Technical Appendices

       In this technical appendices I discuss the data and calculations presented in the text. I divide the appendices into chapters of the book.
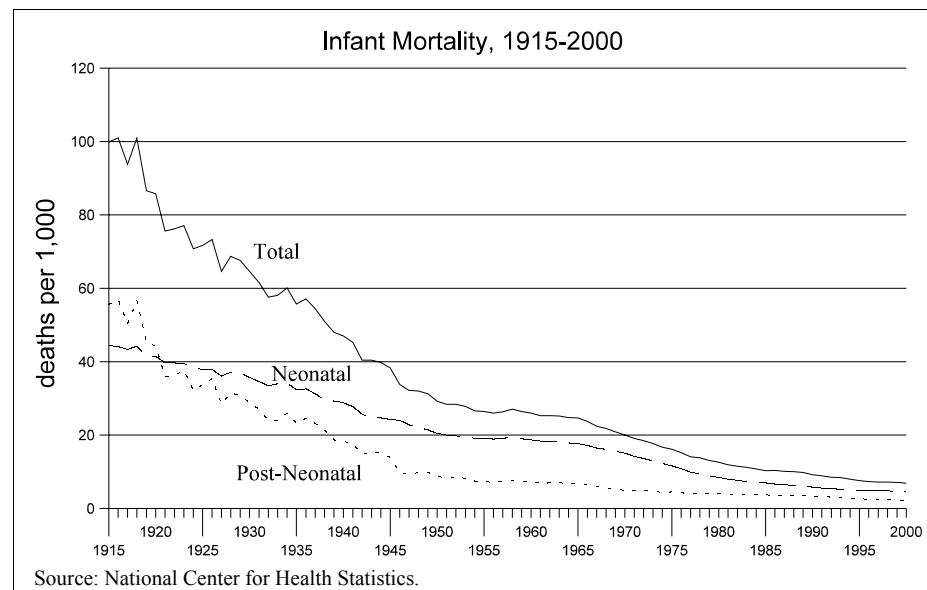
Chapter 3 – Success and Failure at the Beginning of Life

The research reported in this appendix is joint with Ellen Meara, and follows from our paper on the subject.[1]

Trends in Infant Survival

Infant mortality has declined substantially in the 20th century, from a rate of 100 per 1,000 in 1915 (or 1 out of every 10 births) to 7 per 1,000 in 2000 (fewer than one in a hundred).[2] The decline in infant mortality in the first half of the century was largely a result of reduced post-neonatal mortality (deaths after the first 28 days of life). Post-neonatal mortality is generally a result of infectious diseases acquired in the home, and was likely reduced by limiting disease incidence and providing antibiotics to aid recover. In the second half of the century, reduced mortality was attributable to fewer deaths in the first month of life, generally in the first week. Neonatal mortality is much more a product of complications of birth, and is treated with sophisticated medical care provided in the prenatal period and shortly after birth.

Infant Mortality, 1915-2000

Source: National Center for Health Statistics.

Data on birth weights and survival

The basic data on the distribution of birth weights and survival are given in the table 3.1 below.[3]

Table 3.1: Data on Birth Weights and Survival

	Share of births			Neonatal mortality		
Birth weight	1950	1985	1998	1950	1985	1998
< 1,000	0.5%	0.6%	0.7%	87.2%	57.2%	39.7%
1,000-1,499	0.6	0.6	0.7	55.1	10.5	4.3
1,500-1,999	1.4	1.3	1.5	21.1	3.4	1.9
2,000-2,499	4.9	4.2	4.6	5.0	1.1	0.7
2,500-2,999	18.1	15.8	16.5	1.3	0.3	0.2
3,000-3,499	37.7	36.6	37.0	0.7	0.2	0.1
3,500-3,999	27.1	29.5	28.8	0.6	0.1	0.1
4,000-4,499	7.7	9.2	8.5	0.8	0.1	0.1
4,500 & up	2.1	1.9	1.5	1.4	0.3	0.1
Total/Average	100%	100%	100%	2.1%	0.7%	0.5%

These data can be used to decompose changes in neonatal mortality into changes in the distribution of birth weights and changes in birth weight-specific survival. In particular, neonatal mortality is defined as:

Neonatal Mortality = $\sum_j$ *Pr[BW $_j$] [Mortality | Birth Weight]$_j$*

Thus, the change in neonatal mortality is given by:

) Neonatal Mortality = $\sum_j$ *) Pr[BW$_j$] [Mortality | Birth Weight]$_j$ +*

$\sum_j$ *Pr[BW$_j$]) [Mortality | Birth Weight]$_j$ +* $\sum_j$ *) Pr[BW$_j$]) [Mortality | Birth Weight]$_j$*

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The first term is the impact of changes in the birth weight distribution on neonatal mortality. The second term is the effect of changes in birth weight-specific survival on neonatal mortality. The last term is the covariance between the two.

As table 3.2 shows, virtually all of the gains in neonatal survival since 1950 are a result of improved survival conditional on birth weight rather than changes in the birth weight distribution.

Table 3.2: Decomposition of Changes in Neonatal Mortality

	1950	1998	Change
Neonatal mortality	2.1%	0.5%	-1.6%
Amount resulting from change in:			
Birth weight distribution			0.3
Birth weight-specific survival			-1.7
Covariance term			-0.2

Comparison of Birth Weight and Other Factors Influencing Neonatal Mortality

One of the important assumptions of this analysis is that conditional on birth weight, only medical care influences neonatal survival, not the wealth of other maternal and environmental factors that influence birth weight. Formally, this statement translates into an assertion that the explanatory importance of factors other than birth weight for neonatal mortality is low once birth weight is included in the regression. In this subsection, I provide evidence for this.

I demonstrate this using data from the National Vital Statistics linked birth-death file for 1990. These data include a record for every birth and indicate the birth weight and gestation age. The data also indicate whether the infant died in the neonatal period.

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The first column of table 3.3 relates neonatal mortality to birth weight. Infants at very low birth weights are substantially more likely to die than are infants born at higher birth weights. As the last row shows, about 33 percent of neonatal mortality can be explained by birth weight.

The second column shows the relation between maternal demographic, behavioral, and health characteristics and neonatal mortality, omitting the birth weight variables. The coefficients on these variables are generally in the expected direction. For example, young and very old mothers have higher neonatal mortality rates, as do women with more medical conditions. Maternal smoking and drinking are not related to outcomes in this regression, although they are when the health conditions are not included as well. Low weight gain substantially increases the risk of infant death. Still, the total explanatory power of all of these variables as a whole is relatively small, about 3 percent.

The third column includes birth weight along with the demographic, behavioral, and medical factors. The coefficients on the birth weight variables are virtually unchanged from the earlier column. The coefficients on the other variables changes substantially. Indeed, most no longer explain neonatal mortality, or do so in the opposite direction. For example, maternal smoking is associated with lower neonatal mortality controlling for birth weight, as is maternal alcohol use. Maternal weight gain has an effect only about one-tenth as large as when birth weight is not included. Thus, all of the effect of maternal smoking and drinking on neonatal mortality, and almost all of the effect of weight gain, occurs through their effect on birth weights. Indeed, the R^2 in this second column is very close to the R^2 when birth weight alone are included in the regression. Thus, these additional variables collectively do not add much to predictions of neonatal mortality once birth weight is controlled for.

Table 3.3: Comparison of Birth Weight and Other Factors in
Neonatal Mortality
[Dependent Variable: Neonatal Death]

Independent variable	(1)	(2)	(3)
Birth Weight (omitted category: 5,000 + g)			
<500 g	.879	—	.875
500-999 g	.371	—	.367
1,000-1,499 g	.063	—	.061
1,500-1,999 g	.021	—	.020
2,000-2,499 g	.003	—	.002
2,500-2,999 g	-.003	—	-.003
3,000-3,499 g	-.005	—	-.004
3,500-3,999 g	-.005	—	-.005
3,000-4,499 g	-.005	—	-.005
4,500-4,999 g	-.004	—	-.005
BW missing	.219	—	.217
Maternal Age			
Maternal Age	—	-.00051	-.00019
Maternal Age^2	—	.0000077	.0000024
Maternal Race (relative to white)			
Black	—	.003	-.001
Other	—	-.0008	-.0005
Maternal education (relative to college degree +)			
0-8 years	—	-.0008	-.0002
9-11 years	—	-.0007	-.0005

12 years	—	-.00004	-.0001
13-15 years	—	-.00011	-.0002
Missing	—	.0046	.0022
Mother married	—	-.002	-.0006
Prenatal care began (relative to no care)			
1st trimester	—	-.018	-.004
2nd trimester	—	-.020	-.004
3rd trimester	—	-.021	-.004
Unknown	—	-.007	-.001
Parity (relative to 3rd or more)			
1st child	—	-.0003	-.0006
2nd child	—	-.0002	-.0003
Unknown	—	.005	-.0006
Tobacco use (relative to no)			
Yes	—	-.0006	-.001
Unknown	—	.0003	.00003
Alcohol use (relative to no)			
Yes	—	-.0001	-.0009
Unknown	—	-.0040	-.0012
Maternal weight gain (relative to 46 or more lbs)			
<16 lbs	—	.019	.002
16-20 lbs	—	.006	.00005
21-25 lbs	—	.003	-.0003

26-30 lbs	—	.002	-.0003
31-35 lbs	—	.002	-.0003
36-40 lbs	—	.001	-.0003
41-45 lbs	—	.001	-.0002
Unknown	—	.009	.001
Plurality (relative to quintuplet or higher)			
Single	—	-.062	.071
Twin	—	-.029	.070
Triplet	—	.013	.067
Quadruplet	—	.043	.039
Controls for maternal health, pregnancy characteristics	No	Yes	Yes
N	4,163,150	4,163,150	4,163,150
R^2	.326	.027	.328

Note: Standard errors are not reported. With a sample of over 4 million observations, virtually all coefficients are statistically significant.

