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BIOTECHNOLOGY AND THE BURDEN OF AGE-RELATED DISEASES

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Working Paper 2001-2
http://www.cpe.uchicago.edu/publication/publication.html

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November 2001

Prepared for a presentation at the RAND Summer Institute (RSI), Demography, Economics, and Epidemiology of Aging Conference, Santa Monica, California, July 14, 2001. I would like to thank the Charles R. Walgreen Foundation and the National Bureau of Economic Research. I gratefully acknowledge financial support from the National Institutes of Health grant (NIA PO1 AG10120-09) and the National Science Foundation grant (SBR 9114981). The views expressed herein are those of the author and not necessarily those of the Center for Population Economics.

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ABSTRACT

A number of studies have attempted to explain the remarkable decline in mortality rates since 1700, and the concurrent improvements in health and increase in life expectancy at birth, especially over the past century. I argue that their findings suggest a new theory of evolution called *technophysio evolution.* Technophysio evolution is the result of a synergism between technological and physiological improvements that has produced a form of human evolution that is biological but not genetic, rapid, culturally transmitted, and not necessarily stable. The most important aspect of technophysio evolution is the continuing conquest of chronic malnutrition due mainly to a severe deficiency in dietary energy. With the improvement in nutrition and physiology came significant economic growth and technological progress; in fact, technophysio evolution appears to account for about half of the economic growth in Europe over the past two centuries. As technophysio evolution has led to longer life and better health, prevalence rates of chronic conditions have declined, and I next turn to an analysis of why, despite lower prevalence rates, the costs of treating chronic conditions have increased. In the final section, I consider the likely trend in the demand for health care services in the future.

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I. Introduction

During the past two decades there have been a number of major advances in constructing time series on the decline in mortality in Western Europe, Japan, and the United States. The data for these time series were obtained from a variety of archives. Both the retrieval and the processing of the data were made possible by the remarkable advances in computer technology, which not only permitted the creation of the time series but enabled linkage to a variety of variables aimed at explaining the improvement in health and longevity over the past three centuries. In my presentation today I focus first on England and France, for which the longest time series exist, but will make use of data from several other countries including Sweden, Norway, the Netherlands, the United States, and Japan.

Figure 1 shows time series for the decline in mortality rates going back to the 1540s in England and to the 1740s in France. These diagrams present the annual crude mortality rates for each country as a scatter of points. The heavy dark line in the center of each scatter shows the underlying trend in the mortality rate.

Figure 1 shows that in both England and France crude mortality rates were much higher in the eighteenth century than they are today: on the order of three to four times higher. A second feature is the much greater volatility of mortality rates in the past than today, with annual death rates sometimes exceeding the secular trend by as much as 50 to 100 percent. It was these mortality crises that initially caught the attention of demographers who were focused on the data of particular localities. They argued that mortality crises accounted for a large part of total mortality during the seventeenth and eighteenth centuries, and that the decline in mortality rates after about 1750 was due largely to the elimination of these crises. The elimination of crisis mortality was, in turn,

attributed to the elimination of periodic famines. However, when the nationwide time series shown in **Figure 1** were partitioned, it turned out that in both the French and the British cases the elimination of crisis mortality, whether related to famines or not, accounted for only a small fraction of the secular decline in mortality rates. About 90 percent of the drop was due to the reduction in the "normal" levels of mortality.

Still another feature of **Figure 1** is the repeated interruption of downward trends in mortality and their reversal. Substantial interruptions and reversals in the downward trend have also been demonstrated during the nineteenth century for the United States, Sweden, and Hungary. Such interruptions and reversals lasted several decades, and prevented even the keenest contemporary observers from appreciating that the growing control of the environment had the capacity to transform human physiology. It was not until World War I that biodemographers and epidemiologists recognized that they were in the midst of a long-term reduction in mortality rates that had not yet run its course.

Just how remarkable the change has been during the past three centuries is summarized by three key figures on life expectancy at birth. In France and England at the beginning of the eighteenth century, and in a few other OECD nations for which some measurement is possible, life expectancy at birth was about 30 years. Today it is in the neighborhood of 76 to 80 years for the high-income nations of OECD. The lowest long-term life expectancy rate at which *Homo sapiens* can survive is about 20 years. Hence over the 200,000-year history of the species, life expectancy at birth has so far increased by about 60 years, and five-sixths of this increase has occurred since 1700. Half of the increase occurred during the past 100 years.

Attempts to explain the remarkable decline in mortality rates since 1700, and the concurrent improvement in health, especially over the past century, have produced significant advances in knowledge. Although many of the new findings are still tentative, they suggest a new theory of evolution that Dora Costa (an economist and biodemographer at MIT) and I call "technophysio evolution."

Technophysio evolution is the result of a synergism between technological and physiological improvements that has produced a form of human evolution that is biological but not genetic, rapid, culturally transmitted, and not necessarily stable. This process is still ongoing in both rich and developing countries. Unlike the genetic theory of evolution through natural selection, which applies to the whole history of life on earth, technophysio evolution applies only to the last 300 years of human history, and particularly to the last century.

Human beings have gained an unprecedented degree of control over their environment—a degree of control so great that it sets them apart not only from all other species, but also from all previous generations of *Homo sapiens.* This new degree of control has enabled *Homo sapiens* to increase its average body size by over 50 percent, to increase its average longevity by more than 100 percent, and to improve greatly the robustness and capacity of vital organ systems.

