A Steep Increase in Domestic Fatal Medication Errors With Use of Alcohol and/or Street Drugs

David P. Phillips, PhD; Gwendolyn E. C. Barker, BA; Megan M. Eguchi

Background: Increasingly, medications are consumed outside of clinical settings, with relatively little professional oversight. Despite this trend, previous studies of medication errors have focused on clinical settings.

Methods: We examined all US death certificates from January 1, 1983, to December 31, 2004 (N = 49 586 156), particularly those with fatal medication errors (FMEs) (n = 224 355). We examined trends in 4 types of FMEs that vary according to the relative importance of alcohol/street drugs and the relative likelihood of professional oversight in the consumption of medications.

Results: The overall FME death rate increased by 360.5% (1983-2004). This increase far exceeds the increase in death rates from adverse effects of medications (33.2%) or from alcohol and/or street drugs (40.9%). The increase in FMEs varies markedly by type. Type 1 (domestic FMEs combined with alcohol and/or street drugs) shows the largest increase (3196%). In contrast, type 4 (nondomestic FMEs not involving alcohol and/or street drugs) shows the smallest increase (5%). Types 2 and 3 show intermediate increases. Type 2 (domestic FMEs not involving alcohol and/or street drugs) increased by 564%. Type 3 (nondomestic FMEs combined with alcohol and/or street drugs) increased by 555%. Thus, domestic FMEs combined with alcohol and/or street drugs have become an increasingly important health problem compared with other FMEs.

Conclusions: These findings suggest that a shift in the location of medication consumption from clinical to domestic settings is linked to a steep increase in FMEs. It may now be possible to reduce FMEs by focusing not only on clinical settings but also on domestic settings.

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IN THE PAST 2 DECADES, THERE HAVE been major changes in the provision of medications.[1-4] Medical care has increasingly shifted from inpatient to outpatient settings[1,2]; thus, medications that once were consumed and monitored in clinical settings are increasingly taken outside the hospital, with reduced professional oversight.[2] More medications that once required prescriptions have become available over the counter.[3] In addition, polypharmacy has increased significantly.[2,4]

These trends have had 2 consequences that affect the safe consumption of medications. The reduction in professional oversight has made it easier to consume medications and alcohol and/or street drugs concurrently, a combination that increases the risk of adverse effects.[5,6] In addition, the patient has been required to play a larger role in monitoring the consumption of medications. Studies of health literacy,[7,8] patient adherence,[9,10] and medication management capacity[11] all suggest that some patients have difficulty in sharing the burden of quality control in health care.

Despite these considerations, efforts to study and reduce medication errors have focused almost entirely on the role of clinical staff in clinical settings.[12-19] Because of this focus, several important questions remain unanswered: (1) What fraction of fatal medication errors (FMEs) occur at home? (2) What fraction of FMEs involve alcohol/street drugs? (3) Are these fractions increasing with time? These questions are addressed in the remainder of this article.

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METHODS

DATA SOURCE

We examined officially generated electronic copies of all US death certificates (N = 49 586 156). The data set begins with January 1, 1983 (when computerized death certificates first listed primary and secondary causes of death), and ends with December 31, 2004 (the latest data year available).[20]

STUDY DESIGN

On the computerized death certificate, accident location is assigned 1 of several codes, including home, school, street, farm, quarry, industrial place, and public building. When analyzing location of accident, we omitted cases in which location was unspecified. No specific codes for health care institutions exist, but a specific code for "home," signifying the home of the decedent, exists.

Table 1. Trends in YPLL From FMEs and From Other Leading Types of Accidents, United States, 1983 to 2004[a]

Variable	*ICD-9-CM*/ *ICD-10* Codes	YPLL		Increase in YPLL (95% CI), %
		1983	2004	
FMEs	E850-E858/X40-X44	126 600	755 264	496.6 (493.0 to 500.1)
Motor vehicle traffic accidents	[b]	1 801 270	1 540 590	–14.5 (–14.7 to –14.3)
Drowning accidents	E910/W65-W69 and W70-W74	260 890	141 922	–45.6 (–46.0 to –45.2)
Accidental falls	E880-E888/W00-W19	145 360	133 661	–8.0 (–8.7 to –7.4)
Fire/flame accidents	E890-E899/X00-X09	171 081	90 303	–47.2 (–47.6 to –46.8)
Nonmedication poisoning	E860-E869 and E924.1/X45-X49	73 571	88 538	20.3 (19.2 to 21.5)
Firearm accidents	E922/W32-W34	75 701	26 125	–65.5 (–66.0 to –65.0)

Abbreviations: CI, confidence interval; FME, fatal medication error; *ICD-9-CM, International Classification of Disease, Ninth Revision, Clinical Modification*; *ICD-10, International Statistical Classification of Disease-Related Health Problems, 10th Revision*; YPLL, years of potential life lost.