The literature has supported this conclusion using other evidence as well. For example, Horbar and Lucy note the difference in mortality between hospitals with and without neonatal intensive care units, and the decline in mortality when neonatal intensive care units are opened.[4] Less formally, the neonatologists we have spoken to believe this to be true from their experience, with the one exception noted next.

Birth Weight and Gestational Age in Explaining Neonatal Mortality

In addition to birth weight, one other aspect of fetal development is relevant for neonatal survival – gestational age. Premature babies are more developmentally impaired than normal term babies, even given birth weight. We would like to incorporate information on gestational age in addition to birth weight, but data limitations prevent this. The older data report only birth weight and not gestational age. Fortunately, this omission is not likely to be substantially important.

The reason is that birth weight and gestational age are tightly linked. Most premature babies are low birth weight, and vice versa. To demonstrate this, I use data from the linked birth and infant death files for 1990. As table 3.4 shows, 95 percent of very low birth weight babies (<1500 g) are preterm (<37 weeks), as are 55 percent of moderately low birth weight babes (1500-2499 g). The remaining low birth weight babies are those suffering intrauterine growth retardation.

Table 3.4: Low Birth Weight and Prematurity

Birth weight	Not premature	Premature	Total
Normal (2,500 g +)	93%	7%	100%
Moderately low (1,500 - 2,499 g)	45	55	100
Very low (<1,500 g)	5	95	100

To compare the predictive power of the two variables for neonatal mortality, the first column of table 3.5 repeats the regression results presented above relating neonatal mortality to birth weight. The second column relates neonatal mortality to gestational age alone. The R^2 is 23 percent, lower than for birth weight, but still large. The third column includes the two variables together. The R^2 in this regression is 34 percent, almost exactly the same as when birth weight alone is used. Thus, birth weight and gestational age are largely picking up the same effects. Further, the coefficients

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on birth weight do not decline greatly when adding gestational age to the model, while the coefficients on gestational age decline by more. Thus, birth weight is a somewhat more accurate predictor of neonatal mortality than gestational age.

This may be a result of the fact that gestational age is measured with error, while birth weights are measured far more accurately. The presence of error argues that birth weight is a good summary of likely birth outcomes.

Table 3.5: Birth Weight and Gestational Age in Neonatal Mortality
[Dependent Variable: Neonatal Death]

Independent variable	(1)	(2)	(3)
Birth Weight (relative to 5,000 + g)			
<500 g	.879	—	.753
500-999 g	.371	—	.286
1,000-1,499 g	.063	—	.043
1,500-1,999 g	.021	—	.017
2,000-2,499 |g	.003	—	.001
2,500-2,999 g	-.003	—	-.004
3,000-3,499 g	-.005	—	-.005
3,500-3,999 g	-.005	—	-.005
3,000-4,499 g	-.005	—	-.005
4,500-4,999 g	-.004	—	-.005
BW missing	.219	—	.191
Gestational Age (relative to 42 + weeks)			
<20 weeks	—	.821	.300
20-27 weeks	—	.398	.115
28-31 weeks	—	.046	.0001

32-35 weeks	—	.008	.001
36 weeks	—	.003	.0005
37-39 weeks	—	-.0002	-.0003
40 weeks	—	-.0005	-.0003
41 weeks	—	-.0004	-.0003
Not stated	—	.023	.007
N	4,163,150	4,163,150	4,163,150
R^2	.326	.228	.336

Note: Standard errors are not reported. With a sample of over 4 million observations, virtually all coefficients are statistically significant.

Cost-Benefit Analysis

The calculation of the cost and benefits of changes in medical treatments for low birth weight babies closely parallels that our joint paper, and is updated to the more recent time period. Some of the details of the analysis are contained in that paper.

Costs. There are two costs to medical innovations for premature infants. The first is the cost during the birth episode itself. A number of analysts have estimated these costs. Lewit et al. and Rogowski are the most recent studies.[5] Both studies use data from the late 1980s. The Lewit et al. study is a national estimate. Rogowski studies a Medicaid population and thus has higher costs. I use the Lewit et al. analysis, although the results are not very sensitive to this. Lewit et al. estimate that average birth costs per low birth weight infant are $15,000 in 1988. Adjusted for medical care inflation, this is about $30,000 today. The Rogowski estimates, by contrast, are about $5,000 to

$10,000 more.

The second medical cost is the long-term cost of caring for disabled children. As noted in the text, about two-thirds of marginal survivors will have some disabilities, and heavier birth weight babies will also have some disability, although less. Based on the medical literature and conversations with specialists in the field, Meara and I assigned complication rates as follows: 68 percent for babies under 1,000 grams; 28 percent for babies between 1,000 and 1,500 grams; and 23 percent for babies between 1,500 and 2,500 grams. In each case, we assume that half of the complications are severe and half are mild.

Children with disabilities use more Medicaid services than do children without disabilities. Average Medicaid spending per disabled person is about $9,000 currently. We assume that the more severely disabled low birth weight infants spend this amount annually for the rest of their life, and the less severely disabled infants spend one-tenth this amount. This is almost certainly an overstatement of expected spending, because disabled children generally do not use this much care (as noted in Lewit et al.). Thus, this overstates the cost increase from saving low birth weight babies. The present value of lifetime Medicaid costs after the birth episode is just under $40,000 per low birth weight infant. Adding the birth and post-birth costs, the present value of lifetime medical spending for a low birth weight infant is about $70,000.

In 1950, there was some care for low birth weight infants, but it was minimal. We assume no additional costs in the birth period beyond those of a routine delivery. There would be some long-term costs for disabled survivors, though. Meara and I estimate that the rate of impairment was the same for surviving infants born under 1,000 grams in 1950, and was higher for infants born between 1,000 and 1,500 grams. Specifically, we assume that such infants had the same rate of

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disability in 1950 as the lightest infants did. This reflects the fact that medical care was less advanced for these infants than it is today and thus rates of complications were higher.

Low birth weight babies who survived in 1950 would have received some medical care, particularly those with developmental problems. We estimate such costs at a tenth of current costs on an annual basis, reflecting the overall amount by which medical spending in 1950 was below spending today. The present value of lifetime medical costs for a low birth weight infant in 1950 was thus about $3,000. The increase in costs from 1950 to 1998 is therefore about $70,000. Table 3.4 shows these cost estimates.

Table 3.6: Costs and Benefits of Changes in Neonatal Intensive Care

	1950	1999	Change
Costs			
Birth episode	$0	$29,000	
Long-term costs	3,000	42,000	
Total	3,000	71,000	$68,000
Benefits			
Expected years of life	55	70	15
Expected quality-adjusted years	48	61	13
Valuation (present value)	$2.0 mn	$2.4 mn	$350,000

Benefits. The health benefits from improved care for low birth weight infants is both longer life and, potentially, higher quality life.

The share of low birth weight infants dying in the neonatal period fell from 17.7 percent in 1950 to 5.1 percent in 1998. Life expectancy for low birth weight infants is likely to be shorter than

for normal birth weight infants. David Barker estimates that low birth weight infants have a 22 percent higher mortality rate than infants as a whole.[6] We assume this 22 percent applies throughout the 1950 to 2000 time period. With this assumption, life expectancy conditional on reaching age 1 was 74 years in 1998. The increased probability of neonatal survival translates into a 15 year increase in life expectancy at age 1 between 1950 to 1998. A small part of this is because life expectancy at age 1 was higher in 2000 than in 1950. Most was because more low birth weight infants survived.

Quality of life is adversely affected by both severe and mild disability. Meara and I estimate that quality of life for severely disabled people is about 0.65 on a scale from death to perfect health. The 0.65 value is equivalent to the quality of life estimated for other serious diseases such as cancer, diabetes, heart disease, and paralysis. We estimate that quality of life for mildly disabled people is about 0.75, and quality of life for a non-disabled person is about 0.95. In comparison to the results of Saigal et al.,[7] these reflect far more severe disability. Thus, we will understate the benefits of saving lives.

The change in quality of life for infants surviving the neonatal period is a mix of two offsetting factors. On the one hand, the average surviving infant at some birth weights has higher quality of life than did infants at the same birth weight in 1950. This is particularly true for babies born between 1,000 and 1,500 grams, where complication rates have declined over time. On the other hand, more very low birth weight babies are surviving now than in 1950, and thus more infants are in the range where complication rates are higher. On net, these two factors roughly cancel out. Quality of life for low birth weight infants is slightly lower in 2000 compared to 1950 but is essentially unchanged. The decline is only 1 percent. Quality-adjusted years of life, therefore,

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increase by the percentage as years of life unadjusted for quality. Because quality is below 1, however, the absolute number of years is lower, about 13 years for the average low birth weight baby.

A year of quality-adjusted life is assumed to be worth $100,000 to the individual involved and her family. We assume that non-disabled and mildly disabled low birth weight infants work and earn much as do normal birth weight infants. Thus, the net financial impact of saving these babies is about zero, and the social value of life to them is $100,000 per year of quality-adjusted life.

