Medical Progress Report

No. 2 October 2005

Older Drugs, Shorter Lives? An Examination of the Health Effects of the Veterans Health Administration Formulary

Frank R. Lichtenberg

Columbia University and
National Bureau of Economic Research

CMP
CENTER FOR MEDICAL PROGRESS
AT THE MANHATTAN INSTITUTE

Executive Summary

This paper examines access to new drugs under the pharmacy benefits management system of the Veterans Health Administration (VHA). The VHA's National Formulary, implemented in 1997, discourages access to new drugs in an effort to control overall pharmaceutical costs. Some public figures have argued that this system should also apply to purchases under the new Medicare drug benefit, making the study of its effects on patient health particularly important.

Only 38% of the drugs approved in the 1990s, and 19% of the drugs approved by the FDA since 2000, are on the VA National Formulary. Only 22% (17) of the 77 priority-review drugs approved since 1997 are on the 2005 National Formulary.

The drugs used in the VA health system from 1999 to 2002 were older than the drugs used in the rest of the U.S. health-care system. For example, the percentages of VA and non-VA prescriptions for drugs less than five years old were 5.6% and 8.6%, respectively, and the percentages for drugs less than fifteen years old were 31.4% and 39.0%.

This paper estimates the impact of the use of new drugs on longevity, based on annual data on Medicaid drug use and mortality by state, disease, and year, for all fifty states during the period 1991-2001. These estimates imply that increased use of older drugs in the VA system, as a result of the Formulary, has reduced mean age at death of its patients by 0.17 years, or 2.04 months; the value of this reduction in longevity may be nearly $25,000 per person.

Moreover, demographic data published by the VA indicate that the life expectancy of veterans increased substantially before the National Formulary was introduced (during 1991-97) but did not increase, and may even have declined, after it was introduced (1997-2002).

There are many proposals in Congress to adopt a system similar to the VA National Formulary for purchases under the new Medicare drug benefit. These data suggest that such a proposal could reduce life span and survival rates among the Medicare population, raising serious questions about the wisdom of these proposals.

Table of Contents

Older Drugs, Shorter Lives?
An Examination of the Health Effects of the Veterans Health Administration Formulary

INTRODUCTION

The Medicare drug benefit (part D) will go into effect on January 1, 2006. Some people have proposed using the VA pharmacy benefit system, including the VA National Formulary*, as a model for the Medicare drug benefit. In this paper, I consider the wisdom of such a policy.

The VA National Formulary generated controversy when it was implemented because Congress "learned that the formulary prevents physicians from meeting the unique health-care needs of individual veterans and is overly restrictive" (Blumenthal and Herdman, 2000). Congress requested that the Institute of Medicine (IOM) review the experience with the National Formulary and formulary systems. The commission found that formularies and formulary systems (the many policies and procedures necessary to manage implementation of formularies) are an essential part of modern health-care systems and that the VHA therefore was justified in creating its National Formulary.[1] However, the IOM committee found almost no data relating the implementation and management of the National Formulary to the quality of the process and outcomes of veterans' care. To this end, this paper supplements and updates the commission's analysis. It reassesses the impact of the National Formulary system, paying particular attention to its impact on VA enrollees' access to new drugs and the relationship such access has to life expectancy and well-being.

To do this, I examine data on the fraction of drugs that are on the National Formulary, by period of FDA approval. I will also update calculations done by the commission on the extent to which priority-review drugs** approved since 1997 are on the National Formulary.

That a drug is not listed on the National Formulary does not necessarily mean that VA patients do not have access to the drug. A drug not listed on the National Formulary may be listed on one of twenty-three Veterans Integrated Service Networks (VISNs) or local formularies[2]; even if it is not, the patient may obtain access via a nonformulary exceptions process. Therefore, to assess the impact of the National Formulary system on the pattern of drug use, it is necessary to examine data on the drugs *actually used* by people in the VA system. The Medical Expenditure Panel Survey provides such data for the years 1996-2002 and allows us to compare VA drug use with non-VA drug use. Using these data, I will show that drugs used in the VA system are older than drugs used in the non-VA sector and that the gap has widened since the National Formulary was implemented.

I will then consider the effect of the VA Pharmacy Benefits Management (PBM) system on an important patient outcome: survival. There are two ways to do this. The first (indirect) way is to estimate the effect of using older drugs on the probability of survival, or life expectancy. I have estimated this effect in several previous papers, and I will present some new estimates here, based on longitudinal data by state, major disease category, and year, during the period 1990-2001. The second (direct) way is to compute estimates of the life expectancy of veterans from 1990 to 2002 (i.e., before and after the VA PBM system was implemented), and to compare them with data on the life expectancy of American men in general (the vast majority of veterans are men). I will compute these estimates from VetPop2001, the VA's official estimate and projection of the number and characteristics of veterans as of September 30, 2001.

** The VA National Formulary is a list of drugs, devices, and supplies that provides the basis for uniform national access to listed agents including drugs, devices, and supplies for all VHA facilities. It was implemented in 1997 by the Veterans Health Administration (VHA) to help control costs and improve the quality of drugs prescribed in the VHA's health-care facilities, which include 172 hospitals, more than 600 ambulatory facilities, and 132 nursing homes.*

*** Priority-review drugs are drugs considered by the FDA to offer significant improvement compared with marketed products, in the treatment, diagnosis, or prevention of a disease.*

ADDITION OF NEW DRUGS TO THE VA NATIONAL FORMULARY

As indicated in the commission report[3], "under current policy, drugs newly approved by the FDA are considered for addition to the VA National Formulary only after a 1-year delay, except in special cases of important new 1P category drugs, that is, new chemical entities classified for priority review by the FDA."[4] In practice, that policy has meant adding new drugs for the treatment of HIV / AIDS with less than a year lag, whereas other 1P drugs have been added only after a year or more. Currently, these decisions are made by a consortium of the Medical Advisory Panel (MAP), VISN formulary leaders, and the VA PBM.[5]

The VHA policy of a one-year waiting period is a safety precaution that allows evidence of adverse drug effects to accumulate. It also provides time to compare the safety, efficacy, or cost-effectiveness of new drugs with existing therapeutic alternatives, or with drugs for similar indications. Such studies are usually not done during the FDA new drug-approval process. Data, especially in the peer-reviewed open literature, to inform a decision (on whether a new drug is an improvement over existing drug therapies) are generally not available until sometime after release, if at all. In fact, Sloan et al. (1997) noted a dearth of pharmacoeconomic or cost-effectiveness studies even beyond a year after market entry of new drugs. Waiting for a year does not guarantee that adequate comparative evaluations will be available.[6]