[a] Following the usual, official practice,[32] we used 75 years as the life expectancy; YPLL was calculated by summing years of life lost before the age of 75 years for each death. As noted in the "Study Design" subsection of the "Methods" section, an FME death certificate is one with FME recorded either as the underlying cause of death or as one of the contributory causes of death. This type of definition was used not only for FMEs but for each cause of death examined. Most FMEs (82.4%) are recorded as the underlying cause of death rather than as a contributory cause. A death recorded as an FME is elsewhere known as a *fatal preventable adverse drug event*.[15] For brevity, we prefer the former term.

[b] The codes for motor vehicle traffic accidents are too numerous to be listed here; the *ICD-9-CM*[21] and the *ICD-10*[22] provide detailed codes.

We analyzed deaths from all causes but focused on officially acknowledged FMEs, classified as codes E850 to E858 in the *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*)[21] and as codes X40 to X44 in the *International Statistical Classification of Disease-Related Health Problems, 10th Revision* (*ICD-10*).[22] Deaths recorded as FMEs involve "accidental overdose of drug, wrong drug given or taken in error, and drug taken inadvertently [and] accidents in the use of drugs and biologicals in medical and surgical procedures."[21,22] Thus, FMEs can result from prescription or over-the-counter medications. Although FMEs are sometimes unrecorded, we assume that persons whose death certificates mention FME are more likely to have been subject to medication error than were those whose certificates do not mention FME. The category "FME" is equivalent to the term *fatal preventable adverse drug events*, used elsewhere.[15]

The *ICD-9-CM/ICD-10* category "FME" excludes accidental deaths from "street drugs" or alcohol (these are assigned a different set of *ICD-9-CM/ICD-10* codes, identified in the table legends). The FME category also excludes suicides and homicides by poisoning. Finally, the FME category excludes adverse effects, where the "correct drug [was] properly administered in therapeutic or prophylactic dosage, as the cause of adverse effect."[21,22] For example, adverse effects comprise cases such as the administration of the correct medicine in the correct dosage to the correct patient but with an unexpected allergic reaction. The *ICD-9-CM/ICD-10* category of adverse effects is equivalent to the term *fatal nonpreventable adverse drug events*, used elsewhere.[15]

To answer the 3 questions posed in the "Introduction," we classified FMEs into 4 exhaustive, mutually exclusive categories, which were established before we examined the data. These 4 categories vary according to the relative importance of alcohol and/or street drugs and according to the relative likelihood of professional oversight in the consumption of medications. We assumed that professional oversight was relatively unlikely for medications consumed at home.

Type 1 FMEs occur in the patient's home, and the death certificate colists alcohol and/or street drugs as contributory causes of death. Type 2 FMEs occur in the patient's home, and the death certificate does not colist alcohol and/or street drugs as contributory causes of death. Type 3 FMEs do not occur in the patient's home, and the death certificate colists alcohol and/or street drugs as contributory causes of death. Type 4 FMEs do not occur in the patient's home, and the death certificate does not colist alcohol and/or street drugs as contributory causes of death.

It is conceivable that death registrars have become increasingly willing to shift FMEs from secondary to primary cause of death (ie, from contributory to underlying cause). Any tendency of this sort would produce a spurious uptrend in FMEs when they are considered as the primary cause of death. To avoid this bias, we defined an *FME death certificate* as one that listed an FME anywhere on the death certificate (ie, as the primary or secondary cause of death). This type of definition was followed throughout this study not only for FMEs but also for each cause of death examined.

STATISTICAL ANALYSIS

Using the computerized death certificates, we examined sex, race (black vs white), age, marital status, geographic region, cause of death, and location of accident (including FME). Following official recommendations[23] and earlier practice,[12,13,16,24-29] we calculate standard errors[30,31] and significance levels, although we examined complete counts, not samples.

RESULTS

One way to measure the health significance of FMEs is to calculate the number of years of potential life lost (YPLL)[32] from this cause of death. Between 1983 and 2004, the YPLL from FMEs increased by 497% (**Table 1**). The YPLL from FMEs is not only increasing but is doing so at an accelerating pace (the quadratic, best-fit regression line curves upward significantly [$b_2 = 1468.63$, $t_{19} = 9.77$, $P < .001$]).[33] (Henceforth, for brevity, we generally provide the raw data and 95% confidence intervals in table and figure legends.)