Babies with severe complications will not earn as much as normal birth weight infants and will collect more benefits. Lewit et al. estimate, for example, that special education costs are about $3,500 per year and that special education would be used particularly by these children. Low birth weight children are also more likely to be left behind a year in school, at a cost of about $4,000. Further, low birth weight babies will frequently receive disability insurance payments, which average about $3,000 per child.

A high-end estimate is that the average low birth weight survivor with severe complications will use about $25,000 per year in services. This amount is equal, for example, to total annual consumption of the elderly, so it is equivalent to saying that society supports such people at the level that it supports the elderly. This is clearly an overstatement, but by overstating costs, we understate the benefits of changes in technology. We thus assume that a year of quality-adjusted life to the severely disabled is worth $75,000 to society.
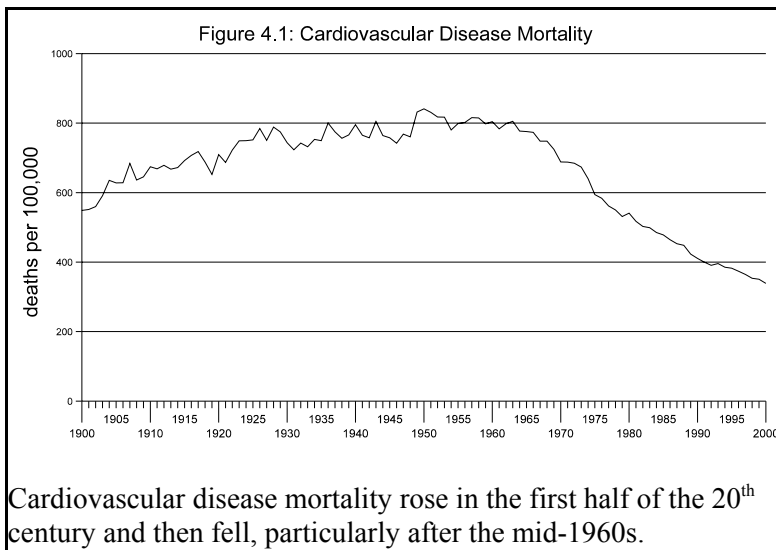
With this valuation, the average low birth weight baby had lifetime benefits of $2.0 million in 1950, and $2.4 million in 1998, for an increase of about $350,000. This amount is about 5 times the cost increase.

Chapter 4 – The Heart of the Matter

This appendix describes the decomposition of cardiovascular disease mortality improvements into intensive treatment, medication, and behavioral and other factors. The research in this appendix is joint with Srikanth Kadiyala.

Basic Trends in Mortality

To set the stage for the analysis, we start by presenting basic trends in cardiovascular disease mortality, and its major components. Figure 4.1 shows cardiovascular disease mortality from 1900 through 2000. The underlying data are from the National Center for Health Statistics, and are adjusted to the age distribution of the population in 2000. The particular year to which the data are age adjusted does not materially affect the trends, although the age adjustment itself has some impact. Mortality rose in the first half of the century and then declined, particularly after the

Figure 4.1: Cardiovascular Disease Mortality

Cardiovascular disease mortality rose in the first half of the 20th century and then fell, particularly after the mid-1960s.

mid-1960s.

Figures 4.2 and 4.3 present coronary heart disease mortality and stroke mortality from 1950 on – the two major components of cardiovascular disease. The decline in heart disease mortality

Figure 4.2: Coronary Heart Disease Mortality

Figure 4.3: Stroke Mortality
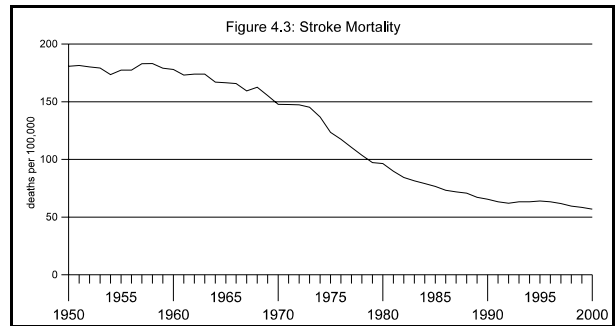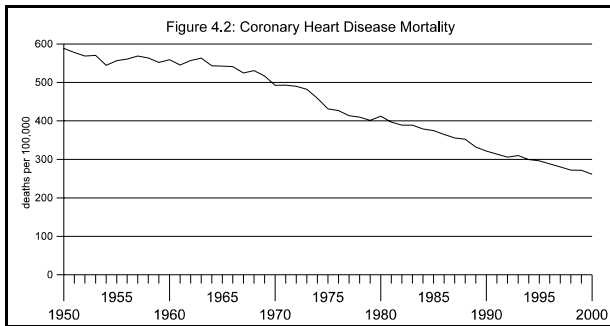
was relatively continuous over the period, at least since the mid-1960s. The decline in stroke mortality was much more concentrated. Stroke declined quite rapidly from the early 1970s through the late 1980s, and has since leveled off.

These figures do not differentiate between changes in incidence of disease and survival conditional on having a disease, so they do not tell exactly why mortality has declined. Still, they illustrate the nature of what needs to be explained.

Prevention and Acute Management

Kadiyala and I start by dividing changes in cardiovascular disease mortality into primary prevention, acute management, and secondary prevention. We do this using data from the Framingham Heart Study. The Framingham data begins in 1948. The study is still ongoing, although the data we have end in 1988. We examine cohorts aged 45-74 in each of 1948, 1958, 1968, and 1978.

Primary prevention is measured as the change in the share of people who have not yet had an acute incident but have one within the next decade. Acute survival is the change in the share of people dying within 90 days of an acute incident. Ninety day survival is a common time period in the literature for acute management.[8] To estimate acute survival by decade, we pool everyone who

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had an acute incident in that decade. For example, all cardiovascular disease incidents from the 1948 cohort that occurred before 1958 are in the 1948 cohort of acute events.

Secondary prevention is measured as 4 year survival for those who survived the 90 day acute interval. Note that secondary mortality is not defined for the full 1978 cohort, since these people had first episodes of cardiovascular disease any time between 1978 and 1988, and we do not have 4 years of complete follow-up data for all people. We use the people that we are able to include – those with incidents at least four year prior to 1988.

All of our sample means are weighted to the 1990 age and sex distribution of the US population as a whole. We measure age in five year increments from 45-49 to 70-74. First incident rates are weighted by the total population in each age group at the beginning of the interval. Acute survival and secondary prevention are weighted by the number of incidents at each age. We form these weights as the product of the age and sex specific 1990 national population times the age and sex specific acute incidence rate in the Framingham data.

The Framingham data do not have people in all age groups in all years. For example, the initial sample in 1948 was aged 30 to 62. We form changes in risk across adjacent decades using the data in all the age-sex cells that are common to those two decades, imposing a minimum of 10 people in an age-sex cell. We then benchmark these changes to the Framingham data from the 1960s. The results on prevention and acute management are given in table 4.1.

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Table 4.1: Prevention and Acute Management in the Framingham Data

	Cohort				Effect of Change:
	1948	1958	1968	1978	
Acute incident in 10 years	20.6%	20.7%	17.3%	15.8%	-1.7%
90 day mortality for acute incident	21.0	19.2	13.4	6.3	-2.4
4 year mortality for acute survivors	19.6	14.8	11.3	6.5	-2.1
10 year cardiovascular mortality	8.9%	7.5%	4.7%	3.0%	-5.9%

Note: Data are age and sex adjusted to the 1990 US population.

Ten year cardiovascular disease mortality is shown in the last row. Mortality fell from 8.9 percent in the decade beginning in 1948 to 3.0 percent in the decade beginning in 1978, for a total change of -5.9 percentage points. The first rows show the components of this decline. As the first row shows, 21 percent of people had an acute incident within a decade of 1948, compared to 16 percent within a decade of 1978. In all time periods, the vast majority of these cases were heart attacks; strokes were a much smaller component.

The last column in the first row indicates if acute incident rates had changed but acute survival and secondary survival had not changed, the expected change in overall mortality would be -1.7 percentage points. Comparing the first three rows indicates that primary prevention, acute management, and secondary prevention are of roughly equal importance in explaining mortality changes, although acute survival has a somewhat greater impact and primary prevention a somewhat smaller impact.

Acute Management

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We begin by understanding the factors leading to lower mortality in the acute phase. Intensive treatment is most obvious explanation. The question is how important this is. The improvement in acute survival over time may be a result of other factors beyond intensive treatment. For example, with fewer people smoking over time, heart attacks might be less severe now than in the past. We use two methods to parcel out the change in acute survival into treatment and risk factor changes. First, we back out the changes that we attribute to risk factors, and assume the residual is a measure of technology. To implement this, we estimated a regression model for acute survival over time, with and without controls for risk factor variables in the period just before the acute incident. The dependent variable is an indicator variable for whether the person survived the acute incident. The independent variables are year dummy variables and pre-event risk factors. The component due to technological change is the effect of the year dummy variables, controlling for the pre-event risk.

We use a linear probability model for ease of interpretation. Table 4.2 shows the results:

Table 4.2: Regression Models Explaining 90-Day Acute Survival
[Dependent Variable: Death in 90 Days]

Independent Variable	Coefficient	Standard Error	Coefficient	Standard Error
Year dummies (relative to 1950s)				
1960s	.019	(.025)	.018	(.025)
1970s	$.068^{**}$	(.027)	$.064^{**}$	(.027)
1980s	$.153^{**}$	(.033)	$.142^{**}$	(.034)
Risk factors:				
Systolic blood pressure	—	—	-.00048	(.00035)

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Cholesterol	—	—	-.000003	(.00018)
Smoker	—	—	-.065[**]	(.019)
Diabetes	—	—	.003	(.026)
BMI	—	—	.011	(.012)
BMI^2	—	—	-.00016	(.00020)
N		1,704		1,704
R^2		.024		.032

Note: Data are from the Framingham Heart Study. Both regressions include age and sex dummy variables. [**] indicates statistical significance at the 5 percent level.