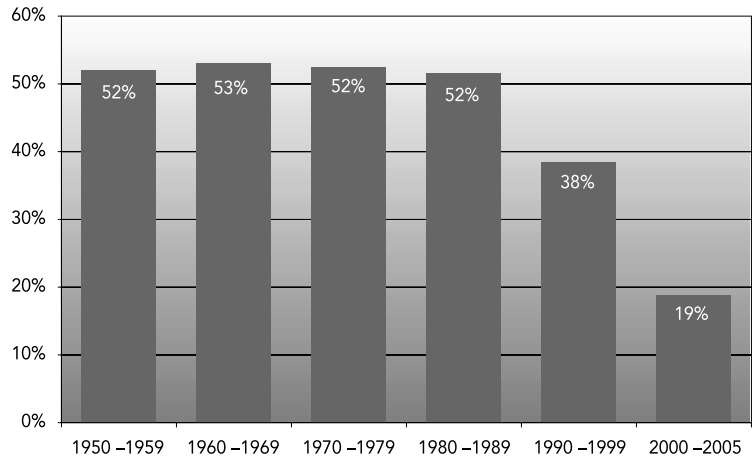
The commission reviewed the forty-two FDA 1P drugs approved in 1996, 1997, and 1998. Ten of the 1P drugs that were introduced before the implementation of the VA National Formulary were included in the initial version. Four drugs were subsequently approved and added, primarily for the treatment of HIV / AIDS. By July 1999, the 28 remaining 1P drugs had either been reviewed and not approved (5), had not been reviewed (21), or were pending (2). The reasons for disapproving additions included "no advantages over contract agents," "evidence regarding efficacy was inconclusive," and "safety / cost concerns." At the same time, the FDA Center for Drug Evaluation and Research 1998 Report to the Nation[7] proposed that 1P drugs "represent an advance in medical treatment" and described a number of the drugs that had been disapproved or not reviewed by the VHA as "notable 1998 new drug approvals." The MAP, VA PBM, and VISN formulary leaders must employ stringent evidentiary requirements for the addition of newly introduced drugs, since few are added to the National Formulary. As far as the committee could determine, however, there is no VHA policy or practice of identifying and reviewing new 1P drugs (for example, the twenty-one "not-reviewed" 1996, 1997, or 1998 1P drugs) or other new-to-market drugs in a systematic way.

VISN and local policies and practices, although variable, appear to be more permissive, so existing or newly introduced drugs are less likely to be added to the National Formulary than to the formularies of other organizations, or to VISN or local formularies. Listed drugs are also less likely to be deleted. One or more VISN or local formularies added 4 of the 5 disapproved 1P drugs and 4 of the 21 non-reviewed 1P drugs. In one case, 18 VISNs added clopidogrel (Plavix), a nationally non-reviewed 1P drug. A decision was then made at the national level not to add this drug to the National Formulary, but it remained on VISN formularies. Changes to these VHA formularies vary considerably from VISN to VISN.

To what extent are FDA-approved drugs listed on the VA National Formulary, so that all VHA patients are guaranteed access to them? To answer this question, I will calculate the percent of drugs approved by the FDA since 1950 on the 2005 VA National Formulary, by decade of FDA approval. I compiled a list of about 1,300 drugs approved, and their approval dates, from the Drugs@FDA Data Files.[8] I determined whether each of these drugs was on the VA National Formulary by examining data in the VA's National Drug File.[9] Figure 1 shows the percent of drugs on the 2005 VA National Formulary, by decade of FDA approval. The fractions of drugs approved in the 1950s, 1960s, 1970s, and 1980s on the VA National Formulary are almost identical: 52-53%. Only 38% of the drugs approved in the 1990s, however, and only 19% of the drugs approved since 2000, are on the VA National Formulary.

The Drugs@FDA Data Files don't indicate whether the drugs approved were priority-review or standard-review drugs. This information is available, though, for drugs approved since 1997 from New Drug Approval Reports, published by the FDA's Center for Drug Evaluation and Research.[10]

Figure 1: Percent of Drugs on 2005 VA National Formulary, by Decade of FDA Approval



The following table shows the number of new molecular entities approved by the FDA since 1997, by review status and formulary status.

	Priority review	Standard review	Total
Listed on 2005 NF	17	14	31
Not listed on 2005 NF	60	98	158
Total	**77**	**112**	**189**

Only 22% (17) of the 77 priority-review drugs approved since 1997 are on the 2005 National Formulary. This is lower than the percentage (33%) of 1P drugs approved in 1996, 1997, and 1998 that the IOM committee reported to be on the National Formulary.

COMPARISON OF VA VERSUS NON-VA USE OF NEW DRUGS

In what follows, I compare use of new drugs in the VA health system with their use in the rest of the U.S. health-care system. I use data from the Medical Expenditure Panel Survey (MEPS), which collects data on a nationally representative sample of families and individuals.[11]

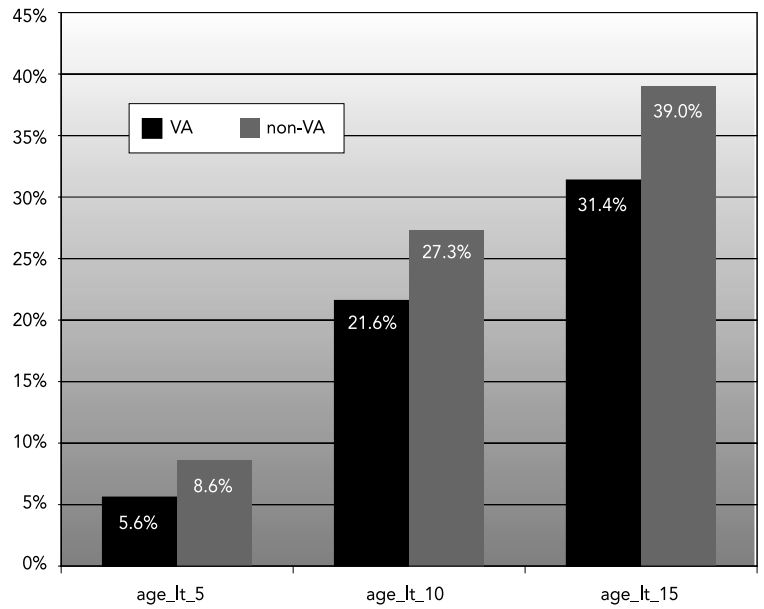
MEPS data are currently available for the years 1996-2002. There is a Prescribed Medicines file for each year. This file contains records of all prescriptions obtained by households in the sample. Each record includes the National Drug Code of the drug and the amount paid for the prescription, by payer. There are twelve payers, and one of these is "Veterans."[12] I will define a "VA prescription" as a prescription for which the amount paid by veterans exceeded zero. In 1999, for example, there were 173,950 prescriptions; 5,083 (2.9%) of these were VA prescriptions.

