Potential risks and prevention, part 4: Reports of significant adverse drug events

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Abstract: A summary analysis of three descriptive studies of significant adverse drug events (ADEs) was conducted.

Case reports of ADEs published in *ClinAlert* during 1976–97 were the source of information on ADEs, including drug-induced deaths, disabilities, and threats to life. The results of the three studies were compared, and recommendations were made.

During the 21-year period, 1520 significant ADEs were reported (29% resulting in death, 15% in permanent disability, and 56% in life threats). Event types were distributed as adverse drug reactions (52%), allergic drug reactions (25%), medication errors (15%), and drug interactions (8%). Only 12% of the drug interactions were classified as having highest significance by one drug information reference, while 32% of the drug interactions were unclassified. Typically, patients were 40–69 years old and relatively healthy or only moderately ill and had received usual dosages. However, 29% of the patients with a drug-induced permanent disability were less than 10 years old. Only 17% of the drugs that could have been monitored by blood level tests were so monitored. The drug categories most commonly involved in ADEs were central-nervous-system agents, antimicrobials, antineoplastics, and cardiovascular agents. The nervous, hematopoietic, cardiovascular, and respiratory systems were affected the most. Faulty prescribing was the most common reason for medication error, and wrong dosage was the most common type of error. A lawsuit was reported in 13% of the cases. Overall, 52% of the cases were judged to have been preventable; of these, 50% could have been prevented by a pharmacist. Litigation was reported for 13% of the cases; settlements and judgments averaged $3.1 million.

A summary analysis of more than 1500 published case reports of ADEs for 1976–97 yielded information on possible risk factors for drug-related deaths, disabilities, and life threats and on which events may have been preventable.

Index terms: Age; Allergies; Anti-infective agents; Antineoplastic agents; Blood levels; Cardiovascular drugs; Central nervous system agents; Dosage; Drug interactions; Drugs, adverse reactions; Errors, medication; Pediatrics; Pharmacists; Prescribing; Toxicity

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Patients often have an adverse effect from their medication, but why this happens is often unknown, and usually little is done to understand these events. The common response is to switch the patient to another medication with a different chemical structure but the same intended effect. This strategy may meet the immediate needs of the patient; however, it does not prevent the adverse effect from occurring in other patients receiving the same or similar drugs.

Because of a lack of scientific investigation of significant adverse drug events (ADEs, or events resulting in death, permanent disability, or a threat to life), practitioners are at a disadvantage in preventing ADEs. Many times, all that can be done is to document the event in the patient's record, change the drug, and advise the patient to avoid the drug (and similar drugs) in the future. Ideally, patients should receive this advice in writing.

Why do some patients have significant adverse events after taking a prescribed drug, while others of the same age and sex experience little problem? A working hypothesis for the uneven distribution of risk involves the heterogeneity within the human population. Thus, significant ADEs may be associated with variables in the exposure (the drug), with patient variables, and with interactions between the two sets of variables.

Many patient variables may represent distinct risks for a significant ADE. Some variables are more important risk factors than others. Abnormal renal and liver functions are important and may contribute significant risk, but what about the contributions of age, weight, the use of

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alcohol, and the severity of illness? There are also many drug exposure variables. If most of the risk factors for a significant ADE can be identified and quantified, then perhaps a predictive model can be built to help screen for high-risk patients. Pharmacists would then have a tool to help decide which patients to monitor most closely.

This report is the last in a series of four on the risks and prevention of significant ADEs. The first study addressed fatal ADEs,[1] the second drug-induced permanent disabilities,[2] and the third drug-induced threats to life.[3] These descriptive studies were conducted to generate hypotheses on what may be potential risk factors for significant ADEs and how these events may be prevented. The results of these studies can be used to design controlled epidemiologic studies to discover the true risk factors for significant ADEs and each factor's relative contribution. This article summarizes the findings of the three studies and makes recommendations.

Methods

Case reports of ADEs published in *Clin-Alert*, a long-standing publication that specializes in abstracting cases of ADEs published in reputable journals, provided the data for the three studies. Each study covered a 20-year period. *Clin-Alert* was selected because of its credibility and because it provided an efficient means of analyzing data. The investigators had compared 30 randomly selected abstracts with the original published case reports and found the *Clin-Alert* reports to be 97% accurate and 98% complete. Each of the studies followed the same methods.

The data for the first three studies were combined and compared. Frequency distributions for each study variable were used as the basis for comparison.