Risk factor changes in the pre-episode period explain only 7 percent of the change in acute survival rates. Smoking is the key variable; the coefficients on the other risk factors are not statistically significant. This regression attributes over 90 percent of the decline in acute mortality to intensive technologies. Since acute mortality fell by about 15 percentage points, this is about 11 percentage points.

The second strategy is to examine particular technologies that contribute to improved survival to see if they can plausibly explain an effect this large. This path has been taken by several studies in the literature, which we follow. Table 4.3 shows the calculations.

The earliest technologies were coronary care units and pre-hospital resuscitation. Goldman and Cook estimated that these technologies contributed significantly to lower mortality in the 1968-76 period.[9] Coronary care units are particularly important for the 4.5 percent of heart attack patients who have cardiac arrhythmia. Studies showed nearly universal survival with a coronary care unit and nearly universal death without. Thus, coronary care units were estimated to reduce mortality

by about 4 percentage points. A combination of basic and advanced pre-hospital resuscitation was estimated to lower acute mortality by about 2 percentage points.

Table 4.3: Impact of Intensive Technologies on Acute Survival

Technology	Mortality Odds Ratio	Use in 1985	Percentage point reduction in mortality
Coronary Care Units			4
Pre-hospital resuscitation			2
Other technologies			4
Medications			
Thrombolytics	.75	.09	.3
Beta-blockers	.88	.48	.7
Aspirin	.76	.30	.9
Anticoagulants	.80	.53	1.4
Nitrates	.94	.93	.7
Intensive procedures			
CABG	.85	.08	.2
Nonprimary angioplasty	.85	.04	.1

Note: Data are from Goldman and Cook and Heidenreich and McClellan.

A number of technologies followed these two innovations. New medications included thrombolytics, beta blockers, aspirin, nitrates, and anticoagulants. Not all of these therapies were new, but their use in heart attack patients was. In addition to these pharmaceutical technologies, there have been two major advances in revascularization surgery: coronary artery bypass grafting, and percuntaneous angioplasty. These technologies have some impact on the acute survival, but

even more impact on secondary survival.

Heidenreich and McClellan have summarized the evidence on the impact of these technologies on 30 day survival after a heart attack.[10] The odds ratios they report, along with the estimate of use in the acute phase, are shown in table 4.3. The last column shows the impact on mortality. In each case, we multiply the estimated odds ratio by the probability of 90 day mortality for the 1960 cohort and by the use in 1985. In total, these technologies explain about 4 percentage points lower mortality. The most important contributors to this were anticoagulation therapy, aspirin, and beta blockers. Thrombolytics have a very big impact on acute survival, but were still used at a relatively low rate in the mid-1980s.

In total, these technologies explain about a 10 percentage point decline in 90 day mortality after a heart attack. Table 4.1 shows a total decline of 13 percentage points in 90 day acute mortality. Thus, these technologies explain about 77 percent of the decline. This is near the amount implied by the residual method. It is also in the range of Heidenreich and McClellan, who estimate that innovations in medical treatment explain 60 to 80 percent of lower mortality. To be conservative, we assume that 77 percent of the reduction in acute mortality is a result of intensive technologies. An additional 7 percent is due to lower smoking. In the absence of more information, we allocate the remaining 16 percent to other, unexplained changes.

The timing of mortality change also matches this pattern. Figure 4.2 shows coronary heart disease mortality declining relatively steadily from the late 1960s on. This is consistent with a continuing diffusion of new innovations for treating heart attacks. Stroke mortality, in contrast, declines much more rapidly, and during a more concentrated period of time. This largely reflects hypertension treatment, as will be discussed. Further, the Framingham data show very little change

in acute survival between the 1948 cohort (having heart attacks in the 1950s) and the 1958 cohort (having heart attacks in the 1960s). But there is a large change over the next two decades, when the technologies were diffusing.

Since acute survival accounts for 38 percent of total changes in survival in the Framingham data, we attribute 29 percent (77 percent times 38 percent) to changes in intensive treatments. An additional 3 percent is attributable to changes in smoking. The remaining 6 percent is attributed to other causes.

Primary Prevention

We next consider the factors leading to improved primary prevention. Lower disease incidence may result from medications to control risk factors or behavioral changes. In principle, intensive medical technologies could influence disease risk. But over the time period we look at, intensive medical procedures were not a major part of primary prevention. Medications are most importantly antihypertensives and cholesterol-lowering drugs. More recently, aspirin has been used in primary prevention. The list of behaviors that may influence risk is lengthy. Standard factors include tobacco, obesity, fat/cholesterol intake, salt use, and heavy alcohol. There are several other medical and social factors that may influence disease risk. These are noted in the text.

Changes in Risk Factors. We start this analysis by understanding which risk factor changes are most important in affecting the incidence of disease. To do this, we once again use data from the Framingham Heart Study. We estimate Cox proportional hazard models for the probability of having a first cardiovascular disease incident. The sample is people without a previous incident.

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After some experimentation, we specified risk factors as: blood pressure (max(0, systolic pressure-140)); cholesterol (max(0, total cholesterol-200)); smoker (yes/no); diabetes (yes/no); obesity (BMI and BMI^2). Blood pressure and cholesterol are both allowed to affect risk non-linearly: at low levels, increasing blood pressure or cholesterol does not affect risk, while at higher levels increases in blood pressure or cholesterol do affect risk. For blood pressure, there is some evidence that both systolic and diastolic pressure influence disease, but the two are highly correlated, so the models fit just as well using systolic pressure only.

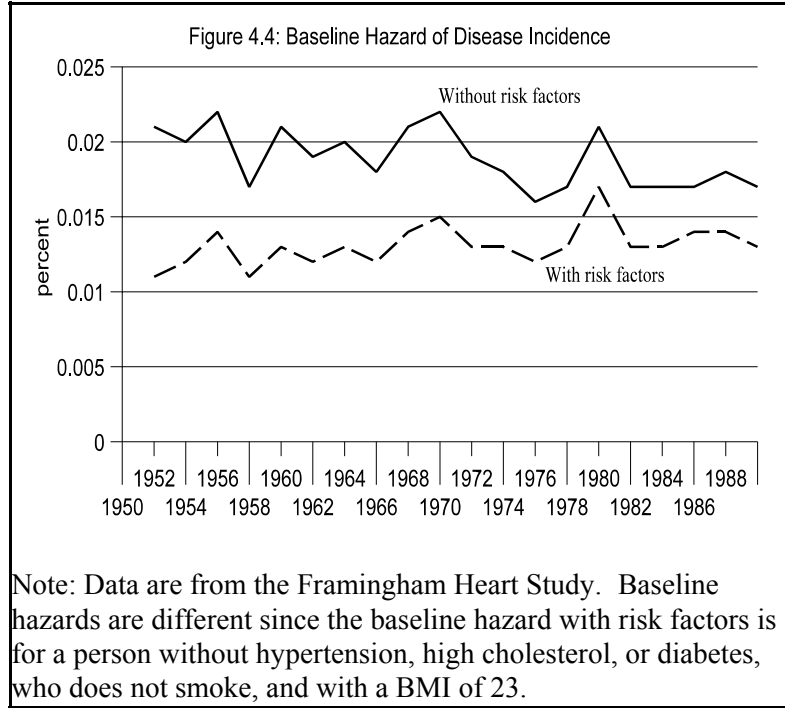The estimates from the proportional hazard models are given in table 4.4:

Table 4.4: Cox Proportional Hazard Models for
Cardiovascular Disease Incidence
[Dependent Variable: Incidence in Next Two Years]

Variable	Odds Ratio	Standard error
Systolic blood pressure	1.019**	(.001)
Cholesterol	1.004**	(.0005)
Smoker	1.284**	(.057)
Diabetic	1.767**	(.107)
BMI	.965	(.028)
BMI^2	1.001**	(.0005)
Number of subjects	4,957	
Number of observations	58,041	
ln(Likelihood)	-19,446	

Note: Hazard models include dummy variables for five year age groups by sex. ** indicates statistical significance at the 5 percent level.

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All of the risk factors significantly affect cardiovascular disease incidence and do so in the expected direction.

The baseline risk hazard indicates how well our model explains the trend in incidence. Adjusted only for age and sex, the incidence of cardiovascular disease risk is falling. If risk factor

Figure 4.4: Baseline Hazard of Disease Incidence

Note: Data are from the Framingham Heart Study. Baseline hazards are different since the baseline hazard with risk factors is for a person without hypertension, high cholesterol, or diabetes, who does not smoke, and with a BMI of 23.

changes explain this trend, the baseline risk level controlling for risk factors should no longer be declining. Figure 4.4 shows that this is the case. Without the risk factors included, the baseline level of risk is falling over time. With the risk factors, it is constant or even increasing slightly. Thus, changes in these risk factors account for all of the reduction in cardiovascular disease incidence.

To measure the importance of different risk factor changes, we use national data from the Health and Nutrition Examination Surveys (NHANES) in 1971-75 and 1988-94. The NHANES are better for this purpose than the Framingham data because they are nationally representative. In addition, the NHANES data have better information on medications. The 1971-75 NHANES contains 4,126 people aged 45-74, and the 1988-94 survey contains 6,401 people.