Figure 2 shows how dramatic the change in the control of the environment after 1700 has been. During its first 200,000 years or so, *Homo sapiens* increased at a exceedingly slow rate. The discovery of agriculture about 11,000 years ago broke the tight constraint on the food supply imposed by a hunting and gathering technology, making it possible to release between 10 and 20 percent of the labor force from the direct

production of food, and also giving rise to the first cities. The new technology of food production was so superior to the old one that it was possible to support a much higher rate of population increase than had been the case prior to c. 9000 B.C. Yet the advances in the technology of food production after the *second* Agricultural Revolution (which began about 1700 A.D.) were far more dramatic than the earlier breakthrough, since they permitted population to increase at so high a rate that the line of population appears to explode, rising almost vertically. The new technological breakthroughs in manufacturing, transportation, trade, communications, energy production, leisure-time services, and medical services were in many respects even more striking than those in agriculture. The twentieth century witnessed a huge acceleration in both population and technological change. The increase in world population between 1900 and 1990 was four times as great as the increase during the whole previous history of humankind. Not only has technological change accelerated dramatically since 1700 but the diffusion of modern technology has also accelerated greatly over the past two centuries.

The most important aspect of technophysio evolution is the continuing conquest of chronic malnutrition due mainly to a severe deficiency in dietary energy, which was virtually universal three centuries ago. In rich countries today some 1800 to 2000 kcal of energy are available daily for work by a typical adult male, aged 20-39. During the eighteenth century, however, France produced less than one-third the current amount of energy for work. And England was not much better off. One implication of these estimates of caloric availability is that mature European adults of the eighteenth and much of the nineteenth century must have been very small and less active by current standards.

Recent studies have established the predictive power of height and weight at early ages with respect to onset of diseases and premature mortality at middle and late ages. Figures 3 and 4 summarize data showing the connection of height and weight to the risk of dying in American and Norwegian cohorts of males. The American cohort turned age 65 around 1910 and the Norwegian cohort turned age 65 about 1980. The two cohorts thus span most of the improvements in health and longevity over the twentieth century. Yet the functions relating height and the body mass index (BMI) to the risk of dying are quite similar. BMI is a measure of weight controlled for height.

Variations in height and weight are associated with variations in the chemical composition of the tissues that make up vital organs, in the quality of the electrical transmission across membranes, and in the functioning of the endocrine system and other vital systems. Nutritional status, as represented by height and weight, thus appears to be a critical link connecting improvements in mortality to improvements in human physiology.

So far I have focused on the contribution of technological change to physiological improvements. The process has been synergistic, however, with improvement in nutrition and physiology contributing significantly to the process of economic growth and technological progress along the lines that I have described elsewhere. Here I merely want to point out the main conclusion. Technophysio evolution appears to account for about half of the economic growth in Europe over the past two centuries. Much of this gain was due to the improvement in human thermodynamic efficiency. The rate of converting human energy input into work output appears to have increased by about 50 percent since 1790.

II. Prospects for Continued Decline in the Burden of Health Care

Both environmental improvements and advances in biomedical technology have contributed to a striking decline in prevalence rates of chronic conditions in high-income countries during the course of the twentieth century. This development is illustrated for the United States by **Table 1**, which compares prevalence rates of Civil War veterans (who were 65 years or older around 1910) and veterans of WWII who were the same ages in the mid-1980s. Even before the impact of alleviating medical intervention is considered, **Table 1** shows that prevalence rates were down by 29 to 52 percent over the course of the seven and a half decades separating the elderly veterans of the two wars. But for two of the disorders, genito-urinary conditions and circulatory diseases, prevalence rates were higher in the mid-1980s than in 1910.

Medical intervention reduced prevalence rates for all six disorders. Such interventions were especially effective in chronic digestive and genito-urinary disorders, where prevalence rates were cut 60 percent and 70 percent respectively. In the cases of musculoskeletal, circulatory, and respiratory disorders, the main impact of medical intervention has been to reduce the severity of the conditions rather than to eliminate them. Whether various medical interventions cured disorders or merely attenuated them, they usually contributed to extending the duration of chronic conditions by postponing death. In other words, medical intervention appears to have had the ironic effect of increasing the duration of some disorders.

It is not yet certain whether environmental improvements and medical interventions have reduced or increased the overall average duration of chronic diseases

over the course of the twentieth century. Preliminary analysis indicates that the average age of onset of chronic disorders among veterans of the Union Army may have begun about 5 years earlier than among veterans of WWII. But this effect is partly offset by an extension in life expectancy at age 50 of about 3 years for the WWII veterans.

Nevertheless, the combined effect of improvements in the environment and in biomedical interventions over the past century has greatly improved the health of the population at middle and late ages. This proposition is supported by **Table 2**, which shows the capacity of Union Army veterans c.1900 to engage in manual labor. By ages 60-64 capacity had declined to about a third of what it had been at its peak, which is about half the proportions shown by current age-earnings profiles. It is also worth noting that peak earnings were reached at about age 35, which is about 15 years earlier than today

Partitioning the decline in prevalence rates into environmental effects and medical intervention effects is quite complex because of the long reach of nutritional and other biomedical insults at earlier ages on the odds of developing chronic diseases at middle and late ages. Although such life-cycle effects have long been suspected in particular diseases, it is only recently that a substantial body of evidence bearing on the interconnections has been amassed. Longitudinal studies connecting chronic diseases at maturity, middle ages, and late ages to conditions *in utero* and infancy were reported with increasing frequency beginning in the 1980s and extending through the 1990s. The exact mechanisms by which malnutrition and trauma at early ages affect waiting time to the onset of chronic diseases are still unclear, but it seems reasonable to infer that

environmental insults during the period when cell growth is rapid could lead to long-lasting impairments of vital organs.

