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Serious medication reactions' frequency and expense in a general medicine department

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Abstract
To evaluate the prevalence and financial impact of medication responses resulting in or extending hospitalization. To find major adverse responses, every patient hospitalized to an internal medicine ward for more than six months was examined. At the time of the adverse drug response (ADR), or at the time of admission, the number of drug classes was tallied. Excess ADR-related hospitalization was calculated using the following methods: a) raw excess length of stay; b) adjustment for age, sex, and the number of drug classes; and c) investigator estimation of excess length of stay. A total of 329 patients were assessed: 212 male and 117 female, with a mean age of 57.2 (males: 52.2, females: 66.2 (P0.05)), ranging from 17 to 95 years.
They spent a total of 3720 days in the hospital (mean stay 11.3 days). 298 patients (mean age 55.7, taking a mean of 2.7 drug classes, staying a mean of 10.7 days in the hospital) had no ADRs; 31 patients (mean age 84, taking 6.3 drug classes, staying a mean of 15.1 days) had ADRs; and 21 patients (mean age 63.6, taking 4.2 drug classes, staying a mean of 19.2 days, P0.01 vs patients without ADRs) had ADRs. Four ADRs (or 13% of ADRs, 40%) were deadly. Raw ADR-related extra hospital stay accounted for 318 days (8.6% of all hospital days), 282 days (7.6% of all hospital days) with multivariate adjustment, and 197 days (5.3% of all hospital days) with investigator estimation. Upon admission, the point prevalence of ADRs was 3%.
There were 5.6 incidents per 1000 patient days in hospitals. ADR-related hospitalizations were about 3% of the total. Moreover, severe ADRs were present in 6.6% of hospitalized patients. ADRs accounted for between 5 and 9% of hospital expenses. ADRs were linked to the pharmacological characteristics of the medications implicated in 24 out of 31 individuals (77%), and some of them may have been preventable.

Keywords: Negative effects of drugs, general medicine

Introduction
A significant portion of total medical expenditures are attributable to adverse drug reactions (ADRs). 3 to 8% of hospital admissions in internal medicine are thought to be connected to Moreover, up to 20% of all hospitalized patients experience ADRs [1, 2], which can happen [3, 4] An adverse drug response, an unintentional overdose, or an underdose accounted for 2.5% of all patients who visited the emergency room of a general hospital, according to prior research [5]. Such study was lacking, however, in that individuals admitted with diagnoses whose association with a drug was not immediately clear were excluded since the diagnosis of a drug-related hospitalization was specified upon admission. In addition, in addition to getting admitted for drug-related diseases, patients may also suffer from adverse drug reactions during their stay in hospital. So, during a 6-month period, we prospectively evaluated every patient admitted to a general medicine department of the same general hospital. We calculated the quantity were hospitalized due to a drug-related diagnosis or experienced a serious adverse drug reaction, and have made an effort to determine risk variables and calculate the excess number of hospital days connected to ADRs.

Metthods
All inpatients at the Dr. Patnam Mahendra medical college, Chevella, Telangana, General medicine departments in 29-bed ward. The patients' admission diagnostic profile demonstrates that this hospital also houses departments for most medical disciplines (Table 1). Severe responses were classified as those that necessitated hospitalizations, were deadly or life-threatening, or required substantial adjustments to the patient's care (likely lengthening hospitalizations). Overdoses performed on purpose were not counted as adverse medication responses. Unlike unintentional overdosing or underdosing.

An expert in drug-induced disorders assessed each instance that was found. They were categorized in accordance with the (augmented), a form of adverse response linked to the pharmacological characteristics of the medications involved, and B (bizarre), a type of adverse reaction unconnected to the pharmacological characteristics and likely allergic (also known as idiosyncratic) [6]. Hence, patients were divided into three groups: those without ADR, those who were hospitalized due to an ADR, and those who experienced a major ADR while receiving medical care. Age, sex, length of hospital stays, amount and kind of medications used (in accordance with the Vidal drug dictionary's classification [7]), and diagnoses were all documented for each patient. The observer also recorded the number of additional hospital days, if any, associated with each adverse response (medical evaluation), taking place at a hospital.