In each of the NHANES years, we divided the sample into 384 cells: 12 age/sex groups; and groups for high blood pressure or not (systolic blood pressure above 140); high cholesterol or not

(total cholesterol above 240); smoker or not; obese or not (BMI greater than or equal to 27); and diabetic or not. Within each group, we measure average systolic blood pressure, average cholesterol, and average BMI and its square. We also measured the share of people in each cell. Not all cells have people in each year.

We then evaluated the cardiovascular disease risk for each cell, using the proportional hazard coefficients from the Framingham data. To get a national risk probability, we weight the cell means using the 1988-94 age and sex distribution of the population. To evaluate the importance of each risk factor to overall changes in disease incidence, we examine the change in the probability of an event based on the observed changes in that risk factor, holding the other factors constant. For example, to determine the impact of smoking on risk, we start with the 1971-75 data. We hold constant the total population in each age, sex, blood pressure, cholesterol, BMI, and diabetes cell. Then, we change the mix between smokers and non-smokers to the 1988-94 proportions. We then add up the total risk in the simulated population. Table 4.5 shows the results:

Start with the first column. The baseline probability of suffering a cardiovascular disease incident is for males aged 45-49 without any of the risk factors. For this group, 10 year disease incidence rates were 16.5 percent in 1971-75 and 14.6 percent in 1988-94, for a reduction of 12 percent.[11] This is very close to the decline in incidence probability between the 1968 and 1978 cohorts in the Framingham Heart Study data (9 percent), which is about the same period of time. Thus, the national data confirms that risk factor changes appear to explain the bulk of lower disease incidence.

Table 4.5: Change in 10 Year Cardiovascular Disease Incidence

	Total	Medication	Other
Probability of event, 1971-75	16.5%		
Probability of event, 1988-94	14.6		
Change resulting from:			
Hypertension	1.7%	0.9%	0.8%
Cholesterol	0.5	0.1	0.4
Smoking	0.5		0.5
Obesity	-0.2		-0.2
Diabetes	-0.1		-0.1
Total	2.4%	1.0%	1.4%

Data are from the National Health and Nutrition Examination Surveys for 1971-75 and 1988-94. Effects on cardiovascular disease risk are based on proportional hazard models from the Framingham Heart Study data.

As the next rows show, the most important factor in this change is reduced blood pressure. Blood pressure decline explains a reduction of 1.7 percentage points in disease risk. Changes in cholesterol and smoking also explain reduced incidence rates, while changes in obesity and diabetes work in the opposite direction. The latter two are quantitatively less important, however.

The importance of changes in hypertension is consistent with figures 4.2 and 4.3. Figure 4.3 shows that mortality from stroke fell particularly rapidly during the 1970s and through the 1980s. As the text noted, the early 1970s was the period when hypertension control became a priority, and when medication and action diffused rapidly.

Medication, Tobacco, and Other Factors. Reduced rates of hypertension and high

cholesterol may result from either increased use of medication or other factors. To estimate the share resulting from increased use of medications, we first determined the mean and standard deviation of blood pressure and cholesterol for people taking medication in 1971-75 and 1988-94. As Table 4.6 shows, medication became vastly more effective, and was used by many more people, in 1988-94 compared to 1971-75.

Table 4.6: Blood Pressure and Cholesterol for People Taking Medication

	1971-75		1988-94	
	Systolic Blood Pressure	Cholesterol	Systolic Blood Pressure	Cholesterol
No previous incident				
Mean (standard deviation)	153 (24)	—	141 (19)	237 (47)
Share taking medication	26%	—	55%	16%
With a previous incident				
Mean (standard deviation)	158 (24)	—	142 (17)	237 (45)
Share taking medication	48%	—	73%	39%
Note: Data are from the NHANES. The sample is people aged 45-74.				

We then simulate how changes in medication usage have affected the incidence of disease. In our simulation, we first increase the share of people in 1971-75 taking anti-hypertensive or cholesterol-lowering medication to the rates in 1988-94. The additional people using medication are a random sample of those with untreated hypertension or high cholesterol. One could imagine that treatments were given more to people at higher risk, but we do not have information on whether this is true. We then draw normal random variables for blood pressure and cholesterol among people who were actually taking medication in 1971-75 or are simulated to take medication. The

random variables have the mean and standard deviation shown in Table 4.6. Thus, new levels of blood pressure and cholesterol are obtained for the 55 percent of hypertensives simulated to be on medication (including the 26 percent already on medication) and the 16 percent of people with high cholesterol simulated to be on medication. Finally, we aggregate the simulated population to the same 384 cells as the original population and then estimate national risk percentages.

As the second column of Table 4.5 shows, about half of reduced hypertension results from increased medication, as does 20 percent of reduced cholesterol. The greater importance of anti-hypertensive medication than of cholesterol-lowering medication is consistent with the much greater share of people on anti-hypertension drugs in 1988-94 than on cholesterol-lowering drugs. Statin drugs were just being introduced in that time period.

The net result is shown in the bottom row of Table 4.5. Roughly 40 percent of primary prevention is a result of better and more commonly used medication. Reduced smoking explains about 20 percent of lower disease incidence. The remaining 40 percent is a result of other factors. We do not know exactly what these other factors are. Some of these factors are likely behavioral. For example, lower use of salt, reduced fat intake, and less heavy alcohol use will all lower hypertension. Other social and environmental changes could affect risk factors as well, however. In the absence of better data, we do not distinguish between these different factors.

We take these shares and apply them to the total change in cardiovascular disease mortality resulting from primary prevention. This gives us an estimate of the mortality impact of these channels through its impact on primary prevention.

<u>Secondary Prevention</u>

As with primary prevention, changes in secondary survival may result from medical advance, behavioral change, and other factors. The range of medical advance is larger in secondary prevention than in primary prevention, however. Intensive treatments provided during the acute or secondary phase can affect secondary survival. In addition, more medications are used for secondary prevention than primary prevention, including nitrates, antiarrhythmia agents, and beta blockers even in patients without hypertension.

Risk Factor Changes. We start by understanding how much of secondary prevention can be explained by changes in risk factors. To do this, we estimate hazard models for the probability of death in the next two years among people who have had an acute incident, using the Framingham Heart Study data. It is important to note that the sample for these estimates is much smaller than the sample for primary prevention. Thus, the results have more potential error associated with them.

After some experimentation, we entered blood pressure, cholesterol, and BMI as averages over the current and previous wave of the Framingham. The fit of the model when average data were used was better than the fit with just current data. (There was no difference in the model with primary prevention, in contrast). In addition to the demographic variables and the risk factors, we included a dummy variable for whether the incident was coronary heart disease or not, dummy variables for the first two waves after the event, and a time trend for additional years after that. None of these additional variables were statistically significant. Table 4.7 reports the results for the risk factors.

Table 4.7: Cox Proportional Hazard Models for Death
Among Acute Phase Survivors
[Dependent Variable: Death in Next Two Years]

Variable	Odds Ratio	Standard error
Systolic blood pressure	1.009**	(.002)
Cholesterol	1.002*	(.001)
Smoker	1.138*	(.090)
Diabetic	1.774**	(.143)
BMI	.912**	(.038)
BMI^2	1.001*	(.001)
Number of subjects	2,022	
Number of observations	11,303	
ln(Likelihood)	-5,231	

Note: Hazard models include dummy variables for five year age groups by sex, a dummy variable for whether the incident was coronary heart disease or not, dummy variables for the first and second waves after the incident, and a time trend for years after that.
**(*) indicates statistical significance at the 5(10) percent level.

The coefficients on the risk factors all have the expected sign, but their statistical significance is not as high as for primary prevention. Cholesterol and smoking, in particular, are only statistically significant at the 10 percent level. Further, the magnitudes of the blood pressure, cholesterol, and smoking coefficients are only half as large in the equation for secondary mortality compared to primary prevention. It is not clear whether this is due to a truly smaller impact on secondary mortality, or to the particular sample.

Changes in risk factors do not account for the bulk of the improvement in secondary survival. Figure 4.5 shows the baseline hazard rate for secondary mortality, with and without the risk factors included. Both hazard rates decline over time. The decline is smaller for the model with the risk factors, but not by a great amount.

Over the entire time period, risk factor changes explain only 5 percent of lower mortality. This rises to about 15 percent over the 1970s and 1980s, when mortality changes were larger. Using the NHANES data yields the same effect – about 15 percent of secondary survival improvement

Figure 4.5: Baseline Hazard of Secondary Mortality

Data are from the Framingham Heart Study. The mean hazard rate is different for the model with and without risk factors because the level of risk is evaluated for a person without hypertension, high cholesterol, or diabetes, who does not smoke, and who has a BMI of 23.
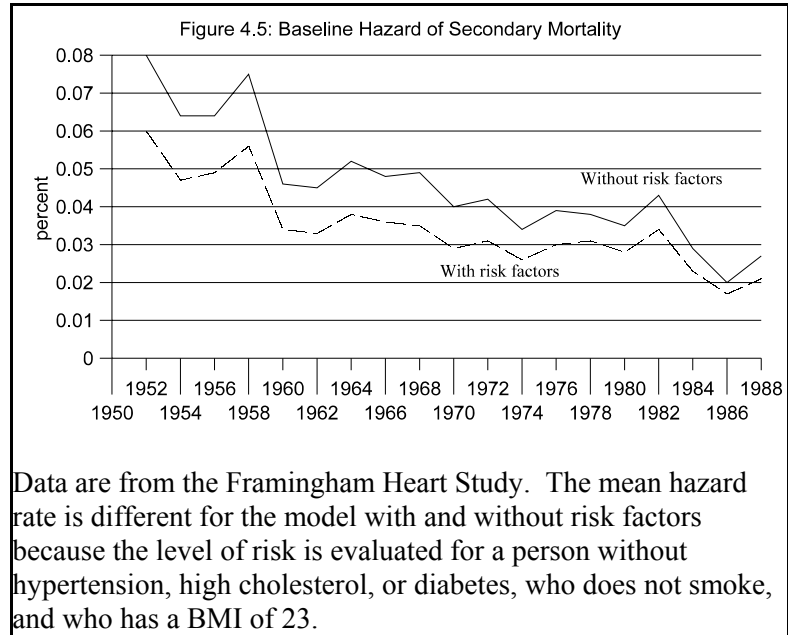
over the 1970s and 1980s is attributable to changes in risk factors.

