Why Women Live Longer than Men

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Ruth C. Fretts, M.D., M.P.H. Harvard Medical School Women around the world have a survival advantage over men sometimes by as much as 10 years. What gives them the upper hand?

t is a fact of life that men enjoy certain physical advantages over women. On average, men are stronger, taller, faster and less likely to be overweight. But none of these attributes seem to matter over the long haul. For whatever the physical virtues of maleness, longevity is not among them.

Women, as a group, live longer than men. In all developed countries and most undeveloped ones, women outlive men, sometimes by a margin of as much as 10 years. In the U.S., life expectancy at birth is about 79 years for women and about 72 years for men. The gender discrepancy is most pronounced in the very old: among centenarians worldwide, women outnumber men nine to one. The gender gap has widened in this century as gains in female life expectancy have exceeded those for males.

The death rates for women are lower than those for men at all ages—even before birth. Although boys start life with some numerical leverage about 115 males are conceived for every 100 females—their numbers are preferentially whittled down thereafter. Just 104 boys are born for every 100 girls because of the disproportionate rate of spontaneous abortions, stillbirths and miscarriages of male fetuses. More boys than girls die in infancy. And during each subsequent year of life, mortality rates for males exceed those for females, so that by age 25 women are in the majority.

For us, these statistics raise two questions: Why do men die so young? And why do women die so old? From the outset we would like to admit that we have no definitive answers to these questions. But the available evidence implicates behavioral as well as biological differences between the sexes, differences in the effects of medical technology, as well as social and psychological factors. Ultimately, our investigation of the gender gap in life span has led us to posit an evolutionary explanation, one that suggests that female longevity is more essential, from a Darwinian perspective, than the prolonged survival of males. The good news is that in spite of this evolutionary imperative, the gap between male and female life expectancy may now be narrowing. The bad news is that some of this convergence may be the result of women suffering more from what used to be considered "male" diseases.

Toxic Testosterone

Comparison of the death rates for men and women in the U.S. at various ages reveals gender differences in mortality patterns [see graph on page 102]. Although death rates are higher for males than females at all ages, the difference between the sexes is more pronounced at certain stages of life. Between 15 and 24 years, for example, the maleto-female mortality ratio peaks because of a sudden surge in male deaths with the onset of puberty. During this period, men are three times more likely to die than women, and most of the male fatalities are caused by reckless behavior or violence. Motor vehicle accidents are the most common cause of death for males in this age group, followed by homicide, suicide, cancer and drowning. Interestingly, a surge in male mortality has been observed in other primates at a similar stage in life: in young adult male macaques, for example, rates of death and "disappearance" are high compared with those of female macaques.

The difference between male and female mortality declines until late middle age, when the mortality ratio plateaus. In the 55- to 64-year-old age group, behavior-related fatalities are still



Hormones, genetics and the fact that women go through menopause may explain why women live longer than men on average.

among the most common causes of death for men and are still much higher in men than in women. Men of this age are more than twice as likely as women to die in car accidents, for example, and almost four times as likely to take their own lives.

Illnesses related to smoking and alcohol consumption also kill more men than women in this age group. But heart disease is the main cause of the gender gap here. Men experience an exponential rise in the risk of heart disease beginning in their 40s; in contrast, women's risk of dying from heart disease does not begin to increase until after menopause, and it approaches the male risk only in extreme old age. Although the gender gap in this age group is smaller than the one described for young adults, the number of people affected by it is far greater. Whereas accidents claim the lives of 45 of every 100,000 young adult males annually, heart disease—the leading cause of death in men and women alike—kills 500 of every 100,000 men between the ages of 55 and 64 every year.

Experts suspect that gender differences in mortality patterns may be influenced at least in part by sex hormones, namely the male hormone testosterone and the female hormone estrogen. The conspicuous peak in the sex-mortality ratio at puberty, for example, coincides with increased testosterone production in men. Because the male hormone has been linked with aggression and competitiveness as well as libido, some researchers ascribe this spike in male mortality to "testosterone toxicity." Later in life, testosterone puts men at risk biologically as well as behaviorally. It increases blood levels of the bad cholesterol (known as LDL, for low-density lipoprotein) and decreases levels of the good one (HDL, for high-density lipoprotein), putting men at greater risk of heart disease and stroke.

Estrogen, on the other hand, has beneficial effects on cardiovascular health, lowering LDL cholesterol and increasing HDL cholesterol. A recent study at the University of Washington suggests that estrogen may exert these effects by regulating the activity of liver enzymes involved in cholesterol metabolism.

Estrogen is also an antioxidant—that is, it neutralizes certain naturally occurring, highly reactive chemicals, called oxygen radicals, that have been implicated in neural and vascular damage and aging. Emerging evidence suggests that treatment with estrogen after menopause reduces a woman's risk of dying from heart disease and stroke, as well as her risk of dying in general. Estrogen therapy has also been shown in some studies to delay the onset of Alzheimer's disease.

