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IS THE HEALTH CARE SYSTEM AT FAULT?

Samuel H. Preston  
Jessica Y. Ho

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Low Life Expectancy in the United States: Is the Health Care System at Fault?

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**ABSTRACT**

Life expectancy in the United States fares poorly in international comparisons, primarily because of high mortality rates above age 50. Its low ranking is often blamed on a poor performance by the health care system rather than on behavioral or social factors. This paper presents evidence on the relative performance of the US health care system using death avoidance as the sole criterion. We find that, by standards of OECD countries, the US does well in terms of screening for cancer, survival rates from cancer, survival rates after heart attacks and strokes, and medication of individuals with high levels of blood pressure or cholesterol. We consider in greater depth mortality from prostate cancer and breast cancer, diseases for which effective methods of identification and treatment have been developed and where behavioral factors do not play a dominant role. We show that the US has had significantly faster declines in mortality from these two diseases than comparison countries. We conclude that the low longevity ranking of the United States is not likely to be a result of a poorly functioning health care system.

Samuel H. Preston  
School of Arts and Sciences  
289 McNeil Building  
University of Pennsylvania  
Philadelphia, PA 19104-6298  
and NBER  
spreston@sas.upenn.edu

Jessica Y. Ho  
3718 Locust Walk, Rm 239  
Population Studies Center  
Philadelphia, PA 19104  
yjho@sas.upenn.edu

The United States falls well behind the world's leaders in life expectancy at birth. Some of the discrepancy is attributable to relatively high infant mortality and some to high mortality from violence among young adults. But the bulk of the discrepancy is attributable to mortality above age 50, an age to which 94% of newborns in the United States will survive according to the 2006 US life table. Life expectancy at age 50 in the United States ranks 29<sup>th</sup> highest in the world in 2006 according to the World Health Organization (WHO 2009). It falls 3.3 years behind the leader, Japan, and more than 1.5 years behind Australia, Canada, France, Italy, Iceland, Spain, and Switzerland. About 4 million Americans reach age 50 each year, so that an average loss of 1.5 years of life years per person means that some 6 million years of potential life are being lost annually. At the conventional value of \$100,000 per additional year of life (Cutler 2004), the relative loss of life in the US above age 50 is valued at roughly \$600 billion annually. Using Japan as a standard, the loss is \$1.3 trillion.

Analysts often juxtapose the poor ranking of the United States in life expectancy and the very high percentage of its gross national product that is spent on health care. In 2007, the United States spent 16% of its GDP on health care, by far the highest fraction of any country (Congressional Budget Office 2007). The conclusion that is often drawn from this combination is that the United States' health care system is extremely inefficient (e.g., Anderson and Frogner 2008).

But measures of population health such as life expectancy do not depend only on what transpires within the health care system – the array of hospitals, doctors and other health care professionals, the techniques they employ, and the institutions that govern access to and utilization of them. Such measures also depend upon a variety of personal behaviors that affect an individual's health such as diet, exercise, smoking, and compliance with medical protocols. The health care system could be performing exceptionally well in identifying and administering treatment for various diseases, but a country could still have poor measured health if personal health care practices were unusually deleterious. This is not a remote possibility in the United States, which had the highest level of cigarette consumption per capita in the developed world over a 50-year period ending in the mid-80's (Forey et al. 2002). Smoking in early life has left an imprint on mortality patterns that remains visible as cohorts age (Preston and Wang 2006; Haldorsen and Grimsrud 1999). One recent study estimated that, if deaths attributable to smoking were eliminated, the ranking of US men in life expectancy at age 50 among 20 OECD

countries would improve from 14<sup>th</sup> to 9<sup>th</sup>, while US women would move from 18<sup>th</sup> to 7<sup>th</sup> (Preston, Gleib, and Wilmoth 2009). Recent trends in obesity are also more adverse in the United States than in other developed countries (OECD 2008; Cutler, Glaeser, and Shapiro 2003).

This paper begins with a review of previous international studies of the comparative performance of health care systems. The review is focused on the major diseases of adulthood, cancer and cardiovascular disease, in the belief that disease-level analyses are more likely to reveal the forces at work than more highly aggregated studies (Garber 2003). In 2005, cancer and major cardiovascular diseases were responsible for 61.0% of deaths in the US at ages 45+ (US National Center for Health Statistics 2008). Because our concern is with mortality per se, the criterion we employ is effectiveness at preventing death, rather than cost-effectiveness or efficiency of resource deployment. These latter criteria have been used in several other recent comparative studies with a financial focus (Garber and Skinner 2008; McKinsey Global Institute 2008).

Health systems can prevent death from a particular disease either by preventing a disease from developing or by effectively treating it once it has developed. A key element in effective treatment is accurate diagnosis. Unfortunately, almost no internationally comparable data exist on the actual incidence of various diseases, which is the appropriate measure of the success of prevention. While cancer appears to be an exception because “incidence” data are published for various cancer registry sites (e.g., at the website of the International Agency for Research on Cancer), the data refer not to the origin of a disease but to its detection, a process that combines actual patterns of incidence with the mechanics of identification. And even if pure measures of it were available, actual disease incidence reflects not only features of a health system but also many other factors of behavioral, social, and genetic origin.

Disease prevalence – the proportion of the population that has been diagnosed with a disease – is even more difficult to interpret. The United States has a higher prevalence than Europe of the major adult diseases, including cancer, heart disease, and diabetes (Thorpe et al. 2007a; Avendano et al. 2009). But higher prevalence could reflect higher incidence, better detection, or longer survival resulting from more successful treatment. Because of these limitations of data and interpretation, our review will focus primarily on disease identification and treatment, elements that are customarily considered to be the provenance of health care systems.

A valuable but not unimpeachable indicator of the effectiveness of treatment is the comparative survival rate of individuals once a disease has been detected. Relatively high survival rates imply either that the disease has been detected unusually early or that treatment is unusually successful. Early detection is valuable to the extent that it permits better therapy. However, if early detection did not alter the clinical course of a disease but only increased the expected length of time from detection to death (so-called “lead time bias”), then it would not be associated with reductions in mortality at the population level despite raising 5-year survival rates (e.g., Gatta et al. 2000).

Because they are not subject to this potential bias, we pay special attention to mortality rates. In particular, in the second half of the paper we investigate comparative mortality trends for prostate cancer and breast cancer. We document that

- effective methods of screening for these diseases have been developed relatively recently;
- these diagnostic methods have been deployed earlier and more widely in the US than in most comparison countries;
- effective methods are being used to treat these diseases; and
- the US has had a significantly faster decline in mortality from these diseases than comparison countries.

### ***International Studies of Cancer***

The United States does well in international comparisons of the frequency of cancer screening. The OECD (2006, 2007) provides 2000-05 data on the percentage of women aged 20-69 in 15 countries who had been screened for cervical cancer during the preceding three years. The US has the highest percentage of women who have been screened in both tabulations.<sup>1</sup> We present evidence below that the US also has exceptionally high screening rates for prostate cancer and breast cancer. Quinn (2003) reports colorectal screening rates in the US that are “quite high” in comparison to Europe but does not provide comparative data. Gatta et al. (2000: 899) also suggest that access to and use of sigmoidoscopy, colonoscopy, and fecal occult blood tests are more common in the US than in Europe. This difference is supported by the finding that

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<sup>1</sup> Ages vary somewhat but the variation is thought to be a “minor threat” to the validity of comparisons (OECD 2006:69). The 15 countries include 6 for whom the recall period is greater than 3 years, the period used in the US.

colorectal cancer patients in the US have less advanced disease at diagnosis than patients in Europe (Ciccolallo et al. 2005).

A higher rate of screening for cancer would produce a higher prevalence of ever-diagnosed cancer in the population, *ceteris paribus*. The elevated prevalence would occur simply because a higher fraction of the population would know about their disease. An additional boost to prevalence would be provided if early detection resulted in reduced mortality. Thus, in view of the higher frequency of screening in the US, we would expect its reported prevalence of diagnosed cancer to be higher than in Europe.

That expectation is confirmed by data from the Health and Retirement Survey and its English and European counterparts. Thorpe et al. (2007a) find that 12.2% of Americans over age 50 report having been diagnosed by physicians with cancer, compared to only 5.4% in a composite of 10 European countries. Avendano et al. (2009) report similar figures for the age range 50-74, with England intermediate between the US and Europe but closer to Europe. Some fraction of these very large differences in prevalence could, of course, be attributable to real differences in disease incidence or to reporting differences, which are discussed briefly below.

Thanks to a large number of cancer registries that record new cancer diagnoses and follow individuals forward from the point of diagnosis, 5-year survival rates for people initially diagnosed with cancer are widely available to provide evidence about the success of detection and treatment. Because of their relative comparability and pertinence to a major disease process, these data are among the best indicators of comparative health system performance. In this summary, we use 5-year relative survival rates, which compare the survival of those diagnosed with cancer to that of an average person of the same age and sex as the person diagnosed.