Results

Frequency of significant ADEs. The frequency of the three types of significant ADEs varied (Table 1). Drug-induced life threats were more frequent than fatal ADEs, and fatal ADEs were more frequent than drug-induced permanent disabilities. Overall, significant ADEs represented 9% of all ADEs reported in *Clin-Alert* from 1976 to 1997.

Reports. Most of the case reports were originally published in medical journals, while only 3% were published in pharmacy journals. Most cases of drug-induced permanent disability were from the legal journal *Medical Malpractice Verdicts, Settlements and Experts*. Most of the reports were from North America and Europe; only a few were from South America, Africa, or the Pacific Rim.

Causality. Sixty-nine percent of the reported ADEs were assessed as being definitely or probably associated with the outcome of interest (Table 2). Type B reactions (idiosyncratic reactions) accounted for 81% of the adverse drug reactions (ADRs).

Mechanisms. Most (52%) of the significant ADEs were ADRs, followed by allergic drug reactions, medication errors, and drug interactions. The most common allergic drug reaction was anaphylaxis. Seventeen percent of the allergic reactions involved immunologic mechanisms that are thus far unclassified. Prescribing was the chief problem in medication errors that resulted in a significant ADE in these studies. Dispensing errors represented 9% of the errors. Most of the drug interactions were category 3 interactions.[4] Only a few of the drug interactions were at the highest levels of significance, categories 1 and 2. Thirty percent of the drug interactions were unclassified.

Patients. Most patients (54%) with a significant ADE were female (Table 3). ADEs were evenly distributed over 10-year age periods. However, the age group 40–69 years represented the bulk of cases. Also, 29% of the cases of drug-induced permanent disability were in children less than 10 years old. Over 80% of the patients were relatively healthy or only moderately ill.

Drugs. Almost all the drugs (91%) were used for the indications listed in *AHFS Drug Information 98* (Table 4).[5] Overall, most of the drugs were prescribed, dispensed, and administered in a hospital. Eighty-nine percent of the patients who had a drug-induced life threat experienced it in a hospital.

Seventy-nine percent of the patients received either usual or below-usual dosages.[5] Forty-nine percent received the suspected drug parenterally, while 42% received it orally. Forty-five percent of the significant ADEs occurred within seven days of starting the drug, while 22% occurred within the first 24 hours. With respect to drug-induced permanent disabilities, 45% occurred within the first 24 hours.

Drug levels were monitored in only 17% of the cases in which they could have been monitored. When monitoring occurred, 88% of the drug levels were either high (twice normal) or very high (more than twice normal).

The drug categories most frequently associated with a significant ADE were central-nervous-system agents, antimicrobials, antineoplastics, and cardiovascular agents; these categories accounted for 64% of the significant ADEs (Table 5). Table 6 lists the specific drugs by type of event.

Events. The significant ADEs most often (68% of the time) affected the nervous, hematopoietic, cardiovascular, and respiratory systems (Table 7). The most commonly occurring precipitating events were anaphylaxis, renal failure, thrombocytopenia, brain damage, and cardiopulmonary arrest.

Errors. A majority (64%) of the medication errors were mistakes, and 81% of the drug-induced life threats were slips (Table 8). Thirty-six percent of the slips involved inattentiveness. Patients received the wrong

Table 1.
Reports of Significant Adverse Drug Events Published in *Clin-Alert*

Item	% Fatal Adverse Drug Events, 1976–95 (n = 447)[1]	% Drug-Induced Permanent Disabilities, 1978–97 (n = 227)[2]	% Drug-Induced Life Threats, 1977–97 (n = 846)[3,a]	All (n = 1520)
Frequency	8	4	15	9
Journal				
Medical	85	43	91	81
Legal	15	56	1	13
Pharmacy	<1	1	4	3
Other	<1	0	3	4
Location				
North America	53	78	56	57
Europe	31	17	34	30
Asia	5	4	6	5
Other	11	1	4	8

[a]The reports for 1982 were not available.