I determined the year in which the FDA first approved the active ingredient of each prescription. I then defined the age of a prescription as the year in which the prescription occurred minus the year in which the FDA first approved the prescription's active ingredient. For example, the age of a 1999 prescription for a drug first approved in 1990 is nine years. I defined three variables indicating whether the age of the prescription was greater than 5, 10, and 15 years.[13] Finally, I calculated the mean values of these three variables, for both VA and non-VA prescriptions, using data for MEPS prescriptions during the years from 1999 to 2002.[14]

Figure 2 (page 4) shows the percent of 1999-2002 VA and non-VA prescriptions for drugs less than 5, 10, and 15 years old. All three measures indicate that the drugs used in the VA health system from 1999 to 2002 were older than the drugs used in the rest of the U.S. health-care system. For example, the percentages of VA and non-VA prescriptions for drugs less than five years old were 5.6% and 8.6%, respectively, and the percentages for drugs less than fifteen years old were 31.4% and 39.0%.

Since we have prescription data both pre- and post-implementation of the National Formulary, we can also assess whether the gap between VA and non-VA drug age widened over time.[15] From 1996 to 2002, new-drug use increased less quickly in the VA health system than in the rest of U.S. health care. The quantity of drugs less than ten years old increased by 1.4 percentage points per year in the non-VA sector, and by 0.6 percentage points per year in the VA sector. The proportion of drugs less than fifteen years old increased by

Figure 2: Percent of 1999-2002 VA and Non-VA Prescriptions for Drugs Less Than 5, 10, and 15 Years Old



Percentages based on 10,495 VA prescriptions and 723,264 non-VA prescriptions. All three differences in percentages are significant (p-value < .001).

1.9 percentage points per year in the non-VA sector and had virtually no increase in the VA sector. These estimates are consistent with the hypothesis that implementation of the VA National Formulary beginning in 1997 reduced use of new drugs in the VA health-care system.

THE EFFECT OF USING OLDER DRUGS ON THE PROBABILITY OF SURVIVAL, OR LIFE EXPECTANCY

We have seen that only 16% of all drugs approved since 1997, and 22% of priority-review drugs, are listed on the 2005 VA National Formulary; that the drugs used in the VA health system from 1999 to 2002 were older than the drugs used in the rest of the U.S. health-care system; and that new-drug use increased more slowly from 1996 to 2002 in the VA health system than it did in the rest of U.S. health care. I will now consider the implications of these facts for a patient outcome that many people might consider the most important and that is undoubtedly the best measured: survival.

In what follows, I present new evidence on the impact of the use of new drugs on longevity, based on annual data on Medicaid drug use and mortality by state, disease, and year, for all fifty states, during the period 1991-2001.

A model based on these data[16] enables us to test the hypothesis that there have been above-average increases in mean age at death (in state-disease cells that have experienced above-average increases in the prescription of new drugs by Medicaid).[17] This analysis enables us to control for many potentially confounding variables, such as unobserved state-specific trends (e.g., state fiscal condition) that might affect mortality and be correlated with Medicaid drug use.[18]

I construct the mortality data from the 1991-2001 Multiple Cause of Death data files.[19] These contain records of every death in the U.S. (about 2 million per year), including data on where the death occurred, exact age at death, and cause of death.

State drug-use information is available for outpatient drugs purchased on or after January 1, 1991, by State Medicaid agencies.[20] In particular, we have quarterly data on the number of prescriptions, by National Drug Code (NDC) and state, for the period 1991-2004.[21]

The Centers for Medicare and Medicaid Services (CMS) data do not contain any information about the diseases for which the drugs were prescribed, but there is a good way to allocate the prescriptions by NDC by disease: by using data in the 1996-2001 Medical Expenditure Panel Survey Prescribed Medicines Files. These files contain about 1.5 million records of individual prescriptions. Each record contains both an NDC and a three-digit ICD9 diagnosis code. Hence, we can determine the relative frequency with which each NDC was used for different diseases. The MEPS diagnosis codes are quite detailed, so I aggregate them (and the mortality data) to broad

disease groups, e.g., cardiovascular disease, cancer, and respiratory disease.

Note that there is a misalignment between the mortality data and the drug-use data: the mortality data pertain to all decedents, i.e., those who had been enrolled in Medicaid and those who hadn't, while the use data pertain only to the Medicaid program. It is reasonable to hypothesize, however, that changes in Medicaid drug use may be correlated, across states and diseases, and over time, with changes in non-Medicaid drug use (e.g., due to spillovers in prescribing). Changes in Medicaid drug use, which can be measured extremely precisely with the CMS data, might be considered a good indicator of changes in overall drug use.

By using data from another source, covering a more recent time period, I can test the hypothesis that the extent of use of new drugs in the Medicaid program is strongly correlated with the extent of use of new drugs in general. I have data from a private company, NDCHealth, on the number of prescriptions, by NDC, state (and five U.S. territories), month (January 2001-December 2003), and payer (Medicaid, other third party, and cash), for six important therapeutic classes of drugs: antidepressants, antihypertensives, cholesterol-lowering drugs, diabetes drugs, osteoporosis / menopause drugs, and pain-management medications.[22] These data show that the extent of new-drug use in the Medicaid program strongly correlates with the extent of the use of new drugs in general. Controlling for disease-state, disease-year, and state-year effects, the data also indicate that longevity (mean age at death) increased more rapidly in state-disease cells experiencing higher increases in post-1990 drug use.

We can use these data to calculate how much of the increase in mean age at death from 1991 to 2001 is attributable to the increasing use of post-1990 drugs. From 1991 to 2001, mean age at death increased by 1.74 years, from 73.24 to 74.99 years, and the fraction of prescriptions that were for post-1990 drugs increased by 0.314. The increase in mean age at death attributable to increasing use of post-1990 drugs is estimated to be 0.79 years.[23] About 46%[24] of the total increase in mean age at death during the period 1991-2001 is attributable to the increasing use of post-1990 drugs. This is similar to the 40% share of longevity increase in fifty-two countries during 1986-2001 that I estimated to be attributable to new drug launches.[25]

The fraction of post-1990 drugs used in the VA health system during 1999-2002 (25.2%) was lower than the fraction of post-1990 drugs used in the non-VA sector (31.9%). The estimates imply that use of older drugs in the VA system reduced mean age at death of its patients by 0.17 years (= 2.53 * [31.9% - 25.2%]), or 2.04 months. Murphy and Topel (2003) argue that the value of a U.S. statistical life-year is not less than $150,000, which would imply that the per-patient value of this reduction in longevity is not less than $25,000.

LIFE EXPECTANCY OF VETERANS, 1991–2002

Demographic data published by the VA enable us to compute the life expectancy of veterans before and after the National Formulary was implemented. Life-expectancy calculations are based on life tables. There are two types of life tables: cohort (or generation) life tables; and period (or current) life tables. The cohort life table presents the mortality experience of a particular birth cohort (e.g., all persons born in the year 1900) from the moment of birth through consecutive ages in successive calendar years. Based on age-specific death rates observed through consecutive calendar years, the cohort life table reflects the mortality experience of an actual cohort from birth until no lives remain in the group. To prepare just a single complete cohort life table requires data over many years. It is usually not feasible to construct cohort life tables entirely on the basis of observed data for real cohorts due to data unavailability or incompleteness (Shryock et al., 1971). For example, a life-table representation of the mortality experience of a cohort of persons born in 1970 would require the use of data projection techniques to estimate deaths into the future (Moriyama and Gustavus, 1972; Preston et al., 2001).