International comparisons of cancer survival rates show a distinct advantage for the US. Using cancer registry data, researchers from the Eurocare Working Group compare 5-year survival rates for cancers of 12 sites that were diagnosed between 1985 and 1989 (Gatta et al. 2000). The aggregate of 41 European registries, which were drawn from 17 countries, had lower survival rates than the US from all cancer sites except the stomach, where differences were small and attributed to differences between the distributions of sites within the stomach. The US data were drawn from the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) database, a population-based cancer registry covering approximately 14% of the US population. For the major sites of lung, breast, prostate, colon, and rectum cancers, US survival

rates were the highest of any of the 18 countries investigated. Cancers first diagnosed on the death certificate (5% in Europe and 1% in the US) were excluded from analysis; if they had been included, the US survival advantage would have increased. The authors discount the possibility that the US advantage was attributable to statistical or registration artifacts.

An updated analysis reached similar conclusions. Based upon period survival data for 2000-02 from 47 European cancer registries, 5-year survival rates were found to be higher in the US than in a European composite for cancer at all major sites (Verdecchia et al. 2007). Table 1 presents the comparative data for all sites for which the US 95% confidence interval was  $<0.025$ . For men (all sites combined), 47.3% of Europeans survived 5 years, compared to 66.3% of Americans. For women, the contrast was 55.8% vs. 62.9%. The male survival difference was much greater than the female primarily because of the very large difference in survival rates from prostate cancer.

Thus, the US appears to screen more vigorously for cancer than Europe and people in the US who are diagnosed with cancer have higher 5-year survival probabilities. Scattered data for cancer of various sites indicate that tumors are typically detected at an earlier stage in the US (Gatta et al. 2000; Sant et al. 2004; Ciccolallo et al. 2005). Of course, all of these phenomena could be the exclusive product of lead-time bias if early detection afforded no benefit for the clinical course of the disease. Below, we present evidence that innovations in diagnosis and treatment of prostate and breast cancer were associated with faster declines in mortality in the US than in OECD countries. Such a pattern would not be observed if lead time bias were the only factor at work, i.e., if early detection conferred no advantage.

### ***International Studies of Cardiovascular Disease***

In contrast to cancer, nations do not have registries for heart disease and stroke. So information about the comparative performance of medical systems in respect to cardiovascular disease is not as systematic and orderly as it is for cancer. One useful source of comparative data is the Health and Retirement Survey (HRS) and its European counterparts, the Survey of Health, Aging, and Retirement in Europe (SHARE). Thorpe et al. (2007a) compare the US to a composite of 10 European countries on the frequency with which people with a particular diagnosis report using medication. Of people aged 50+ diagnosed with heart disease, 60.7% of Americans and 54.5% of Europeans report being on medication. The proportions using

medication after a stroke are comparable at 45.1% and 44.6%. Of those reporting high cholesterol levels, 88.1% of Americans report being medicated vs. 62.4% of Europeans.<sup>2</sup> Crimmins, Garcia, and Kim (2009) show that a much higher fraction of Americans are using lipid-lowering drugs at a particular age than in Japan, the Netherlands, or Italy, even though proportions with elevated cholesterol in these countries are similar to or higher than that in the US.

Among those reporting high blood pressure in HRS and SHARE, the proportions reporting taking medication for the condition are similar in the US (88.0%) and Europe (88.9%) (Thorpe et al. 2007a). However, when actual measures of blood pressure are used rather than self reports, the position of the US improves. Wolf-Maier et al. (2004) employ regional or national samples in the US, Canada, and five European countries. Hypertension is defined as the population of persons who have systolic blood pressure of 160+ or diastolic blood pressure of 95+ or who are using antihypertensive medication. Of persons aged 35-64 with hypertension, 77.9% were being treated in the US, compared to a range of 41.0% - 62.4% in the other six countries. Among those with hypertension, 65.5% were being *successfully* treated in the US (i.e., their levels were reduced below the hypertension-defining threshold), compared to 24.8% to 49.1% in the other countries.

Survival data for cardiovascular disease start not from the point of diagnosis but from an acute event of heart attack or stroke. An OECD study, following up on a study by the TECH network, computed one-year case fatality rates for people hospitalized for acute myocardial infarction (AMI) in Australia, Canada, Denmark, Finland, Sweden, Great Britain, and the US. The samples were sometimes regionally rather than nationally representative. Among the seven countries in 1996, the US had the third lowest case-fatality rate for males aged 40-64 and the second-lowest rate for men aged 85-89. For women at these ages, the US ranked fourth and first (Moise 2003). Part of the explanation of the better performance of the US may be related to its unusually aggressive treatment regime. Of the seven countries, the US had the highest proportion of male and female patients in both age intervals undergoing revascularization operations (percutaneous transluminal coronary angioplasty or coronary artery bypass graft) (Ibid.; see also

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<sup>2</sup> The US figure for cholesterol is drawn from the Medicare Expenditure Panel Survey because HRS did not gather this information.



Technological Change in Health Care (TECH) Research Network 2001).<sup>3</sup>

One study has explicitly linked more aggressive surgical treatment in the US to better outcomes. It compared Canadians and Americans who had just experienced an AMI and who enrolled in a drug trial (Kaul et al. 2004). Data are not nationally representative but rather reflect the patient-base of hospitals participating in the trial. Americans had a small but statistically significant advantage in 5-year survival. Controlling many baseline characteristics, the hazard rate was 17% higher in Canada. When revascularization was added to the model, it was associated with a 28% reduction in the hazard rate and its addition reduced the international difference to an insignificant 7%. The authors conclude that "...our findings are strongly suggestive of a survival advantage for the US cohort based on more aggressive revascularization" (Ibid., p. 1758).

OECD (2003) has conducted a large international study of ischaemic stroke, which accounts for roughly 88% of stroke cases except in Japan, where it represents about 70%. They calculate in-hospital 7-day and 30-day survival rates for patients newly admitted with ischaemic stroke. For both men and women aged 65-74, the US ranking on 7-day survival rates was 3<sup>rd</sup> out of 9; at ages 75+, it was 2<sup>nd</sup> out of 9 for both sexes. For 30-day hospital survival rates at ages 65-74, the US was 2<sup>nd</sup> for women and tied for 2<sup>nd</sup> with two others among men. At ages 75+, the US 30-day survival rate was 1<sup>st</sup> for men and 2<sup>nd</sup> for women. Counting all deaths and not simply deaths in the hospital, and limiting comparison to six regions including two in Canada, the US survival rate ranked 1<sup>st</sup> for men aged 65-74 and 75+ and second for women in these ages. However, the US one-year survival rate among this set of populations was considerably poorer, ranking 5<sup>th</sup> of 6 for men aged 65-74 and 4<sup>th</sup> of 6 for men aged 75+. For women at these two ages, the rankings were 4<sup>th</sup> and 3<sup>rd</sup>. Consistently in these rankings, the US position was better at 75+ than at 65-74.

Carotid endarterectomy (surgical removal of plaque from inside the carotid artery) is used to prevent stroke or the recurrence of stroke. Such surgery is much more common in the US than in any of 11 comparison OECD countries (OECD 2003). We are unaware of any studies linking this surgery to international patterns of stroke mortality, but a randomized clinical trial reports a large survival advantage for persons undergoing the procedure (Halliday et al. 2004).

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<sup>3</sup> Data on treatments at ages 85-89 were not available for Spain or the United Kingdom.

### ***Contrary Evidence? “Mortality Amenable to Medical Care”***

The Commonwealth Fund (2008) has recently issued a “scorecard” on US health system performance that consists of 37 indicators. The highly publicized report concludes that the United States lags far behind its peers in measures of health system performance. Most of the indicators use benchmarks that are established by consultation with experts or by values in best-performing states. But several are based on international comparisons. The international index that receives the most attention is “Mortality amenable to medical care”, on which the US currently ranks last among 19 countries. This index is developed and applied in Nolte and McKee (2008), where amenable deaths are described as “deaths from certain causes that should not occur in the presence of timely and effective health care” (p. 59). Only deaths below age 75 are included, which constitute 43.2% of deaths in the US in 2005 (US National Center for Health Statistics 2008). For some causes of death, an earlier age cutoff is used.

The distribution of major causes of death included among the “amenable causes” is provided for the US, the United Kingdom, and France (Nolte and McKee 2008). A majority of amenable deaths in all three countries is attributed to ischemic heart disease and other circulatory diseases, even though only half of ischemic heart disease deaths are included because some are believed not to be amenable to health care. That rule of thumb is clearly a poor substitute for an effort to attribute international variation in mortality from ischemic heart disease to its various components, including health care systems and behavioral and social factors.<sup>4</sup> The authors note that a similar rule of thumb could have been introduced for cerebrovascular diseases, which constitute at least a quarter of the “amenable” deaths in the US and UK. But it would have been no more satisfactory for that cause of death.

In view of the studies that show that the US does relatively well in treating cardiovascular disease, it seems inaccurate to attribute its high death rates from these causes to a poorly performing medical system. And these diseases contribute a majority of their set of amenable deaths, rendering the totality of amenable causes problematic. A related objection could be raised to the inclusion of diabetes deaths in the set. On the other hand, prostate cancer is excluded from the list of amenable causes despite the fact that the 5-year survival rate from prostate cancer in the US is above 99% and the disease can be readily identified (see below).

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<sup>4</sup> The strategy adopted by Nolte and McKee is no different from saying that genetic factors play some role in cardiovascular mortality and, as a consequence, attributing half of international variation in cardiovascular mortality to genetic factors.