Table 1: Diagnostic categories at admission in 329 consecutives patients hospitalized over a 6-month period.

Alcohol-related disorders and alcoholism	28.3%
Depression, anxiety, and panic attacks	17.0%
Suicide attempts	14.6%
Social reasons	11.2%
Falls	10.6%
Neurological disorders	5.8%
Seizures	2.7%
Stroke	3.0%
Rheumatological disorders	5.5%
Bronchopulmonary disorders	4.2%
Cancer	2.7%

Three distinct approaches were used to calculate the additional hospital days attributed to adverse medication reactions: The precise number of hospital days for patients hospitalized due to an ADR was provided in all three. The calculations for patients who had an ADR in the hospital included:

1. The raw number of extra hospital days, or the difference between the mean hospital stay for patients without an ADR and the raw individual hospital stay of patients who experienced an ADR.
2. The adjusted number of extra hospital days, calculated as the difference between the mean hospital stay for patients without an adverse drug reaction (ADR) and the mean hospital stay for patients with an ADR, after adjusting the length of stay for age, sex, and the number of medication classes (multivariate regression analysis).
3. The number of additional hospital days that the patient's attending physician estimates (see above).

According to the computation technique utilized, the total number of excess days was equal to the sum of the excess days connected to ADRs resulting in admission or occurring in a hospital, yielding three findings. The cost of extra hospital days was calculated by dividing the total number of extra days by the hospital administration's reference daily hospital cost, which is 1923.90 FF (287.15 Euros or £ 240.46) for this medical department. The hospital will bill insurance companies or the healthcare system using this value.

For quantitative and qualitative variables, respectively, regression analysis and analysis of variance with or without covariates were used in the statistical analysis. Using Systat A, analyses were conducted. At 0.05, the statistical significance level was chosen.

Result

General traits of the population as a whole

335 individuals were admitted to the ward between December and June 2018, the six-month research period. The study's sample size was 329 (98.2%). The six individuals that were excluded were hospitalized for a single night due to an urgent issue unrelated to drugs.

Table 2 lists the general population characteristics. $ Age, length of hospital stays, and number of drug classes were all significantly different between men and women, with the latter being older, staying in the hospital for longer, and using more medications from various classes. $ In Figure 1, the relationship between hospital stays duration and age and the number of drug classes was shown to be significant (duration=6.71+1.6number of drug classes, r=0.33, P0.001). Age and the number of drug classes were likewise associated (age + number of drug classes = 0.64 + number of drug classes, r = 0.66, P 0.001) (Figure 2). The link between the length of the hospital stays and the number of medication classes was no longer significant (P=0.16) when age was taken into consideration. Age and gender were the main drivers of hospital stay length across the board, independent of ADR status.

Adverse effects of drugs

Thirty-one of the 329 patients experienced substantial adverse drug reactions; in 10 cases, the ADR led to hospital admission, and in 21 other cases, the ADR occurred while the patient was hospitalized. There were 298 patients who experienced no negative medication reactions. Table 3 lists the characteristics of these groupings. No one who was hospitalized due to an ADR experienced another ADR while receiving medical care.

In comparison to other patients, those hospitalized for ADRs were older, more frequently female, and used more medication classes.

Patients who experienced major ADRs during their hospital stays were not always older than those who did not, but they were more typically female and used more medication classes. $ 14 out of 21 patients with ADRs hospitalized for all ADRs i.e. connected to the pharmacological characteristics of the medications. Table 4 lists the relevant adverse medication response since some individuals experienced several responses at once the overall number of responses is larger than the total number of people experiencing the reactions, whether they occur concurrently (for example, dehydration and hypotension, or a fall and hip fracture). None of the negative medication responses were brand-new at the time of the occurrence, meaning they weren't listed in the Summary of Product Characteristics. Patients without ADR are included in the regression between age and length of hospital stay (duration=0.10+0.19 age, r=0.43, P0.01).

Table 5 displays drug use, with percentages and 95% two-sided confidence intervals for both those used by the general population and those implicated in ADRs.

