%	7.2	1		30 518	94%	8.3	1		61 747	93%	7.7	1	
Day-hospital	28 48	8%	1.8	0.25	0.24-0.26	1954	6%	1.3	0.16	0.15-0.17	4802	7%	1.6	0.20	0.20-0.21
Not urgent admission ^a	8332	27%	2.2	1		7599	25%	2.2	1		15 931	26%	2.2	1	
Urgent admission ^a	22 897	73%	10.3	2.26	2.21-2.32	22 919	75%	13.2	2.82	2.75-2.90	45 816	74%	11.6	2.51	2.47-2.56

^a calculated only among ordinary admissions.

Distribution of DAMA: distribution of absolute and relative number, index for DAMA, odd ratio with confidence interval (CI) 95%, stratified for sex

	Female t*					Male			Total t*						
	n.	%	1000	OR	CI 95%	n.	%	t* 1000	OR	CI 95%	n.	%	1000	OR	CI 95%
Socio-demograp	ohic char	racteris	tics of	patients	5										
Age class															
0 years	618	2%	1.8	0.18	0.17-0.20	713	2%	1.9	0.15	0.14-0.16	1331	2%	1.9	0.17	0.16-0.18
01-05 years	759	2%	6.3	0.64	0.59-0.69	990	3%	5.7	0.45	0.42-0.48	1749	3%	5.9	0.55	0.53-0.58
06-14 years	516	2%	4.3	0.44	0.40-0.48	699	2%	4.1	0.32	0.30-0.35	1215	2%	4.2	0.39	0.36-0.41
15-24 years	4277	13%	15.4	1.58	1.53-1.64	2396	7%	10.3	0.82	0.78-0.86	6673	10%	13.1	1.23	1.19-1.26
25-44 years	15 505	45%	9.8	1		9686	30%	12.5	1		25 191	38%	10.7	1	
45-64 years	5305	16%	4.1	0.42	0.41-0.43	8780	27%	6.4	0.51	0.49-0.52	14085	21%	5.3	0.49	0.48-0.50
65-74 years	2597	8%	3.0	0.30	0.29-0.31	4318	13%	4.0	0.32	0.31-0.33	6915	10%	3.5	0.33	0.32-0.34
75-84 years	2851	8%	3.1	0.32	0.30-0.33	3593	11%	4.5	0.35	0.34-0.37	6444	10%	3.8	0.35	0.34-0.36
85 years and more	1649	5%	3.7	0.38	0.36-0.40	1297	4%	6.1	0.49	0.46-0.52	2946	4%	4.5	0.42	0.40-0.43
Citenzhip															
Europe Union	28 226	83%	5.1	1		28 741	89%	5.8	1		56 967	86%	5.5	1	
Extra EU	5851	17%	13.7	2.7	2.62-2.78	3731	11%	15.3	2.65	2.56-2.74	9582	14%	14.3	2.64	2.58-2.70
Residence															
Italy	31 442	92%	5.3	1		29 757	92%	5.8	1		61 199	92%	5.6	1	
Other Country	2635	8%	54.4	10.74	10.31-11.19	2715	8%	54.0	9.77	9.38-10.17	5350	8%	54.2	10.78	10.47-11.09
Veneto ^b	28 162	90%	5.1	1		25 809	87%	5.5	1		53 971	88%	5.3	1	
Other Region ^b	3280	10%	7.6	1.48	1.43-1.54	3948	13%	8.8	1.59	1.54-1.64	7228	12%	8.2	1.54	1.51-1.58
Own province ^c	24 637	87%	5.1	1		22 641	88%	5.5	1		47 278	88%	5.3	1	
other province ^c	3525	13%	5.6	1.09	1.06-1.13	3168	12%	5.7	1.04	1.00-1.08	6693	12%	5.6	1.07	1.04-1.10
Own ULSS ^d	16 271	66%	4.6	1		16 611	73%	5.6	1		32 882	70%	5.1	1	
Extra ULSSd	8366	34%	6.4	1.38	1.34-1.42	6030	27%	5.2	0.93	0.91-0.96	14 396	30%	5.8	1.15	1.13-1.17

^a calculated only among ordinary admissions.

sive behavior. Pregnant women are usually apprehensive about their own and their fetus's health and finding such women more likely to be cases of DAMA than women in other diagnostic categories could be due to physicians favoring these DAMA to avoid the risk of legal problems. Patients who are discharged against the doctor's orders have to sign a form releasing the hospital of all liability [23]. This form is designed to protect the hospital and its employees against any legal action and inform patients that the hospital and its employees cannot be held liable for any subsequent morbidity or mortality. With the recently increased focus on continuity of care,

however, experts have also expressed concern about the professional - and in some cases legal - responsibility that may derive from patients leaving against medical advice, whether they sign such a form or not [24]. A further study investigating this particular issue would be desirable.

For other diagnostic categories, our study confirmed the findings of a previous study [17], i.e. that the two hospital diagnoses most frequently ending in cases of DAMA are substance abuse and poisoning. As a previous study, hospital protocols are needed to treat alcohol and opioid withdrawal with a view to containing cases of DAMA [5].

^b calculated only among Italians.

calculated only among Veneto residents.
dealculated only among Veneto residents.
dealculated only among Veneto residents admitted in their own province.

