Mismedicating the Elderly—Says Who?

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It hardly seems possible that three, relatively obscure, Ivy League academicians could trash the collective reputations of nearly every practicing physician in this country and get away with it. Not long ago, that's exactly what happened.

Sharon Willcox, David Himmelstein, MD, and Steffie Woolhandler, MD, writing in *The Journal of the American Medical Association (JAMA)*,[1] accused American doctors of wrongly medicating nearly one fourth of the country's entire senior-citizen population. This estimate was a conservative one, said the authors of this Harvard-based study; the true incidence of "inappropriate prescribing for the elderly" was probably closer to 32%. In an accompanying *JAMA* editorial, Harvard's Jerry Gurwitz, MD, added that "this was only the tip of the iceberg."[2]

Having appeared in a respectable journal, these numbers promptly sprang to life. The reaction in the popular press was swift and predictable:

- "Wrong Drugs Given to 1 in 4 of Elderly," hollered the same-day headlines in *The New York Times*.[3]
- "Frightening . . . horrifying . . ." gasped *Time* magazine,[4] " . . . medications that are notorious."
- "More than 6.6 million elderly Americans not in nursing homes are prescribed a dangerous or inappropriate medication every year," blared the Associated Press.[5]
- "The nation's biggest drug problem," claimed *USA Today*, "is the poor prescribing practices of doctors."[6]

Having touched off a firestorm, Himmelstein and Woolhandler showed no inclination to douse the flames. In *Time* magazine,[4] Himmelstein said, "It's a sad commentary on the prescribing practices of many doctors in this country." In the same vein, Woolhandler remarked to *The New York Times*,[3] "Based on my own clinical practice, I knew it was a problem." Though Woolhandler was not surprised by the study's findings, she found them deeply disturbing, said the *Times*. What disturbed Himmelstein, confided *USA Today*,[6] was the number of elderly patients taking drugs that were likely to do more harm than good. "The quickest and easiest route to get the patient out of the doctor's office is to write a prescription. And in the day of the 7-minute office visit, that's what doctors resort to."

No mugging of the medical profession would be complete without a few extra licks from Sidney M. Wolfe, MD, of Public Citizen Health Research Group. "Young and old are being given the wrong drugs, the wrong doses and the wrong combinations," said Wolfe to *USA Today*.[6] ". . . This new study . . . reflects an abysmal ignorance on the part of doctors." The Harvard researchers had merely confirmed what Wolfe knew all along: medicine is a game best played by a few smart guys sitting behind big piles of journals. The rest of us abysmally ignorant numskulls should be tarred, feathered, and sent packing. This was merely one more example of our incompetence, documented in *JAMA* for all to see.

Surely, such "landmark research" deserves a much, *much* closer look. Nearly 7 months after publishing the Harvard study, *JAMA* printed a series of highly critical responses.[7] This time around, however, there was no burst of outrage in the national press, and unfortunately, none of these rebuttals unearthed the basic methodological flaws of the Harvard study.

At first glance, the study seems simple and straightforward. Take one list of medications "contraindicated for the elderly," crossmatch it against a database of pills actually ingested by the elderly, extrapolate the results to the general population, and Bingo! You have instant sound bites on the evening news. Perhaps the slickest part of the Harvard study, however, was in utilizing both a drug list and a database that others had already created. With the laborious parts of their study completed in advance, all that remained for the authors was number crunching and the banking of a $22,631 grant from the

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Robert Wood Johnson Foundation (documentation on file at the Robert Wood Johnson Foundation, Princeton, NJ, 1993; grant No. 022608). Little did it matter that the adopted drug list was not what they claimed it to be or that their 7-year-old database bore no resemblance to present-day prescribing practices.