According to Nolte and McKee (2008), males in the United States had a faster fall in mortality from non-amenable causes of death (an 8% decline) than from amenable ones (4%) between the latest two readings, 1997/8 and 2002/3. This anomaly suggests either flaws in the index or the unimportance of medical care relative to other factors that are operating.

Causes of death whose inclusion in Nolte and McKee's list of amenable causes at older ages is more defensible are influenza and pneumonia. Mortality from both causes is heavily influenced by smoking (Centers for Disease Control and Prevention 2002), so the international distribution of mortality is a product of factors beyond the health care system. On the other hand, influenza is partially immunizable and death from pneumonia can often be avoided through administration of vaccines or antibiotics or improvements in hospital sanitation.

The US ranks 9<sup>th</sup> of 23 OECD countries in the proportion of the population above age 65 offered an annual influenza vaccination (OECD 2007). Figure 1 demonstrates that the 2000-04 age-standardized death rate from influenza at ages 50+ in the United States is among the lowest of the 16 countries investigated. The US fares less well in mortality from pneumonia, ranking 6<sup>th</sup> worst among the 16 countries investigated (Figure 2). However, the ranking is somewhat deceiving because its death rate is closer to all but one of the better-ranked countries than to the five countries with higher rates. The US death rate from pneumonia at ages 50+ is actually below the weighted or unweighted mean for the other 15 countries.

### ***Disease Prevention***

Medical procedures and survival rates are indicators of what happens to individuals whose health problems come to the attention of the health care system. But a health care system can also help prevent serious health problems from occurring in the first place. Of course, early identification of a disease is also preventative medicine in the sense that it may prevent death. But access to preventive medicine would appear to be an especially problematic area in the United States because 47 million people lack any form of health insurance (DeNavas-Walt, Proctor, and Smith 2007).<sup>5</sup> Such people are less likely to see a doctor and thus to receive routine testing that might detect the early stages of a disease and prevent its clinical manifestations (Institute of Medicine 2001). They are also less likely to receive advice about health maintenance

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<sup>5</sup> It has been claimed that this number includes 10 million people who are in fact covered by Medicaid insurance but who fail to report it (Ohsfeldt and Schneider 2006).

and disease prevention (Ibid.).

An additional factor that may inhibit disease prevention in the US is the shortage of primary care physicians. The US scores in the bottom group of 6 out of 18 OECD countries on a scale of the adequacy of primary care (Macinko, Starfield, and Shi 2003). The scale is built from items relating to policy, finances, and personnel. In turn, the adequacy of primary care may be related to disease prevention (Ibid.)

The best indication of the success of prevention is disease incidence. But international data on disease incidence are nil. As noted earlier, disease prevalence is higher in the US than in a European composite for cancer, heart disease, stroke, chronic lung disease, and diabetes (Thorpe et al. 2007a). However, such a difference could result from higher incidence in the US, better detection, or longer survival after detection. It could also result from reporting differences, e.g., a greater inclination to report disease in the US. But a careful study by Banks et al. (2006) using biomarkers suggests that morbidity differences between England and the US at ages 55 to 64 are real and not a result of differences in reportage. One related study found that, faced with the same set of health-related vignettes, Americans were less likely to report themselves as disabled than the Dutch (Kapteyn, Smith, and van Soest 2007).

Even if incidence data were available, analysts would have to disentangle the role of personal behavioral and social histories from that of health system performance. And these are not always readily distinguishable. Are the historically high rates of smoking in the US attributable to the failure of the US public health system to stem the smoking tide? The fact that Canada had for many years the second highest consumption of cigarettes per adult (Forey et al. 2002) makes it appear that geographic factors, perhaps related to conditions for growing or importing tobacco, had more to do with consumption patterns than did health systems. And public health authorities were not passive in the US. The US Surgeon General's (1964) report on the health hazards of cigarette smoking was the first major indictment of the habit by a government authority and it was quickly followed up with a massive anti-smoking media campaign (Cutler and Glaeser 2006). The US had the largest reduction in manufactured cigarettes consumed per adult of any country between 1970 and 2000 (Forey et al. 2002). Some of that decline was likely attributable to public health efforts (Cutler and Glaeser 2006).

However it is achieved, the high prevalence of disease in the US adds considerably to health expenditure. Thorpe et al. (2007b) combine comparative prevalence data on 10 conditions

in HRS (in the US) and SHARE (in Europe) with Agency for Healthcare Research and Quality data on expenditure per medical condition for the population aged 50+. Their 95% confidence intervals on the per capita cost of higher disease prevalence in the US are \$1,195 to \$1,750 per year, or 12.7 to 18.7% of total personal health care spending among those aged 50+.

Inefficiencies in the health care system are not solely responsible for high per capita health expenditures in the US; the high prevalence of major diseases is also substantially implicated (see also Michaud et al. 2009).

### ***Case Study I. Prostate Cancer***

Accounting for 31,000 deaths in 2000, prostate cancer was, after lung cancer, the second leading cause of cancer deaths among US men that year (US National Center for Health Statistics 2002). Unlike most chronic diseases, it is not associated with cigarette smoking (Lumey et al. 1997). A link with exercise has been suggested in several studies but a review article found that “conclusions were quite variable... odds ratios [of developing prostate cancer] for men engaged in high levels of activity ranged from 0.2 to over 2.0” (Torti and Matheson 2004). Dietary risk factors are suspected but not well established. The risk of prostate cancer is somewhat higher for men with a high body mass index, but the risk is less than for other cancers (Crawford 2003). Genetic factors, some of them associated with race, appear to be important in the risk of developing prostate cancer (Li et al. 2007). Its relatively flat landscape of behavioral risk factors, together with its medical preventability, make mortality from prostate cancer a purer indicator of health system performance than mortality from many other chronic diseases of adulthood.

#### ***A. Prostate Cancer Screening***

The Digital Rectal Examination (DRE) and Prostate Specific Antigen (PSA) test are the primary screening tools for prostate cancer. As a screening test, DRE is of limited value because it cannot investigate the entire prostate gland (Ilic et al. 2006). It is more difficult to detect cancer with DRE than with the PSA test (Harris and Lohr 2002). The PSA test has the added benefits of being easy to perform, relatively inexpensive, and reproducible (Constantinou 2006).

The PSA blood test for the presence of prostate cancer was approved by the Food and Drug Administration in 1986 (Shampo 2002). The test enables the detection of high and/or

rapidly increasing levels of an antigen that often signals the presence of prostate cancer. High levels of the antigen can also be produced by other conditions; confirmation of cancer is made by transrectal ultrasound-guided biopsy (TRUS).

The PSA test is somewhat controversial. One reason is that, like many other medical screens, the PSA test can produce a false positive – a report of potential cancer when it is not present. According to a summary of studies of the sensitivity and specificity of PSA testing, an average of 75% of those with PSA readings above 4.0 ug/l have prostate cancer and 71% of men with prostate cancer have a PSA reading above 4.0 ug/l (Bunting 2002). However, the main reservation about the use of the PSA test is that treatment for prostate cancer can produce impotence and/or incontinence. Because of these side effects, several organizations have recommended against PSA testing for men over 75 (U.S. Preventive Services Task Force 2008). On the other hand, the American Cancer Society and the American Urological Association recommend that the PSA test should be offered annually to men over 50 with at least a 10-year life expectancy.

By reputation the US has been the world leader in PSA testing, especially in the early years after the test was developed (Hsing, Tsao, and Devesa 2000; Levi et al. 2000; Vercelli et al. 200; De Koning et al. 2002; Bouchardy et al. 2008). Table 2 compiles the latest data that we were able to locate on the frequency of PSA testing in various countries or regions. The age ranges used and the survey dates are not identical from country to country, preventing exact comparisons. The United States has the highest recorded percentage ever tested at older ages (prevalence) as well as the highest percentage tested in a recent period (incidence).<sup>6</sup>

Evidence about the efficacy of PSA testing from randomized controlled trials has been mixed. The Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial began in 1993 and involved 76,693 US men aged 55-74. After 7 to 10 years of follow up, the death rate from prostate cancer did not differ significantly between the study and control group. As noted by the authors, one possible explanation of the negative result is that PSA testing is already so frequent in the US (see Table 2) that high levels of screening were already present among the control group. Furthermore, many cancers had already been identified in both treatment and control groups (Andriole et al. 2009). Results of the study are most reasonably interpreted as

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<sup>6</sup> Of the two sources of US data presented in Table 2, the BRFSS data are less reliable because they are based on a telephone survey with a low response rate.

addressing the question of whether mortality advantages would pertain to *extending* PSA testing in a population in which half of men are already being tested every two years.

The second trial, the European Randomized Study of Screening for Prostate Cancer, was more than twice as large and was conducted in a region where prostate cancer screening is much less common. The trial began in the early 1990's in 7 European countries and included a total of 162,243 men between the ages of 55 and 69. The study found that offering PSA screening to the treatment group reduced the death rate from prostate cancer by 20% (rate ratio of 0.73, 95% CI, 0.56 to 0.90). The absolute reduction was 0.71 prostate-cancer deaths per 1,000 men. The median and average follow up times were 9 and 8.8 years, respectively; death rates in the two study groups began diverging after 7 to 8 years and continued to diverge subsequently (Schröder et al. 2009).