Unlike the cohort life table, the period life table does not represent the mortality experience of an actual birth cohort. Rather, the period life table presents what would happen to a hypothetical (or synthetic) cohort if it experienced throughout its entire life the mortality conditions of a particular period in time. Thus, for example, a period life table for 2002 assumes a hypothetical cohort subject throughout its

lifetime to the age-specific death rates prevailing for the actual population in 2002. The period life table may thus be characterized as rendering a "snapshot" of current mortality experience and shows the long-range implications of a set of age-specific death rates that prevailed in a given year. Official government estimates of U.S. life expectancy are based on period life tables (Arias, 2004); my calculations of the life expectancy of veterans will also be based on period life tables.

Calculation of the life table is derived from the probability of death, which depends on the number of deaths and the midyear population for each age group observed during the calendar year of interest. The VA publishes historical data on and projections of the number of deaths and the number of living veterans, by age group and year, 1990-2030.[26] Data for 1991-2002 are shown in Table 2 (see Appendix, page 16). The top part of the table shows the number of veteran deaths during the year, by age group. The middle part shows the number of veterans alive at the beginning of the year, and the bottom part shows the mortality rate.[27]

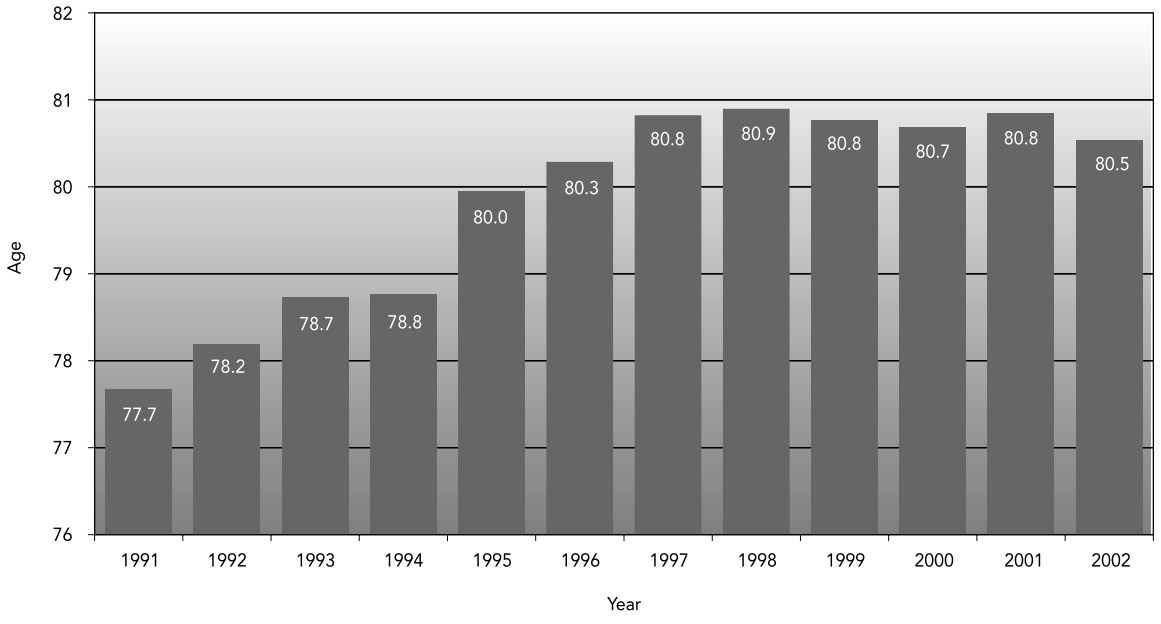
Estimates of veterans' life expectancy during the period 1991-2002 are shown in Figure 3. Since the estimates are based on rough approximations, the average *level* of life expectancy should be viewed with caution. The mean value of life expectancy during the entire period is 6.6 years *higher* than the mean value of the life expectancy of all U.S. males at birth[28] (over 94% of veterans alive in 2002 were male).

Figure 3 indicates that veterans' life expectancy increased substantially before the National Formulary was introduced (during 1991-1997) but did not increase, and may even have declined, after it was introduced (1997-2002). Figure 4 juxtaposes the path of veterans' life expectancy with the path of life expectancy of all U.S. males at birth. The life expectancy at birth of all U.S. males increased after-as well as before-1997, although the rate of growth declined by about a third.

CONCLUSION

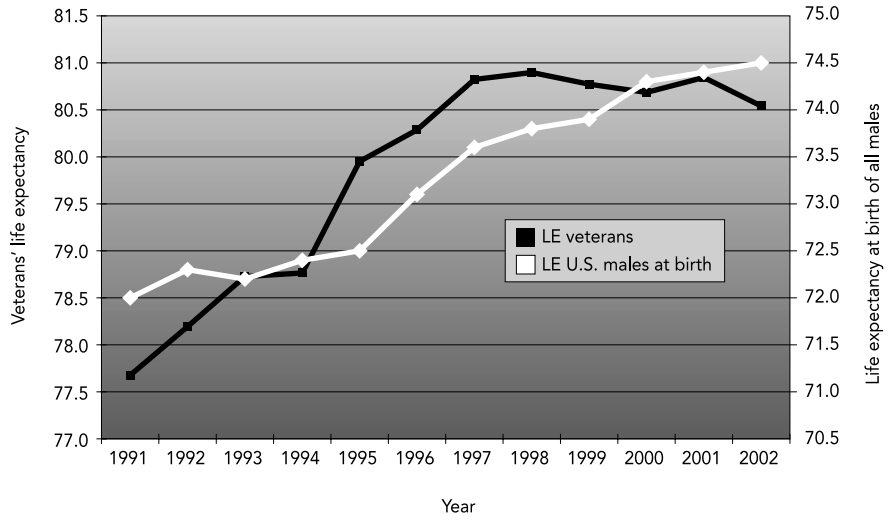
In this paper, I have examined access to new drugs under the Pharmacy Benefits Management system

Figure 3: Life Expectancy of Veterans, 1991–2002



Source: Author's calculations based on VetPop2001 State and National Tables (http://www.va.gov/vetdata/demographics/VP2001sn.htm).

Figure 4: Veterans' Life Expectancy vs. Life Expectancy at Birth of All U.S. Males



of the Veterans Health Administration. Since 1997, the VA National Formulary has played a key role in that system.