In 1983, the YPLL from FMEs was approximately the same as from most other major types of accident. By 2004, however, there were more YPLL from FMEs than from every other major type of accident, except for motor vehicle traffic accidents (Table 1). Indeed, by 2004, FMEs were responsible for far more YPLL than were all accidents from falls, firearms, drowning, fire and flames, and nonmedication poisonings combined.

For any cause of death, yearly increases in YPLL could be driven by 2 factors: (1) the average age at death could be decreasing yearly and (2) the number of deaths

could be increasing yearly. The FME death rate increased steeply, by 360.5% (**Figure 1** and **Table 2**), whereas the average age at death for FMEs decreased only slightly, by 4.8%. Thus, YPLL for FMEs increased mainly because of the 360.5% increase in the FME death rate.

The increase in the FME death rate is much greater than the increase in any comparison category in Figure 1 and Table 2. For example, the death rate from all accidents combined decreased slightly, as did the death rate from all causes combined. Except for FMEs, the death rates for the 5 major types of accidents listed in Table 1 all decreased in the study period.[23] There were relatively moderate increases in other categories: surgical errors (42.9%), adverse effects of medications (33.2%), and deaths from alcohol and/or street drugs (40.9%). The FME death rate is not only increasing steeply but at an accelerating rate (b_2=0.8, t_{19}=7.19, $P<.001$).[33]

The increase in FMEs varies markedly by type (**Figure 2**A and **Table 3**). Type 1 (domestic FMEs combined with alcohol and/or street drugs) shows the largest increase, 3196%. In contrast, type 4 (nondomestic FMEs not involving alcohol and/or street drugs) shows the smallest increase, 5%. Types 2 and 3 show similar, intermediate increases. Type 2 (domestic FMEs not involving alcohol and/or street drugs) increased by 564%.

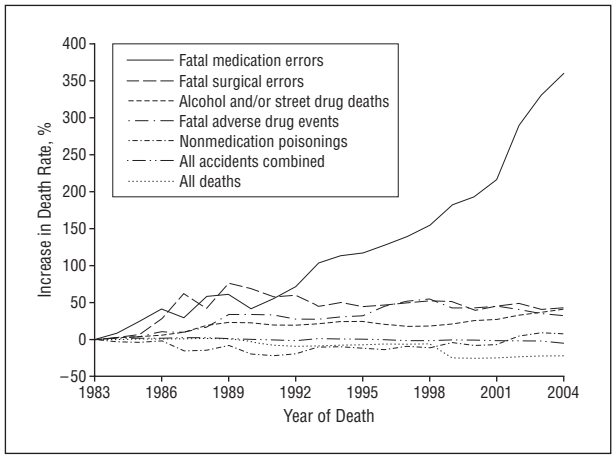

Figure 1. Trends in the US death rate from fatal medication errors and from other causes of death (January 1, 1983–December 31, 2004).

Type 3 (nondomestic FMEs combined with alcohol and/or street drugs) increased by 555%. Type 1 FMEs increased steeply and at an accelerating rate (b_2=10.90, t_{19}=8.69, $P<.001$).[33]

Because of these differential trends, type 1 FMEs have become more important in relation to other types of FMEs. In 1983, type 1 FMEs constituted only 2.32% of all FMEs; by 2004, this percentage was 7 times larger (16.65%). In 1983, there were few type 1 FMEs (n=92) and many more type 4 FMEs (n=1175), a ratio of 0.08 (92/1175). By 2004, the situation was reversed: there were many type 1 FMEs (n=3792) and relatively few type 4 FMEs (n=1541), a ratio of 2.46 (3792/1541).

Type 1 FMEs comprise 3 components: (1) medication errors (2) occurring at home (3) in conjunction with alcohol/street drugs. Figure 2B and Table 3 display the separate trends for each component. All FMEs increased by 360%, all fatal accidents at home increased by 69%, and deaths from alcohol and/or street drugs increased by 41%. Thus, each component separately increased by relatively moderate amounts; in contrast, the combination of the 3 components increased steeply, by 3196%.

