Human Longevity, Individual Life Duration, and the Growth of the Oldest-Old Population

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CHAPTER 10. CAUSES OF DEATH AMONG THE OLDEST-OLD: AGE-RELATED CHANGES IN THE CAUSE-OF-DEATH DISTRIBUTION

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Introduction

In this chapter, age-related changes in the cause-of-death distribution are investigated. Vital statistics for the Caucasian population of the United States in 1991–1994 are analysed, with focus on differences between the oldest-old (85+) and the younger-old (65–84).

The distribution of deaths by cause reflects various characteristics of the population, including ecological environment, behaviour and life styles, genetic profiles of the population, availability of and accessibility to medical services, and the level of medical technology (Preston 1976; Vallin and Meslé 1988). The cause-of-death structure differs between males and females and varies substantially with age (Horiuchi 1999: Figure 2; National Institute of Population and Social Security Research 1999: Table 5.26).

Age-related changes in the cause-of-death distribution provide valuable information for ageing research for at least two reasons. First, the age variations should reflect physiological and behavioural changes with age. For example, if some organs of old persons tend to deteriorate faster than others, diseases of the organs are likely to be more prevalent causes of death at older ages. Second, age variations in the cause-of-death composition give important clues on individual differences in longevity. Suppose some persons are highly susceptible to particular diseases and they tend to die at younger ages from those diseases. Fewer of them are likely survive to older ages, thereby making those diseases less prevalent causes of death at older ages.

The cause-of-death distribution among the oldest-old is of particular importance for studying relationships between senescence and disease development. Causes of death that are prevalent at very old ages may be particularly strongly related to senescent processes.

The peculiar age pattern of mortality among the oldest-old adds to the importance of their cause-of-death structure. The age-associated increase of total (i.e., all-cause) mortality tends to slow down at very old ages in humans (Horiuchi and Wilmoth 1998; Thatcher, Kannisto, and Vaupel 1998) and a number of other species (Vaupel *et al*. 1998; Horiuchi

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2003). The mortality deceleration suggests that survivors to oldest ages may have genetic, environmental, and behavioural characteristics that are considerably different from those of the rest of the population. Observations of centenarians indicate that they are not the weakest segment of population but healthy people with special endowments (Perls, Silver, and Lauerman 2000). Characteristics of these special persons may be reflected in the cause-of-death profile of the oldest-old.

The age pattern of death rate at adult ages differs among major causes of death (Simms 1946; Kohn 1963; Horiuchi and Wilmoth 1997), suggesting that the cause-of-death structure of the oldest-old may be significantly different from those of the other age groups. Cause-specific death rates that rise with age steeply at ages 30–54 and cause-specific death rates that increase rapidly at ages 65–89 are considerably different, with only a few overlaps (Horiuchi *et al*. 2003).

The cause-of-death distribution among the oldest-old is important for medical economics as well. It has been found that the cost of medical services in the period preceding the death of an old patient tends to decline with age (Lubitz, Beebe, and Baker 1995; Scitovsky 1988, 1994; Temkin-Greener *et al*. 1992). This is partly because very old patients tend to be treated at less expensive hospitals and aggressive high-risk treatments are less likely to be applied to them. But the age-associated cost decline is also attributable to age differentials in the disease pattern (Perls and Wood 1996).

Causes of death reported in death certificates are not fully reliable (e.g., Crombie *et al*. 1995; reviewed in Manton and Stallard 1984: Chapter 2.3). Thus, a number of medical researchers studied autopsy findings and clinical records of old decedents and identified causes of death and other pathological conditions that are widely observed in very old persons. Puxty, Horan, and Fox (1983) reported that pneumonic diseases were the most common cause of death in old patients admitted acutely to hospital. Ishii, Hosoda, and Maeda (1980) listed bronchopneumonia, encephalomalacia (softening of the brain), myocardial infarction, gastric cancer, arteriosclerosis, and myocardial hypertrophy as the most prevalent diseases among the Japanese decedents who were 80 years or older. Klatt and Meyer (1987) examined autopsy and other medical records of 32 centenarians and concluded that atherosclerosis, neoplasia, and bronchopneumonia were common—but diabetes mellitus, obesity, hypertension, and cerebrovascular accident were absent or rare. Bordin *et al*. (1999) compared autopsy results between 114 extremely old decedents (97 years and older) and 151 younger ones (65–74) in Italy and found that extremely old persons tended to die of cardiovascular and respiratory diseases, and in most cases, of acute events.