Table 2: Characteristics of the overall study population

	Total	Men	Women
Number	329	212	117
Mean age (range)	57.2 (16-95)	52.5 (17-95)	66.2* (16-95)
Mean duration of stay	11.3 (1-50)	9.7 (1-50)	14.2* (1-49)
in days (range) Mean number of drug classes (range)	2.9 (0-8)	2.6 (0-8)	3.4* (0-8)

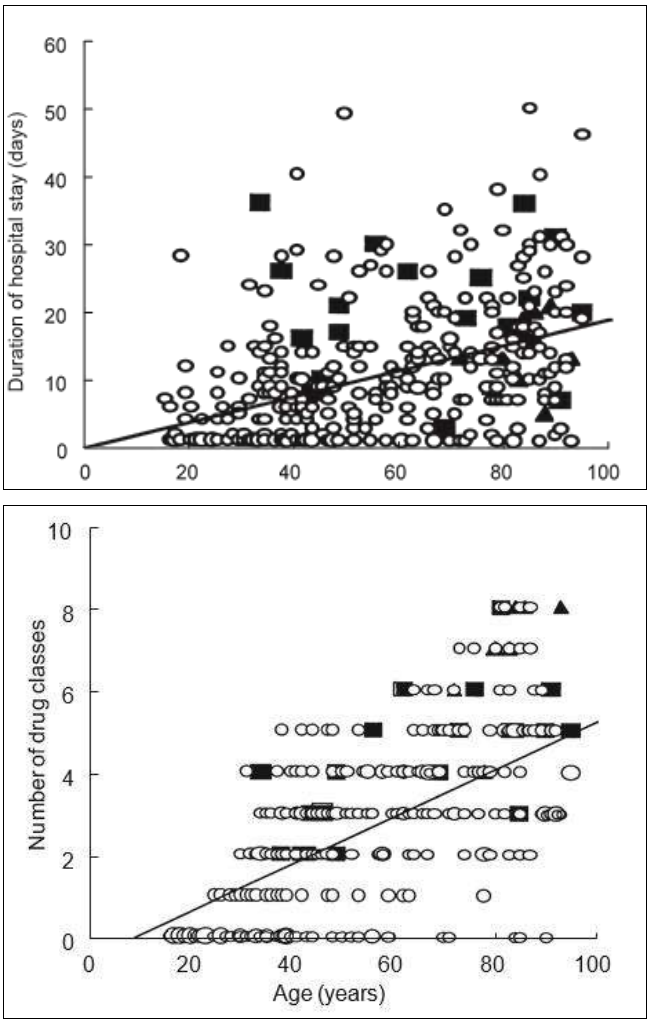

Fig 1: Relationship between duration of hospital stay and age, for patients with no adverse drug reaction (circles).

Patients admitted because of an adverse drug reaction (triangles) and patients having an adverse reaction in hospital (squares) are also indicated. The regression shown between age and duration of hospital stay is for patients without ADR (duration=−0.10+0.19×age, r=0.43, $p<0.01$).
Figure 2 Relationship between age and number of drug classes for all patients without adverse drug reaction (circles). Patients admitted because of an adverse drug reaction (triangles) and patients having an adverse reaction in hospital (squares) are also indicated. The regression shown between number of drug classes and age is for patients without ADR (number of drug classes= −0.53+0.058×age, r=0.64, $p<0.01$).

Duration of hospital stay

Patients with ADRs who were hospitalized did not stay in the hospital much longer than those who were not admitted for ADRs, but those who were already there did. We adjusted the length of hospital stays in the various groups by age, sex, and the number of medication classes used since these variables were associated to the length of hospital stays (analysis of covariance).
Table 6 provides the least squares adjusted mean lengths of stays for the three groups.
Patients who were hospitalized due to ADRs spent marginally less time in the hospital after correction than patients who were not admitted due to ADRs (albeit this was not significant); patients who had an ADR in the hospital stayed longer than the other two groups.