The Goteborg, Sweden component of the European trial followed 20,000 randomly selected men aged 50–66 for 10 years. Half were invited for biennial PSA testing, with 10,000 men serving as passive controls for whom diagnosis of metastatic prostate cancer was monitored by using the Swedish Cancer Registry. The risk of being diagnosed with *metastatic*, i.e., advanced, prostate cancer was reduced by 48.9% in the PSA treatment group relative to controls ( $p < .01$ ) (Aus et al. 2007).

According to SEER, after the PSA test was introduced in the late 1980s, the recorded incidence of prostate cancer in the US rose from 119/100,000 in 1986 to a peak of 237/100,000 in 1992 (SEER 2008).<sup>7</sup> The proportion of tumors that are metastatic was 25% of newly-diagnosed tumors in 1980 and only 4% in 2002 (Etzioni et al. 2008). Consistent with more extensive screening, the United States identifies prostate cancer at an earlier stage, on average, than Sweden (Stattin et al. 2005), Japan (Ogawa et al. 2008), or the United Kingdom (Collin et al. 2008). Stage at diagnosis is particularly important in prognosis – if detected at an early stage, prostate cancer can be treated by radical prostatectomy or radiotherapy.

## ***B. Prostate Cancer Treatment***

Once prostate cancer is detected, a variety of treatments can be employed, including radical prostatectomy, radiation by beam (external beam radiotherapy) or implanted seeds (brachytherapy), or hormone therapy. “Watchful waiting” is also an option. Since 1991, radical

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<sup>7</sup> The data are for males and refer to the age-adjusted rates for all ages.

prostatectomy has been the most common treatment for localized prostate cancer in the US. It serves as the initial treatment for over a third of newly-diagnosed patients (Harris and Lohr 2002). Observational studies have described apparent survival advantages from radical prostatectomy and radiation therapy (e.g., Wong et al. 2006; Trock et al. 2008) but not always from hormone therapy alone (Lu-Yao et al. 2008). The questions of possible selection bias that are always present in observational studies add uncertainty to these results.

Uncertainty has been reduced by several recent reports of randomized clinical trials. A key study of Scandinavian men examined survival after diagnosis of prostate cancer. Men were randomly assigned to radical prostatectomy or to watchful waiting (Bill-Axelsson et al. 2005). Some of those assigned to prostatectomy did not have the operation, and some of those assigned to watchful waiting pursued radiation or hormonal therapy. Nevertheless, after a median follow-up period of 8.2 years, the group assigned to prostatectomy had cumulative proportions dead from prostate cancer that were lower by 44%, rates of disease progression that were lower by 67%, and rates of distant metastasis that were lower by 40%. All comparisons were statistically significant (Ibid.).

A randomized trial of variation in radiation dosage reported a highly significant beneficial effect on survival of heavier doses (Pollack et al. 2002). Another randomized trial of adjuvant radiotherapy enrolled 425 men with pathologically advanced prostate cancer who had undergone radical prostatectomy between 1988 and 1997. Adjuvant radiotherapy significantly reduced the risk of PSA relapse and disease recurrence, although improvements in survival were not statistically significant (Thompson et al. 2006).

Several randomized clinical trials evaluate the use of hormone therapy as an adjunct to surgery or radiation in high risk patients; the value of hormone therapy used alone or as primary therapy has only been assessed by observational studies. A population-based cohort study found that primary androgen deprivation therapy does not improve survival in elderly men compared with conservative management (no surgery, radiation, or hormone therapy) (Lu-Yao et al. 2008). However, three phase III randomized trials have shown that a combination of radiotherapy and androgen suppression improve survival relative to radiotherapy alone (Bolla et al. 2002, Hanks et al. 2003, and Pilepich et al. 2005).

Population-based information about the frequency of various treatments of prostate cancer is much skimpier than information about the use of the PSA test. Among US men aged



65-80 in SEER who were diagnosed with low grade tumors between 1991 and 1999, 25.5% received no treatment within six months of diagnosis, 9.6% received hormone therapy, and the remaining 64.8% received either radiation or prostatectomy (Wong et al. 2006).

Scandinavian countries rarely use radical therapies – radical prostatectomy or radiation – and rely primarily on watchful waiting or hormone therapy for palliation (Fleshner, Rakovitch, and Klotz 2000; Sandblom et al. 2000). For example, the fraction of patients treated with curative intent in Norway was only 3% in 1985-1989 and rose to 6% in 1990-1994. In 1990-1994, radical prostatectomy was used to treat only 3.0 and 3.3% of all patients diagnosed with prostate cancer in Norway and Sweden, respectively (Kvåle et al. 2007). Low levels of surgery and radiation therapy are also reported in Japan (Ogawa et al. 2008).

Differences in treatment approach also exist between the US and the UK, with US approaches generally being more aggressive, particularly in the use of surgery (Collin et al. 2008). A survey of American and Canadian urologists indicated that American urologists tended to have a more aggressive approach to case identification and surgical intervention. They were also more likely to perform radical prostatectomy on patients over the age of 70 (Fleshner, Rakovitch, and Klotz 2000).

### ***C. Prostate Cancer Survival***

The combination of earlier detection and aggressive treatment in the US has produced greatly improved survival chances for men diagnosed with prostate cancer. 5-year relative survival rates in the US increased from 71% to 83% between 1984-86 and 1987-89, whereas European rates improved from 55% to 59% during the same period (Post et al. 1998). According to SEER (2008), the US 5-year relative survival rate had increased to 99.2% for those diagnosed in 2000.

Gatta et al. (2000) compared international survival rates for cancers diagnosed between 1985 and 1989. All of the European countries considered had lower prostate cancer survival rates than the US. European patients had a 4.1 times greater risk of dying in the first year after diagnosis, suggesting that earlier diagnosis plays an important role in these survival differences (Ibid.). The updated study whose results are presented in Table 1 found that 5-year survival rates for prostate cancer in 2000-02 were 99.3% in the US compared to 77.5% in Europe.

#### ***D. Prostate Cancer Mortality***

Population-level data on mortality have one distinct advantage over data on survival rates among those newly diagnosed: they are not subject to lead-time bias. If one country is diagnosing cancer sooner than another but early diagnosis does not alter the clinical course of the disease and delay or prevent death, then that country will enjoy no advantage in mortality as a result of its earlier diagnoses. When early diagnosis improves prognosis, population-level mortality is responsive to the timeliness of diagnosis. It is also responsive to the efficacy of treatments employed regardless of stage at diagnosis. Mortality data has a similar advantage relative to recorded incidence and prevalence data, both of which are subject to lead-time bias.

In order to investigate whether the relatively aggressive use of PSA testing and therapy in the United States has produced an unusually rapid decline in mortality from prostate cancer, we have used World Health Organization data on deaths by cause and population by five-year age groups. We have chosen a group of 15 economically developed OECD countries for purposes of comparison: Australia, Austria, Canada, Finland, France, Germany, Greece, Italy, Japan, the Netherlands, Norway, Spain, Sweden, Switzerland, and United Kingdom.

Figure 3 compares levels of age-standardized death rates per 100,000 (all ages combined) in the United States to the unweighted mean death rate in these 15 comparison countries.<sup>8</sup> With the exception of 1985, the US had higher death rates each year from 1980 to 1995. Beginning in 1996, the US had lower rates and the US advantage grew every year thereafter. By 2003, the US had death rates that were 20.4% lower than the mean of the comparison countries. Mortality rates among men 60-79 were lower in 1997 than in any year since 1950 (Tarone, Chu, and Brawley 2000). Baade, Coory, and Aitken (2004) note that changes in risk factors and in the accuracy of or procedures for recording cause-of-death information are unlikely to be responsible for the observed trends.

Declines in prostate cancer mortality have been attributed to both PSA screening and improvements in treatment (Baade et al. 2004; Potosky, Feuer, and Levin 2001; Bouchardy et al. (2008), Kvåle et al. (2007), Collin et al. (2008).) An individual-level population model that used counterfactuals to simulate US mortality and incidence of advanced-stage prostate cancer concluded that two-thirds of the decline in mortality between 1990 and 1999, and 80% of the

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<sup>8</sup> These rates are taken from the International Agency for Research on Cancer (<http://www-dep.iarc.fr/>), which extracts the World Health Organization mortality data and standardizes the rates to the world population in 1960 (Segi world standard).

decline in distant-stage incidence, was attributable to expanded PSA testing (Etzioni et al. 2008).

To test whether the faster mortality decline in the US was statistically significant, we use a negative binomial regression in a fixed-effects model applied to data for these 16 countries for the period 1982 to 2005. The dependent variable is the log of the number of deaths from prostate cancer in a particular age, country and year cell, with population size in a particular cell used as the exposure. Independent variables are a set of age group identifiers, a set of period identifiers, a dummy variable for the US, and a set of US/period interactions. Six 4-year-wide time periods are used, beginning with 1982-85 and ending with 2002-05. 1982-1985, the period before PSA testing was begun, is chosen as the reference period. Significance tests recognize the clustering of observations by country. Results are presented in Table 4.