The fractions of drugs approved in the 1950s, 1960s, 1970s, and 1980s on the 2005 VA National Formulary are almost identical: 52-53%. Only 38% of the drugs approved in the 1990s, however, and 19% of the drugs approved since 2000, are on the VA National Formulary. Only 22% (17) of the 77 priority-review drugs approved since 1997 are on the 2005 National Formulary. This is lower than the percentage (33%) of priority-review drugs approved in 1996, 1997, and 1998 that the IOM committee reported to be on the National Formulary.

The drugs used in the VA health system from 1999 to 2002 were older than the drugs used in the rest of the U.S. health-care system. For example, the percentages of VA and non-VA prescriptions for drugs less than five years old were 5.6% and 8.6%, respectively, and the percentages for drugs less than fifteen years old were 31.4% and 39.0%.

The percent of drugs less than ten years old increased by 1.4 percentage points per year in the non-VA sector, and by 0.6 percentage points per year in the VA sector, during 1996-2002. The percent of drugs less than fifteen years old increased by 1.9 percentage points per year in the non-VA sector and had virtually no increase in the VA sector. These estimates are consistent with the hypothesis that implementation of the VA National Formulary beginning in 1997 reduced the use of new drugs in the VA health-care system.

I presented estimates of the impact of use of new drugs on longevity, based on annual data on Medicaid drug use and mortality by state, disease, and year, for all fifty states during the period 1991-2001. The estimates implied that the use of older drugs in the VA system reduced mean age at death of its patients by 0.17 years, or 2.04 months. Murphy and Topel (2003) argue that the value of a U.S. statistical life-year is not less than $150,000, which would imply that the per-patient value of this reduction in longevity is not less than $25,000.

I used demographic data published by the VA to compute the life expectancy of veterans before and after the National Formulary was implemented. Veterans' life expectancy increased substantially before the National Formulary was introduced (during 1991-1997) but did not increase, and may even have declined, after it was introduced (1997-2002). The life expectancy at birth of all U.S. males increased after- as well as before-1997, although the rate of growth declined by about a third.

There are many proposals in Congress to adopt a system similar to the VA National Formulary for purchases under the new Medicare drug benefit. These data suggest that this shift could reduce well-being, life span, and survival rates among the Medicare population, raising serious questions about the wisdom of these proposals.

About the Author

Professor Frank Lichtenberg currently serves as the Courtney C. Brown Professor of Business at the Columbia University Graduate School of Business as well as a research associate of the National Bureau of Economic Research. His work has focused on how new technologies affect the productivity of companies, industries and nations. Dr. Lichtenberg's studies have ranged from the impact of pharmaceutical innovation to the consequences of leveraged buyouts for efficiency and employment. This research has earned numerous fellowships and awards, including the 1998 Schumpeter Prize and a 2003 Milken Institute Award for Distinguished Economic Research, as well as grants by the National Science Foundation, the National Institute of Standards and Technology, Merck and Co., the Fulbright Commission, and the Alfred P. Sloan Foundation. He has worked for several U.S. government agencies, including the Department of Justice and the Congressional Budget Office, as well as taught at Harvard University and the University of Pennsylvania.

Dr. Lichtenberg received a BA in history from the University of Chicago and an MA and PhD in economics from the University of Pennsylvania.

REFERENCES

Arias, E. (2004), "United States Life Tables, 2002," *National Vital Statistics Reports*, vol. 53, no 6. Hyattsville, Md.: National Center for Health Statistics.

Blumenthal, David, and Roger Herdman, eds. (2000), *Description and Analysis of the VA National Formulary*, VA Pharmacy Formulary Analysis Committee, Division of Health Care Services (Washington, D.C.: National Academies Press), http://www.nap.edu/catalog/9879.html.

Lichtenberg, Frank R. (2005), "Pharmaceutical Knowledge-Capital Accumulation and Longevity," in *Measuring Capital in the New Economy*, ed. Carol Corrado, John Haltiwanger, and Dan Sichel (Chicago: University of Chicago Press, forthcoming).

_____ (2005), "Availability of New Drugs and Americans' Ability to Work," *Journal of Occupational and Environmental Medicine* 47 (4), April, 373-380.

_____ (2005), "The Effect of Access Restrictions on the Vintage of Drugs Used by Medicaid Enrollees," *American Journal of Managed Care* 11 (January).

_____ (2005), "The Impact of New Drug Launches on Longevity: Evidence from Longitudinal Disease-Level Data from 52 Countries, 1982-2001," *International Journal of Health Care Finance and Economics* 5, pp. 47-73.

_____ (2005), "Home, or Nursing Home? The Effect of Medical Innovation on the Demand for Long-Term Care" (March), working paper.

_____ (2005), "The Impact of Increased Use of HIV Drugs on Longevity and Medical Expenditure: An Assessment Based on Aggregate U.S. Time-Series Data" (February), working paper.

_____ (2004), "The Effect of Drug Vintage on Survival: Micro Evidence from Puerto Rico's Medicaid Program," NBER Working Paper No. 10884 (November), http://www.nber.org/papers/w10884.

_____ (2004), "Sources of U.S. Longevity Increase, 1960-2001," *Quarterly Review of Economics and Finance* 44, no. 3 (July): 369-89.

_____ (2004), "The Expanding Pharmaceutical Arsenal in the War on Cancer," NBER Working Paper No. 10328 (February), http://www.nber.org/papers/w10328.

_____ (2003), "The Effect of New Drugs on HIV Mortality in the U.S., 1987-1998," *Economics and Human Biology* 1: 259-66.

_____ (2003), "Pharmaceutical Innovation, Mortality Reduction, and Economic Growth," in *Measuring the Gains from Medical Research: An Economic Approach*, ed. Kevin M. Murphy and Robert H. Topel (Chicago: University of Chicago Press), 74-109.

_____ (2001), "Are the Benefits of Newer Drugs Worth Their Cost? Evidence from the 1996 MEPS," *Health Affairs* 20, no. 5 (September/October): 241-51.

_____ (2000), "The Effect of Pharmaceutical Utilisation and Innovation on Hospitalisation and Mortality," in *Productivity, Technology, and Economic Growth*, ed. B. van Ark, S. K. Kuipers, and G. Kuper (Kluwer Academic Publishers).

_____ (1996), "Do (More and Better) Drugs Keep People Out of Hospitals?," *American Economic Review* 86 (May): 384-88.

Lyles A, Luce B, Rentz A. (1997) Managed care pharmacy, socioeconomic assessments, and drug adoption decisions. *Social Science & Medicine*. 1997; 45:511-521.

Massachusetts Outpatient Formulary Guide. 1999. Mather DB, Sullivan SD, Augenstein D, Fullerton PDS, Atherly D. Incorporating Clinical Outcomes and Economic Consequences into Drug Formulary Decisions: A Practical Approach. *The American Journal of Managed Care*. 1999; 5(3):277-285.

Moriyama, I. M., and S. O. Gustavus (1972), *Cohort Mortality and Survivorship: United States Death-Registration States, 1900-68. Vital Health Statistics*, vol. 3, no. 16. Hyattsville, Md.: National Center for Health Statistics.