Weinberg *et al*. (1989) indicated that infectious causes were the leading etiology for deaths in a nursing home. In another institutionalized population, the most common causes of death were bronchopneumonia, congestive heart failure, metastatic carcinoma, pulmonary embolism, myocardial infarction, and cerebrovascular event, in descending order (Gross *et al*., 1988). According to a study of centenarians in France (not based on autopsies), heart failure, respiratory failure, and chronic respiratory infection were among most prevalent diseases in morbid processes leading to 376 deaths (Allard *et al*., 1996). Hadley (1992) reviewed a number of autopsy studies and concluded that causes of death among the oldest-old were generally characterized by a high proportion of deaths due to cerebrovascular diseases and pneumonia, a low proportion of deaths due to cancers, and a relatively high proportion of deaths from chronic ischemic heart disease in comparison with acute myocardial infarction.

As for identifiability of cause of death, Kohn (1982) reviewed autopsy results of more than 200 decedents at age 85 and over, and reported that a clear manifestation of specific diseases was lacking in at least 30 percent of the cases. He proposed, therefore, "senescence" should be accepted as a cause of death. This argument was not supported by later studies that identified specific causes for most deaths among the extremely aged (Puxty *et al*. 1983; Bordin *et al*, 1999).

Although these clinical and pathological reports provide substantially more detailed and more accurate data on causes of death than death certificates, they are not without limitations. The decedents are often limited to patients of a certain hospital or residents of a certain nursing home and do not necessarily represent a regional or national population. The number of deaths is small, making it difficult to study age trajectories of the cause-of-death distribution, particularly with respect to less prevalent diseases. Thus, in research on causes of death, clinical reports and vital statistics based on death certificates should complement each other. An examination of death certificates of centenarians in Minnesota showed that congestive heart failure, atherosclerosis, neurological/mental conditions, and poorly defined conditions were major reported causes of deaths of centenarians (Gessert, Elliott, and Haller 2002). The present study uses U.S. vital statistics for investigating age-related changes in the distribution of causes of death among old persons in the large national population, with special attention to the oldest-old.

Data

Vital statistics on deaths in the U.S. from 1991 to 1994 are used in this study. Selected information on each death certificate is available on CD-ROMs published by the National Centre for Health Statistics (NCHS) of the USA (1997, 1998). The analysis is limited to White U.S. residents, because the focus of this study is on age variations in the cause-of-death structure in the elderly population, and reported ages among the Black elderly in the U.S. are not highly accurate (Preston *et al*. 1996, 1998). Data in the four calendar years are pooled together, in order to increase the statistical reliability of results for relatively uncommon causes of death.

The four calendar years (1991–1994) fall in the ICD9 period. Causes of death in the period were recorded according to the Ninth Revision of the International Classification of Diseases (ICD9). Although the data set includes multiple cause-of-death information, this study focuses on the "underlying cause of death," which is "(a) the disease or injury which initiated the train of events leading directly to death, or (b) the circumstance of the accident or violence which produced the fatal injury" (World Health Organization 1977:763). Multiple cause-of-death data are complicated and may require development of innovative statistical methodologies, which is beyond the scope of this paper.