The coefficient of the interactive variable for US observations during the period 2002-05 is -0.274, which is significant at  $p < .001$ . Compared to expectations based upon country and year, the US had roughly 27% lower mortality in 2002-05 than it did in 1982-85. (The US/2002-2005 variable is always significant at  $p < 0.001$  regardless of reference period used). Likewise, the coefficient of the US/period interactive variable for the 1998-2001 period is -0.215 and is also significant at  $p < .001$ . So the US had significantly faster declines in mortality than did comparison countries between 1982-85 and both 1998-2001 and 2002-05.

Mortality trends from prostate cancer may be affected by “attribution bias”: people who have had prostate cancer detected may be more likely to have their death ascribed to it even though some other morbid process were actually responsible (Feuer et al. 1999). Such bias, combined with more aggressive screening, would produce a rise rather than a fall in prostate cancer mortality. This bias may account for the rise in prostate cancer mortality in the late 80s and early 90s (Figure 3), but it obviously would minimize rather than accentuate the actual decline that is observed between 1982-85 and 2002-05.

African Americans have prostate cancer death rates that are among the highest in the world (Crawford 2003). Perhaps the most prominent explanation of the racial disparity is that dark skin inhibits the absorption of Vitamin D, which is highly protective against prostate cancer (Li et al. 2007). A more tenuous connection to the health care system among African Americans is probably also a factor. Nevertheless, a sharp decline in prostate cancer mortality in the US is evident among both whites and African Americans. Both whites and blacks had rates that peaked in the early 1990s. Between 1992/3 and 2004/5, the death rate declined by 32.2% for African

Americans and by 36.3% for whites (Ibid.). The absolute decline in rates was much larger for African Americans. The 5-year survival rate for blacks increased from 68.4% for those diagnosed in 1986, the year when PSA testing was approved, to 97.0% for those diagnosed in 2000. Among whites, the improvement was from 79.0% to 99.8% (SEER 2008).

### ***Case Study II. Breast Cancer***

Breast cancer is the most common cause of cancer death among women in a majority of high income countries (Vainio and Bianchini 2002). In contrast to prostate cancer, there are important behavioral risk factors for breast cancer. These include childlessness or low parity, late age at first birth, obesity, and use of hormone replacement therapy (Das et al. 2005; Levi et al. 2005). Thus, trends in mortality are more difficult to interpret as exclusively reflecting medical factors. But, like prostate cancer, breast cancer is highly amenable to medical intervention through screening and therapy.

#### ***A. Breast Cancer Screening***

Mammography, breast self-examination, clinical breast examination (CBE), and magnetic resonance imaging (MRI) are used to screen for breast cancer. No randomized trials of CBE alone have been completed, and case-control and ecological studies have provided only limited evidence for its efficacy in reducing mortality from breast cancer (Vainio and Bianchini 2002). Breast self-examination is an appealing screening method because it is noninvasive, but it has weak ability to detect breast cancer (Elmore et al. 2005). Two randomized trials of breast self-examination have been conducted, and neither found evidence of mortality reduction. The International Agency for Research on Cancer (IARC) has concluded that there is inadequate evidence for the efficacy of CBE and breast self-examination in reducing breast cancer mortality (Vainio and Bianchini 2002). The US Preventive Services Task Force also found evidence from trials involving CBE and breast self-examination to be inconclusive (Humphrey et al. 2002). The third technique, MRI, is mainly employed in high risk patients and after conventional diagnostic procedures have already been conducted (Veronesi et al. 2005). Because of its high cost (approximately 10 times that of mammography) and its relatively low specificity, MRI is not a feasible tool for routine screening in the general population (Elmore et al. 2005).

Thus, mammography is currently the most important diagnostic tool for breast cancer. It

is the only screening test that has been shown to reduce mortality from breast cancer in randomized trials and population studies (Veronesi et al. 2005; Wells 1998). The International Agency for Research on Cancer (IARC) concluded that there is sufficient evidence from randomized trials that offering of mammography to a treatment group reduces breast cancer mortality in women aged 50-69, by an average of 25%. After adjusting for the effect of non-acceptance of the screening invitation, this figure rises to 35% (Vainio and Bianchini 2002). The US Preventive Services Task Force reviewed eight randomized controlled trials of offering mammograms to treatment groups and concluded that, for studies of that were designated as of fair quality or better, the relative mortality risk for women aged 40-74 was 0.84 (95% CI, 0.77 to 0.91) (Humphrey et al. 2002; see also Gøtzsche and Nielsen 2009). While some concerns have been raised concerning flaws in the trials' design and execution, in-depth independent reviews have concluded that they do not negate the trials' results (Quinn 2003).

The National Cancer Institute and the American Cancer Society (ACS) issued the first formal guidelines for mammography in 1977, advocating screening for all women over the age of 50 (Wells 1998). Currently, all major US medical organizations recommend screening mammography for women over the age of 40 (Elmore et al. 2005; Ahern and Shen 2009). The US is the only country that strongly endorses screening mammography for women under age 50 (Jatoi and Miller 2003); recent evidence has supported the efficacy of screening in the age group 40-49 (Humphrey et al. 2002).

Use of mammographic screening in the United States increased very rapidly; the percentage of women aged 50-64 who reported having a mammogram in the past 2 years increased from 31.7% in 1987 to 73.7% in 1998 (Breen et al. 2001). Screening programs generally began later in Europe than in the US (Møller et al. 2005). The start dates for organized screening programs in the countries under investigation range from 1986 to 1999 (Shapiro et al. 1998; Jatoi and Miller 2003).

Table 3 presents international data on the frequency of screening for breast cancer in recent years. In the early-to-mid 90s, the United States had the highest frequency of mammograms in the nine countries for which we are able to locate data. The OECD has collected more recent data which shows that, while the frequency of mammograms has increased in the US, it has grown faster in a number of other countries. Of the 19 countries shown in Table 2, the United States ranks 6<sup>th</sup> in the proportion of women in or around the age interval 50-69 who

had received mammograms in the previous two years.

Consistent with the relatively high frequency of mammograms in the US, Sant et al. (2004) found that breast cancer is diagnosed at what is, on average, a later stage in Europe than in the US.

### ***B. Breast Cancer Treatment***

In OECD countries, the large majority of cases of breast cancer are treated surgically. Surgery is often supplemented with some combination of radiotherapy, hormone therapy, and chemotherapy (i.e., adjuvant therapy). Descriptions of the Halsted mastectomy, which served as the treatment of choice for breast cancer for almost a century, were first published in 1894 (Veronesi et al. 2002). It was later replaced by the modified radical mastectomy, which was popular in the 1980s (Cotlar et al. 2003). Neither the original Halsted radical mastectomy nor the modified radical mastectomy were introduced on the basis of evidence from randomized clinical trials; however, observational studies confirm an enormous survival advantage for surgery relative to no surgery (e.g., Sant et al. 2004).

In most high income countries, breast conserving surgery (BCS, also known as lumpectomy) is currently the most common primary treatment for breast cancer (Veronesi et al. 2005). Relative to total mastectomy, its advantages are reduced disfigurement and morbidity rather than mortality (Wood 1994). After 20 years of follow-up in a randomized trial, Fisher et al. (2002) report finding no differences in disease-free survival, distant-disease-free survival, or overall survival between women who underwent lumpectomy alone compared to those having a total mastectomy (see also Veronesi et al. 2002). In 1990, the National Institutes of Health Consensus Development Conference recommended breast conservation therapy for the majority of women with Stage I or II breast carcinoma.

Radiation treatment of breast cancer was first used in 1896, but equipment and techniques have improved substantially, particularly since the 1960s (Ragaz et al. 1997). The Early Breast Cancer Trialists' Collaborative Group conducted a meta-analysis of 36 trials of radiotherapy. They found that the local recurrence rate with radiotherapy and surgery was three times lower than with surgery alone, and that radiotherapy was associated with 6% reduction in the relative risk of death due to breast cancer (odds ratio, 0.94) (Early Breast Cancer Trialists' Collaborative Group 1995). Ragaz et al. (1997) found that, after 15 years of follow-up, women assigned to

chemotherapy plus radiotherapy had a 33% reduction in the recurrence rate and a 29% reduction in mortality from breast cancer compared to women treated with chemotherapy alone.

Adjuvant systemic multi-agent chemotherapy and tamoxifen have been estimated to reduce mortality (in terms of the relative reduction of the annual odds of death) by 27% and 47%, respectively (Early Breast Cancer Trialists' Collaborative Group 1998a, 1998b). These figures are derived from the meta-analyses of all randomized trials of any aspect of treatment for early breast cancer that began before 1990. There were 47 trials of adjuvant polychemotherapy involving 18,000 women (Early Breast Cancer Trialists' Collaborative Group 1998a). Greater benefits were reported in women under the age of 50, who experienced with significant reductions in recurrence and mortality of 35% and 27%. For women between 50 and 69, these figures were 20% and 11% (Ibid.).