In part, the small effect of risk factor changes in this time period is a result of offsetting trends. Blood pressure and smoking among people with cardiovascular disease declined greatly in the Framingham data. But diabetes rates were increasing. Since the impact of diabetes is estimated to be relatively much larger in the secondary prevention setting, the overall effect of risk factor changes is blunted. The increase in diabetes is somewhat particular to Framingham. In the NHANES data, diabetes rates were about the same from the early 1970s to the early 1990s. The difference might be due to self-report of diabetes in the NHANES compared to laboratory assessment in the Framingham data, but this seems unlikely, since diagnosis of existing cases was

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probably increasing over the period. In fitting the results to aggregate data, we assume that 15 percent of reduced secondary mortality is a result of an improved risk profile, consistent with the NHANES and Framingham data over the 1970s and 1980s.

We parcel out the change in risk factors into pharmaceuticals, tobacco, and other effects using the same methodology as for primary prevention. Medication explains the bulk of the change in risk factors. Blood pressure fell substantially among those with established cases of disease, and a substantial amount of this is because of increased medication usage. Smoking rates were virtually unchanged for survivors of a cardiovascular disease incident. This may reflect the impact of medical care on saving smokers who suffer from cardiovascular disease. In any case, the general reduction in smoking was not a big contributor to secondary prevention. Other factors explain some part of the decline in mortality, but a relative small share.

Intensive Treatments. Some of secondary survival is attributable to intensive treatments. The surgical technologies noted above have their primary impact on mortality beyond the acute phase. Bypass surgery, for example, has relatively little impact on mortality during the first few months after a heart attack, but a much greater impact a few years later. Angioplasty is the same way. These impacts would not be picked up by the risk factors discussed above.

We estimate the impact of these interventions using the same methodology as above. We first determined from the clinical literature the impact of these surgical techniques on survival. The most recent evaluation is from Mark et al. using data from the 1980s.[12] Mark et al. estimate that 5 year survival for bypass surgery patients was about half of what it would have been if those patients had been treated medically. (The effect of bypass surgery is greatest in patients with more disease,

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who fare poorly on medical management.) For angioplasty, the odds ratio is about 75 percent. The

Mark et al. intervention compared these surgeries to medical management as it was practiced in the

1980s. For our comparison, we want to evaluate surgery relative to medical management in the

1950s. To do this, we use the Heidenreich and McClellan estimate of the impact of medical

management on acute survival and combine that with the impact of surgery relative to medical

management. We assume that the medications in medical management affect only acute survival,

having no effect on secondary survival. Thus, the decline in mortality risk in the first 90 days

persists but does not get larger. We then multiply the effect of surgery relative to 1980s

management by the implied change in mortality of 1980s management relative to 1950s

management.

The result is shown in the first column of table 4.8. Relative to technology several decades

ago, 5 year survival after CABG or angioplasty is 40 to 60 percent lower.

Table 4.8: Impact of Intensive Technologies on Post-Acute Survival

Technology	Mortality Odds Ratio	Use in 1985	Percentage point reduction in mortality
Total			1.8
CABG	.39	.11	1.3
Angioplasty	.59	.06	.5

Note: See text for data sources.

Data on the use of these technologies after a heart attack comes from community studies in

Minneapolis.[13] In the mid 1980s, about 10 percent of patients received CABG and another 5 percent

received angioplasty. This matches well with Medicare data.[14]

The net impact is shown in the last column of the table. Use of surgical technologies following heart attacks can explain about 2 percentage points, or 14 percent of lower secondary mortality.

Non-Acute Pharmaceutical Use. In addition to these surgical technologies, pharmaceuticals are used in the post-acute period that help prevent disease recurrence. These pharmaceuticals have effects that are independent of the traditional risk factors. The most common medications used for post-acute management are aspirin, beta blockers, anticoagulants such as heparin and warfarin, and (now) ACE inhibitors. In the late 1980s, however, ACE inhibitors were generally not used for secondary prevention, so we omit this technology.

Several meta-analyses have estimated the impact of post-acute pharmaceutical use on mortality.[15] These estimates, except for ACE inhibitors, are shown in Table 4.9. The clinical literature also has estimates of the use of these technologies post-MI.[16] Table 4.9 shows these estimates as well. The last column reports the total impact on survival. These therapies reduce mortality by about 3.2 percentage points, or 24 percent of the total decline in secondary mortality.

Table 4.9: Impact of Post-Acute Medication on Survival

Technology	Mortality Odds Ratio	Use in 1985	Percentage point reduction in mortality
Total			3.2
Beta blockers	.77	.44	2.0
Aspirin	.83	.15	0.5
Anticoagulants	.78	.16	0.7
Note: See text for data sources.			

There is some interaction between the medications here and control of risk factors, particularly hypertension. Beta blockers are a common antihypertensive, and reduce heart disease risk more generally. To account for this, we reduce the pharmaceutical component of hypertension in the secondary prevention setting by half. This accords with evidence from the NHANES that about half of people taking an antihypertensive are using beta blockers.

Summary. We estimate that changes in risk factors explain 15 percent of reduced secondary mortality, changes in intensive treatments explain another 14 percent, and changes in post-acute use of medications 24 percent. In total, this adds to about 50 percent of secondary mortality. It is not clear what is responsible for the other half. There are certainly other medical interventions that we are not capturing. Other behavioral changes might also be important, however, as might the variety of social and environmental factors noted in the text. We do not have a ready way to parcel out these different factors.

In the absence of better data, we use two strategies to deal with the residual. First, we assign the residual to non-medical factors. This allows us to form a lower bound for the impact of medical advance on technology. We are also somewhat more certain of the technologies we have captured than the other factors. A second strategy is to attribute the residual in the same way we do the part we can identify.

Summary and Comparison to Other Literature

Table 4.10 shows the summary of factors influencing cardiovascular disease mortality. The

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first panel is our base case, where the unknown component of secondary prevention is assigned to non-medical factors. Intensive technology explains about one-third of better health. Non-acute medications are just over one-quarter, and behavioral and other factors are near 40 percent. The second panel instead apportions the residual component of secondary prevention to intensive treatment, post-acute medications, and behavioral and other factors based on the share we can explain. The shares are relatively similar.

Table 4.10: Summary of Factors Explaining Better Health

| Factor | Explanation | | | |
	Intensive Technology	Medication	Tobacco	Other
Assigning Unknown to Other				
Primary prevention	—	12%	6%	10%
Acute management	29%	—	3%	6%
Secondary prevention	5%	11%	-1%	19%
Total	34%	22%	8%	36%
Assigning Unknown Equally to All Categories				
Primary prevention	—	12%	6%	10%
Acute management	29%	—	3%	6%
Secondary prevention	9%	21%	-1%	5%
Total	38%	33%	7%	21%

Note: The totals are combined using the data in Table 4.1 showing that primary prevention explains 28 percent of reduced mortality, acute management explains 38 percent, and secondary prevention explains 34 percent.

A reasonable summary of this evidence is that each of the three factors – intensive technology, medications, and non-medical factors – explain about a third of mortality reduction.

While there is considerable uncertainty about the specific assumptions in the estimation, this uncertainty does not substantially affect the conclusions drawn. As noted in the chapter, the conclusions about the return to intensive technologies and behavioral research are robust to even very large changes in the mix of factors explaining better health. While we certainly make errors, we hope many of these will offset each other.

These results are consistent with other evidence in the medical literature. These findings are summarized in Table 4.11. Lee Goldman and Francis Cook were the first to analyze changes in cardiovascular disease mortality, considering the period from 1968 to 1976. They concluded that 54 percent of reduced mortality was a result of lifestyle improvements, most importantly reduced serum cholesterol levels and fewer people smoking. There was little effective medication for high cholesterol at that time, so this would have been entirely non-medical. An additional 19 percent was due to medical management of patients with heart disease or hypertension, in both cases predominantly through medication, and 21 percent was a result of intensive treatment of patients with disease.

Pamela Sytkowski, William Kannel, and Ralph D'Agostino, investigators on the Framingham Heart Study, have analyzed the sources of better health in the Framingham data.[17] Those authors estimate that about two-thirds of mortality reduction is a result of better risk factor control, and one-third is a result of acute treatments. Sytkowski, Kannel, and D'Agostino do not decompose the change in risk factor profiles into medical and behavioral factors although they speculate that both are important.