The early 1980s established the connections of alcoholic consumption and smoking during pregnancy to the damaging of the central nervous system of fetuses. Although suggested as early as 1968, evidence confirming that protein-calorie malnutrition (PCM) could cause permanent impairment of central nervous system function accumulated in the 1990s. New evidence also indicated that iodine deficiency *in utero* and severe to moderate iron deficiency during infancy could also cause permanent neurological damage.

Perhaps the most far-reaching studies connecting early age insults and chronic conditions at later ages were those undertaken by the Environmental Epidemiological Unit of the British Medical Research Council at the University of Southampton. Based on studies of a large sample of birth records linked to medical records at middle and late ages, they reported that such conditions as coronary heart disease, hypertension, stroke, type II diabetes, and autoimmune thyroiditis began *in utero* or in infancy, but did not become apparent until mid-adult or later ages. Although numerous questions were raised about the validity of these findings during the first half of the 1990s, the second half of the decade witnessed a substantial expansion of research into the connection between characteristics before age one and the later onset of chronic diseases (or premature mortality). The strongest evidence for such links that has emerged thus far pertains to hypertension, coronary heart disease (CHD) and type II diabetes. A review of 32 papers dealing with the relationship between birth weight and hypertension concluded that there was a significant tendency for blood pressure at middle ages to increase as birth weight

declined. Investigators have found evidence of a connection between anthropometic measures of the neonate and later coronary heart disease in Finland, India, and Sweden.

The theory of a nexus between environmental insults *in utero* or at early ages and the onset of chronic diseases at later ages suggests that the rapid advances in public health technology between 1890 and 1950 should contribute to a continuing decline in the prevalence rates of chronic diseases and perhaps even to an acceleration of this decline. The first half of the twentieth century witnessed an avalanche of new technologies that improved the environment, including the cleaning up of the water supply, the cleaning up of the milk supply, the widespread draining of swamps, the improvement of garbage disposal and sewage systems, the rapid reduction in the use of animals (especially in cities) for transportation, the switch to electricity and to fuels with a lower carbon content than had been used previously, and the rapid advance in obstetric technology and neonatal care. This period also witnessed significant improvements in the diversity of the food supply throughout the year and the beginnings of dietary supplements that improved year-round consumption of vitamins and other trace elements.

Evidence indicating that these improvements had an effect on longevity during middle and late ages are contained in a recent study undertaken at the Max Planck Institute for Demographics Research in Rostock, Germany. This study found strong correlations between month of birth and longevity samples of middle-aged men from Austria, Denmark and Australia. The connection appears to be related to the relatively poor quality of the diet available to mothers during winter months for the first third of the twentieth century. Using correlation analysis and other statistical techniques, the study concludes that approximately one-third of the variance in longevity after age 50 was due

to environmental influences during the months following conception. Very similar results have been found for the Union Army veterans who were born two generations earlier.

Comparison of the Union Army data with those in the Health and Retirement Survey indicates that there was a substantial decline in the number of chronic diseases at all ages between 50 and 70. **Table 3** shows that over the course of the twentieth century the number of chronic conditions declined by about two-thirds at each age interval. The average annual rate of decline was about 1.3 percent.

Evidence that the rate of decline in chronic and disabling conditions may be accelerating has been reported by the investigators at the Center for Demographic Studies at Duke University who have made use of data obtained from National Long Term Care Surveys conducted between 1982 and 1999. This study reported an average annual decline of about 1.7 percent in disability rates during the 17-year period. However, when this period was broken into three parts, there was a statistically significant acceleration in the rate of decline during the second and third parts of the period as compared with the first part. The study attributes the acceleration to a variety of health and socio-economic factors, including the level of education, which increased markedly and rapidly during the first half of the twentieth century.

Does the mounting evidence of the long-term decline in the prevalence rate of chronic diseases, and what also may be an acceleration in the long-term rate of decline, mean that the "supply" of treatable chronic diseases is declining? I use the word supply in order to distinguish the physiological burden of health care from the demand for health care services, which may rise even if the physiological burden remains constant, or

declines. Moreover, I use a different definition of the burden of disease than that employed by the World Health Organization and the World Bank. They treat death as the maximum burden of disease, as it should be from an ethical standpoint. However, from a financial standpoint, death terminates health care expenditures on a particular individual. Consequently to address the question of whether declines in physiological prevalence rates will relieve current fiscal pressures on the health care systems of OECD nations, it is necessary to weight the existence of a particular chronic disease by the cost of treating that condition, which generally increases with age.

Such an index is shown in **Figure 5**. In this figure the burden of per capita health care costs, which is based on U.S. data, is standardized at 100 for ages 50-54. **Figure 5** shows that the financial burden of health care per capita rises slowly in the fifties, accelerates in the sixties, accelerates again in the seventies, and accelerates even more rapidly after the mid-eighties. The financial per capita burden at age 85 and over is nearly six times as high as the burden at ages 50-54. Notice that the financial burden of health care for ages 85 and over is over 75 percent higher per capita than at ages 75-79. However, the physiological prevalence rate (number of conditions per person) is roughly constant at ages 80 and over.

Costs rise, even though the number of conditions per person remains constant, because the severity of the conditions increases or because the cost of preventing further deterioration, or even partially reversing deterioration, increases with age. It should be kept in mind that standard prevalence rates merely count the number of conditions, neglecting both the increasing physiological deterioration with age and the rising cost of treatment per condition. **Figure 5** indicates that to forecast the future financial burden of

health care, it is necessary to make use of a function of the age-specific cost of health care, such as that shown in **Figure 5**.