The increase in FMEs pervades nearly all major demographic groups (**Figure 3**). Only children from birth to the age of 9 years display no increase in FMEs. Although the FME increase is pervasive, it is particularly strong for persons aged 40 to 59 years and particularly weak for those 60 years and older (Figure 3A). The rise in FMEs is significantly larger for males and white individuals (Figure 3B) and pervades all 9 officially designated geographic regions (geographic data available on request).[23]

These trends helped change the age distribution of persons dying of FMEs (Figure 3). In 1983, middle-aged decedents, aged 40 to 59 years, constituted only 17.9% of all FMEs; by 2004, this percentage had increased to more than half of all FMEs (53.2%). In contrast to FMEs, the age distribution for all deaths combined barely changed between 1983 and 2004.[23]

COMMENT

Unlike almost all other causes of death, the FME death rate has increased steeply in recent years (by 360.5%).

Table 2. Trends in the US Death Rate From FMEs and From Other Causes of Death, 1983 to 2004

Variable	*ICD-9-CM/ICD-10* Codes	No. of Deaths		Increase in Death Rates (95% CI), %[a]
		1983	2004	
FMEs	E850-E858/X40-X44	3954	22 770	360.5 (345.4 to 376.5)
Surgical error	E870-E876/Y60-Y69	395	706	42.9 (26.6 to 62.0)
Alcohol and/or street drugs	291-292, 303, 304.0-304.5, 304.7-304.8, 305.0, 305.2-305.7, 305.9, 357.5, 425.5, 535.3, 571.0-571.3, 655.5, 790.3, 760.7, 980, E860.0/E24.4, F10-F16, F19, G31.2, G62.1, G72.1, I42.6, K29.2, K70, K85.2, K86.0, O35.4, P04.3, Q86.0, R78.0, T51, X65, Y15, Y90, Y91	29 414	51 814	40.9 (38.9 to 42.9)
Adverse drug events	E930-E949/Y40-59	3132	5219	33.2 (27.5 to 39.3)
Nonmedication poisonings	E860-E869, E924.1/X45-X49	2163	2902	7.3 (1.5 to 13.4)
All accidents combined	E800-E869, E880-E929/V01-V99, W00-W99, X00-X59, Y85-Y86	120 537	148 601	−1.4 (−2.2 to −0.7)
All deaths	Not applicable	2 022 000	2 401 000	−5.0 (−5.2 to −4.9)

Abbreviations: See Table 1.
[a] Rates were calculated using population data from the 2007 statistical abstract of the United States.[34]

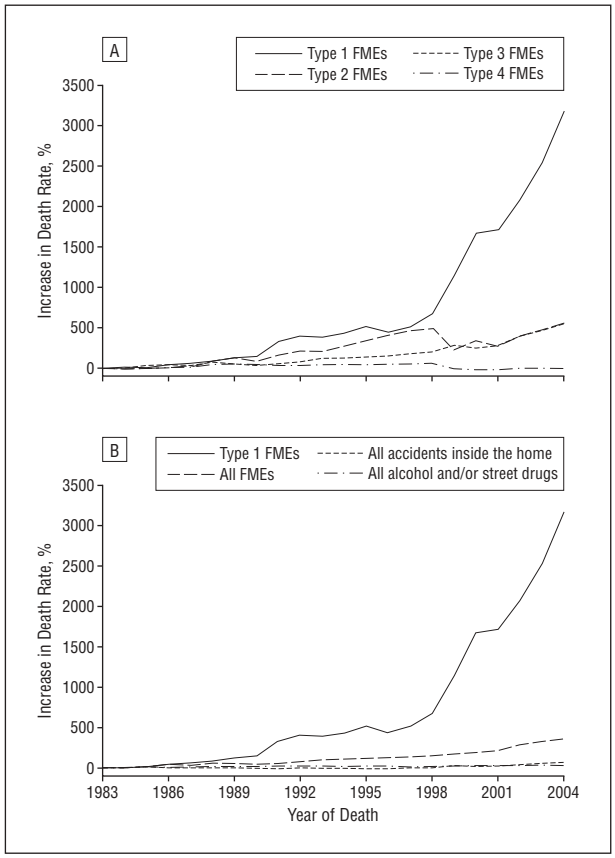

Figure 2. Trends in the US fatal medication error (FME) death rate by type of circumstance in which the FME occurs (A) and for various comparison groups (B) (January 1, 1983–December 31, 2004).