Table 2.
Assessment of Significant Adverse-Drug-Event Reports

Item	% Fatal Adverse Drug Events, 1976–95 (n = 447)[1]	% Drug-Induced Permanent Disabilities, 1978–97 (n = 227)[2]	% Drug-Induced Life Threats, 1977–97 (n = 846)[3,a]	All (n = 1520)
Causality				
Definite	10	23	11	13
Probable	46	47	63	56
Possible	44	30	26	31
Adverse drug reactions[b]	58	43	50	52
Type A	34	9	7	19
Type B	66	91	93	81
Drug allergies	19	0	35	25
Anaphylactic	22	0	52	45
Cytotoxic	35	0	29	30
Immune complex related	19	0	4	7
Cell mediated	2	0	0	1
Other[c]	22	0	16	17
Medication errors	17	54	4	15
Prescribing	67	57	42	58
Administration	17	24	41	24
Dispensing	4	11	13	9
Other	11	8	3	8
Interactions	6	2	11	8
Category 1	4	0	2	2
Category 2	8	20	10	10
Category 3	38	40	47	44
Category 4	8	0	8	10
Category 5	0	0	4	3
Unclassified	42	40	29	32

[a]The reports for 1982 were not available.
[b]Type A = pharmacologic and dose related, type B = idiosyncratic.
[c]Angioedema, pneumonitis, drug fever, acute pulmonary infiltration, chronic pulmonary fibrosis, drug-induced asthma, Stevens-Johnson syndrome, and toxic epidermal necrolysis.

dosage in 35% of the cases, poor monitoring (either at baseline or during therapy) in 18%, and an inferior drug in 13%.

The high rate of significant ADEs in children below the age of 10 years deserves special mention. Most of these adverse events involved permanent disabilities caused by overdoses. Most could have been prevented by computerized monitoring and the oversight of a pharmacist.

Lawsuits. Lawsuits with financial judgments were reported in 199 (13%) of the cases of significant ADEs (Table 9). The physician was the primary defendant most of the time. The most common reasons for bringing suit were overdose (20%), poor or no monitoring (19%), and improper treatment (15%). The drug was misdispensed in 6% of the cases. Financial judgments were awarded by verdict rather than by settlement 57% of the time and ranged from $20,000 to $127 million, with a mean of $3,127,890.

Preventability. Fifty-two percent of the significant ADEs were assessed as preventable (Table 10). Of the drug-induced permanent disabilities, 83% could have been prevented. A pharmacist could have prevented 50% of the preventable significant ADEs. The most common preventive strategies included pharmacist monitoring, computer screening, better laboratory monitoring, and assessing risk before placing the patient on a potentially toxic drug.

Discussion

The analysis of the collective data from the three studies revealed some surprises. The most striking finding, in the author's opinion, was that most patients with a significant ADE received normal or below-normal dosages. Ignoring medication errors, this finding suggests patient factors are at play, not the least of which may be a genetic predisposition. Although the oral route is generally considered the safest, this study found that the oral route is more commonly associated with significant ADEs.

That 9% of all *Clin-Alert* reports represented a major adverse outcome was not surprising. This may not mean that 9% of all ADEs in the population are of major importance as defined in the methods. This is because the *Clin-Alert* reports may not be representative of all ADE events.

About one fifth of the significant ADEs were allergic drug reactions,

Table 3.
Patient Variables Associated with Significant Adverse-Drug-Event Reports

Patient Variable	% Fatal Adverse Drug Events, 1976–95 (n = 447)[1]	% Drug-Induced Permanent Disabilities, 1978–97 (n = 227)[2]	% Drug-Induced Life Threats, 1977–97 (n = 846)[3,a]	All (n = 1520)
Sex				
Female	53	53	54	54
Male	47	47	46	46
Age (yr)				
<10	13	29	8	12
10–19	7	5	8	7
20–29	7	13	11	10
30–39	12	10	13	12
40–49	13	16	13	13
50–59	16	10	16	15
60–69	16	13	18	17
>69	17	5	14	13
Patients status				
Relatively healthy	40	36	9	21
Moderately ill	36	38	76	60
Severely ill	20	21	15	17
Terminally ill	4	4	0	2

[a]The reports for 1982 were not available.

Table 4.
Drug Variables Associated with Significant Adverse-Drug-Event Reports

Drug Variable	% Fatal Adverse Drug Events, 1976–95 (n = 447)[1]	% Drug-Induced Permanent Disabilities, 1978–97 (n = 227)[2]	% Drug-Induced Life Threats, 1977–97 (n = 846)[3,a]	All (n = 1520)
Officially indicated	87	83	97	91
Setting where drug started				
Hospital	56	57	89	67
Outpatient	41	38	5	29
Other	3	5	6	4
Dosage				
Below usual	2	7	7	6
Usual	64	43	82	73
Two to three times usual	26	15	6	12
More than three times usual	7	34	5	9
Route				
Oral	42	29	46	42
Parenteral	46	63	46	49
Other	13	9	8	9
Duration (days)				
<1	25	45	12	22
1.1–7	20	13	29	23
7.1–30	22	11	28	23
31–365	22	17	24	22
>365	10	15	8	10
Blood levels				
Testing available[b]	40	24	15	24
Blood drawn if testing available	10	20	24	17
Levels high or very high if blood drawn[c]	72	100	94	88