What, then, can be said about the likely movements in the curve of the relative burden of health care costs at ages 50 and over during the next generation? **Figure 6** lays out 3 possibilities. The first possibility is that there will be a proportional downward shift in the curve (Case A). This is the curve implied by using the change in the average prevalence rate, which implies a shift downward at a constant average rate at all ages. The example shown in **Figure 6** implies a decline in average prevalence rates of 1.2 percent per annum, which locates all of the points in Case A at about two-thirds of the previous level. If I had used 1.5 percent, the points on the Case A curve would all be located at about 60 percent of the original level.

A second alternative, shown as Case B in **Figure 6**, is that the curve of disease burden by age will shift to the right. The Case B curve was constructed on the assumption that over the course of a generation the average age of onset of chronic conditions is delayed by about 5 years. This assumption is supported by a number of epidemiological studies in the Netherlands, Britain, the United States, and elsewhere. This forecast is based partly on the evidence that the average age of the onset of chronic disabilities has been declining since the start of the twentieth century.

It is also based on studies of the relative cost of health care by years before death. These studies have produced the curve shown in **Figure 7**, which is standardized on the average costs of health care for all persons age 65 and over in the U.S. Medicare program. **Figure 7** shows that 5 years before the year of death, annual health cost is virtually the same as all annual Medicare costs per capita. By the second year before

death the cost has risen by about 60 percent, and in the year of death the annual cost exceeds the average by over four times. Indeed, expenditure on persons during their last two years of life account for 40 percent of all Medicare expenditures.

The pattern portrayed in **Figure 7** has not changed significantly over the past two decades. The relative constancy in health care costs by years before death supports Case B in **Figure 6**, since it implies that no matter how far to the right the health care curve shifts, age-specific costs will eventually rise sharply as the proportion of persons who die in any given age category increases.

Figure 6 shows a third possibility, Case C. In that case, the curve of age-specific health costs twists. At ages 50 through 64 the curve shifts downward, while at ages above 65 the curve rises. The downward shift before age 65 is due to a presumed acceleration in the delay in the onset of chronic disease and an initially slower rate of deterioration. The sharper rise after age 65 is partly due to diffusion of the most expensive interventions and partly to the assumption that the more effective interventions of the future will also be more expensive.

III. Forecasting Trends in the Demand for Health Care Services

So far I have focused purely on the economic burden of treatable chronic conditions. Figures 5 and 6 focused on the cost-adjusted supply of treatable conditions. I now want to consider the likely trend in the demand for health care services by consumers. **Table 4** presents the change in the structure of consumption in the United States between 1875 and 1995. The trend in the structure of consumption in other OECD nations has been quite similar. The term "expanded consumption" takes account of the fact that as income

has increased, consumers have preferred to take an increasing share of their real income in the form of leisure, rather than in purchasing more commodities as would be possible if they did not reduce their hours of work.

One notable feature of **Table 4** is the change in the share of income spent on food, clothing, and shelter, which has declined from 75 percent of expanded consumption to just 12 percent over the 120-year period. Another striking change is the share of income spent on health care, which has increased nine-fold, from one percent of expenditures to nine percent.

For purposes of forecasting, the most important feature of **Table 4** is the last column, which presents the long-term income elasticities for each category of expenditures. The income elasticity is defined as the percentage increase in expenditures on a given commodity that will occur with a one-percent increase in income. Notice that the income elasticities for food and clothing are quite low, which means that the share of these items in total consumption will continue to decline. An income elasticity of one means that the share of a given item in total consumption will remain constant. Notice that shelter, which includes most consumer durables, is closer to, but still below one. On the other hand, the income elasticities for health care, education, and leisure are all well above one. The income elasticity of 1.6 means that income expenditures on health care in the U.S. are likely to rise from a current level of about 14 percent of GDP to about 21 percent of GDP in 2040.

Is that bad? Should such a development be avoided? Should governments seek to thwart consumer demand for health care services? Such a policy would be necessary only if OECD nations lacked the resources to provide that much health care. However,

the growth in productivity of traditional commodities, including food, clothing, shelter, and consumer durables, will release the resources required to provide expanded health care. In the U.S. a century ago, it took about 1700 hours of work to purchase the annual food supply for a family. Today it requires just 260 hours. If agriculture productivity grows at just two-thirds of its recent rates, then by 2040 a family's annual food supply may be purchased with about 160 hours of labor.

A recent study of the role of the change in the benefits and costs of health care conducted by investigators at the National Bureau of Economic Research (NBER) concluded that the benefits of health care services over the past 40 years have more than justified their costs. They suggest a fundamental repositioning of the public debate about medical care, from how governments can limit spending to how to get the most out of the spending that is untaken. NBER investigators have also suggested changing the methods of health care financing so that the consumer demand for increasingly effective services is not unnecessarily thwarted.

Table 1
Comparison of the Prevalence Rates of Selected Chronic Conditions among Union Army Veterans in 1910 and World War II Veterans in the Mid-1980s (in Percent)

Disorders	1 Union Army Veterans	2 World War II Veterans before Alleviating Intervention	3 Annual Rate of Decline in Prevalence Rates before Alleviating Intervention	4 World War II Veterans after Alleviating Intervention	5 Annual Rate of Decline in Prevalence Rates after Alleviating Intervention
Musculoskeletal	67.7	47.9	0.4	42.5	0.6
Digestive	84.0	49.0	0.7	18.0	2.0
Genito-urinary	27.3	36.3	+0.4	8.9	1.5
Central nervous, endocrine, metabolic, or blood	24.2	29.9	+0.3	12.6	0.9
Circulatory	90.1	42.9	1.0	40.0	1.1
Respiratory	42.2	29.8	0.5	26.5	0.6

Note: + indicates an increase in prevalence rates. The term "before alleviating intervention" in Column 2, refers to interventions that alleviated existing chronic conditions, not interventions that prevented chronic conditions from occurring, as in the use of penicillin to prevent rheumatic heart disease from occurring.