This increase is particularly steep for decedents aged 40 to 59 years, for whom FMEs increased by 890.8%. Type 1 FMEs (domestic FMEs combined with alcohol and/or street drugs) have increased even more sharply, by 3196%. Thus, various types of FMEs and FMEs in general have become increasingly important public health problems. We considered whether the 360% increase in all FMEs resulted from an equally steep increase in the number of prescriptions. However, per capita prescriptions increased relatively moderately (by 73.6%).[37,38]

In addition, we considered several alternative explanations for the 3196% increase in type 1 FMEs. These FMEs comprise 3 components: (1) medication errors (2) occurring at home (3) in combination with alcohol and/or street drugs. It seems implausible that the increase in type 1 FMEs could have been generated by equally steep increases in any of these components. The increase for the combination of the 3 components in type 1 FMEs far exceeds the increase for any single component: all FMEs, 360%; all fatal accidents at home, 69%; and deaths from alcohol and/or street drugs, 41%. Various indicators of substance use or abuse show little or no evidence of increase during the study period. Alcohol consumption per capita decreased (by 17.1%) between 1983 and 2004.[39] The number of illicit drug users declined from 14.1% of the population in 1979 to 6.2% in 1998 and increased only slightly between 1999 and 2004 (from 6.3% to 7.9%).[40,41] Although changes in the use of alcohol/street drugs might have contributed to the increase in FMEs, it is difficult to understand how these changes could be the primary reason for the dramatic increase in FMEs. In sum, the steep increase in type 1 FMEs seems unlikely to have been driven by any single component.

We also considered whether the steep increase in type 1 FMEs could result from changes in classification practices. It is difficult to understand how these putative changes could account for much of the increase in type 1 FMEs for several reasons. The increase in type 1 FMEs is unlikely to result from increased misclassification of "accident at home" because 2 different methods of coding home yield similar findings. Accidents at home were coded since 1979, whereas deaths at home were coded since 1989. The 2 different coding procedures reveal similarly steep increases in FMEs at home. For 1989 to 2004, accidents at home involving FMEs and alcohol and/or street drugs (type 1) increased by 1342% (222 cases in 1989), whereas deaths at home involving FMEs and alcohol and/or street drugs increased by 1831% (167 cases in 1989). None of the increases in Figure 1 and Figure 2 seem to be generated by the change from *ICD-9-CM* to *ICD-10* on January 1, 1999. The lines in these figures display no "break" at the *ICD-9-CM/ICD-10* juncture, and all increases are evident in each *ICD-9-CM/ICD-10* period.

The observed 22-year increase in FMEs is unlikely to have been generated by an increased willingness to code deaths as medication errors for 2 reasons. (1) Attention to medication errors surged with publication of the Institute of Medicine report *To Err Is Human*. This study received "tremendous attention from both the public and the healthcare industry,"[42(p174)] and a survey showed that the report was "the most closely followed health policy story of the year."[43(p2041)] Given the "increased-willingness-to-code hypothesis," FMEs should increase relatively little in the year before *To Err Is Human* appeared and by much more in the year after this report appeared. However, the opposite is true: we found that FMEs increased by only 5.8% in the year after the report and by much more (13.1%) in the year before the report. In addition, in the 15 years before this report appeared (in late 1999), FMEs increased substantially (Figure 1). (2) The FME increase varies markedly by demographic group. To explain these findings, the increased-willingness-to-code hypothesis would require complex, large, yearly, accelerating changes in reporting practices in a 22-year period. Each year, death registrars would need to be increasingly willing to classify deaths as FMEs, particularly for white individuals, males, and the middle aged. We found no studies documenting yearly changes in classification practices for some groups rather than others. In sum, the evidence suggests that the 3196% increase in type 1 FMEs is unlikely to be generated primarily by reporting artifacts.

We found that FMEs increase most steeply in domestic settings, where professional oversight is least likely. This provides fresh evidence for (1) evaluating patients' capacity to manage their own medicines, (2) educating patients about the risks associated with their prescriptions, and (3) monitoring patient performance. It may be appropriate to include not only physicians and nurses but also pharmacists in these efforts.

We found a steep increase in deaths from a combination of medications and alcohol and/or street drugs. This

Table 3. Trends in the US FME Death Rate by Type of Circumstance in Which the FME Occurs and for Various Comparison Groups, 1983 to 2004[a]

Variable	No. of Deaths		Increase in Death Rates, % (95% Confidence Interval)[b]
	1983	2004	
FMEs			
Type 1	92	3792	3195.8 (2628.7 to 4049.8)
Type 2	1040	8634	563.8 (523.4 to 609.1)
Type 3	118	967	555.3 (448.3 to 706.2)
Type 4	1175	1541	4.9 (−2.8 to 13.2)
All	3954	22 770	360.5 (345.4 to 376.5)
All accidents inside the home	16 191	34 317	69.5 (66.4 to 72.7)
All alcohol and/or street drugs	29 414	51 814	40.9 (38.9 to 42.9)

Abbreviation: See Table 1.