The purpose of the Harvard study, we are told, was "to examine the amount of inappropriate drug prescribing for Americans aged 65 or older *living in the community* [italics added]."[1] Having said that, the authors promptly produced a list of "hazardous" drugs co-opted directly from a 1991 paper by Beers et al[8]: "Explicit Criteria for Determining Inappropriate Medication Use *in Nursing Home Residents* [italics added]." The Beers criteria had been "specifically" devised for "a population older than 65 years, and frail enough to reside in a nursing home."

Very plainly, Beers and coauthors were not talking about ordinary old people living in their own homes. Ordinary, everyday physicians know the difference, without being told, between robust, 65-year-old gadflies, and the "frail, elderly patients confined to nursing homes." My repeated MEDLINE searches produced no evidence that the human body's ability to detoxify drugs ceases abruptly on the 65th birthday. Whether giving a Darvon pill to a healthy 65-year-old constitutes a mortal sin is left for the reader to decide.

Next, for their database of drugs ingested by senior citizens, the Harvard group selected the 1987 National Medical Expenditure Survey (NMES).[9] By its own description, the NMES contains an oversampling of the elderly, the poor, the functionally impaired, and black and Hispanic minorities. It is taken as an act of faith that, for use in the Harvard study, NMES numbers were validly extrapolated to the general, home-dwelling, over-65 population. But having accepted this as factual, one must further ask: "Is it fitting and proper to reach 1994 conclusions on the basis of 1987 drug-prescribing data?" Apparently so—at least in the eyes of the authors, who dismiss the question by simply asserting that prescribing patterns of physicians "probably hadn't changed dramatically" in those years.[1] This presumption, perhaps, is the Harvard study's most glaring fallacy.

While prescribing patterns are not easily documented, there exists one readily available yardstick of changing trends: *Pharmacy Times*'s[10] annual ranking of the top-200 drugs marketed in the United States, the best-seller list of the pharmaceutical industry. As a group, drugs included among the top-200 comprise 52% of all new and refill prescriptions in the United States. Any product failing to make the *Pharmacy Times* list accounts for no more than 0.1% of all new and refill prescriptions.

Given a few hours in the periodical room, the patterns of prescription writing become remarkably clear. Tables 1 and 2 include the lists of forbidden drugs, the ranking of those drugs on the *Pharmacy Times* top-200 list, and the alleged number of prescriptions written for these drugs for elderly patients in 1994.

For us old-timers, reading the pill names in the column labeled "inappropriate drugs" in Table 1 is like reading the roll call of long-lost friends. Every single one of these drugs has known better times: most are fading fast, and several are effectively dead and buried. It is obvious that the use of these medications is declining. Since 1987, Butazolidin has been totally withdrawn from the market, and Vasodilan and Cyclospasmol are no longer mentioned in the *Physicians' Desk Reference (PDR)*.[11]

Checking locally, I find that not one drugstore in the county has stocked either Nembutal or Seconal in more than 5 years. "If you really need 'em, we can get 'em," they say, "from the warehouse, 200 miles away." Meprobamate, once the leader of its class, now sits in a dusty bottle on the back shelf; only two pharmacists I spoke with remember filling their last prescription. Diabinase faded from popularity more than a decade ago, and scarcely anyone uses Dalmane these days.

Already the drug list has dwindled by nearly one half. Here the plot thickens. Even though Butazolidin is no longer available in drugstores, and Cyclospasmol and Vasodilan are virtually unobtainable, the Harvard study credits physicians with prescribing these three drugs more than 500,000 times for older patients in 1994.[1] The explanation for this incongruous statement, of course, lies in the study's 7-year-old database that lingers on, long after these pills vanished from the marketplace.

Let's see now: one of the forbidden drugs is gone forever, two are no longer in the *PDR*, and five others are rarely prescribed. Only four of the remaining drugs made the current best-seller list, and of these, only Darvon finished among the top 50. Yet somehow, using this ragtag assortment of pills, doctors still managed to mismedicate a full one fourth of the over-65 United States population? Incredible!