Table 3Distribution of DAMA: distribution of absolute and relative number, index for DAMA, odd ratio with confidence interval (CI) 95%, stratified for sex

	Female		Male		Total										
	n.	%	t* 1000	OR	CI 95%	n.	%	t* 1000	OR	CI 95%	n.	%	t* 1000	OR	CI 95%
Clinical condition															
Sustance abuse	715	2%	69.6	20.38	18.84-22.04	2089	6%	89.6	20.66	19.70-21.66	2804	4%	83.5	23.94	22.99-24.92
HIV	80	0%	22.1	6.15	4.86-7.68	145	0%	18.9	4.04	3.41-4.78	225	0%	19.9	5.34	4.66-6.10
Psychiatric	3676	11%	23.9	6.67	6.43-6.92	3166	10%	25.6	5.52	5.32-5.74	6842	10%	24.7	6.65	6.48-6.83
Trauma	1754	5%	17.3	4.82	4.57-5.05	3308	10%	23.8	5.12	4.93-5.31	5062	8%	21.1	5.66	5.49-5.83
Poison	315	1%	35.3	9.95	8.87-11.17	337	1%	46.4	10.20	9.12-11.41	652	1%	40.2	11.01	10.17-11.93
Burn	9	0%	7.2	1.96	0.90-3.74	28	0%	12.4	2.62	1.74-3.80	37	0%	10.5	2.79	1.96-3.85
Infectious disease	1080	3%	6.4	1.76	1.65-1.87	1738	5%	9.3	1.97	1.88-2.07	2818	4%	7.9	2.10	2.02-2.18
Cancer disease	1186	3%	2.6	0.70	0.66-0.74	1785	5%	3.7	0.77	0.73-0.81	2971	4%	3.1	0.82	0.79-0.85
Other	15 119			1		19 876	61%	4.7	1		34 995	53%	3.8	1	
Pregnancy, childbirth and the postnatal period	⁷ 10 143	30%	11.2	3.08	3.01-3.16										

HIV/AIDS-related and psychiatric disorders were also strongly associated with DAMA, here again confirming previous findings [25-27]. In a prospective study that developed and validated a DAMA prediction tool, psychiatric patients who were cases of DAMA were more likely to have thought that their hospital stay would be brief, so it was the initial "treatment agreement", rather than the nature of their hospitalization, that appeared to be at odds with these patients' expectations [28]. Such cases nonetheless pose an ethical dilemma for health care providers, who must balance respect for their patients' desire to leave with ensuring that they receive the most appropriate care [23]. It sometimes proves quite difficult to respect a patient's wishes without placing their life at risk, and their decision-making capacity may be open to question. It may also be unclear to the treating physician whether the psychiatric disorder is interfering with such decisions [23], but there is clinical evidence to suggest that, despite their altered way of thinking and mood, psychiatric patients are not necessarily less able than others to make appropriate health care decisions [29].

Admissions for surgery seem to be less liable to cases of DAMA (as already reported, [17]), and this is hardly surprising because patients admitted for surgical procedures have to put their lives in their doctors' hands and they are well aware that their health problems cannot be solved outside the hospital. After an operation, patients need a few days to feel autonomous again, by which time they are usually discharged by their doctors. The DAMA rate is low for cancer too, probably here again because cancer patients do not seek solutions for their health problems outside the hospital and they consider their in-hospital care unavoidable.

The likelihood of a given patient leaving a hospital as a case of DAMA changes with age.

For the time being, no accurate assessments have been conducted on the real reasons why patients opt for DAMA, so it is impossible to estimate what proportion of DAMA could be prevented. Our study points to certain characteristics of admissions associated with DAMA. At the time of admission, it may be crucial to identify cases at risk of DAMA and thus plan their course of hospital care with this in mind, as well as organizing follow-up care for after they leave hospital. Patients who are cases of DAMA should be followed up either by means of telephone consultations or with visits from primary physicians or nurses to check on the patient's condition, preferably

within a week of their leaving hospital, depending on their condition. Such approaches would have a good chance of containing the poor outcomes of cases of DAMA [5]. To shed more light on the actual motives behind cases of DAMA, it would also be extremely useful to include questions on the reasons for their decision in the forms that such patients are required to sign [30].

Our study suffers from several limitations. The main weakness of our study lies in that the structure of the available database does not allow for us to adjust for confounding variables, though the use of this routinelyrecorded, unrestricted and unselected population-based registry ensured that the data were not distorted by research hypotheses and provided an overall picture of the DAMA phenomenon. A second limitation concerns the fact that it is only in Italy that cases of patients who fail to attend a day hospital appointment are defined as cases of DAMA, meaning that our findings are not comparable with reports on this phenomenon from other countries, and also giving rise to a partial discrepancy with the DAMA figures for ordinary hospitalizations, for which patients have to deliberately sign a form requesting to be discharged against medical advice [31, 32]. Finally, we were unable to include two important factors in our analysis, relating to patients' level of education and their employment status – both of which parameters are strongly associated with people's perception of their state of health - because the regional registry does not record these details [33, 34].

In conclusion, this study identified admission factors associated with patients being discharged from hospital against medical advice. Identifying patients at risk of becoming cases of DAMA is an important step towards designing approaches to limit this phenomenon. Further research is needed to see how to assure a better quality of care and improve outcomes for these patients, and how best to care for and support this challenging patient population [35].

Conflict of interest statement

There are no potential conflicts of interest or any financial or personal relationships with other people or organizations that could inappropriately bias conduct and findings of this study.

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