It is well known that causes of death reported on death certificates are not highly accurate. A number of studies comparing death certificates and autopsy findings in several countries (including Australia, Germany, Iceland, Italy, Japan, and U.S.A.) have indicated errors in death certificates (Asnaes, Frederiksen, and Fenger 1983; Engel *et al*. 1980; Gloth and Burton 1990; Hasuo *et al*. 1989; Kircher *et al*. 1985; Kiyohara *et al*. 1989; Lee 1989; Maclaine, Macarthur, and Heathcote 1992; McKelvie 1993; Modelmog, Rahlenbeck, and Trichopoulos 1992; Mollo *et al*. 1986; Nielsen, Bjornsson, and Jonasson 1991; Poli *et al*. 1993). The number of deaths for each cause of death in vital statistics should not be automatically accepted at its face value. Nevertheless, if used with caution, cause-of-death statistics are an important source of information on health and mortality. Suppose similar age patterns of mortality are found for certain diseases that have some common pathological, physiological, or epidemiological characteristics. Then the age patterns may be related to the characteristics, possibly providing some clues on interactions between senescent processes and development of those diseases.

Method

For each age–sex category and each selected cause of death, the proportion of all deaths in the age–sex group that are attributable to the cause can be calculated. Age patterns and sex differentials of those proportions are compared among different causes of death. In this study, the proportion is denoted by $d_{ijk} = D_{ijk}/D_{\bullet jk}$, where D_{ijk} is the number of deaths due to the underlying cause i for the age group j and sex category k; and $D_{\bullet jk}$ is the number of all deaths for the age group j and sex category k.

Five-year age intervals from 0–4 to 95–99, and 100+, are used in the analysis of 35 selected cause-of-death categories (Figure 3). Although age variations in the cause-of-death distribution are examined for the entire age range, the focus of this study is on old ages. Hereafter, "old age" indicates 65 years and over, "oldest-old age" 85 years and over, and "younger-old age" 65–84 years.

The 95% confidence interval of the proportion is estimated using the standard procedure of Gaussian-distribution approximation. This approximation should be appropriate for most of the proportions in old age, because the data set is large and the selected causes of death are generally prevalent at old ages. (However, for several proportions computed from very small numbers of deaths, the approximation is not necessarily appropriate, so that confidence interval estimates for the proportions may not be accurate and the lower boundaries of the intervals may even become negative.)

There are a few different statistical approaches to mortality variations by age and cause. Age trajectories of *death rate* were previously compared among various causes of death (Simms 1946; Kohn 1963; Vallin and Meslé 1988: Chapter 10). This type of study includes age patterns of cause-specific life table ageing rate (Horiuchi and Wilmoth 1997, 1998) and calculation of cause-specific Gompertzian slopes (Horiuchi *et al*. 2003). Another type of statistics is the proportional distribution of deaths, which can be obtained in at least two ways: the distribution of deaths *by age for each cause*, as investigated by Vallin and Meslé (1988: Chapter 7), and the distribution of deaths *by cause within each age group*, as examined in this study. The distribution of deaths by age for each cause and sex is computed as $D_{ijk}/D_{i\bullet k}$, and the distribution of deaths by cause within each age–sex group is computed as $D_{ijk}/D_{\bullet jk}$.

Thus at least three different types of analysis must be distinguished: (a) age trajectories of cause-specific death rates, (b) age-distributions of cause-specific deaths, and (c) age variations in the cause-of-death structure. They are closely interrelated but have different strengths and limitations, thus complementing each other. In (a), it is not always easy to compare age patterns of cause-specific mortality. Death rates for most degenerative diseases rise steeply with age, making their age trajectories appear fairly similar. This problem applies to (b) as well. Age distributions of deaths for many degenerative diseases may look similar, with peaks concentrating in the narrow age range between 70 and 85. In contrast, age trajectories of (c) tend to be clearly distinguishable from each other, because the cause-of-death distribution measures *relative* differences in the prevalence of causes of death, independently of age-related changes in the total mortality and the total number of deaths. In (c), however, if the proportion of deaths from a certain cause declines with age, it is not clear whether the mortality from the cause decreases or increases with age (unless additional information is provided). The decline of the proportion may be due to an age-related decrease of the cause-specific mortality, or its relatively slow increase with age.

Selection of Causes of Death

Two sets of cause-of-death categories, nine broad categories (Figures 1 and 2) and thirty-five more specific categories (Figure 3) are used. Their definitions in terms of ICD9 codes are listed in Tables 1 and 2.