Table 2

Average Capacity of Union Army Veterans to Engage in Manual Labor, by Age, c. 1900 (percent)

Age	Capacity to Engage in Manual Labor
50-54	0.75
55-59	0.56
60-64	0.34
65-69	0.17
70-74	0.08
75 and over	0.04

Note: Capacity at prime ages = 100

Table 3

Average Number of Chronic Conditions per Union Army Veteran and per White Male in HRS

Age	c. 1900	1992-96	Average Annual Rate of Decline (%)
50-54	3.3	1.0	1.3
55-59	4.5	1.4	1.2
60-64	5.6	1.6	1.3
65-69	6.2	1.9	1.3

Table 4

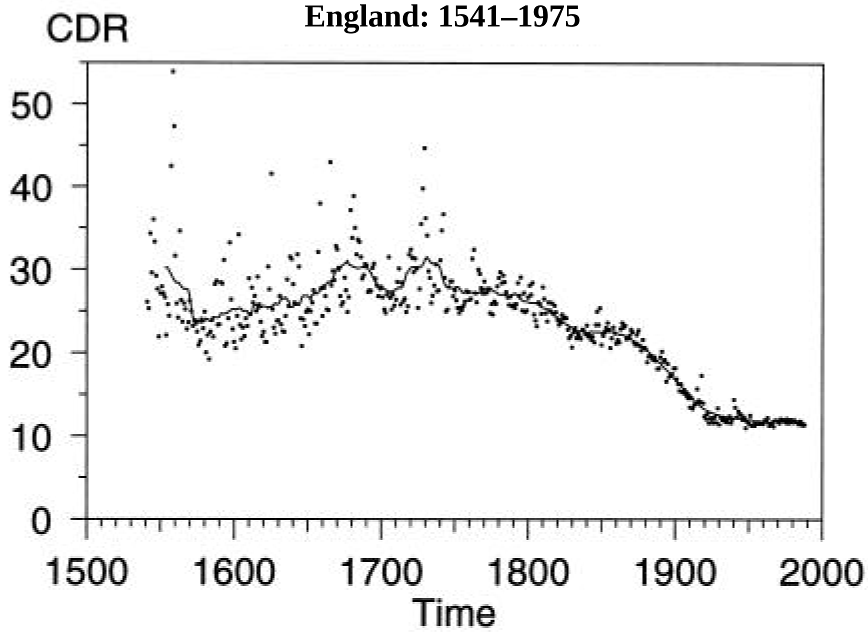
The Long-Term Trend in the Structure of Consumption and the Implied Income Elasticities of Several Consumption Categories

Consumption Class	Distribution of Consumption (%) 1875	1995	Long-Term Income Elasticities
Food	57	12	0.2
Clothing	14	4	0.3
Shelter	16	14	0.7
Health Care	2	23	1.6
Education	1	12	1.6
Other	10	37	1.1

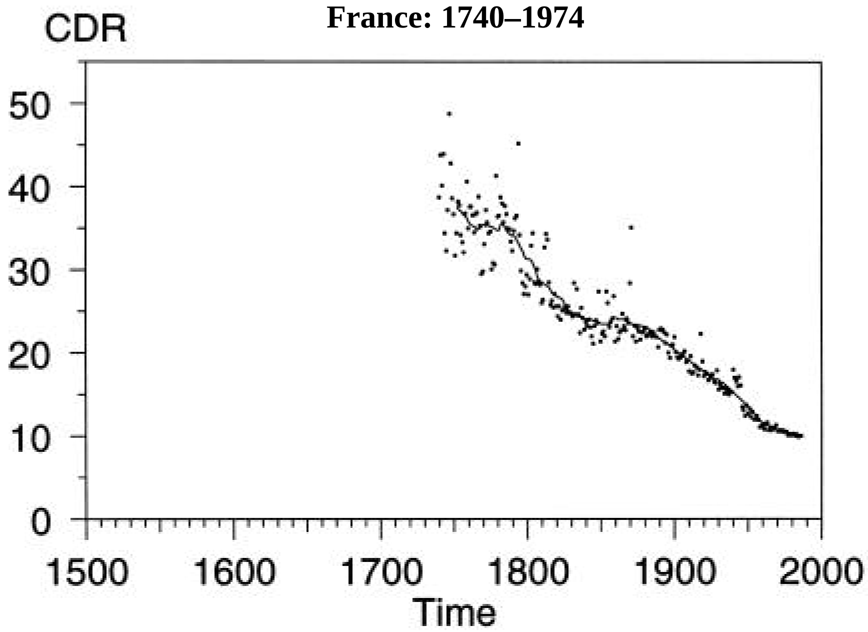
Figure 1

The Secular Trends in Mortality Rates in England and France

PART A
England: 1541–1975



PART B
France: 1740–1974



Note: Each diagram shows the scatter of annual death rates around a 25-year moving average.