[a]The reports for 1982 were not available.
[b]The percentage of blood level monitoring usually available for the drugs discovered.
[c]Twice normal or greater.

perhaps because of the large category of unclassified allergic reactions defined the protocol. These reactions are thought to have an antigen–antibody component; however, the mechanism of the reaction is not well-known.

Only 12% of the drug interactions were in categories 1 and 2; most were in category 3, and many were unclassified. Why this is happening warrants investigation.

Most of the patients were female; females may be more susceptible or may be more willing to share their drug reactions with their physician. The finding that most of the significant ADEs occurred in middle-aged people is remarkable and raises the question of whether this is because this age group is now the largest and thus takes the most medication. Only a controlled epidemiologic study will be able to determine whether age is a true risk factor for a significant ADE. About a third of the drug-induced permanent disabilities occurred in patients less than 10 years of age; more investigation is needed to see what is contributing to these pediatric drug misadventures. Until then, this category of patients warrants special monitoring.

Most of the patients were in relatively good health or were only moderately ill. It has traditionally been believed that the patients most vulnerable to the negative effects of drugs are the very sick. This study suggests this may not be true; again, a controlled study is needed.

Many drugs could have been monitored by blood level testing but were not. The earliest case report reviewed was from 1976, long after the arrival of clinical pharmacy.

It was not unexpected that antimicrobial, antineoplastic, and cardiovascular agents were the drug categories most commonly associated with significant ADEs. Of note, however, was that central-nervous-system agents were the category second most commonly associated with ADEs and the category most frequently linked

to fatal ADEs and drug-induced life threats.

The list of drugs most commonly associated with significant ADEs (Table 6) is intriguing. The list of drugs in the medication error column is strikingly similar to the list of commonly used "high-alert" drugs published by the Institute for Safe Medication Practices.[6] Warfarin barely made the "most common" list in the summary analysis, and digoxin and potassium did not. Perhaps the potential toxicity of these drugs is so well-known that monitoring is universal and publishing one more ADE report is not believed to be helpful.

The organ systems most frequently affected by ADEs were the central nervous system, blood, cardiovascular system, and respiratory system. Organs involved most often in drug-induced permanent disabilities were the brain, eyes, and ears. Most of the drugs doing the damage can be monitored by blood level testing.

Anaphylaxis was the most common precipitating allergic event. This finding, coupled with the high proportion of allergic drug reactions, has important implications for pharmacists. Renal damage was not a major problem, however. Other organs may be more vulnerable to ADEs than the kidneys.

Most of the medication errors were knowledge errors (mistakes) rather than lapses in attention (slips). This finding is consistent with the finding that many of the errors involved prescribing problems, especially incorrect dosages and poor drug selection. Again, these results represent opportunities for pharmacists.

Although only 13% of the cases involved a lawsuit resulting in a financial judgment, *Clin*-Alert abstracts only one legal journal. It is unknown how many of the cases originally published in the medical, pharmacy, and nursing journals abstracted by *Clin-Alert* were also involved in a lawsuit. Almost a third of the lawsuits associated with a drug-induced life threat involved misdispensed drugs. The pharmacy profession lags behind the grocery industry in bar coding products and in using bar-code readers to avoid mistakes. Bar-coding technology was discovered more than 20 years ago.[7]

The reasons for the lawsuits were essentially the same as the reasons for the errors: overdoses, poor or no

Table 5.
Drug Categories Most Commonly Associated with Significant Adverse-Drug-Event Reports

Drug Category	% Fatal Adverse Drug Events, 1976–95 (n = 447)[1]	% Drug-Induced Permanent Disabilities, 1978–97 (n = 227)[2]	% Drug-Induced Life Threats, 1977–97 (n = 846)[3,a]	All (n = 1520)
Central-nervous-system agents	24	16	26	24
Antimicrobials	17	18	20	19
Antineoplastics	17	15	7	11
Cardiovascular agents	12	5	11	10
Blood formation and coagulation drugs	4	5	5	5
Hormones	8	7	2	4
Fluids and electrolytes	2	7	3	3
Autonomic agents	2	1	4	3
Other	14	26	21	20

[a]The reports for 1982 were not available.