[a] We classified FMEs into 4 exhaustive, mutually exclusive categories, which were established before we examined the data. These 4 categories vary according to the relative importance of alcohol/street drugs and according to the relative likelihood of professional oversight in the consumption of medications. Type 1 FMEs occur at home, when the death results from a combination of medication error and alcohol/street drugs. Type 2 FMEs occur at home, when the death results from medication error with no involvement of alcohol and/or street drugs. Type 3 FMEs occur outside the home, when the death results from a combination of medication error and alcohol and/or street drugs. Type 4 FMEs occur outside the home, when the death results from medication error with no involvement of alcohol and/or street drugs. In 10.9% of FMEs, the FME accident occurs in conjunction with other types of accidents. In these cases, one cannot determine from the death certificate whether the code "accident at home" refers to the FME, to some other accident, or to both. Consequently, this 10.9% of FME cases was omitted in all analyses that examined location of accident. In the remaining, single-accident FME cases, 31.2% did not specify the location of the accident. These cases were excluded from all analyses that examined location of accident. The proportion of FMEs excluded in these analyses does not vary significantly by year ($b = .001$, $t_{20} = 1.28$, $P = .11$). Table 1 and Table 2 provide the *International Classification of Diseases* codes for causes of death analyzed.

[b] Rates were calculated using population data from the 2007 statistical abstract of the United States.[34]

provides fresh evidence for (1) screening patients for use, misuse, or abuse of alcohol and/or street drugs; (2) taking extra precautions when prescribing medicines with known dangerous interactions with alcohol and/or street drugs; and (3) emphasizing to the patient the risks of mixing medicines with alcohol and/or street drugs.

In addition to possible changes in policy and clinical practice, it also seems advisable to expand research on medication errors. Much of this research has focused on elderly patients and clinical settings.[12-17] The present findings suggest that more research should be devoted to middle-aged patients and domestic settings.

The use of official computerized death certificates provides significant advantages. These data enable us to examine many FME cases for the entire United States for several decades. Using these data, we can study FMEs in various settings (including the home) and under various circumstances (including the involvement of alcohol and/or street drugs).

On the other hand, this data set has significant limitations. First, it does not provide much detail per FME (eg, dosage or detailed drug), and it allows us to examine only the most severe medication errors (those that are fatal). In addition, although we can study FMEs arising at home, we cannot perform the parallel analysis of FMEs arising in medical settings. Partly because of these limitations, this study has left several important questions unanswered. We documented steep increases in FMEs, but we did not measure the separate increases for each type of medication, whether prescribed or over the counter. Research on this topic may need to await further data. Detailed information on deaths from individual medications is available only recently, from 1999 to 2004.

It now seems clear that a rapidly increasing number of FMEs occur in domestic settings, but the detailed reasons for this increase are not yet clear. We do not yet know what types of error play the largest role. In addition, we do not yet know what type of alcohol and/or street drug

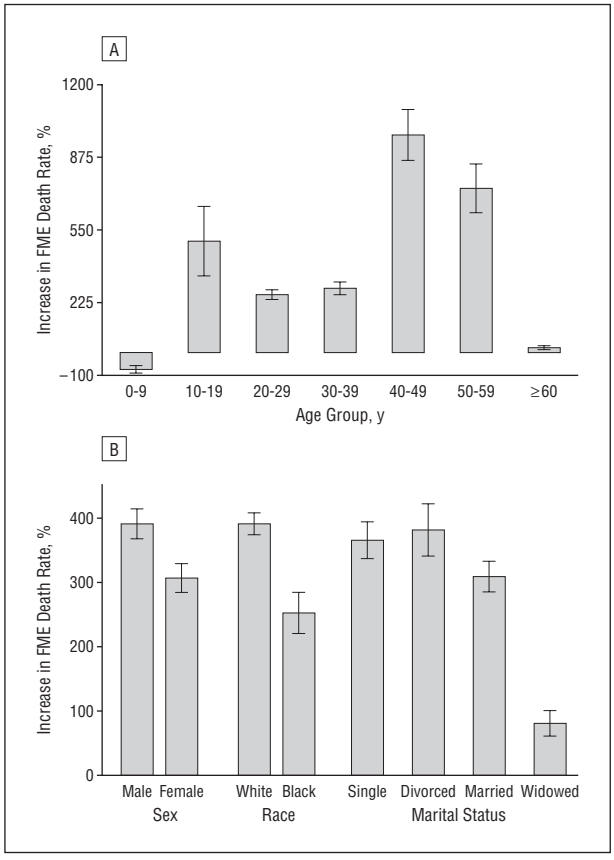

Figure 3. Increase in US fatal medication error (FME) death rates by age group (A) and various demographic characteristics (B) (January 1, 1983-December 31, 2004). Error bars represent 95% confidence intervals, calculated according to formulas for the ratio of rates provided by Daly and Bourke.[30] Information on population is taken from the statistical abstracts of the United States.[34-36] The age groups examined are as defined in the statistical abstracts of the United States. The analysis of marital status is restricted to persons 18 years and older.

consumption contributes most to the increase in FMEs. For example, we do not yet know whether the increase in FMEs is produced mostly by occasional drinkers or by heavy drinkers.