Figure 2

The Growth of the World Population and Some Major Events in the History of Technology

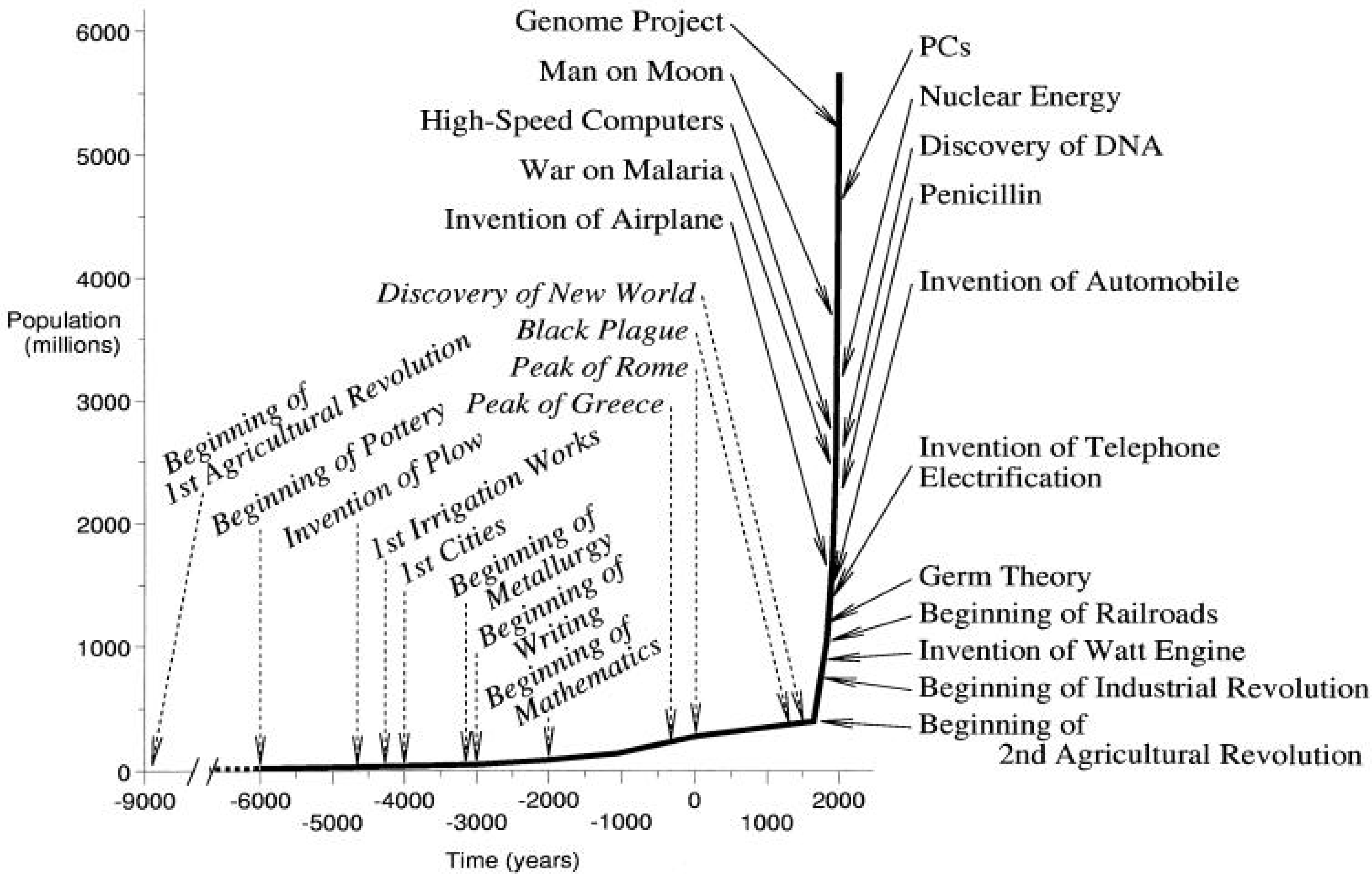


Figure 3

Relative Mortality Risk among Union Army Veterans and among Norwegian Males

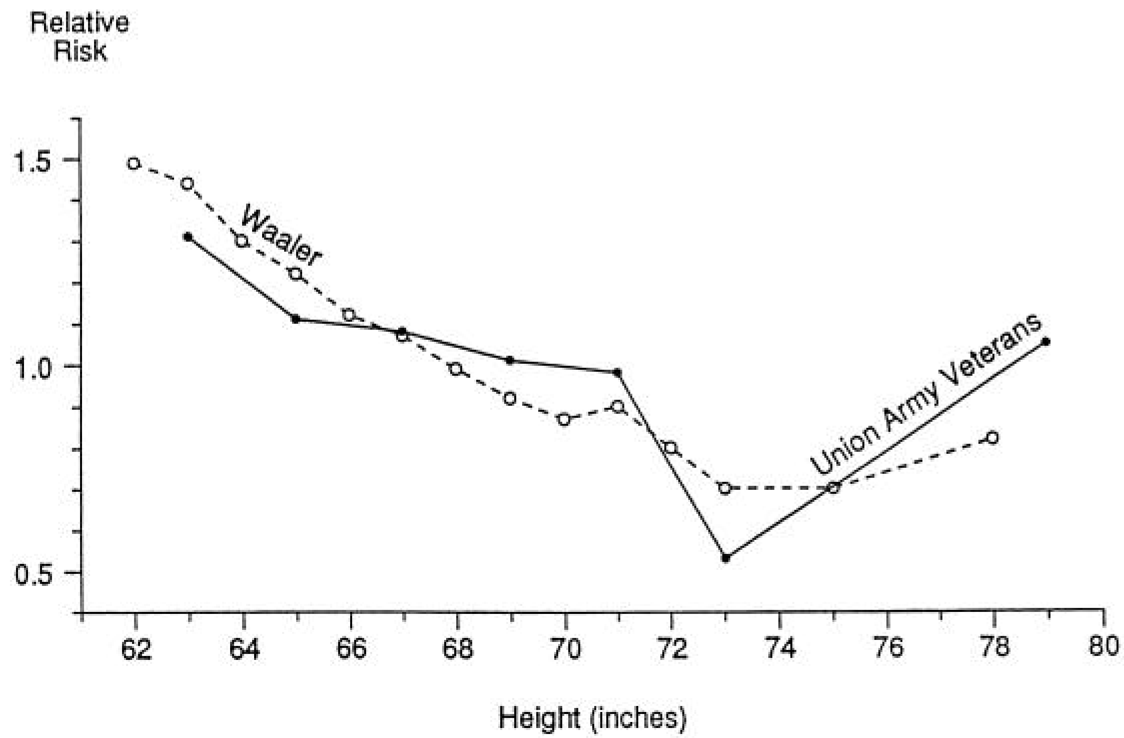


Figure 4

Relative Mortality Risk by BMI among Men 50 Years of Age, Union Army Veterans around 1900 and Modern Norwegians