Excess hospital days due to ADRs

The patients hospitalized because to ADR spent a total of 139 days in the hospital. (1) Utilizing the raw data from Table 6: a mean excess of 8.5 days per patient with in-hospital ADR, for a total excess of 178.5 days, added to the 139 days in patients hospitalized for ADRs yielded a total excess of 317.5 days, out of a total excess of 3720 days for the entire population (8.5%).
(2) Using figures from Table 6 that have been adjusted for age, sex, and the number of medication classes, 142.8 more days were added to the 139 days mentioned above, making a total of 281.8 days (7.6% of all hospital days).
(3) Utilizing medical estimates of extra length attributable to ADRs, as determined by the patient's attending physician, a total of 58 days were added to the 139 days for a total of 197 days (5.3% of all days), according to the estimations.
When the cost of a hospital day in internal medicine is multiplied by these 317.5, 281.8, or 197 extra days, the cost over six months was (91167, 80919, and 56568Rs). Moreover, Table 7 shows annual expenses overall, annual costs per ward bed, and annual costs per patient with an ADR.

Table 3: Characteristics of patients admitted for ADR (ADRA), with ADR in hospital (ADRH), and without ADR (No ADR)

	No ADR	ADRA	ADRH	All ADR
Number	298	10	21	31
Type A	—	10	14	24
Men/Women	198/100	2/8*	12/9*	14/17*
Mean age	55.8	83.9*†	63.5	70.2*
(range)	(16–95)	(72–93)	(34–95)	(34–95)
Mean number of drug classes (range)	2.7 (0–8)	6.3*† (4–8)	4.2* (2–8)	4.9* (2–8)

Table 4: ADR description

ADR	Number of cases	Drugs	Comments
Allergy	8	antibiotics (6)	All occurred in hospital
skin reactions (4)		calcium heparinate (1),	
angioedema (1)		fluoxetine (1)	
bronchospasm (1) Orthostatic hypotension	6	antihypertensive drugs, neuroleptics	Often with falls, resulting in one
		tricyclic antidepressants	hip fracture, with fatal outcome outcome in an elderly

			patient
Dehydration	5	diuretics for hypertension or heart failure	In elderly patients
Sleepiness and falls	5		Associated with the two previous disorders
Hypokalaemia	3	diuretics and digoxin	One case of dysrhythmia with favorable outcome
Dysrhythmia	3	digoxin, - with b-adrenoceptor blocker (1) - with diuretic (1)	
Hypoglycaemia	3	insulin (1),	In elderly patients with decreased
		sulphonamides (2)	food intake without dose adjustment
Gastro-intestinal disorders	5		
$ candidosis	1	antibiotic treatment,	
epigastric pain	3	NSAIDs	
duodenal haemorrhage	1	NSAID	Fatal outcome
Neurological: extrapyramidal signs	1	neuroleptics	
Confusion and agitation	1	first dose of viloxazine	
Renal failure	1	gentamycin	Fatal renal failure
Thrombocytopenia with	1	low molecular weight heparin	95-year-old woman, fatal outcome
thrombosis Urinary retention	1	trihexyphenidyle	Resulted in discovery of prostate carcinoma

Prevalence and incidence of adverse reactions

The incidence rate during hospitalizations was 5.6 per 1000 patient-days (21 cases over 3720 patient-days in hospital); the prevalence of reactions during hospitalizations can be calculated as the number of days with reaction over total hospital days, i.e.: 5.3 to 8.5% depending on computation method used, considering the duration of adverse reactions. The point prevalence of adverse drug reactions at admission was 3%: 10 of 329 admissions.

Discussion

A substantial amount of the illness burden in the general population is caused by drugs. It can be evaluated at several times, such as when a patient is admitted to the hospital, when they are out-patients, or when they are generally non-hospitalized. Recent literature, which is outlined below, provides some evidence of these frequencies: The fact that these studies were conducted in various settings and using various retrieval techniques, and that some of them only took adverse reactions into account while others also included involuntary overdosing or underdosing, and that some of them only took clinically obvious reactions into account while others also looked for biological disturbances make them somewhat difficult to compare [8]. Overall, this research provide consistent findings, though:

Table 5: Frequency of ADRs for each drug class.