Table 6.
Drugs Most Commonly Suspected of Inducing Significant Adverse Drug Events[a]

Adverse Drug Reaction	Allergy	Error	Interaction	All[b]
Valproic acid	Heparin	Theophylline	Methotrexate	Methotrexate
Trimethoprim–sulfamethoxazole	Dextran	Valproic acid	Antineoplastic agents	Heparin
Vancomycin	Sulfasalazine	Gentamicin	Trimethoprim–sulfamethoxazole	Trimethoprim–sulfamethoxazole
Methotrexate	Carbamazepine	Halothane	Levamisole	Valproic acid
Immune serum globulin	Chlorhexidine	Potassium chloride	Bleomycin	Phenytoin
Cyclophosphamide	Cefazolin	0.9% sodium chloride injection	Clozapine	Sulfasalazine
Lithium	Lisinopril	Doxorubicin	Filgrastim	Cyclophosphamide
Aspirin	Rifampin	Lithium	Hydrochlorothiazide	Vancomycin
Bleomycin	Trimethoprim–sulfamethoxazole	Neomycin	Hydralazine	Carbamazepine
Procainamide	Methyldopa	Lidocaine	Lithium	Lithium
Streptokinase	Diatrizoate	Morphine sulfate	Trimethoprim	Ciprofloxacin
Amiodarone	Penicillamine	Oxytocin	Warfarin	Cyclosporine
Diatrizoate		Corticosteroids		Streptokinase
Diphtheria and tetanus toxoids and pertussis vaccine				Diatrizoate
Polio vaccine				Doxorubicin
Propofol				Diphtheria and tetanus toxoids and pertussis vaccine

[a]Listed in order of decreasing frequency.
[b]All drugs causing all events by all mechanisms.

Table 7.
Organ Systems and Precipitating Events Associated with Significant Adverse-Drug-Event Reports

Organ System and Precipitating Event	Fatal Adverse Drug Events, 1976–95 (*n* = 447)[1]	Drug-Induced Permanent Disabilities, 1978–97 (*n* = 227)[2]	Drug-Induced Life Threats, 1977–97 (*n* = 846)[3,a]	All (*n* = 1520)
Organ system (%)				
Nervous	10	48	12	17
Hematopoietic	15	0	22	17
Cardiovascular	15	7	19	16
Respiratory	11	1	22	16
Digestive, hepatic, and biliary	23	5	4	9
Renal and urinary	4	4	10	7
Visual	0	19	0	3
Ear, nose, and throat	0	11	0	2
Other	22	4	10	13
Precipitating event (no.)				
Anaphylaxis	4	0	101	105
Renal failure	6	5	58	69
Thrombocytopenia	6	0	61	67
Brain damage	0	42	0	42
Cardiopulmonary arrest	17	0	18	35
Agranulocytosis	11	0	23	34
Toxic epidermal necrolysis	8	0	22	30
Hemorrhage	2	0	27	29
Neutropenia	4	0	25	29
Hypotension	2	0	25	27
Pulmonary edema	2	0	25	27
Pseudomembranous colitis	6	0	17	23
Aplastic anemia	9	0	12	21
Hepatic failure	18	3	0	21
Hepatitis	18	0	3	21

[a]The reports for 1982 were not available.

Table 8.
Medication Errors Associated with Significant Adverse-Drug-Event Reports

Item	% Fatal Adverse Drug Events, 1976–95 (*n* = 447)[1]	% Drug-Induced Permanent Disabilities, 1978–97 (*n* = 227)[2]	% Drug-Induced Life Threats, 1977–97 (*n* = 846)[3,a]	All (*n* = 1520)
Error category				
Mistake	66	72	19	64
Slip	34	28	81	36
Reason for slip				
Inattentiveness	3	41	68	36
Reading	9	10	0	8
Poor communication	0	2	16	4
Other	88	47	16	52
What happened				
Wrong dosage	41	29	48	35
Poor monitoring	17	22	3	18
Poor drug selection	23	7	16	13
Incorrect administration	4	13	7	9
Unauthorized drug	6	10	16	9
Other	9	20	10	15

[a]The reports for 1982 were not available.

monitoring, and improper treatment. The financial judgments were impressive. A judgment of $1 million will pay for many pharmacists and a sophisticated, user-friendly computer system with money left over.