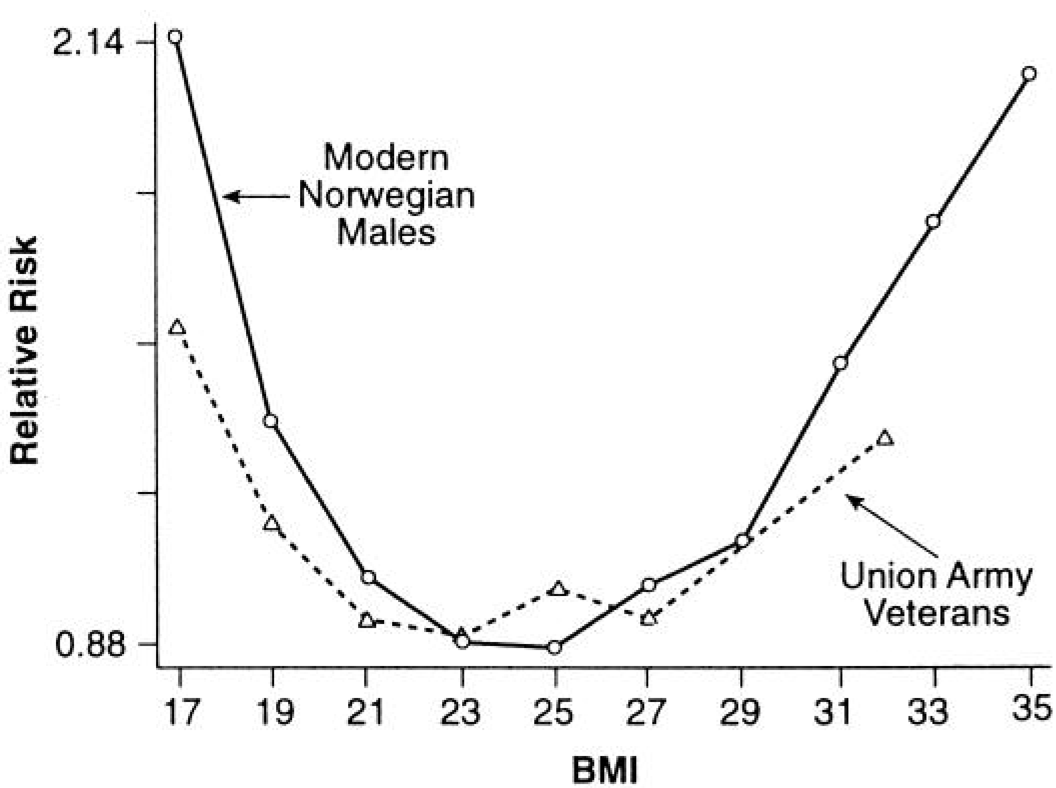
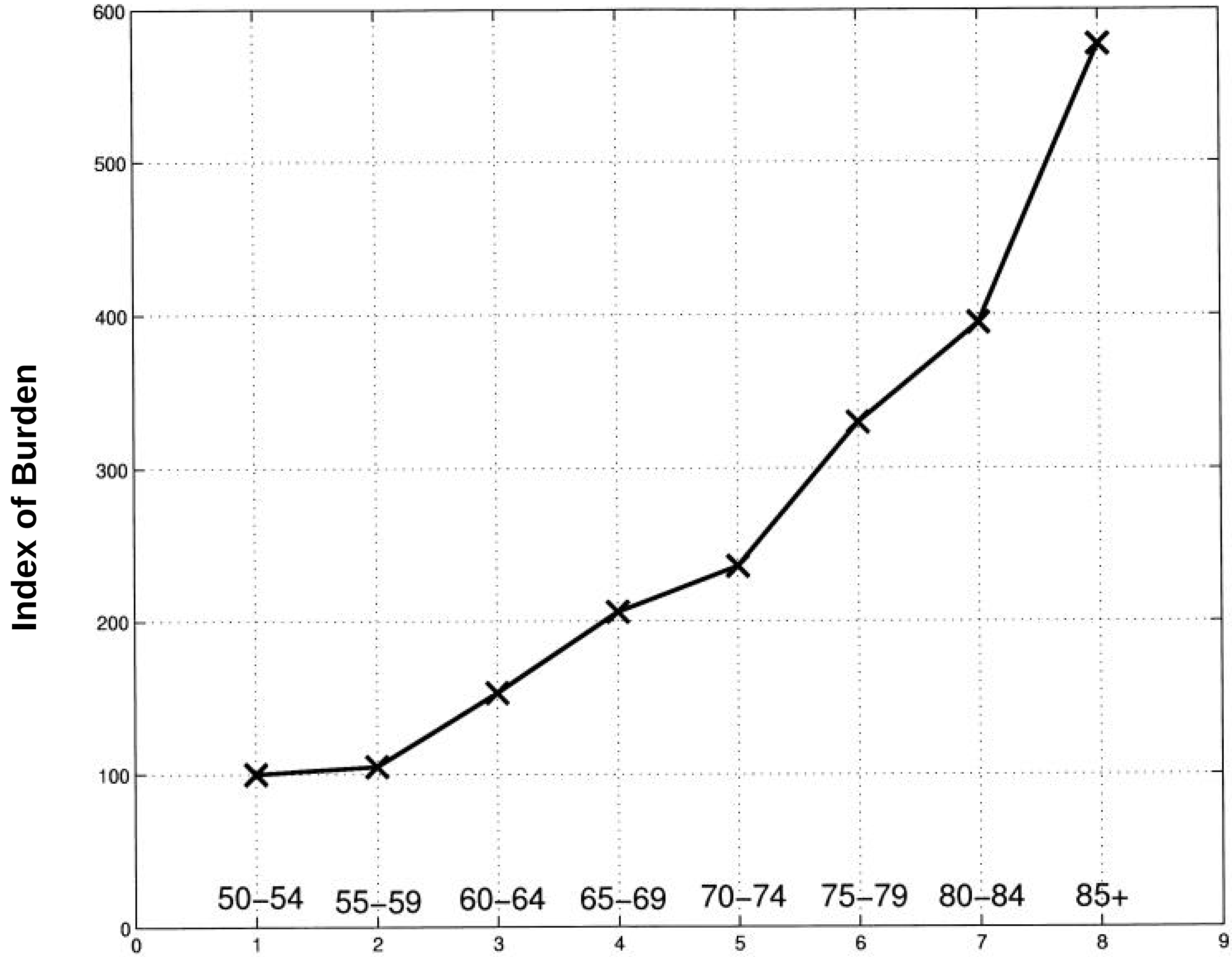