Cole et al. first reported the clinical efficacy of tamoxifen for disseminated breast cancer in 1971. The Early Breast Cancer Trialists' Collaborative Group summarized the results of 55 randomized controlled trials involving more than 37,000 women. Compared to a placebo, adjuvant tamoxifen resulted in annual reductions of 26% in recurrence and 14% in death. Among women treated for five years, these figures rose to 50% and 28%, respectively (Early Breast Cancer Trialists' Collaborative Group 1998b; Osborne 1998) Tamoxifen produces significant benefits in women of all age groups (Jaiyesimi et al. 1995; Early Breast Cancer Trialists' Collaborative Group 1998b). Following pharmacologic and clinical evaluations, the US Food and Drug Administration approved tamoxifen for the treatment of metastatic breast cancer in postmenopausal women in 1977. Tamoxifen was also approved as the initial endocrine therapy for disseminated breast cancer in premenopausal women.

Information on international differences in breast cancer treatment is limited. A comparison of the Eurocare and SEER registry data found that 97% of women in SEER were treated surgically compared to 90% in the Eurocare registries. Lymphadenectomy rates were slightly more extensive in the US, and more axillary lymph nodes were examined in the US (Sant et al. 2004). Hughes (2003) compared patterns of breast cancer care in Belgium, Canada (Manitoba and Ontario), France, Italy, Norway, Sweden, United Kingdom (England), and the United States. During the latest period investigated, 1990-93, at least 90% of women diagnosed with breast cancer received a mastectomy or breast-conserving surgery in all areas except Ontario, where the figure was 82%, and England (71%). The use of radiotherapy with BCS has

also risen over time and varied considerably among countries. Among women receiving BCS in 1995-97, Belgium, France, Canada and the UK had the highest proportions of women receiving radiation therapy. The US ranked below these countries and above Sweden and Italy (Ibid.)

Adjuvant chemotherapy became standard treatment for breast cancer patients in the US in the late 1970s (Ragaz et al. 1997). Tamoxifen began to be widely used in the late 1970s and early 1980s after the Nolvadex Adjuvant Trial Organization trials demonstrated its effectiveness (Mariotto et al. 2002). It has since become the most widely prescribed antineoplastic agent for treatment of breast cancer in the United States and Great Britain (Jaiyesimi et al. 1995). Between 1975 and 2000, the percentage of breast cancer patients receiving chemotherapy in the US increased from essentially 0 to 80%, while tamoxifen use increased from 0 to 50% (Berry et al. 2006). Starting in the mid-1980s, tamoxifen use in the UK also increased rapidly. By 1990, 50% of women with breast cancer over the age of 50 in the Thames region were receiving tamoxifen (Blanks et al. 2000). Unfortunately, we have not found comparable international data on the use of chemotherapy and tamoxifen. Variations in stage and type of tumor, age of patient, type of surgery, and other factors make it impossible to reliably compare the few national or regional data that exist.

### ***C. Breast Cancer Survival***

Several studies have compared international survival rates from breast cancer. As noted above, the survival advantage of US breast cancer patients compared to their European counterparts is well documented. The US survival advantage is particularly sharp among older women (Hughes 2003). International differences in survival are challenging to interpret, but three studies using cancer registry data for European and American women cancer survival have attributed the survival differences from breast cancer to earlier diagnosis and more aggressive care in the US. These factors have also been introduced to explain better breast cancer survival rates in the US than in Canada (Ugnat et al. 2005).

Gatta et al. (2002) found that European breast cancer patients diagnosed 1985-89 had significantly lower five-year relative survival rates than American patients (73% vs. 82%). None of the 17 European countries had higher five-year relative survival than the US. In the first year after diagnosis, the risk of death from breast cancer was much higher in European than American patients. Survival rates fell with increasing age at diagnosis in both the US and Europe, but the



fall was more marked in Europe. Gatta et al. suggest that the survival rate differences may be attributable to earlier diagnosis in the US.

The most thorough study compared American and European women diagnosed with breast cancer between 1990 and 1992 (Sant et al. 2004). The five-year survival rate was higher in the US than in Europe (89% vs. 79%), and survival for each stage-at-diagnosis category was also higher in the US. Early-stage tumors were more frequent in the US (41% of cases) than in Europe (29%). Treatment was more aggressive in the US, where 97.1% of women underwent surgery compared to 90.2% in Europe. In the US, 50.7% of women had 15+ lymph nodes evaluated for metastasis, compared to 27.8% in Europe. The overall relative risk of death was 37% higher among European women (95% confidence interval 25-50%). The excess risk was reduced to 20% by adjustment for surgical intervention, which was associated with a 90% reduction in mortality. Adjustment for stage at diagnosis reduced the relative risk to 12% and further adjustment for the number of lymph nodes evaluated to determine cancer progression reduced the excess risk of death among the European women to an insignificant 7%. Introducing information on the use of radiotherapy did not alter the relative risk of European women. Thus, the higher survival rate in the US appears to be a result both of earlier diagnosis and more aggressive treatment.

The most recent study compared cancer survival differences between Europe and the US in 2000-2002 based on period rather than cohort survival data. As shown in Table 1, the five-year survival rate for breast cancer was 79.0% in Europe, compared with 90.1% in the US. Verdecchia et al. (2007) hypothesize that these differences were most likely due to differences in timeliness of diagnosis.

Trends in screening and in survival in the US are consistent with the idea that earlier screening improves survival. The increase in the percentage of American women aged 50-64 with a mammogram in the previous two years from 32% in 1987 to 74% in 1998 was accompanied by an increase in five-year survival rates from 79% for those diagnosed in 1985 to 91% for those diagnosed in 2000 (SEER 2008).

#### ***D. Breast Cancer Mortality***

In many developed countries, breast cancer mortality rates began declining around 1990 (Veronesi et al. 2005; Botha et al. 2003). It is unlikely that the declines in mortality were caused

by changes in the major risk factors for the disease. In fact, the risk factor profile of women in high income countries has, if anything, become less favorable over the past few decades as a result of rising obesity and delayed and reduced childbearing (Levi et al. 2005). Reductions after 2002 in the use of hormone replacement therapy could work in the opposite direction but the risk is sufficiently small (Writing Group for the Women's Health Initiative Investigators 2002; Chlebowski et al 2003), and lags sufficiently long, that the decline should not be reflected in a data series that ends in 2005. Chu et al. (1996) rule out changes in coding or ascertainment as contributors to the mortality decline in the US, noting that there had been no coding changes affecting breast cancer and that no systematic problems with ascertainment were identified after 1989.

Studies of trends in breast cancer mortality have attributed the declines mainly to earlier detection – in particular, rising rates of mammographic screening – and improved treatment (Veronesi et al. 2005; Levi et al. 2005; Chu et al. 1996). A careful, detailed simulation for the US by Berry et al. (2006) concluded that “We can say with high probability that both screening and adjuvant therapy have contributed to the reductions in U.S. breast cancer mortality observed from 1975 (and especially from 1990) to 2000. Our best estimate is that about two-thirds of the reduction is due to therapy and one-third to screening” (Berry et al. 2006:36). Using less precise methods, Blanks et al. (2000) reached a similar conclusion about the decline in breast cancer mortality in England and Wales from 1990 to 1998. Evidence that states with greater use of mammography had greater mortality declines between 1992 and 1999 supports the link between screening and mortality (Das et al. 2005).

We hypothesize that the US has had a faster decline in breast cancer mortality than the comparison countries because it took better advantage of technological advances in screening and treatment. Mortality data alone do not permit us to distinguish between the effects of screening and treatment, but that distinction is not central to judging the effectiveness of a health care system.

Figure 4 shows the annual age-standardized death rate in the United States and the average for our 15 OECD countries since 1980. Clearly, the US has had a faster decline in breast cancer mortality than average among the comparison countries. Is the faster decline in the US statistically significant? To answer this question, we repeat the approach used for prostate cancer, using WHO data files on deaths by cause and population by five-year age groups. We

employ negative binomial regression on data at ages 50+ (in five-year wide age groups until 85+). The dependent variable is the log of the number of deaths from breast cancer in a certain age group for a particular country and time period. Independent variables are a set of age group identifiers, a set of period identifiers, a dummy variable for the US, and a set of US/period interactions. We designate six 4-year-wide time periods, beginning with 1982-85 and ending with 2002-05, and choose 1982-85 as the reference period. Because of the rapid increase in the proportion of women receiving mammograms from less than a third in 1987 to 74% in 1998, a reference period in the early 1980s appears appropriate. Significance tests recognize the clustering of observations by country. Results are presented in Table 4.

Using 1982-85 as the reference period, we find that the US/2002-05 interaction term is significant at .01. With a coefficient of -.126, the coefficient implies that mortality in the US has fallen 13% faster since 1982-85 than in other countries. US interactive coefficients for 1994-97 and 1998-2001 are also negative and significant at 5%. The interactive variable, US/2002-2005, is always significant at  $p < 0.01$  regardless of which date is selected as reference period (not shown). Thus, the US has experienced a significantly faster decline in breast cancer mortality than comparison countries.

### *Summary*

We have demonstrated that mortality reductions from prostate cancer and breast cancer have been exceptionally rapid in the United States relative to a set of peer countries. We have argued that these unusually rapid declines are attributable to wider screening and more aggressive treatment of these diseases in the US. It appears that the US medical care system has worked effectively to reduce mortality from these important causes of death.