Consider Persantine (dipyridamole), which by the researchers' estimates, doctors prescribed 4,832,889 times for elderly patients in 1994.[1] The Harvard researchers point out that as a blood thinner, Persantine is no better than common aspirin; its only legitimate indication is with warfarin in the treatment of patients with artificial heart valves. Here, they set the record straight: "Only 36,000 Americans (half of them older than 65 years) underwent valve replacement in 1987. Even assuming a long life expectancy, artificial heart valve recipients cannot account for many of the 1.8 million older people using dipyridamole in 1987."

What they fail to mention is that Persantine, also a

Table 1. Drug Prescribing for the Elderly: the 1994 Harvard-Based Study vs *Pharmacy Times* Rankings

Inappropriate Drugs*	1994 Prescriptions Written for Noninstitutionalized Elderly†	*Pharmacy Times* Ranking Among Top-200 Prescription Drugs‡			Comment
		High Mark, Ranking (y)	1987	1994	
Sedative, hypnotic					
Diazepam (Valium)	1,547,111	#1 (1973–77)	#19	#145, #149	
Chlordiazepoxide (Librium, Libraz, Limbitrol)	1,135,497	#21 (1982)	§	§	
Flurazepam (Dalmane)	578,459		#66	§	
Meprobamate (Miltown, Equanil, Equagesic)	538,278	#6 generic (1971)	§	§	
Pentobarbital (Nembutal)	60,696	#48 (1972)	§	§	
Secobarbital (Seconal)	25,459	#57 (1977)	§	§	
Antidepressants					
Amitriptyline (Elavil)	1,966,922	#27 (1977)	#105, #148	#72	
NSAIDS					
Indomethacin (Indocin)	1,300,212	#11 (1973)	#138	§	
Phenylbutazone (Butazolidin)	83,327		§	§	Off market after 1992
Hypoglycemics					
Chlorpropamide (Diabinase)	1,638,666	#21 (1982)	#76	§	
Analgesics					
Propoxyphene (Darvon, Darvon-N, Darvocet)	2,412,308	#2 (1973)	#15	#24, #42, #80	
Pentazocine (Talwin)	105,118	#54 (1973)	§	§	
Dementia prescriptions					
Isoxsuprine (Vasodilan)	221,376		§	§	No longer listed in PDR after 1987
Cyclandelate (Cyclospasmol)	198,835		§	§	No longer listed in PDR after 1988
Antiplatelet prescriptions					
Dipyridamole (Persantine)	4,832,889		#51, #88	§	Indications changed in 1987 from antianginal to antiplatelet
Muscle relaxants					
Cyclobenzaprine (Flexeril)	263,671		#46	#125, #159	
Methocarbamol (Robaxin)	134,589		§	§	
Carisoprodol (Soma)	149,108		§	§	
Orphenadrine (Norgesic, Norflex)	174,069		§	§	
Antiemetics					
Trimethobenzamide (Tigan)	99,990		§	§	

**According to the criteria of Beers et al[8] for nursing home patients.*
†According to the Harvard-based study by Wilcox et al.[1]
‡From annual listings of "top-200 drugs of the year."[10]
§Not ranked within the top 200 new and refilled drug prescriptions in the United States, according to Pharmacy Times.
NSAIDS denotes nonsteroidal antiinflammatory drugs; PDR, Physicians' Desk Reference.

vasodilator, was originally prescribed as an alternative to nitroglycerin. The FDA-approved indications for Persantine in the 1987 *PDR* reads thus: "Possibly effective for long-term therapy of chronic angina pectoris. Prolonged therapy may reduce the frequency of, or eliminate, anginal episodes, improve exercise tolerance, and reduce nitroglycerin requirement."[12(p717)] Contrast this with the FDA-approved statement in the 1988 *PDR* 1 year later and 1 year after the database: "Persantine is indicated as an adjunct to coumarin anticoagulants in the prevention of post-operative thromboembolic complications of cardiac valve replacement."[13]