Murphy, Kevin M., and Robert H. Topel (2003), "The Economic Value of Medical Research," in *Measuring the Gains from Medical Research: An Economic Approach*, ed. Murphy and Topel (Chicago: University of Chicago Press), 41-73.

Preston, S. M., P. Heuveline, and M. Guillot (2001), *Demography: Measuring and Modeling Population Processes* (Oxford: Blackwell).

Sales, Mariscelle M., et al. (2005), "Pharmacy Benefits Management in the Veterans Health Administration: 1995 to 2003," *American Journal of Managed Care* (February): 104-12.

Shryock, H. S., J. S. Siegel, et al. (1971), *The Methods and Materials of Demography*, vol. 2. U.S. Bureau of the Census. Washington, D.C.: U.S. Government Printing Office.

Sloan FA, Whetten-Goldstein K, Wilson A. Hospital pharmacy decisions, cost containment, and the use of cost-effectiveness analysis. *Social Science & Medicine*. 1997; 45(4):523-533.

United States General Accounting Office (2001), "VA Drug Formulary: Better Oversight Is Required, but Veterans Are Getting Needed Drugs," report to the ranking member, Committee on Veterans' Affairs, U.S. Senate (January), GAO-01-183.

United States General Accounting Office (1999), "VA Drug Formulary: VA's Management of Drugs on Its National Formulary," GAO report to the ranking minority member, Committee on Veterans' Affairs, U.S. Senate (December), GAO / HEHS-00-34.

ENDNOTES

1. An Institute of Medicine committee agreed to assist Congress with this review, in part because the committee saw in the VHA example an opportunity to understand and anticipate problems that all publicly funded programs are likely to encounter in this new age of pharmaceuticals. Congress asked the committee to review the restrictiveness of the National Formulary, its impact on the costs and quality of care in the VHA, and how it compared with formularies and drug-management practices in the private sector and in other public programs, especially Medicaid. Further, it found that the "VA National Formulary was not overly restrictive, and the limited available evidence suggests that it has probably meaningfully reduced drug expenditures without demonstrable adverse effects on quality." However, the committee also concluded that there were "manifold opportunities to improve the management of the formulary system used by the VHA," i.e., that the National Formulary lacked systems to ensure that: (1) new drugs are expeditiously reviewed for inclusion; (2) access to medically necessary exceptions to the formulary is consistently in place systemwide; (3) therapeutic interchange is accomplished in a flexible and consistent way, sensitive to patient risks, across the far-flung VHA system; and (4) views of critical constituencies of providers and patients are represented in the management of the National Formulary.

2. The list of drugs on the National Formulary is readily available (http://www.vapbm.org/PBM/natform.htm). However, lists of drugs on only a few of the VISN formularies are available (see, e.g. http://www.visn20.med.va.gov/webRx/rxbyname.html), and these are not in a uniform format.

3. IOM Report, 50. Blumenthal, David, and Roger Herdman, eds. (2000), *Description and Analysis of the VA National Formulary*, VA Pharmacy Formulary Analysis Committee, Division of Health Care Services (Washington: National Academy Press) <http://www.nap.edu/catalog/9879.html>

4. VHA Directive, 97-047. Veterans Health Administration, Department of Veterans Affairs, Washington, DC 20420, July 24, 2001, VHA DIRECTIVE 2001-044, http://www.vapbm.org/directive/vhadirective.pdf.

5. Although the final authority was vested initially in a VA PBM Executive Steering Board made up of officials from various units of the VHA central office, this board never became operational.

6. Lyles et al., 1997; Massachusetts Outpatient Formulary Guide. 1999; see also VA drug-class reviews at http://www.dppm.med.va.gov/newsite/reviews.html.

7. See http://www.fda.gov/cder/reports/rptntn98.pdf.

8. See http://www.fda.gov/cder/drugsatfda/datafiles/default.htm.

9. The National Drug File (http://www.vapbm.org/natform/NDF0305.EXE) contains data on specific products (identified by National Drug Code [NDC]). Each record includes a National Formulary indicator (YES or NO) and the name of the generic drug to which the NDC corresponds. I considered a generic drug to be on the formulary if any product corresponding to that drug was on the formulary. The fraction of *products* listed on the formulary is smaller than the fraction of *drugs* listed on the formulary. For example, only a subset of a drug's dosage forms and strengths may be listed on the formulary.

10. See http://www.fda.gov/cder/rdmt/default.htm.

11. Drawn from a nationally representative subsample of households that participated in the prior year's NCHS National Health Interview Survey. The objective is to produce annual estimates for a variety of measures of health status, health-insurance coverage, health-care use and expenditures, and sources of payment for health services. Statisticians and researchers use these data to generalize to people in the civilian noninstitutionalized population of the United States.

12. The other payers are: self or family; Medicare; Medicaid; private insurance; Champus/Champva; other federal, state and local government; workers' comp; other insurance; other private payers; and other public payers.

13. I defined the following three variables:

$AGE\_LT\_5_i$ = 1 if the age of prescription i was less than 5 years
= 0 otherwise
$AGE\_LT\_10_i$ = 1 if the age of prescription i was less than 10 years
= 0 otherwise
$AGE\_LT\_15_i$ = 1 if the age of prescription i was less than 15 years
= 0 otherwise

14. Although the VA National Formulary was launched in 1997, it may not have been fully implemented right away. To allow for this possibility, I compare VA with non-VA prescriptions beginning in 1999.

15. I did this by estimating regressions of the form:

$$AGE\_LT\_5_i = \beta_0 + \beta_1 VAi + \beta_2 YEARi + \beta_3(VAi * YEARi) + \varepsilon_I \quad (1)$$

where

VA_i = 1 if prescription i is a VA prescription
= 0 otherwise
$YEAR_i$ = the year in which prescription i occurred

If $\beta_3 < 0$, the percentage of new drugs is growing less rapidly (or declining more rapidly) in the VA health system than it is in the rest of the U.S. health-care system.

Estimates of β_2, β_3, and $(\beta_2 + \beta_3)$ for the three different drug-age measures are shown in the following table:

dependent variable	AGE_LT_5	AGE_LT_10	AGE_LT_15
β_2	0.000436	0.013539	0.019322
std. err.	0.000123	0.000194	0.000215
t-stat	3.54	69.88	89.89
p-value	0.0004	<.0001	<.0001
β_3	0.000552	-0.00773	-0.01889
std. err.	0.001203	0.00189	0.002097
t-stat	0.46	-4.09	-9.01
p-value	0.6464	<0.0001	<0.0001
$\beta_2 + \beta_3$	0.000988	0.005809	0.000431
std. err.	0.001196	0.00188	0.002086
t-stat	0.83	3.09	0.21
p-value	0.4091	0.002	0.8362

For AGE_LT_5, the VA vs. non-VA difference in the rate of increase of new drug use (β_3) is not statistically significant. However, for the other two age measures, the difference is negative and significant.