Finally, Maria Hunink, Lee Goldman, Anna Tosteson, Murray Mittleman, Paula Goldman, Lawrence Williams, Joel Tsevat, and Milt Weinstein built a simulation model to examine changes in cardiovascular disease mortality over the 1980s.[18] They concluded that 15 percent of mortality reduction over the 1980s resulted from acute treatment for heart attacks, 29 percent resulted from medical and surgical treatment of coronary artery disease, 25 percent resulted from primary prevention of risk, and 29 percent resulted from better risk factor control in people with pre-existing disease. The total role of intensive technologies in better health is the 15 percent case fatality plus some share of the 29 percent from treating patients with coronary artery disease. While an exact division of this amount is not available, it is likely to come close to the 33 percent presented here. The authors do not divide risk factor control into medication and lifestyle changes.

Table 4.11: Other Studies of Cardiovascular Disease Mortality

	Study		
	Goldman and Cook	Sytkowski et al.	Hunink et al.
Time period	1968-76	1950-80	1980-90
Intensive treatment	21%	33%	15%*
Non-acute medication	19%	47%	85%
Behavioral/other	54%		

* Estimate includes only case fatality for AMI. Authors estimate 29 percent of reduced mortality is from medical/surgical treatment of coronary artery disease, which includes some intensive treatment.

Social Status and Mortality

One of the hypotheses about improved health that has been put forward in the literature is that cardiovascular disease mortality is related to the nature of work. People in higher status

positions or with more job control are healthier than people in lower status positions. We do not have direct measures of job status in our data, but we do have measures of education. People who are better educated are on average in higher status jobs than people who are less well educated. We thus examined how education is related to cardiovascular disease health.

To do this, we estimated our models in the Framingham data including indicators for whether the person had a high school degree or some college education. In no regression were the education variables statistically significantly related to risk. Their coefficients were small, and the coefficients on the other variables were not materially affected. Education changes are thus not a major part of better health.

Chapter 5 – The Power of the Pill

In this appendix, I summarize the costs and benefits of treatment changes for people with depression. The work in the appendix is my own, but I am greatly aided by data provided by Ernst Berndt, Susan Busch, Richard Frank, Anupa Bir, and Sharon-Lise Normand. The interested reader is referred to the publications cited in the text. The data were originally collected by Berndt, Busch, and Frank, and I refer to it with their names.

Trends in Depression Diagnosis

The text notes the increase in diagnosis of depression over time. The source of the data on diagnosis rates is the National Ambulatory Medical Care Survey. I include as depressed anyone with a primary ICD-9 diagnosis of 296.2x and 296.3x (major depression), as well as other forms of depression given by ICD-9 codes 300.4x, 309.0x, 309.1x, and 311.xx. While major depression is strictly defined only as the first two codes, most primary care physicians seem to code depression rather loosely, and past studies using claims data generally use an expansive definition of patients.[19]

Figure 5.1 shows primary care physician diagnoses of depression over

Diagnosis of Depression , 1980-1998

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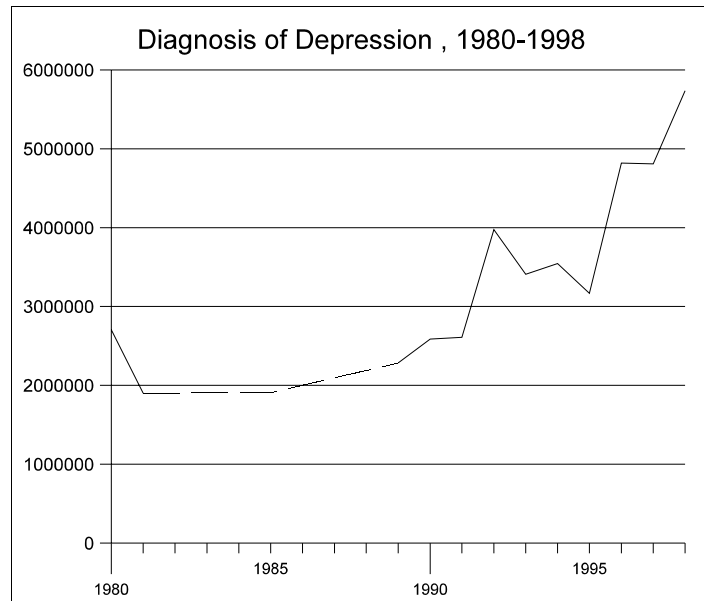
time. The number of diagnoses rose from about 200,000 in the mid-1980s to over 500,000 today.

The Costs and Benefits of Treatment Changes

The costs and benefits of treatment changes are calculated from the Berndt, Busch, and Frank data. The Berndt, Busch, and Frank data are from a number of large employers nationwide. There are over 2,000 episodes of major depression (defined as ICD-9 codes 296.2x and 296.3x) each year. The data are divided into episodes of treatment, periods of 90 days or more after a period without service use. To look at outpatient care for mental illness, Berndt, Busch, and Frank limit the sample to episodes without a hospitalization. Since hospitalization rates are falling over time, this works to overstate the growth of costs. Reimbursement is calculated for each episode and is based on all services used.

Efficacy of Treatment

Berndt, Busch, and Frank summarize the data into 34 types of care provided. To judge the efficacy of each treatment category, Berndt, Busch, and Frank, along with Bir and Normand convened an expert panel of psychiatrists and psychologists familiar with the clinical literature. This panel rated the efficacy of each treatment path for many different demographic groups.

Not all possible treatments were calculated for each demographic group. About 25 to 30 percent of cases were unrated by the panel. This is typically because the number of people in the cells was sufficiently small that it was not worth having the panel rate the efficacy of that combination. The share of episodes that are unrated falls over time, as more people receive standard therapy. Berndt, Bir, Busch, Frank, and Normand take three approaches to the unrated cases. The

first approach removes the unrated cases from the sample. The second approach assumes that the unrated cases have the worst possible outcome. The third approach assumes they have the median outcome. In forming my estimates, I follow the first approach. This understates the gains from care improvement, since the untreated cases likely received below average care.

The first step in the analysis is to translate these remission rates into expected weeks spent in full or partial depression. I designed a simulation model to do this. Data from Keller et al.[20] showed the path of remission from depression for a sample of people that was largely untreated. The data are for people with full or partial recovery, the latter defined as at least a 50 percent reduction in symptoms. I separated the data into the probability of full and partial recovery using the share of each group 3 months into the depressive spell, based on the clinical trials literature. The Keller et al. data are for specific periods of time after a depressive episode begins: one week, one month, three months, six months, and one year. I linearly interpolated between these intervals to form a remission probability by week.

The Berndt et al. expert panel estimated the probability of full and partial remission for different demographic groups after 16 weeks of treatment. I used these data to estimate remission probabilities under the different treatment paths for every week after the episode began. To do this, I assumed that treatment has no effect during the first two weeks of therapy. The two week interval with no improvement is designed to reflect the fact that most antidepressants do not take effect until about two weeks. I assumed that after this interval, the remission probability increased by the same percentage at all periods of time as the experts assessed the efficacy at 16 weeks.

As an example of this methodology, the estimates of the probability of full or partial remission for a person not receiving mental health care are: 3 percent after 1 week; 20 percent after

1 month; 35 percent after 3 months; 50 percent after 6 months; and 70 percent after 1 year. For the

group treated with maximum efficacy, the probabilities are: 3 percent after 1 week; 54 percent after

1 month; 63 percent after 3 months; 72

percent after 6 months; and 93 percent

after 1 year. Remission probabilities are

lower for less efficacious treatment

paths. Figure 5.1 shows this comparison.

Figure 5.1: Probably of Recovery from Depression

With these weekly estimates of

remission probabilities, I formed the

expected number of weeks in full and

partial remission under different
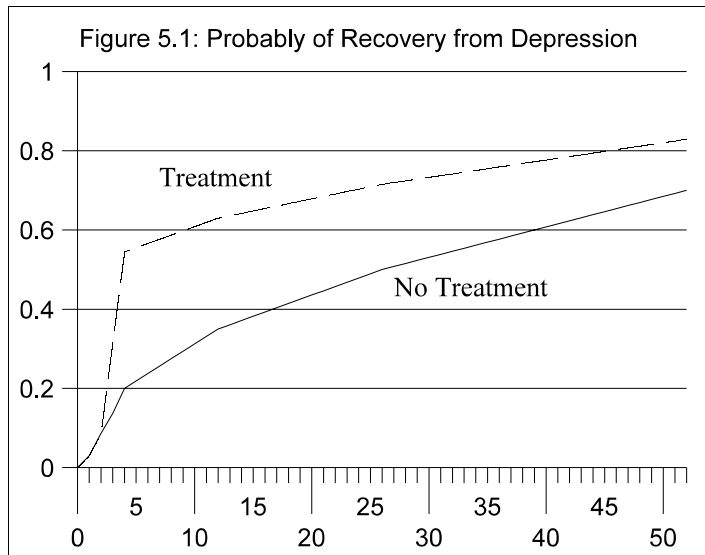
treatment paths. Without treatment, the estimates suggest that the typical person with depression

will experience 29 weeks with no recovery and 14 weeks with partial recovery. For the most

efficacious treatment, that falls to 17 weeks with no recovery and 16 weeks with partial recovery.

Note that weeks of partial recovery increase in this simulation, as a result of the large fall in time

spent with no recovery.

I experimented with including a relapse probability in the calculations, and thus more time

spent depressed. The literature suggests a 30 percent relapse probability for untreated remission.

But little is known about how relapse compares under different types of care. Since I am looking

only at the first year of treatment, when relapse will be smaller, I ultimately did not include this

effect.

Health Benefits of Depression Treatment. The health gains from depression treatment result from the fact that people spend less time depressed, which raises their quality of life. To value these gains, one needs to know the quality disutility to assign to being depressed. The literature has a number of estimates of quality reduction associated with depression, cited in the text.[21] The estimates range from -0.1 to -0.6 on a scale where 0 to 1 is the difference between death and perfect health. A rough consensus is a value of about -0.4. I use this as the quality disutility for full depression. For partial recovery, I assume half this loss and use a quality disutility of -0.2.