Once the indications for Persantine changed, sales plummeted; 7 years later, no form of dipyridamole remains on the top-200 list. Make no mistake about it: physicians did not write 4.8 million Persantine prescriptions for the elderly in 1994! The numbers just don't wash. No drug ranked so low could possibly be used daily by 1.8 million senior citizens.* Perhaps Willcox, Himmel-

**By comparison, Valium, Darvon, and Elavil each walloped Persantine on the top-200 list, but none of these three is prescribed even half as often, at least by the Harvard researchers' estimates. One of these figures is not correct. Clearly the 1987 numbers for Persantine were extrapolated to 1994.*

Table 2. Antihypertension Agents Prescribed for the Elderly: the 1994 Harvard-Based Study vs *Pharmacy Times* Rankings

Inappropriate Drugs*	1994 Prescriptions Written for Noninstitutionalized Elderly†	*Pharmacy Times* Ranking Among Top-200 Prescription Drugs‡		
		High Mark, Ranking (y)	1987	1994
Antihypertensives				
Propranolol (Inderal)	4,995,356	#2 (1982)	#23, #57, #153, #198	§
Methyldopa (Aldomet, Aldoril)	3,663,512	#9, #35 (1982)	#40, #102	§
Reserpine (Serpasil, Salutensin)	1,467,226	#12 generic (1970)	§	§

**According to the criteria of Beers et al[8] for nursing home patients.*
†According to the Harvard-based study by Wilcox et al.[1]
‡From annual listings of "top-200 drugs of the year."[10]
§Not ranked within the top 200 new and refilled drug prescriptions in the United States, according to Pharmacy Times.

stein, and Woolhandler should have said, "If, over the last 7 years, physicians had not changed their drug-writing habits, they would probably still be writing 4,832,889 Persantine prescriptions for their elderly patients in 1994."

The Harvard study lays claim to the best of both worlds, taking its data from 1987 and its standards from 1994. One could easily forget that prescribing Persantine in 1987 was perfectly appropriate, based on standards of the day. Likewise, Vasodilan and Cyclospasmol were also legitimate drugs in 1987, since, at that time, both were still classified as possibly effective based on reviews by the National Academy of Sciences and the National Research Council.[12,14]

Next, notice that blood pressure pills are considered separately on Table 2 of this editorial. While the original Beers list consisted of 23 inappropriate drugs, the Harvard paper lays claim to only 20, omitting the three antihypertensives, Inderal (propranolol), Aldomet (methyldopa), and Serpasil (reserpine), which they determined were too controversial. However, after stating that they had excluded these three drugs, they included them anyway, in both table and text, along with their observation that the percentage of elderly being mismedicated was probably 32% rather than 23.5%.

Reserpine, though seldom prescribed anymore, is still a perfectly legitimate second-line drug.[15,16] Aldomet, to this day, remains the number 1 antihypertensive drug in large areas of the world. Inderal was recommended by the 1988 National Institutes of Health National Committee on High Blood Pressure as a "step-one" (first choice) blood pressure medicine.[17] Back in 1988, we were congratulating ourselves, because with such medicines we had lowered stroke mortality by 40% in 15 years.[17] Why should patients who are doing well on one of these pills be switched and retitrated onto newer, costlier products, only to face a whole new gamut of side effects?*

The Harvard researchers cannot have it both ways: either include these drugs and we will argue about them, or exclude them altogether and stop implying that the situation is probably far more drastic than the numbers indicate.

Finally, one must ask whether we have reached the point at which everyone over age 65 who is taking this or that particular pill can be labeled "wrongly medicated." For decades now, many physicians have tried Darvon before resorting to stronger narcotics. Often it works. Consider also the case of Indocin (indomethacin): while it is no longer the drug of choice, it is cheap and many patients have taken it for years with no problems. Are these drugs potentially hazardous? Of course they are—as are aspirin, Tylenol, and Ex-Lax. Perhaps the more pertinent question is: "Can anyone name 20 medications that could *not* under any circumstances be branded potentially hazardous to somebody?"