Drug class	Number of users (% use frequency)	Number of ADRs	% ADR in users	confidence interval
Antibiotics	122 (37.1)	6	4.9	1.8–10.6
Antidepressants	85 (25.8)	9	10.6	4.9–19.2
Neuroleptics Anxiolytics Hypnotics	95 (28.8)	2	2.1	0.3–7.4
Antihypertensives	36 (10.9)	4	11.1	3.1–26.6
Diuretics	61 (18.5)	3	4.9	1.0–13.7
Antiarrhythmics	40 (12.2)	0	0	0–8.8
Digitalics	45 (13.7)	3	6.7	1.4–18.3
Anticoagulants oral	20 (6.1)	0	0	0–17.0
injectable	11 (3.3)	1	4	0.23–41.0
NSAIDs	38 (5.4)	3	7.9	1.7–21.4
Antiparkinsonian	10 (3.0)	1	10	0.25–44.0
Antidiabetic agents	15 (4.5)	3	20	4.3–48.1
Lipid lowering agents	12 (3.6)	1	8.3	0.2–38.5
Steroids	4 (1.2)	0	0	0–60.2
Hormone	3 (0.9)	1	33.3	0.8–90.6
replacement therapy Muscle relaxants	15 (4.6)	0	0	0–21.8
Analgesics	98 (29.8)	0	0	0–3.7

Table 6: Duration of hospital stay in raw figures, and after correction for age, sex, number of drug classes

		No ADR	ADRA	ADRH
Number of patients		298	10	21
Mean duration of stay in days		10.7	13.9	19.2*
(range)		(1–50)	(5–21)	(3–36)
Corrected duration of stay (±s.e. Mean)		10.9±0.5	8.3±2.9	17.7±1.9*†

Table 7: Estimated costs of adverse drug reactions in a 29-bed ward of general medicine in FF, Euros

	Unit	Raw estimate	Corrected estimate	Medical evaluation
Months	Rs	91169	80918	56 568
		76354	67 769	47376
Yearly cost	Rs	1221 676	1 084310	758 016
	Rs	182 339	161 837	113136
	Rs	152 709	135 538	94752
Yearly cost per	Rs	42126	37390	26138
hospital bed	Rs	6287	5580	3901
		5265	4673	3267
Cost per ADR	Rs	19704	17488	12226
patient	Rs	2940	2610	1824
		2463	2186	2528

a) Chrishilles *et al*study [9].'s of 3170 individuals over 65 years old in the outpatient population discovered 10% adverse responses, of which 10% (0.7% of the total) were hospitalised as a result of this reaction. Prince *et al*. [10] identified 293 adverse reactions in 10184 individuals (2.8%), of which 71 (0.7%) required hospitalizations. Schneider *et al*. [11] found 707 adverse reactions in 463 patients overall (5.1%), of whom 105 (0.8%) required admission. These investigations of the general population can be contrasted with three studies on patients treated with digitalis, which reported that 0.7, 0.8, and 0.8% of hospital admissions were due to side effects and overdoses from digitalis [12-14].
Overall, 5–10% of patients experience negative medication responses, and just under 1% of patients are admitted to the hospital as a result.

b) Upon hospital admission: As previously mentioned, ADRs that result in hospital admission happen prior to admission and are generally more severe than other responses. They account for 10% of outpatient hospitalizations and affect less than 1% of the overall population. These cross-sectional models are more prevalent.
Results from several recent papers [15-26] are summarized in Table 8, where the percentage of patients admitted for drug-related reactions ranges from 3% to 20%, with smaller numbers occurring in extremely specialised fields like cardiology and larger numbers occurring in the elderly or in internal medicine. In all, 520 drug-related hospitalizations were discovered in these 13 publications' studies of 9420 patients, or 5.5%, excluding underdoses. This number is close to that discovered by Einarson [1], who collated 36 papers published between 1966 and 1989, with an overall admission rate for ADRs of 5%.
It is noteworthy how closely the data from the admissions and outpatient studies resemble each other.

c) Less studies have been conducted in hospitals; they require that all hospitalised patients be followed up on during their hospital stay, as opposed to the easier cross-sectional studies after admission. Patients may also face more surveillance while in the hospital. Variations in the literature may be explained by changes in the level of scrutiny: Six studies [27–29] were located between 1990 and 1995, and the outcomes are displayed in Table 9. There are between 64 and 36000 patients involved, with a mean of 3% overall and a range of 1.5% to over 20%. (in HIV-positive patients). One extremely sizable research overshadows this finding. For 13872 patients, the other data reveal a total of 875 ADRs, or 6.3%. to the patient population studied, and the way in which the reactions were looked for and ascertained, the figures are quite consistent overall. The data suggest that drug-related diseases occur in 5–7% of the general treated population, Despite significant differences across the studies, associated 10% of those cases (or 0.7% of the population) require hospitalisation. This accounts for around 5% of all hospital hospitalisations, and responses happen in roughly 5% of those cases all patients staying in medical wards at hospitals.