The thirty-five causes are mutually exclusive but not exhaustive. The set of thirty-five categories was developed through a trial-and-error process of combination, division, and elimination. Initially, the 282-category system prepared by NCHS (1998) was used, and

Table 1. ICD9 codes of the broad cause-of-death categories for Figures 1 and 2.

Broad cause-of-death category	ICD9 code
Infectious and parasitic diseases	001–139
Neoplasms	140–239
Heart diseases	390–398, 402, 404–429
Cerebrovascular diseases	430–438
Other diseases of the circulatory system	401, 403, 440–459
Diseases of the respiratory system	460–519
Congenital and perinatal disorders	740–779
Other diseases	240–389, 520–739, 780–799
External Injuries	E800–E999

Table 2. ICD9 codes of causes of death selected for Figure 3.

Cause of death	ICD9 code
septicemia	038
malignant neoplasms	140–208
diabetes mellitus	250
nutritional deficiencies	260–269
anemias	280–285
mental disorders	290–319
Parkinson's disease	332
multiple sclerosis	340
chronic rheumatic heart disease	393–398
hypertensive disease	401–404
acute myocardial infarction	410
coronary atherosclerosis	414
pulmonary embolism	415.1
heart failure	428
haemorrhagic stroke	430–432
infarctive stroke	433–434
other cerebrovascular diseases	435–438
atherosclerosis	440
aortic aneurysm	441
pneumonia	480–486
influenza	487
chronic bronchitis	491
emphysema	492
peptic ulcer	531–533
hernia of abdominal cavity	550–553
intestinal obstruction without mention of hernia	560
chronic liver disease and cirrhosis	571
renal failure	584–586
diseases of the integumentary system	680–709
senility without mention of psychosis	797
motor vehicle accidents	E810–E825
accidental falls	E880–E888
inhalation and ingestion accidents	E911–E912
suicide	E950–E959
homicide	E960–E978

categories with small numbers of deaths at old ages (less than 0.3% of all deaths at ages 65 and over) were mostly eliminated. (However, several cause-of-death categories which seemed important for ageing research were not eliminated even though their proportions were less than 0.3%.)

Some categories appeared to be heterogeneous mixtures of diseases. For example, the 282-category system includes "renal failure, disorders resulting from impaired renal function, and renal sclerosis, unspecified" as a single category. An apparently heterogeneous category like this one was, if possible, divided into subcategories, and the d_{ijk} pattern was examined for each subcategory.

In general, a category whose major subcategories exhibited similar age patterns in old age was not divided. Such categories include malignant neoplasms, nutritional deficiencies, anemias, mental disorders, chronic rheumatic heart disease, hypertensive disease, hemorrhagic stroke, infarctive stroke, pneumonia, ulcer of stomach and duodenum, chronic liver disease and cirrhosis, diseases of the integumentary system, motor vehicle accidents, suicide, and homicide.

A few remarks are needed about some of the cause-of-death categories. Diseases grouped together as "infectious and parasitic diseases" in ICD9 (001–139) constitute a less comprehensive category than the name usually implies. This group does not include some infectious diseases that are common in old age, such as influenza and kidney infections, as well as many types of pneumonia, bronchitis, chronic hepatitis, rheumatism, and various inflammations in the heart. In ICD9, these diseases are classified according to the organ systems (circulatory, respiratory, digestive, genitourinary, etc.) The ICD9 category of "infectious and parasitic diseases" mainly consists of highly contagious diseases that are prevalent in economically underdeveloped countries, such as cholera, diphtheria, tetanus, measles, typhus, and malaria.