This conclusion is consistent with other evidence that we have reviewed on the performance of the US health care system: screening for other cancers also appears unusually extensive; 5-year survival rates from all of the major cancers are very favorable; survival rates following heart attack and stroke are also favorable (although one-year survival rates following stroke are not above average); the proportion of people with elevated blood pressure or cholesterol levels who are receiving medication is well above European standards.

These performance indicators pertain primarily to what happens after a disease has developed. It is possible that the US health care system performs poorly in preventing disease in

the first place. Unfortunately, there are no satisfactory international comparisons of disease incidence. Individuals report a higher prevalence of cancer and cardiovascular disease in the United States than in Europe, and biomarkers confirm the higher prevalence of many disease syndromes in the US compared to England and Wales. Higher disease prevalence is *prima facie* evidence of higher disease incidence, although it could also be produced by better identification (e.g., through screening programs) or better survival. The history of exceptionally heavy smoking in the US, and the more recent massive increase in obesity, suggest that a high disease incidence in the US could not be laid entirely at the feet of the health care system.

Evidence that the major diseases are effectively diagnosed and treated in the US does not mean that there may not be great inefficiencies in the US health care system. A list of prominent charges include fragmentation, duplication, inaccessibility of records, the practice of defensive medicine, misalignment of physician and patient incentives, limitations of access for a large fraction of the population, and excessively fast adoption of unproven technologies (Garber and Skinner, 2008; Cebul et al. 2008; Commonwealth Fund 2008). Some of these inefficiencies have been identified by comparing performance across regions of the United States. Of course, the fact that certain regions do poorly relative to others does not imply that the US does poorly relative to other countries. And many of the documented inefficiencies of the US health care system add to its costs rather than harm patients.

Just as we are not addressing issues of efficiency on the production side, we are not treating patient welfare as the main outcome. Practices that produce greater longevity do not necessarily enhance well-being. This potential disparity is central to the controversy involving PSA testing, which uncovers many cancers that would never kill patients but whose treatment often produces adverse side effects.

The question that we have posed is much simpler: does a poor performance by the US health care system account for the low international ranking of longevity in the US? Our answer is, “no”.

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Table 1. Five-Year Relative Survival Rates for Cancer of Different Sites, US and European Cancer Registries\*

<u>Site</u>	<u>5-year survival rate (%)</u>	
	United States	Europe
Prostate	99.3	77.5
Skin melanoma	92.3	86.1
Breast	90.1	79.0
Corpus uteri	82.3	78.0
Colorectum	65.5	56.2
Non-Hodgkin lymphoma	62.0	54.6
Stomach	25.0	24.9
Lung	15.7	10.9
All malignancies (men)	66.3	47.3
All malignancies (women)	62.9	55.8

\*Based on period survival data for 2000-02

Source: Verdecchia et al. (2007).

Table 2. Indicators of Frequency of PSA Testing Among Males

A. Percent of Men Ever Receiving a PSA Test

Country	Percentage of Men Ever Receiving a PSA Test	Year	Age Group	Source
Australia	49%	2003	40+	1
Austria	54.6%	2006-2007	40+	2
Canada	47.5% <sup>6</sup>	2000-2001	50+	3
France	36%	2005	40-74	4
Italy	31.4%	2003	50+	5
Netherlands (Rotterdam)	12.7% <sup>6</sup>	1994	55-74	6
Switzerland (Vaud and Neuchâtel Cantons)	10%	“Early 1990s”	65+	7
United States	75% (BRFSS)	2001	50+	8
	62.7% (NHIS) <sup>1</sup>	2005	50-79	9

B. Percent of Men Recently Receiving a PSA Test

Country	Percentage of Men Receiving a PSA Test in the Past x Years	x	Year	Age Group	Source
Australia	27%	2	1995/1996	50+	10
Austria	31.1%	1	2006-2007	40+	2
Belgium (Limburg Province)	23%	1	1996-1998	40+	11
Canada	26%	1	2000-2001	40+	12
Italy	15.9%	1	2002	50+	5
Netherlands (Rotterdam)	20.2%	3	1997-2000	55-74	13
Norway (3 counties)	7%	1	1999	50-65	14
Spain (Getafe City)	20.9%	2	1997-1999	55+	15
Sweden	25.3% <sup>2</sup>	1	2002	50+	16
United Kingdom	7%	1	1999-2001	45-84	17
United States	57% (BRFSS)	1	2001	50+	8
	48.4% (NHIS) <sup>1</sup>	2	2005	50-79	9

<sup>1</sup> This figure does not include men with a history of prostate cancer.

<sup>2</sup> According to Sennfalt, Carlsson, and Varenhorst (2006), 430,000 PSA tests were performed in Sweden in 2002. We assume that all were performed on men aged 50+. The UN Population Division’s estimates for Sweden’s male

population (aged 50+) for 2000 and 2005 were retrieved from the UN Statistics Division's Common Database and interpolated to give a figure for 2002 of 1,699,442.

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Table 3. Percentage of Women Receiving a Mammogram in Previous Two Years: 1994 and 2003<sup>1</sup>

Country	Earlier Year				Later Year			
	% Screened	Year	Age Group	Source	% Screened	Year	Age Group	Source
Australia	51.4	1996-7	50-69	1	55.6	2003-2004	50-69	10
Austria	23.1 35.7	1995	40-79 50-54	2				
Belgium	49.2	1997	50-69	3	54.0	2003	50-69	10
Canada	50	1994	50+	4	70.6	2003	50-69	10
Finland					87.7	2003	50-59	10
France					72.8	2003	50-69	10
Hungary					60.2	2003	45-65	10
Iceland					62.0	2003	40-69	10
Ireland					79.5	2003	50-64	10
Italy					29.0	2000	55-69	11
Japan					2.6	2003	50-69	10
Luxembourg					62.4	2003	50-69	10
Netherlands	53.2	1994	50-69	5	79.0	2003	50-75	11
New Zealand					62.3	2003	50-64	10
Norway					98.0	2003	50-69	10
Portugal					60.1	2003	50-69	10
Spain	28	1994	40-70	6				
Sweden					83.6	2004	50-74	10
Switzerland <sup>2</sup>	20	1992-3	50-64	7	27.0	2002	50-69	11
United Kingdom <sup>3</sup>	63.9	1995	50-64	8	74.7	2003	50-64	10
United States	66.5	1994	50-64	9	76.0	2003	50-69	10

<sup>1</sup> For later years, when there are two observations for the same country we use survey rather than program data in order to maximize comparability with the US (this affected only Canada and the Netherlands).

<sup>2</sup> For 1992-93, the data for Switzerland is for the canton of Vaud only, and the screening interval is 1 year.

<sup>3</sup> For the UK, the recall period is 3 years.

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Table 4. Coefficients of Negative Binomial Regression Predicting the Log of the Number of Deaths from Prostate and Breast Cancer

<u>Variable</u>	<u>Coefficient</u> (standard error)	
	<i>Prostate Cancer</i>	<i>Breast Cancer</i>
Constant	-10.37*** (0.079)	-7.657*** (0.067)
Age		
50-54	0.000 (-)	0.000 (-)
55-59	1.166*** (0.026)	0.247*** (0.013)
60-64	2.159*** (0.026)	0.413*** (0.019)
65-69	3.013*** (0.032)	0.550*** (0.024)
70-74	3.744*** (0.034)	0.721*** (0.029)
75-79	4.384*** (0.038)	0.925*** (0.032)
80-84	4.942*** (0.041)	1.157*** (0.038)
85+	5.455*** (0.047)	1.520*** (0.046)
Period		
1982-1985	0.000 (-)	0.000 (-)
1986-1989	0.0586*** (0.010)	0.0350*** (0.011)
1990-1993	0.103*** (0.016)	0.0276 (0.015)
1994-1997	0.0837*** (0.023)	-0.00241 (0.028)
1998-2001	0.0242 (0.029)	-0.0741* (0.037)
2002-2005	-0.0529 (0.036)	-0.114** (0.042)
Observation from US	0.125 (0.080)	0.108 (0.082)

Observation from US in

1982-1985	0.000 (-)	0.000 (-)
1986-1989	-0.0229* (0.010)	-0.0216* (0.011)
1990-1993	-0.00278 (0.015)	-0.0225 (0.015)
1994-1997	-0.0850*** (0.023)	-0.0585* (0.028)
1998-2001	-0.215*** (0.029)	-0.0892* (0.036)
2002-2005	-0.274*** (0.036)	-0.126** (0.040)

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\*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$