Note that this estimate of health benefits is only part of the possible gains. Depressed people are more likely to commit suicide than people who are not depressed, and these savings should be included as well, net of the avoided pain from future time not spent depressed. The literature is not clear on whether treatment efficacy is related to suicide. Without good data I do not include any effect from reduced suicide.

Economic Benefits of Depression Treatment. The economic benefits of depression treatment are those associated with the ability to work and earn. Several papers in the literature provide the basis for these estimates. The most recent contribution is by Ettner et al., which I follow.[22] I include two economic benefits. The first is the additional time a person spends at work when treated compared to not being treated. Ettner et al. estimate that people with depression are about 7 percent less likely to be employed than are people without a psychiatric disorder. The average person without a psychiatric disorder earns about $25,000 per year (in the early 1990s). Multiplying these two numbers, I estimate that each year being depressed results in nearly $2,000 less income. I assume this loss is suffered during times of full depression, but that people with partial recovery

return to work at that point.

In some cases, this loss may be split between the employer and the employee, if the person is on leave from a job some of the time. While this matters for the income of the person, it does not matter for society as a whole. Losses to both employers and employees are losses to society as a whole. Thus, I count the two together.

The second benefit is greater productivity on the job. People who are depressed are not as productive on the job as people who are not depressed. Ettner et al. estimate that earnings are about 6 percent lower for workers who are depressed than for workers who are not depressed. I assume that this lower productivity applies to people with both full and partial depression. This loss is multiplied by the number of weeks the person spends in either full or partial depression.

This calculation ignores one long-term economic benefit of treating depression: the fact that people treated for depression may stay in school longer and get more education. Estimates suggest that early onset depression is associated with less schooling and thus a reduction in future earnings.[23] But no estimates indicate the extent to which a shorter duration of depression increases educational attainment. In the absence of such estimates, I omit this factor.

Preview of Comparisons

To examine the impact of changes in medical care, I divide the population into two groups: people newly diagnosed with depression, and people who were previously diagnosed and switched from another therapy to SSRIs.

<u>Costs and Benefits of Treatment Changes Among The Newly Treated</u>.

The first part of the analysis considers the costs and benefits of treating people for depression who were otherwise undiagnosed. I consider a person who was not diagnosed with depression in 1991 and the corresponding person diagnosed with depression and treated with an SSRI in 1996.

Table 5.1 shows the costs and benefits of treatment change for this group. According to the Berndt, Bush, and Frank data, treatment with an SSRI costs about $673 on average, including physician and psychotherapy visits that sometimes accompany the use of SSRIs. We do not know exactly what treatments people would have received were they not diagnosed with depression. I assume that the person would have had 2 office visits, costing about $100. The same cost would be approximately right for an office visit and anxiolytic medication. Thus, the net cost increase is thus about $600.

Table 5.1: Costs and Health Impact of Treatment for Newly Diagnosed Depressed People

	1991	1996	Change
Average Cost	$100	$673	$573
Weeks with full symptoms	27.9	17.7	-10.2
Weeks with partial symptoms	13.5	17.0	3.5

The benefits from this additional treatment is significantly lower time spent depressed. Using the model above, the amount of time a depressed person will spend with severe symptoms falls by 10.2 weeks with SSRI treatment. Three and a half of these weeks are spent with partial symptoms, but most are symptom free. With a quality of life disutility from unremitted depression

of -0.4 and of partially remitted depression of -0.2, the improvement in quality of life is .07 years. At a value of $100,000 per year, this totals $6,500.

In addition to these health benefits are the economic benefits of more time and work and higher productivity on the job. Using the methodology above, this is about $600 of increased productivity. These benefits are summarized in table 5.2. The benefits are 10 times greater than the costs.

Table 5.2: Benefits of Treating Depression

	Change
Health Benefits	$6,500
Economic Benefits	$589
- Value of additional weeks at work	$388
- Value of increased productivity	$201

Costs and Benefits of Treatment Changes Among Those Treated

The second part of the analysis considers the costs and benefits of treatment changes among those who were diagnosed with depression prior to SSRIs but had access to new therapies with the advent of SSRIs. Table 5.3 shows the treatment changes that occurred between 1991 and 1996. Over this time period, the share of patients treated with psychotherapy only or TCAs fell, and the share of patients treated with SSRIs increased. Other therapy includes treatments such as lithium, potentially with other medications. Many of these medications (including lithium) are not associated with improved outcomes for patients with major (or unipolar) depression.

Table 5.3: Treatment Changes Among those Diagnosed with Depression

	1991	1996	Change
Psychotherapy only	51%	48%	-3%
TCA (with or without psychotherapy)	6	1	-5
SSRI (with or without psychotherapy)	18	28	10
Other	25	23	-2

Because the 1991 to 1996 time period is relatively short, the treatment changes are not particularly large over this time period. For example, SSRI use was already at 18 percent by 1991 and TCA use had already declined to 6 percent. A longer time period would show even more dramatic changes in treatments.

Table 5.4 shows costs and benefits of treatment changes over this time period. Average spending per person with depression was constant over the time period, at about $500 per case. The reason for this was noted in the text: Including physician visits as well as medication, an episode of SSRI care is about the same cost as an episode of TCA therapy. A full course of psychotherapy is more expensive than either of these two, but many people do not stay in that option for the full course. At the number of visits people actually experience, the cost of psychotherapy is about the same as the cost of medication.

Because of the switch from psychotherapy in particular, the average person with depression received more effective care in 1996 than in 1991. The reduction is about one half week with any symptoms.

Table 5.4: Costs and Benefits of Treatment Changes for Patients with Depression

	1991	1996	Change
Average Cost	$504	$505	$1
Weeks with full symptoms	22.9	22.1	-0.8
Weeks with partial symptoms	15.3	15.5	0.2

Note: Costs are in real ($1996) dollars.

The health and economic benefits of this change are shown in table 5.5. The health benefits are about $500, which come from the reduction in time spent with severe depressive symptoms. The economic benefits are another $50. The net benefits are thus about $550. This is not large, but it does show a benefit.

Table 5.5: Health and Economic Benefits of Less Time Depressed

	Change
Health Benefits	$538
Economic Benefits	$48
Value of additional weeks at work	$30
Value of increased productivity	$18

Chapter 6 – Medical Care: Of What Value?

The chapter describes a calculation comparing the benefits of medical technology change resulting from cardiovascular disease and infant mortality and the costs of medical advance in the medical system as a whole. In this appendix, I explain the details of this calculation.

The appendix for chapter 3 presented data showing that the average low birth weight infant lives an additional 15 years today over 1950. Given the share of low birth weight babies in the population, this translates into 0.6 years of additional longevity per infant born. Because of reduced cardiovascular disease mortality, the average person lives an additional 4½ years today over 1950. About two-thirds of this, or nearly 2.7 years of life, is attributable to medical care improvements. Combining these two values yields an additional 3.4 years of life attributable to medical advance.

The benefits of this advanced can be found assuming a value for a year of life. At a value of $90,000 per year, reflecting the fact that not all years will be in good health, the gains in longevity are worth $50,000.

Medical spending in 1950 was about $500 per person per year. Over the course of a person's lifetime, this is about $10,000 in present value. In 1990, annual medical spending per person was near $4,000. Over the course of a person's life, this is about $60,000 in present value. The increase in medical spending as a whole is therefore about $50,000 in present value, about equal to the longevity improvements from better treatment of low birth weight infants and people with cardiovascular disease.

Notes

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2. Data on infant mortality are from the United States, Centers for Disease Control and Prevention, National Centers for Health Statistics.

3. Data for 1950 are from H.C. Chase, *A Study of Infant Mortality from Linked Records: Comparison of Neonatal Mortality from Two Cohort Studies, United States, January-March 1950 and 1960*, United States, National Center for Health Statistics, Vital and Health Statistics, Series 20, Number 13, June 1972.

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7. Saroj Saigal, David Feeny, Peter Rosenbaum, William Furlong, Elizabeth Burrows, and Barbara Stoskopf, "Self-Perceived Health Status and Health-Related Qualify of Life of Extremely Low Birth Weight Infants at Adolescence", *Journal of the American Medical Association*, 276(6), August 14, 1996, 453-459; Saroj Sagal, Peter L. Rosenbaum, David Feeny, Elizabeth Burrows, William Furlong, Barbara L. Stoskopf, and Lorraine Hoult, "Parental Perspectives of the Health Status and Health-Related Quality of Life of Teen-Aged Children Who Were Extremely Low Brith

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8.   See Mark McClellan, Barbara J. McNeil, and Joseph P. Newhouse, "Does More Intensive Treatment of Acute Myocardial Infarction In the Elderly Reduce Mortality?: Analysis Using Instrumental Variables." *Journal of the American Medical Association,* 272(11):859-866, September 21, 1994.

9.   Lee Goldman and E. Francis Cook, "The Decline in Ischemic Heart Disease Mortality Rates: An Analysis of the Comparative Effects of Medical Interventions and Changes in Lifestyles", *Annals of Internal Medicine*, 1984; 101: 825-836.

10.   Paul Heidenreich and Mark McClellan, "Accounting for Changes in Survival for Heart Attack Patients", in David Cutler and Ernst Berndt, eds., *Medical Care Output and Productivity*, Chicago: University of Chicago Press, 2001.

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