16. Consider the following econometric model:

$$AGE\_DEATH_{ijt} = \beta\ POST1990\%_{ijt} + \alpha_{ij} + \delta_{it} + \gamma_{jt} + \varepsilon_{ijt} \qquad (2)$$

where

AGE_DEATH_{ijt} = mean age at death from disease i (i = 1,2,…,16) in state j (j = 1,2,…,50) in year t (t=1991,1992,…,2001)

$POST1990\%_{ijt}$ = the % of Medicaid prescriptions for disease i in state j in year t that contain active ingredients approved by the FDA after 1990

α_{ij} = a fixed effect for disease i in state j

δ_{it} = a fixed effect for disease i in year t

γ_{jt} = a fixed effect for state j in year t

ε_{ijt} = a disturbance

The model is to be estimated via weighted least squares, weighting by N_DEATH_{ijt}, the number of deaths from disease i in state j in year t.

17. I.e., prescriptions that contain active ingredients approved by the FDA after 1990.

18. These are controlled for by including the γ_{jt}'s. The econometric specification is similar to the one that I used in a previous paper, "The Impact of New Drug Launches on Longevity: Evidence from Longitudinal Disease-Level Data from 52 Countries, 1982-2001." In that paper, however, the measure of drug availability was the *cumulative number of drugs launched* for a given disease in a given country (and the data were subject to left-censoring). The data available for this study are superior in an important respect: we have very extensive data on *drugs actually prescribed*.

19. See http://www.nber.org/data/deaths.html.

20. See http://www.cms.hhs.gov/medicaid/drugs/drug5.asp.

21. There are about 700 data files: one for each state in each year.

22. I used these data to estimate the following equation:

$$tot\_prod\_age_{cjt} = \pi\ mdcd\_prod\_age_{cjt} + \alpha_{cj} + \delta_{ct} + \gamma_{jt} + \varepsilon_{cjt}$$

where

$tot\_prod\_age_{cjt}$ = the mean age (number of years since FDA approval) of *all* prescriptions in therapeutic class c (c = 1,2,…,6) in region j (j = 1,2,…,55) in month t (t=1,2,…,36)

$mdcd\_prod\_age_{cjt}$ = the mean age of Medicaid prescriptions in therapeutic class c in region j in month t

α_{cj} = a fixed effect for therapeutic class c in region j

δ_{ct} = a fixed effect for therapeutic class c in year t

γ_{jt} = a fixed effect for region j in year t

ε_{cjt} = a disturbance

The estimate of π was positive and highly significant (p-value <.0001), which indicates that the extent of use of new drugs in the Medicaid program is strongly correlated with the extent of use of new drugs in general. I will now present the statistics pertaining to β from estimation of eq. (2):

β	2.53
std. err.	0.45
t-stat	5.65
p-value	<.0001

The estimate of β is positive and highly significant.

23. $\beta = \Delta * POST1990\% = 2.53 * 0.314$.

24. = 0.79 / 1.74.

25. Lichtenberg, "The Impact of New Drug Launches on Longevity."

26. See http://www.va.gov/vetdata/demographics/VP2001sn.htm.

27. Since the age groups are five years wide, the probability of surviving from the beginning of age group a to the beginning of age group (a+1) is approximately $S_{at} = (1 - M_{at})^5$. The probability of surviving from the first age group (age < 20) to the beginning of age group a is is $H_{at} = S_{1t} * S_{2t} * \ldots * S_{a-1,t}$. The probability that a person in the first age group will die in age group a is $Q_{at} = (H_{a+1,t} - H_{at})$. The life expectancy of a person in the first age group in year t is is $E_t = \Sigma_a Q_{at} A_a$, where A_a= the mean age at death of a person dying in age group a, which I assume to be the midpoint of the age interval. For example, I assume that deaths of people aged 75-79 occur at age 77.5. I assume that people dying after age 100 die at age 102.5.

28. While there are some reasons to expect the mean value of E_t to be lower than the mean value of the life expectancy of all U.S. males at birth-serving in the military may impair one's future health-there are other reasons to expect it to be greater. E_t is based on a population of individuals who have been veterans, i.e., who lived long enough to serve in the armed forces (e.g., did not die in infancy) and who survived serving in the armed forces. It would be more appropriate to compare E_t with the life expectancy of all U.S. males at age twenty, for example. Such data are available for some years (it was 73.25 for 1989-1991 and 75.6 in 2002) but are not available annually (Arias, 2004, Table 11).

Appendix

Table 1: Priority Review Drugs Approved After 1997 Not Listed on 2005 National Formulary

ABARELIX	MIFEPRISTONE
ACAMPROSATE	NATALIZUMAB
ADEFOVIR	NITAZOXANIDE
ALITRETINOIN	NITISINONE
ALOSETRON	NITRIC OXIDE
ANAGRELIDE	ORLISTAT
APREPITANT	OSELTAMIVIR
ARSENIC	PEGVISOMANT
AZACITIDINE	PEMETREXED
BEVACIZUMAB	PEMIROLAST
BEXAROTENE	PIOGLITAZONE
BIMATOPROST	RALOXIFENE
BORTEZOMIB	REPAGLINIDE
CAPECITABINE	RIFAPENTINE
CASPOFUNGIN	ROFECOXIB
CELECOXIB	SACROSIDASE
CETUXIMAB	SIROLIMUS
CINACALCET	SODIUM OXYBATE
DALFOPRISTIN/QUINUPRISTIN	TEGASEROD
DAPTOMYCIN	TEMOZOLOMIDE
EPIRUBICIN	THALIDOMIDE
EPTIFIBATIDE	THYROTROPIN ALFA
ERLOTINIB	TIROFIBAN
FOMIVIRSEN	TREPROSTINIL
FONDAPARINUX	TROGLITAZONE
GANIRELIX	UNOPROSTONE
GEFITINIB	VALRUBICIN
KETOTIFEN	VERTEPORFIN
LEFLUNOMIDE	ZANAMIVIR
LEPIRUDIN	ZOLEDRONIC