The assessment that over half of the significant ADEs were preventable is encouraging, as is the finding that pharmacists could have prevented half of the preventable ADEs. Monitoring by pharmacists, computer screening programs, and laboratory tests might be able to eliminate almost 55% of preventable events.

Many middle-aged, relatively healthy patients with normal renal function received normal or below-normal dosages and still had a significant ADE. It may be that these seemingly normal patients had deficiencies in the cytochrome P-450 isoenzymes responsible for metabolizing the drug suspected of causing the ADE. Perhaps patients with an unexplainable, significant ADE should be phenotyped to discover if they are deficient in such enzymes.

The limitations of this study are similar to those listed for the study described in part 1.[1] The findings are suitable for generating hypotheses and form the basis of further investigation.

On the basis of these results, the following recommendations are proposed:

1. If pharmacy is a clinical profession, more should be done to protect patients from ADEs, and this function should become a primary function of pharmacists.
2. Standards on how to report significant ADEs should be developed.
3. Using such standards, pharmacists should publish more ADE reports and should become the practitioners most frequently reporting such events.
4. Patients receiving potentially toxic drugs should receive baseline and ongoing monitoring of blood drug levels and renal and liver function.
5. Patients receiving potentially toxic drugs that can be monitored by blood levels should always be monitored in this way until a lack of toxicity is demonstrated.
6. The drug interactions identified in these studies should be examined further, especially in terms of how

they are classified in drug interaction texts.

7. Patients who are relatively healthy or only moderately ill, patients who receive usual dosages of drugs, and middle-aged patients should not be overlooked in therapeutic drug monitoring. Further pharmacokinetic and genetic research should be conducted to discover why these patients have significant ADEs.
8. More up-to-date, detailed computer programs linking patient, laboratory, and drug data should be developed to prevent significant ADEs.
9. The profession should promote and help to implement computerized order entry by physicians.
10. Pharmacists need to document and publish cases in which they have prevented a significant ADE. Estimates of cost savings should be included.
11. The profession should discuss and develop procedures for reimbursement for the prevention of significant ADEs.
12. Well-designed epidemiologic studies of significant ADEs are needed.

Table 9.
Lawsuits Associated with Significant Adverse-Drug-Event Reports

Item	Fatal Adverse Drug Events, 1976–95 (*n* = 447)[1]	Drug-Induced Permanent Disabilities, 1978–97 (*n* = 227)[2]	Drug-Induced Life Threats, 1977–97 (*n* = 846)[3,a]	All (*n* = 1520)
No. (%) lawsuits with financial judgment	61 (14)	127 (56)	11 (1)	199 (13)
Defendant (%)				
Physician	44	33	45	37
Hospital	23	20	9	20
Pharmacist	3	5	36	6
Other	30	42	9	36
Principal reason for lawsuit (%)				
Overdose	16	22	18	20
Poor or no monitoring	21	19	9	19
Improper treatment	10	19	0	15
Misdispensed drug	0	13	27	6
Contraindicated drug	18	0	0	5
Prolonged treatment	3	6	9	5
Other	32	21	36	29
Financial judgments (%)				
Verdict	57	59	36	57
Settlement	43	41	64	43
Amount awarded ($)				
Range	35,000–9,000,000	20,000–127,000,000	32,000–8,000,000	20,000–127,000,000
Mean	1,061,318	4,385,087	1,152,182	3,127,890

[a]The reports for 1982 were not available.

Table 10.
Preventability of Significant Adverse Drug Events

Item	% Fatal Adverse Drug Events, 1976–95 (*n* = 447)[1]	% Drug-Induced Permanent Disabilities, 1978–97 (*n* = 227)[2]	% Drug-Induced Life Threats, 1977–97 (*n* = 846)[3,a]	All (*n* = 1520)
Preventable events	67	83	50	52
If event preventable, preventable by a pharmacist	57	40	50	50
Method of prevention				
Pharmacist monitoring	27	18	22	23
Computerized screening	17	13	18	17
Better laboratory test monitoring	25	10	9	14
Patient risk assessment	8	8	8	8
Earlier discharge[b]	0	5	13	7
Patient counseling	6	3	7	6
Physician education	3	9	2	4
Double-checking[b]	0	6	3	3
Unclear	4	7	0	3
Other	10	22	19	16

[a]The reports for 1982 were not available.
[b]Method not included in criteria for this study.

Conclusion

A summary analysis of more than 1500 published case reports of ADEs for 1976–97 yielded information on possible risk factors for drug-related deaths, disabilities, and life threats and on which events may have been preventable.

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