One of the most bothersome things about the Harvard study is the lumping of terms. "Potentially inappropriate," "ineffective," "hazardous," and "contraindicated" all wound up meaning about the same thing. By the time this notion reached the headlines of *The New York Times*, the buzzword was "wrong." This, of course, is an outrageous sort of wrongness, one that screams aloud for tighter controls of the medical profession and stiffer regulations on the pharmaceutical industry.

The Harvard study entitled "Inappropriate Drug Prescribing for the Community-Dwelling Elderly"[1] is deeply flawed. It portrays medication guidelines designed

**Like Persantine, propranolol no longer ranks among the top-200 prescribed drug products. It is literally impossible for 1,774,370 home-dwelling senior citizens to have received propranolol prescriptions in the year 1994, as alleged by the Harvard researchers.*

for nursing homes as the proper standard of care for otherwise healthy elderly people. It is rooted in an obsolete database, its numbers are grossly exaggerated, its conclusions far-fetched, and its motives questionable. In short, there is no factual basis for the assertion that one in four older Americans are being prescribed the wrong drugs by their doctors.

Finding fault with physicians is like shooting fish in a barrel. Hardly a week passes that someone doesn't tattle on doctors these days, each new allegation more damning than the last. After years of being hammered in the headlines and picked apart by sound bites, few physicians bother to defend our profession anymore. We may think it is useless to do so, but the unfortunate truth is that unchallenged allegations never go away. By ignoring them, we are labeled guilty, no matter how far-fetched the charge.

Take the statement "wrong drugs given to 1 in 4 of elderly," stamp it with the *JAMA* seal of approval, print it in *The New York Times*, and suddenly you've created an undying, hard-copy statistic, to be quoted and requoted forever: heavy artillery in the arsenals of those who would reshape medicine to their own grand designs. *That's* what all the fuss is about.

In the flurry of editorial outrage that followed the Harvard study, *USA Today* pointed grimly into Dr Sidney M. Wolfe's black bag of statistics[6,18]:

- More than 659,000 people a year are hospitalized for adverse drug reactions, two thirds of which may be due to poor prescribing practices.
- More than 16,000 car crashes a year are due to adverse reactions to prescription drugs.
- More than 61,000 people suffer drug-induced Parkinson's symptoms.
- More than 41,000 people a year are hospitalized for ulcers caused by drugs.
- More than 3300 older Americans die of ulcers caused by arthritis medications each year.
- More than 1500 die from hip injuries suffered during drug-induced falls.

Tell us, please, exactly who verifies these numbers, anyway?

Occasionally, the biggest insights appear in the smallest print. The Harvard study ends by acknowledging the "inspiration and data" of Sidney Wolfe, MD, and his book *Worst Pills Best Pills*.[19] By pure coincidence, the Beers paper[8] concludes with a list of its participants: among them, Sidney M. Wolfe, MD, Public Citizen Health Research Group, Washington, DC. Could it be that in Dr Wolfe we have found the missing link? With such a direct connection, surely the Harvard researchers knew perfectly well they were passing off nursing home criteria as the proper standards for healthy senior citizens.

If Himmelstein considers this study a sad commentary on American doctors, then perhaps he should reflect on the caliber of research flowing these days from major universities. If the prescribing practices of American physicians were no more accurate than the Harvard researchers' study, the streets of our country would be littered with the dead. While we may speculate why professors from reputable institutions would go to such extremes proving things that simply are not true, we may never know whether this study is the result of shoddy workmanship, preconceived bias, or deliberate deception. Whatever the case, it is little more than an underhanded potshot at working doctors, and it is time someone said so aloud.

Meanwhile, the drum keeps beating and the uninterrupted stream of outrageous, unchallenged statistics continues to flow through the daily press. An item in the January 3, 1995, *USA Today* reads, ". . . 140,000 die each year from side effects or reactions to prescription drugs, says a report based on Food and Drug Administration data."

Let's face it, the practice of medicine is a potentially hazardous profession.

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