Figure 5. Relative Burden of Health Care by Age, U.S. Data circa 1996



Age
(average burden of 50-54 year-olds = 100)

Figure 6
How Will the Curve of Relative Disease Burden Shift?

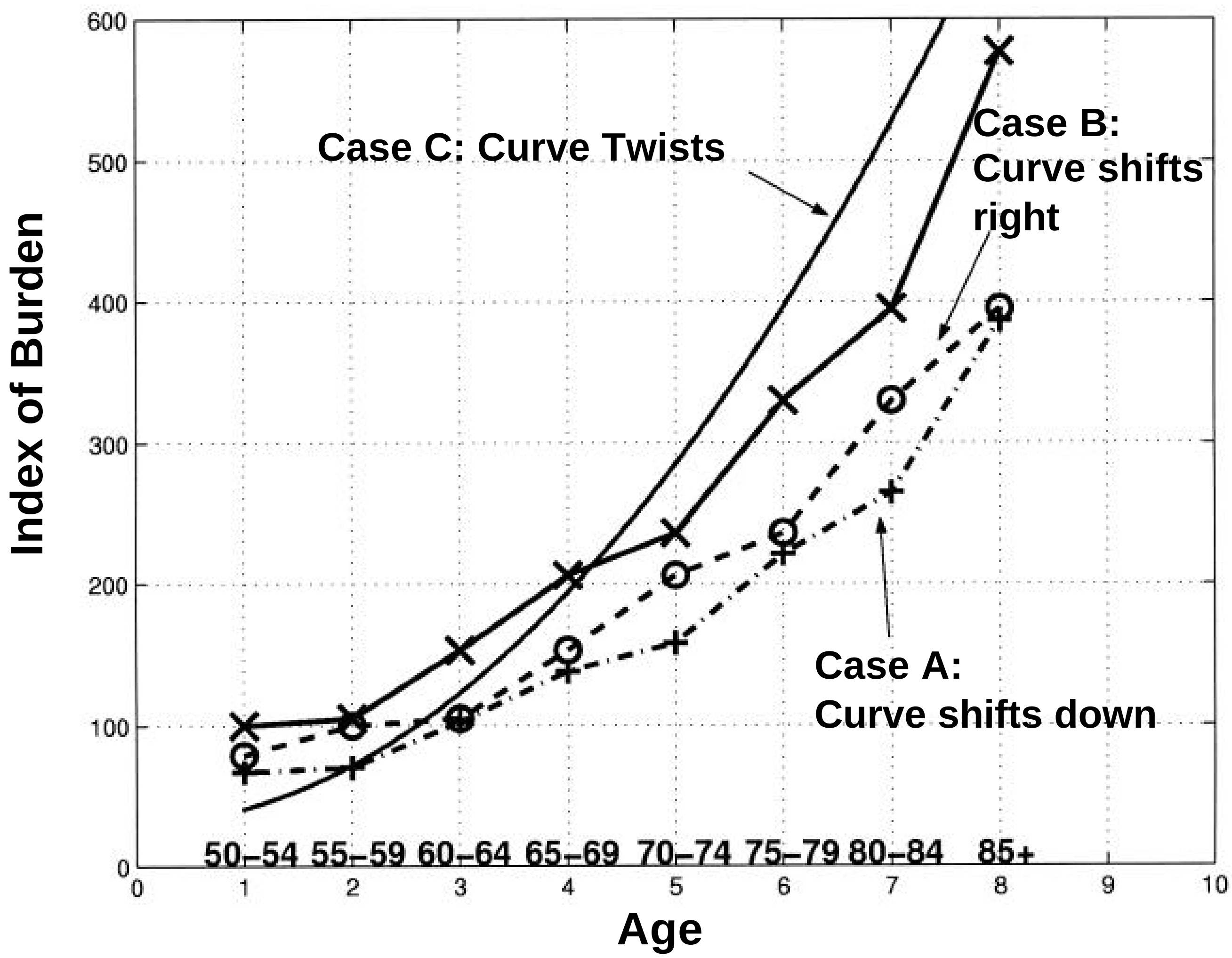


Figure 7. Index of Average Annual Health Care by Year before Death