Recent changes in medical care have shifted the location in which many medications are consumed from clinical to domestic settings. The present findings suggest that this shift is linked to a steep increase in FMEs. It may now be possible to reduce FMEs by focusing not only on clinical settings but also on domestic settings.

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REFERENCES

1. American Hospital Association. TrendWatch chartbook 2007: trends affecting hospitals and health systems. http://www.aha.org/aha/research-and-trends/chartbook/2007chartbook.html. Accessed June 17, 2007.
2. National Center for Health Statistics. *Health, United States, 2005, With Chartbook on Trends in the Health of Americans.* Hyattsville, MD: National Center for Health Statistics; 2005.
3. Blenkinsopp A, Bradley C. Patients, society, and the increase in self medication. *BMJ.* 1996;312(7031):629-632.
4. Gorard DA. Escalating polypharmacy. *QJM.* 2006;99(11):797-800.
5. US Department of Veterans Affairs. Complications of antiretroviral therapy: recreational drugs and antiretroviral therapy. http://www.hiv.va.gov/vahiv?page=cm-314_rec_drugs. Accessed October 28, 2007.
6. Substance Abuse and Mental Health Services Administration. Report to Congress on the prevention and treatment of co-occurring substance abuse disorders and mental disorders. http://www.samhsa.gov/reports/congress2002/. Accessed September 28, 2007.
7. Baker DW, Wolf MS, Feinglass J, Thompson JA, Gazmararian JA, Huang J. Health literacy and mortality among elderly persons. *Arch Intern Med.* 2007;167(14):1503-1509.
8. Nielsen-Bohlman L, Panzer AM, Kindig DA, eds. *Health Literacy: A Prescription to End Confusion.* Washington, DC: National Academies Press; 2004.
9. Col N, Fanale JE, Kronholm P. The role of medication noncompliance and adverse drug reactions in hospitalizations of the elderly. *Arch Intern Med.* 1990;150(4):841-845.
10. The Boston Consulting Group. The hidden epidemic: finding a cure for unfilled prescriptions and missed doses. http://www.bcg.com/publications/publications_splash.jsp. Accessed August 10, 2007.
11. Kripalani S, Henderson LE, Chiu EY, Robertson R, Kolm P, Jacobson TA. Predictors of medication self-management skill in a low-literacy population. *J Gen Intern Med.* 2006;21(8):852-856.
12. Phillips DP, Bredder CC. Morbidity and mortality from medical errors: an increasingly serious public health problem. *Annu Rev Public Health.* 2002;23:135-150.
13. Phillips DP, Christenfeld N, Glynn LM. Increase in U.S. medication-error deaths between 1983 and 1993. *Lancet.* 1998;351(9103):643-644.
14. Aspden P, Wolcott J, Bootman JL, Cronenwett LR, eds. *Preventing Medication Errors: Quality Chasm Series.* Washington, DC: National Academies Press; 2006.
15. Gurwitz JH, Field TS, Harrold LR, et al. Incidence and preventability of adverse drug events among older persons in the ambulatory setting. *JAMA.* 2003;289(9):1107-1116.
16. Phillips DP, Jarvinen JR, Phillips RR. A spike in fatal medication errors at the beginning of each month. *Pharmacotherapy.* 2005;25(1):1-9.
17. Barker KN, Flynn EA, Pepper GA, Bates DW, Mikeal RL. Medication errors observed in 36 health care facilities. *Arch Intern Med.* 2002;162(16):1897-1903.
18. Pirmohamed M, James S, Meakin S, et al. Adverse drug reactions as cause of admission to hospital: prospective analysis of 18,820 patients. *BMJ.* 2004;329(7456):15-19.
19. Gandhi TK, Weingart SN, Borus J, et al. Adverse drug events in ambulatory care. *N Engl J Med.* 2003;348(16):1556-1564.
20. National Center for Health Statistics. *Mortality Detail File, 1983-2004.* Hyattsville, MD: National Center for Health Statistics; 1987-2007. Computer Data File.
21. Public Health Division, NSW Health. Annotated International Classification of Diseases: Ninth Revision, Clinical Modification: Fifth Edition, October 1995. http://www.health.nsw.gov.au/public-health/icd/icd9.htm. Accessed December 2, 2006.