"Hypertensive disease" (ICD9 code 401–404) and "atherosclerosis" (ICD9 code 440) are essentially "residual" categories after major diseases related to hypertension and atherosclerosis are placed in other categories (e.g., acute myocardial infarction, coronary atherosclerosis, haemorrhagic stroke, infarctive stroke). "Hypertensive disease" does not include those involving vessels of the heart, brain, or eye; and "atherosclerosis" does not include atherosclerosis of cerebral, coronary, mesenteric, or pulmonary arteries. Data on deaths that are reported as due to "diabetes mellitus" may be difficult to interpret, partly because Type 1 diabetes and Type 2 diabetes are not distinguished in ICD9, and partly because, when a person dies from a heart disease that was caused by diabetes mellitus, the underlying cause of death tends to be reported as heart disease, rather than diabetes mellitus, possibly deviating from WHO's definition of the "underlying cause of death." Special caution is also needed for "pulmonary embolism", which tends to be seriously under-diagnosed (Bordin *et al*. 1999; Green and Donald 1976; Poli *et al*. 1993).

Distribution of Deaths by Broad Cause-of-Death Categories

Figure 1 displays age variations in the number of deaths for both sexes combined in the U.S. White population during the four-year period from 1991 to 1994. The deaths are divided into nine broad cause-of-death categories. The figure indicates that the distribution is peaked in the age range of 80–84 and that heart diseases and neoplasms are the most dominant causes. However, it is difficult to draw more detailed information from the figure.

Figure 2 shows age variations in the proportional distribution of deaths by cause. Congenital and perinatal disorders are the main cause of death in the first year of life but their proportion

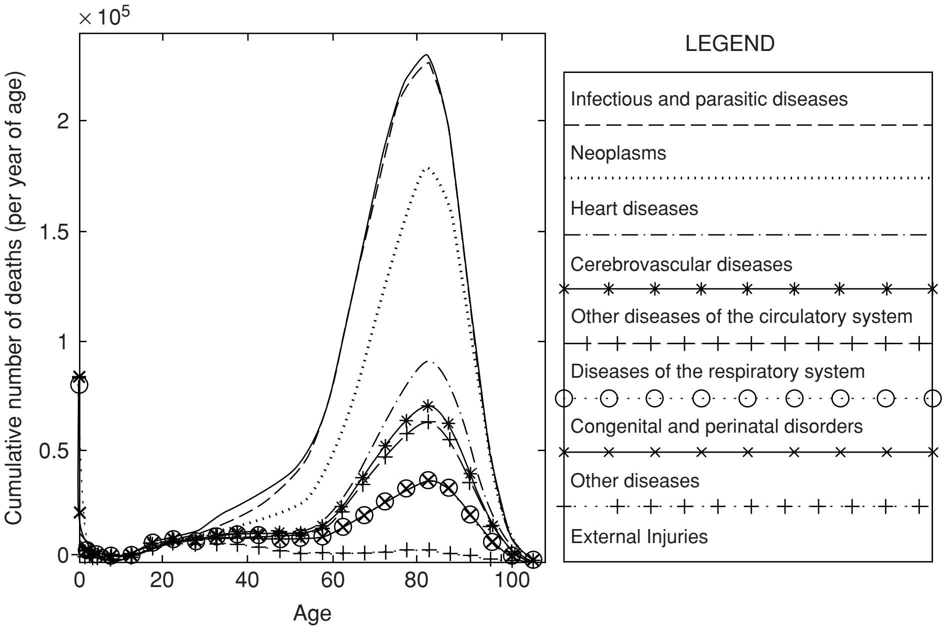

Figure 1. Cumulative number of deaths by cause, U.S. Whites, 1991–1994 combined. Each cause-of-death category corresponds not to a curve, but to the area between the two adjacent curves. For example, the number of deaths from heart diseases is represented by the vertical distance between the dotted line and the dash-dot line.

becomes almost negligible in adult years. The dominant cause of death at young ages is external injuries, which include accidents, poisoning, suicide, and homicide. About three-quarters of deaths around age 20 are due to external injuries. The proportion of deaths due to infectious and parasitic diseases remains low in both childhood and old age, but is notably high between the late 20s and the late 40s because of HIV infection.

The proportion of deaths from neoplasms rises steeply between ages 20 and 60. About 40 percent of deaths around age 60 are attributed to neoplasms. The proportion declines steeply after age 60, to only a few percent of deaths among centenarians. The proportion of deaths due to heart diseases increases with age throughout adult years. Also the proportion of deaths from cerebrovascular diseases rises with age up to around 90. About one-tenth of deaths at old ages is attributable to diseases of the respiratory system. The proportion of deaths due to respiratory diseases increases gradually with age.