How does our study stack up against these numbers? We discovered a fairly modest percentage of admissions—3%—that were attributable to medication responses. A community hospital with a number of speciality departments serves as our location. And as the department practises general medicine, it accepts patients who are not accepted to the specialist wards. Among these patients are many people who struggle with alcoholism (28% of those admitted patients), or who have attempted suicide with drugs (14.6%). Adverse medication responses account for roughly 5.5% of hospitalisations when these are omitted. All of these events were type A, occurring in elderly individuals who were taking multiple medication classes and 90% of them had associated heart failure and 60% had renal failure 6.3% of hospitalised patients experienced significant drug adverse reactions. 17 out of 25 hospitalised events (type A reactions) occurred in 14 out of 21 individuals, which suggests that they may have been anticipated and possibly averted. Individuals who experienced negative side effects were older and used more prescription medications. Older patients spent more time in the hospital and required more medication. Women also had higher ADRs, were older, consumed more medicines, and spent longer in hospitals. Hence, it is crucial to correctly account for age, sex, and the number of medication classes taken when calculating the extra hospital days linked to ADRs.

Table 8: Summary of published work on drug related hospital admissions.

Source (reference)	Study population	Total number of patients in study	*Number* admitted for ADR	%
Chan *et al.* [15]		1701	34	2
Col *et al.* [16]	Elderly patients	315	53	17
Garijo *et al.* [17]		1847	72	3.9
Hallas *et al.* [18]	Pneumology	313	11	3.5
Hallas *et al.* [19]	Cardiology	366	15	4
Hallas *et al.* [8]	Internal Medicine	333	27	8.1
Hallas *et al.* [20]	Internal Medicine and Geriatrics	607	85	14
Hallas *et al.* [21]	Gastro-entrology	328	32	9.8

Hallas *et al.* [22]	Geriatrics	294	33	11.2
Lin & Lin [23]		2695	109	4
Lindley *et al.* [24]	Elderly patients	416	26	6.3
Smucker *et al.* [25]	Elderly patients	100	9	9
Van Kraaij *et al.* [26]	Elderly patients	105	14	13.3

Table 9 Adverse drug reactions in hospitalized patients.

Source	Study population	Total number of patients in study	Number with ADR	%
Carbonin *et al.* [27]		9148	532	5.8
Classen *et al.* [3]		36653	648	1.8
Foreman *et al.* [28]	Elderly	64	1	1.6
Harb *et al.* [4]	HIV+	390	79	20.3
Lindley *et al.* [24]	Elderly patients;	416	77	18.5
O'Neil *et al.* [29]	Test of methods	3146	133	4.2

It is noteworthy to notice that patients with drug-related admissions had shorter hospital stays than patients with non-drug related disorders after adjusting for age and treatment (perhaps a sign of the number of underlying diseases and their severity). As these ailments often had straightforward treatments (such as discontinuing or modifying medication dosage), the shorter stay may have been caused by quicker diagnosis times for these conditions. According on how they are calculated, excess drug-related hospital days total between 5.3 and 8.5% of all hospital days. The best estimate may be based on age, sex, and treatment-corrected durations, which results in a total of 7.6% of hospital days.

Conclusion

Maybe, these drug-related incidents might have been avoided.

Most likely not for type B reactions, which are unpredictable unless there is a known allergy. A cursory analysis of the type A responses reveals that many of them, including the fatal ones, may have been preventable, saving a significant amount of money on healthcare resources as well as reducing patient suffering. Compared to the 70% in our study, a different study has shown that up to 65% of adverse medication responses may be preventable [32]. Any intervention programme that could demonstrate its effectiveness would quickly turn out to be affordable. In this one 29-bed unit, eliminating half of the preventable significant adverse responses (which account for 35% of all reactions) would yield annual savings of more than 50000.

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