Table 2: Demographic Data on Veterans, 1991–2002

Age	<20	20–24	25–29	30–34	35–39	40–44	45–49	50–54	55–59
Year				**Number of deaths**					
1991	29	797	1991	3699	5615	5512	7956	13935	32570
1992	18	683	1787	3543	5475	5738	8993	13506	29977
1993	20	691	1637	3527	5580	6251	9496	13406	27185
1994	14	584	1409	3215	5271	6228	9988	13849	25735
1995	14	638	1427	3052	5436	7311	10371	14405	23842
1996	21	500	1317	2561	4869	7672	10479	14872	22953
1997	12	359	1069	1894	3901	6470	9309	15935	22261
1998	20	339	915	1569	3282	6005	8565	16240	21803
1999	21	317	852	1559	3180	6101	8686	16766	21815
2000	26	339	804	1480	2901	6085	9382	17090	22316
2001	14	211	481	891	1269	2985	6717	20013	24679
2002	14	217	441	871	1223	2805	6411	17562	27536
Year				**Number alive**					
1991	9799	416155	1118642	1583546	1871072	3021445	3212103	2470216	2884391
1992	9152	425139	1095812	1563619	1838404	2616539	3476386	2525059	2706603
1993	10996	407650	1056779	1530989	1822089	2314835	3603409	2601574	2572738
1994	10668	380275	1022324	1486256	1794793	2093929	3632480	2707654	2469478
1995	10007	339934	997708	1436028	1757751	2014915	3539528	2818806	2401227
1996	9600	311544	959625	1369790	1711676	1994150	3080630	3188829	2392406
1997	9560	298061	910085	1306040	1664757	1953326	2670969	3448520	2447173
1998	11414	281820	850631	1251681	1623225	1935096	2364019	3571336	2522529
1999	12075	271341	794328	1208118	1574231	1901448	2136143	3599190	2627044
2000	13273	271794	731274	1178937	1513691	1853422	2047712	3506113	2736305
2001	12397	279966	680278	1133104	1443688	1807612	2028176	3049288	3097870
2002	11806	288274	647974	1074531	1374989	1762558	1989379	2642851	3350445
Year				**Mortality rate**					
1991	0.29%	0.19%	0.18%	0.23%	0.30%	0.18%	0.25%	0.56%	1.13%
1992	0.19%	0.16%	0.16%	0.23%	0.30%	0.22%	0.26%	0.53%	1.11%
1993	0.18%	0.17%	0.15%	0.23%	0.31%	0.27%	0.26%	0.52%	1.06%
1994	0.13%	0.15%	0.14%	0.22%	0.29%	0.30%	0.27%	0.51%	1.04%
1995	0.14%	0.19%	0.14%	0.21%	0.31%	0.36%	0.29%	0.51%	0.99%
1996	0.22%	0.16%	0.14%	0.19%	0.28%	0.38%	0.34%	0.47%	0.96%
1997	0.12%	0.12%	0.12%	0.14%	0.23%	0.33%	0.35%	0.46%	0.91%
1998	0.17%	0.12%	0.11%	0.13%	0.20%	0.31%	0.36%	0.45%	0.86%
1999	0.17%	0.12%	0.11%	0.13%	0.20%	0.32%	0.41%	0.47%	0.83%
2000	0.20%	0.12%	0.11%	0.13%	0.19%	0.33%	0.46%	0.49%	0.82%
2001	0.11%	0.08%	0.07%	0.08%	0.09%	0.17%	0.33%	0.66%	0.80%
2002	0.12%	0.08%	0.07%	0.08%	0.09%	0.16%	0.32%	0.66%	0.82%

Table 2: continued

	60–64	65–69	70–74	75–79	80–84	85–89	90–94	95–99	100+
Year					**Number of deaths**				
1991	61621	104716	113083	68660	37928	14562	12145	7363	389
1992	58209	100658	121607	77208	41710	16947	9666	7257	473
1993	54272	98586	128719	87154	45661	19817	8558	6668	634
1994	54067	96092	134463	101214	52555	23786	8169	5779	881
1995	51587	90015	132434	111112	58516	26980	7883	4839	1248
1996	47809	86339	130454	123205	67517	30734	8476	3955	1341
1997	44230	82143	126255	133820	77411	34091	9955	3216	1282
1998	39818	77806	123336	140020	88097	38132	11813	2850	1094
1999	36815	75360	117970	144006	100265	42534	13442	2615	882
2000	35158	72729	111965	145840	113313	48560	15176	2522	747
2001	34010	69091	108732	145378	126039	55853	16967	2692	615
2002	33407	63605	104324	141866	138797	64751	19082	3251	524
Year					**Number alive**				
1991	3411319	3629402	2841425	1212401	428894	118004	44549	24699	1210
1992	3280921	3582956	3006289	1390541	478689	139659	39586	21975	1605
1993	3220731	3420484	3102584	1585517	538255	160723	36886	18317	2182
1994	3093889	3269916	3160623	1791865	610826	183154	36140	15309	3072
1995	2904906	3174385	3127011	2001480	711421	207446	38979	12461	3219
1996	2709998	3073918	3065441	2202117	822732	231802	46110	10142	3015
1997	2546293	2961703	3030949	2333979	946382	259477	54415	8969	2503
1998	2423731	2908251	2894063	2414230	1081604	292019	61742	8289	1991
1999	2330482	2797107	2771807	2467836	1228022	333524	70175	8300	1735
2000	2268468	2629168	2696118	2446893	1377969	390683	79509	9125	1461
2001	2263150	2455383	2615913	2403775	1522182	454261	89562	11053	1245
2002	2318244	2311788	2525306	2380480	1615623	524584	100940	13208	1137
Year					**Mortality rate**				
1991	1.81%	2.89%	3.98%	5.66%	8.84%	12.34%	27.26%	29.8%	32%
1992	1.77%	2.81%	4.05%	5.55%	8.71%	12.13%	24.42%	33.0%	29%
1993	1.69%	2.88%	4.15%	5.50%	8.48%	12.33%	23.20%	36.4%	29%
1994	1.75%	2.94%	4.25%	5.65%	8.60%	12.99%	22.60%	37.8%	29%
1995	1.78%	2.84%	4.24%	5.55%	8.23%	13.01%	20.22%	38.8%	39%
1996	1.76%	2.81%	4.26%	5.59%	8.21%	13.26%	18.38%	39.0%	44%
1997	1.74%	2.77%	4.17%	5.73%	8.18%	13.14%	18.30%	35.9%	51%
1998	1.64%	2.68%	4.26%	5.80%	8.15%	13.06%	19.13%	34.4%	55%
1999	1.58%	2.69%	4.26%	5.84%	8.16%	12.75%	19.16%	31.5%	51%
2000	1.55%	2.77%	4.15%	5.96%	8.22%	12.43%	19.09%	27.6%	51%
2001	1.50%	2.81%	4.16%	6.05%	8.28%	12.30%	18.94%	24.4%	49%
2002	1.44%	2.75%	4.13%	5.96%	8.59%	12.34%	18.90%	24.6%	46%

The Center for Medical Progress is dedicated to articulating the importance of medical progress and the connection between free-market institutions and making medical progress both possible and widely available throughout the world. It encourages the development of market-based policy alternatives to sustain medical progress and promote medical innovation.

The Manhattan Institute is a 501(C)(3) nonprofit organization. Contributions are tax-deductible to the fullest extent of the law. EIN #13-2912529

MANHATTAN INSTITUTE FOR POLICY RESEARCH

52 Vanderbilt Avenue • New York, NY 10017
www.manhattan-institute.org

Non-Profit
Organization
US Postage
PAID
Permit 04001
New York, NY