Figure 1. Age Standardized Death Rates at Ages 50+ From Influenza, 2000-2004

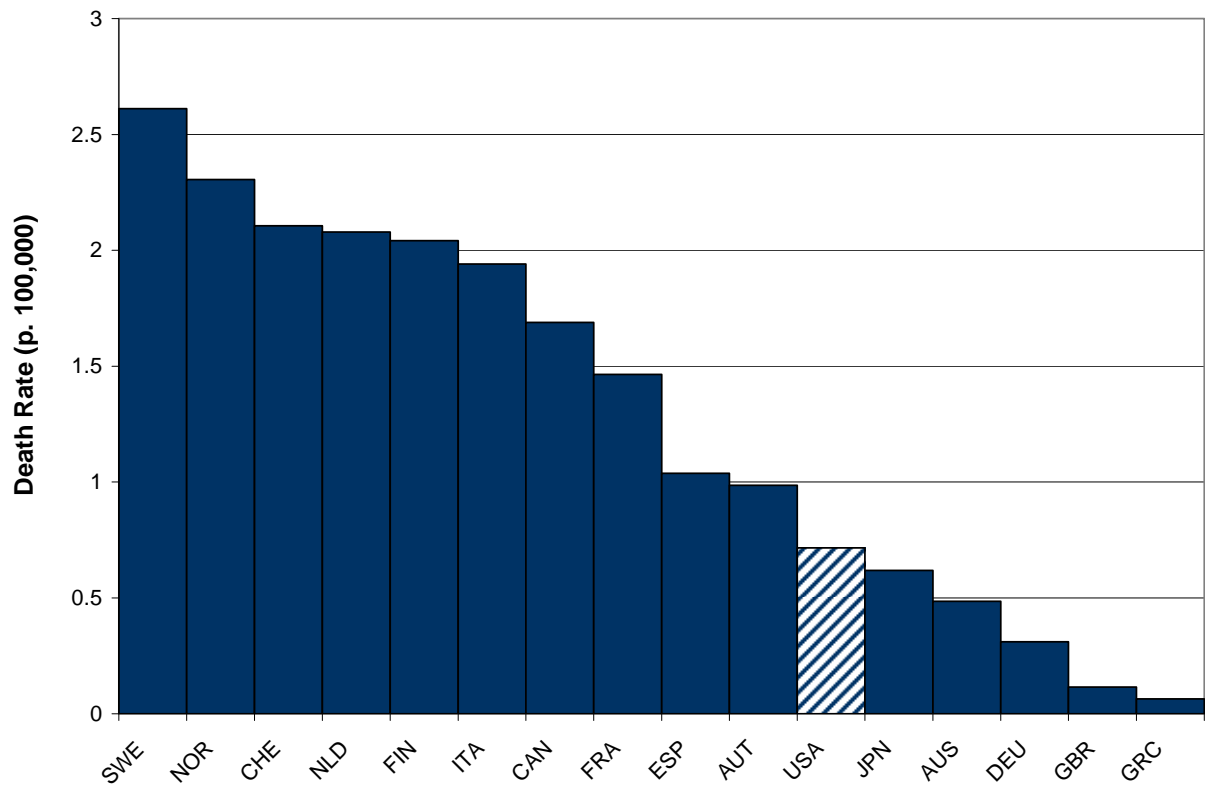


Figure 2. Age Standardized Death Rates at Ages 50+ From Pneumonia, 2000-2004

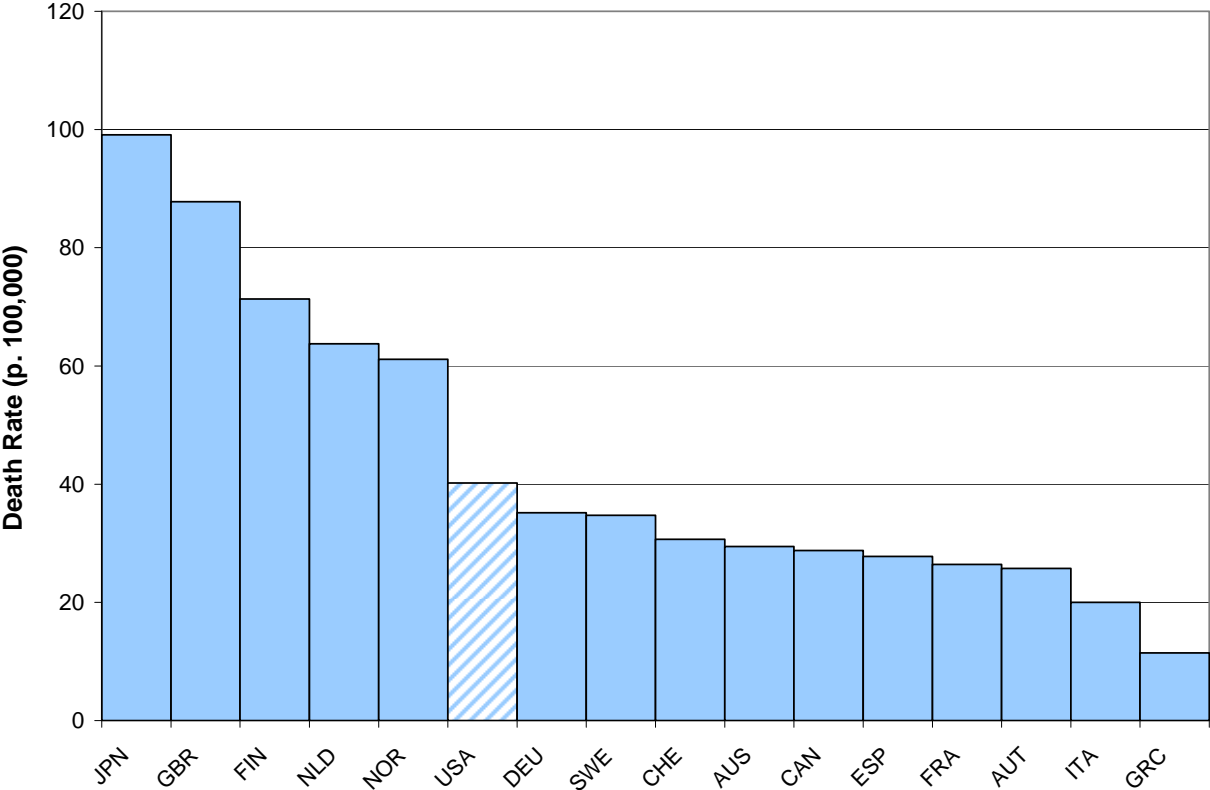


Figure 3. Age-Standardized Death Rates From Prostate Cancer, 1980-2005

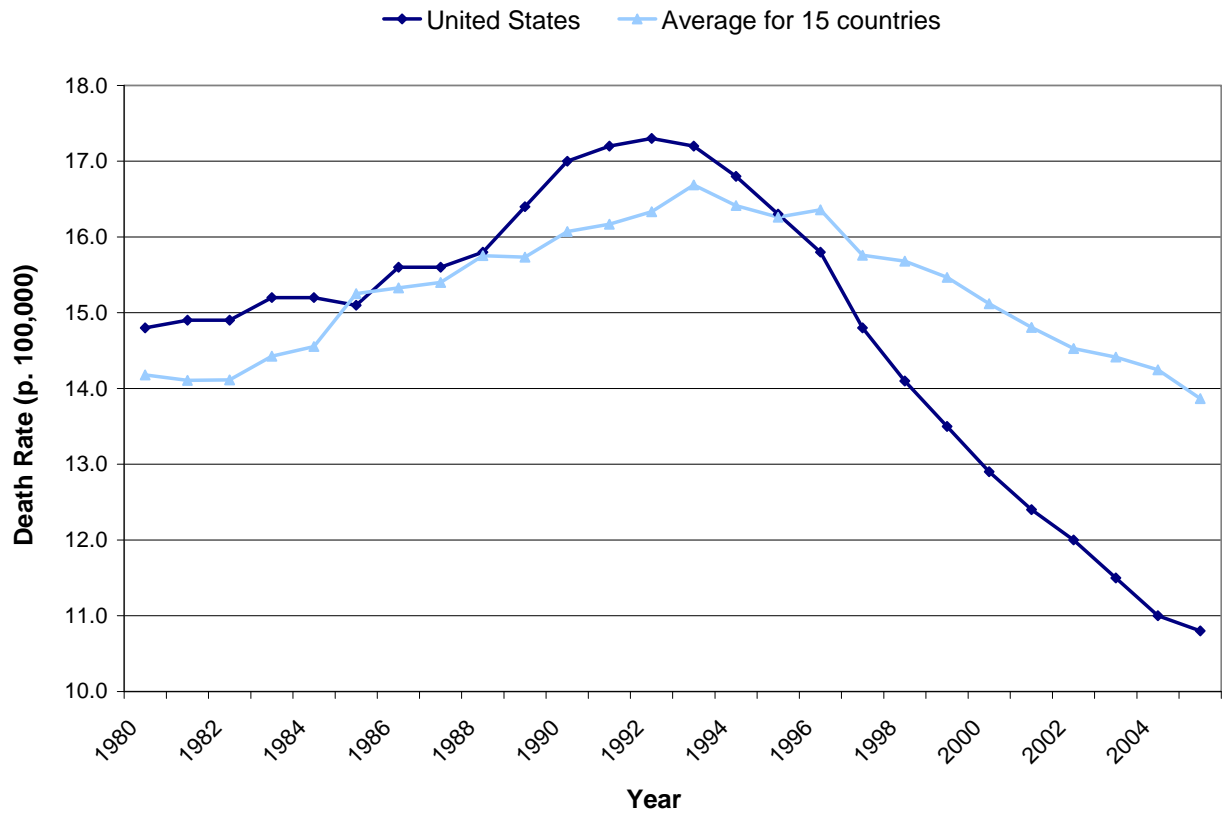


Figure 4. Age-Standardized Death Rates From Breast Cancer, 1980-2005