It is important to note that with the exception of this evidence regarding estrogen therapy, the relation between sex hormones and mortality patterns is still speculative. Furthermore, any attempt to explain mortality patterns must include the recognition that these trends are relatively recent. As the graph on the next page shows, the two divergences we have been discussing did not emerge until the middle of the century. Before that time, the sex-mortality ratio was constant across age groups for which data are available. The recent changes can probably be accounted for by two societal factors: improvements in obstetrical care, which have dramatically reduced women's risks of dying in childbirth, and an increased availability of guns and cars, which has contributed to more accidental and violent deaths in young males.

Historical Advantage

Although the reasons women live longer than men may change with time, it seems likely that women have been outliving men for centuries and perhaps longer. Even with the sizable risk conferred by childbirth, women lived longer than men in 1900, and it appears that women have outsurvived men at least since the 1500s, when the first reliable mortality data were kept. Sweden was the first country to collect data on death rates nationally; in that country's earliest records, between 1751 and 1790, the average life expectancy at birth was 36.6 years for women and 33.7 years for men. Death rates in less developed countries, whose citizens have limited access to cars, guns and maternal care, also provide a measure of mortality before modernity. At present, the only countries in which male life expectancy exceeds that for females are those with longstanding sexual discrimination including Bangladesh, India and Pakistan—where social pressures and practices such as female infanticide and bride-burning result in unique "losses" of females.

The fact that women live longer than men does not, however, mean that they necessarily enjoy better health. It could be that women live with their diseases, while men die from them. Indeed, there is a difference between the sexes in disease patterns, with women having more chronic nonfatal conditions—such as arthritis.

osteoporosis and autoimmune disorders—and men having more fatal conditions, such as heart disease and cancer.

Survival of the Fittest

To understand better the forces that control human aging and longevity, we have tried to determine whether the longer life span of females might be part of some grand Darwinian scheme. Gender differences in longevity have been observed in other members of the animal kingdom: in fact, in almost all species that have been observed in the wild, females tend to live longer than males. Female macaques live an average of eight years longer than males, for example, and female sperm whales outlive their male counterparts by an average of 30 years.

It seems that a species' life span is roughly correlated with the length of time that its young remain dependent on adults. We have come to believe that when a significant, long-term investment of energy is required to ensure the survival of offspring, evolution favors longevity—in particular, female longevity. Indeed, we believe that the necessity for female longevity in the human reproductive cycle has determined the length of the human life span.

We start with the assumption that the longer a woman lives and the more slowly she ages, the more offspring she can produce and rear to adulthood. Longlived women therefore have a selective advantage over women who die young. Long-lived men would also have an evolutionary advantage over their short-



COMPARISON OF DEATH RATES

Differences in the death rates of U.S. men and women have changed over the past century. Mortality has been consistently higher for men than for women at all ages (the male-to-female mortality ratio is more than one). In recent decades, however, this discrepancy has become even more pronounced at certain stages of life. SOURCE: Social Security Administration

er-lived peers. But primate studies suggest that men's reproductive capacity is actually limited more by their access to females than by life span. Hence, the advantage of longevity for men would not be nearly as significant as it is for women. And because males historically are not as involved in child care as females, in the not so distant evolutionary past the survival of a man's offspring depended not so much on how long he lived as on how long the children's mother lived.

One might think that the existence of menopause halts the transmission of a woman's genes and thus contravenes the evolutionary argument for female longevity. We think just the opposite: menopause confers a selective advantage and promotes longer life by protecting females from the increased mortality risk associated with childbirth at advanced age. Even today this increase in risk is considerable: a woman in her 40s is four to five times more likely to die in childbirth than a 20-year-old.

When menopause evolved, maternal mortality would have been much greater. If offspring require a significant maternal investment of time and energy to survive—which human children most certainly do—then there probably comes a point in a woman's life when it is more efficient to pass on her genes by caring for the children and grandchildren she already has than by producing and nurturing more children, risking death and the death of her existing children in the bargain. The argument that menopause is an evolutionary adaptation was first developed in 1957 by George C. Williams, now at the State University of New York at Stony Brook, and recent anthropological studies have supported it. Because human children are dependent for such a long time, continued health and longevity may enhance older women's contribution to the gene pool even when they can no longer reproduce.

In our own studies of centenarians, we have found that a surprising proportion of women who lived to be 100 or more gave birth in their 40s. One of our subjects had even had a child at the age of 53. We found that, overall, 100-year-old women were four times as likely to have given birth in their 40s as a control group of women, born in the same year, who died at the age of 73. This observation reinforces our suspicion that longevity is

linked with fecundity at an advanced age. Of course, we do not mean that having a baby in middle age makes a woman live longer. Rather, it seems that the factors that allow certain older women naturally to conceive and bear children a slow rate of aging and perhaps also a decreased susceptibility to the diseases associated with aging—also improve these women's chances of living a long time.

We propose that women's longevity edge over men may simply be a by-product of genetic forces that maximized the length of time during which women could bear and raise children and perhaps assist with grandchildren as well. Moreover, male longevity may simply be a function of the fact that men must carry the genes that ensure longevity to pass them on to their daughters. Thus, the necessity of female longevity in the human species may be the force that has determined the natural life span for both men and women.