22. World Health Organization. International Statistical Classification of Disease-Related Health Problems, 10th Revision. http://www.who.int/classifications/apps/icd/icd10online/. Accessed December 2, 2006.
23. National Center for Health Statistics. *Vital Statistics of the United States, 1993: Volume II: Mortality: Part A: Section 7.* Washington, DC: Public Health Service; 1997.
24. Phillips DP, Christenfeld N, Ryan NM. An increase in the number of deaths in the United States in the first week of the month: an association with substance abuse and other causes of death. *N Engl J Med.* 1999;341(2):93-98.
25. Phillips DP, Paight DJ. The impact of televised movies about suicide: a replicative study. *N Engl J Med.* 1987;317(13):809-811.
26. Phillips DP, Carstensen LL. Clustering of teenage suicides after television news stories about suicide. *N Engl J Med.* 1986;315(11):685-689.
27. Phillips DP, Ruth TE, Wagner LM. Psychology and survival. *Lancet.* 1993;342(8880):1142-1145.
28. Phillips DP, Liu GC, Kwok K, Jarvinen JR, Zhang W, Abramson IS. The Hound of the Baskervilles effect: natural experiment on the influence of psychological stress on timing of death. *BMJ.* 2001;323(7327):1443-1446.
29. Phillips DP, Jarvinen JR, Abramson IS, Phillips RR. Cardiac mortality is higher around Christmas and New Year's than at any other time: the holidays as a risk factor for death. *Circulation.* 2004;110(25):3781-3788.
30. Daly LE, Bourke GJ. *Interpretation and Uses of Medical Statistics.* 5th ed. Oxford, England: Blackwell Science Ltd; 2000:544.
31. Altman DG, Machin D, Bryant TN, Gardner MJ, eds. *Statistics With Confidence: Confidence Intervals and Statistical Guidelines.* 2nd ed. London, England: BMJ Books; 2000:46-47.
32. NCHS definitions: years of potential life lost. National Center for Health Statistics Web site. http://www.cdc.gov/nchs/datawh/nchsdefs/yearsofpotentiallifelost.htm. Accessed May 18, 2007.
33. Kleinbaum DG, Kupper LL, Muller KE, Nizam A. *Applied Regression Analysis and Other Multivariable Methods.* 3rd ed. Pacific Grove, CA: Duxbury Press; 1998.
34. US Census Bureau. The 2007 Statistical Abstract: The National Data Book . http://www.census.gov/compendia/statab/2007/2007edition.html. Accessed January 18, 2007.
35. US Census Bureau. Statistical Abstract of the United States 1985: National Data Book and Guide to Sources (105th ed). http://www.census.gov/prod/www/abs/statab1951-1994.htm. Accessed January 18, 2007.
36. US Census Bureau. The 2006 Statistical Abstract: The National Data Book. http://www.census.gov/compendia/statab/2006/2006edition.html. Accessed January 18, 2007.
37. Pharmaceutical Manufacturers Association. *Statistical Fact Book.* Washington, DC: Pharmaceutical Manufacturers Association; 1991.
38. NDC Health. *National Prescription Audit.* Yardley, PA: NDC Health; 1991-1998.
39. National Institute on Alcohol Abuse and Alcoholism. Apparent per capita ethanol consumption for the United States, 1850-2004. http://www.niaaa.nih.gov/Resources/DatabaseResources/QuickFacts/AlcoholSales/default.htm. Accessed May 4, 2007.
40. Office of National Drug Control Policy. Fact sheet: drug use trends: October 2002. http://www.whitehousedrugpolicy.gov/publications/factsht/druguse/. Accessed August 28, 2007.
41. Substance Abuse and Mental Health Services Administration. *Results From the 2004 National Survey on Drug Use and Health: National Findings.* Rockville, MD: Office of Applied Studies; 2005. NSDUH series H-28, DHHS publication (SMA) 05-4062.
42. Stelfox HT, Palmisani S, Scurlock C, Orav EJ, Bates DW. The "To Err is Human" report and the patient safety literature. *Qual Saf Health Care.* 2006;15(3):174-178.
43. Altman DE, Clancy C, Blendon RJ. Improving patient safety: five years after the IOM report. *N Engl J Med.* 2004;351(20):2041-2043.