The Secret to Living Longer

If female longevity is the product of evolutionary forces, then one might wonder what physiological mechanisms have evolved to support the preferential survival of women over men. As we have mentioned, sex hormones are thought to be important factors in determining the relative susceptibilities of the genders to aging and disease. Less obvious is the contribution that menstruation might make to longevity. Because of the monthly shedding of the uterine lining, premenopausal women typically have 20 percent less blood in their bodies than men and a correspondingly lower iron load. Because iron ions are essential for the formation of oxygen radicals, a lower iron load could lead to a lower rate of aging, cardiovascular disease and other age-related diseases in which oxygen radicals play a role. Indirect support for this theory comes from studies at the University of Kuopio in Finland and the University of Minnesota Medical School. In these studies, male volunteers who made frequent blood donations had less oxidation of LDL cholesterol-a key step in the development of atherosclerosis and heart disease.

Women also have a slower metabolism than men—a distinction that makes them more prone to obesity. But there may also be an inverse relation between metabolic rate and life span. Evidence of this link comes from animal studies of food restriction, which slows metabolic processes: in experiments sponsored by the National Institute on Aging, monkeys that ate 30 percent less of the same diet as their free-feeding peers seemed to age more slowly.

Studies of so-called clock genes in microscopic worms have also demonstrated the connection between metabolic rate and life span. Siegfried Hekimi of McGill University has observed that worms with particular mutations in these genes live five times as long as normal animals and have much slower physiological functions. Although it is still not known why men's metabolism rates are faster than women's, it is becoming clear that this difference is present almost from the moment of conception, when male embryos divide faster than female ones. The faster metabolic rate may make men's cells more vulnerable to breakdown, or it may simply mean that the male life cycle is completed more promptly than the female one.

Finally, chromosomal differences between men and women may also affect their mortality rates. The sex-determining chromosomes can carry genetic mutations that cause a number of life-threatening diseases, including muscular dystrophy and hemophilia. Because women have two X chromosomes, a female with an abnormal gene on one of her X chromosomes can use the normal gene on the other and thereby avoid the expression of disease (although she is still a carrier of the defect). Men, in contrast,

PERCENT OF U.S. POPULATION THAT IS FEMALE



Women outnumber men by age 25, when they make up 50.3 percent of the U.S. population; by age 100, women comprise 81.7 percent. SOURCE: Social Security Administration (1990 data)

have one X chromosome and one Y chromosome, and so they cannot rely on an alternative chromosome if a gene on one of the sex chromosomes is defective.

This disadvantage became more ominous when, in 1985, researchers at Stanford University reported the discovery on the X chromosome of a gene critical to DNA repair. If a man has a defect in this gene, his body's ability to repair the mutations that arise during cell division could be severely compromised. The accumulation of such mutations is thought to contribute to aging and disease.

There is also increasing interest in women's second X chromosome as a longevity factor in and of itself. Although one of the two Xs is randomly inactivated early in life, the second X seems to become more active with increasing age. It may be that genes on the second X "kick in" and compensate for genes on the first X that have been lost or damaged with age. This compensation could have a sizable influence, as it appears that roughly 5 percent of the human genome may reside on the X chromosome. In recent years the X chromosome has also become the focus of the search for genes that might directly determine human life span.

Closing the Gender Gap

Men and women alike have seen profound gains in life expectancy in this century. Since 1900, the average national increase in life expectancy in developed countries has been 71 percent for women and 66 percent for men. This increase cannot be explained by physiological or evolutionary theories. Rather, swift changes in knowledge of health and disease, changes in lifestyle and behavior, and advances in medical technology have greatly improved the chances of both sexes' living to old age.

In the past two decades, however, there has been a notable deceleration in the extension of life expectancy in women. The reasons for this decline are still being debated. Some researchers feel that women in developed countries are close to reaching the natural limits of human life span, and so their gains in life expectancy must inevitably diminish.

But some sociologists have discounted this reasoning, pointing instead to women's changing roles in society. As more women have taken on behaviors and stresses that were formerly confined to men—

smoking, drinking and working outside the home—they have become more likely to suffer from diseases that were traditionally considered "masculine." Mortality from lung cancer, for example, has almost tripled in women in the past two decades. Smoking seems to be the "great equalizer" for men and women: current actuarial data from Bragg Associates in Atlanta show that on average middle-aged female smokers live no longer than male smokers do.

In part because of these factors, men's and women's death rates in the U.S. have begun to converge in the past 20 years. But it is primarily the reduction in male mortality, as opposed to the increase in female mortality, that is narrowing this gender gap. In general, the higher a nation's level of social and economic development, the greater the life expectancy for both men and women and the greater the convergence in the two figures.

Research on sex hormones, sex chromosomes and gender-specific behavior is sure to further understanding of the human body well beyond the questions posed by the longevity gender gap. In exploring this intriguing phenomenon, investigators will undoubtedly find clues to how both men and women can live longer and more healthy lives.

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