Distribution of Deaths by Specific Causes

Figure 3 shows age patterns of the proportion of deaths for thirty-five selected causes. Vertical dotted lines are drawn at ages 65 and 85, indicating the lowest boundaries of “old

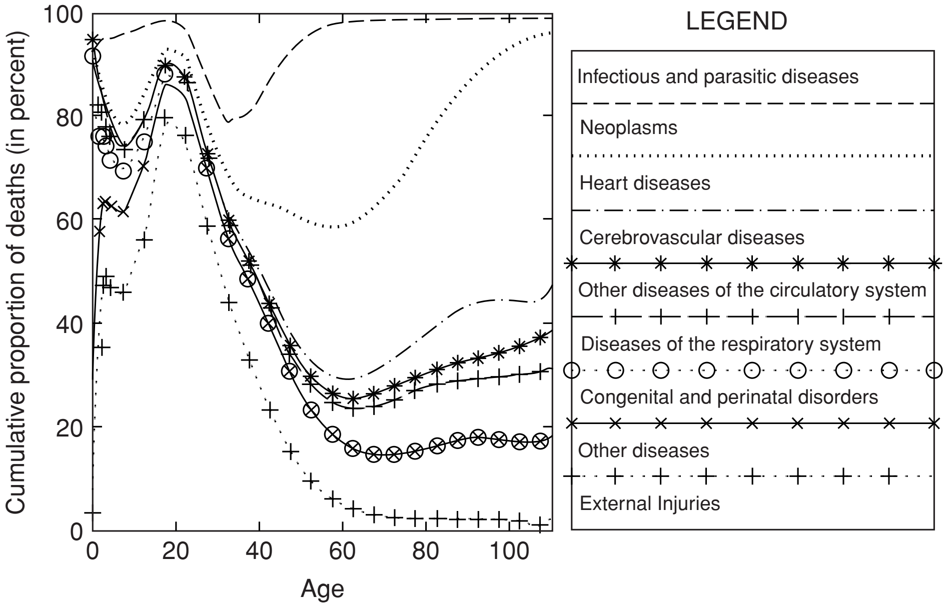

Figure 2. Age-related changes in the distribution of deaths by cause, U.S. Whites, 1991–1994 combined. Each cause-of-death category corresponds not to a curve, but to the area between the two adjacent curves. Namely, the proportion of deaths at the given age that are attributable to the cause-of-death category is indicated by the vertical distance between two adjoining curves. For example, the proportion of deaths from heart diseases is represented by the distance between the dotted line and the dash-dot line. The dotted line shows the proportion of all deaths at the given age from causes *other than* infectious and parasitic diseases and neoplasms. At age 60, the dotted line indicates 59 percent. The dash-dot line shows the proportion of all deaths from causes *other than* infectious and parasitic diseases, neoplasms, and heart diseases. At age 60, the dash-dot line indicates 29 percent. Thus, the difference (i.e., the vertical distance) between the two curves is the proportion attributable to heart diseases, which is 30 (59 minus 29) percent at age 60. (In this example, age 60 is chosen for simplicity, but actually the proportions are not given for single-year ages but for five-year age intervals, and points placed at the middle of the intervals are linked by curves.)

age" and "oldest-old age", respectively. The age trajectories in old age can be classified into three patterns: upward, downward, and bell-shaped. The proportion of deaths due to a certain cause may ascend with age (upward), descend with age (downward), or ascend then descend with age (bell-shaped). (There was no reversed bell-shaped pattern or consistently flat pattern.) We limit the label "bell-shaped" to those with peaks near age 85, and consider those with peaks near the beginning or end of the old-age range ("left-hooked" or "right-hooked") as special versions of "downward" or "upward", respectively. Only three curves in Figure 3 are identified as bell-shaped: Parkinson's disease for males and females, and

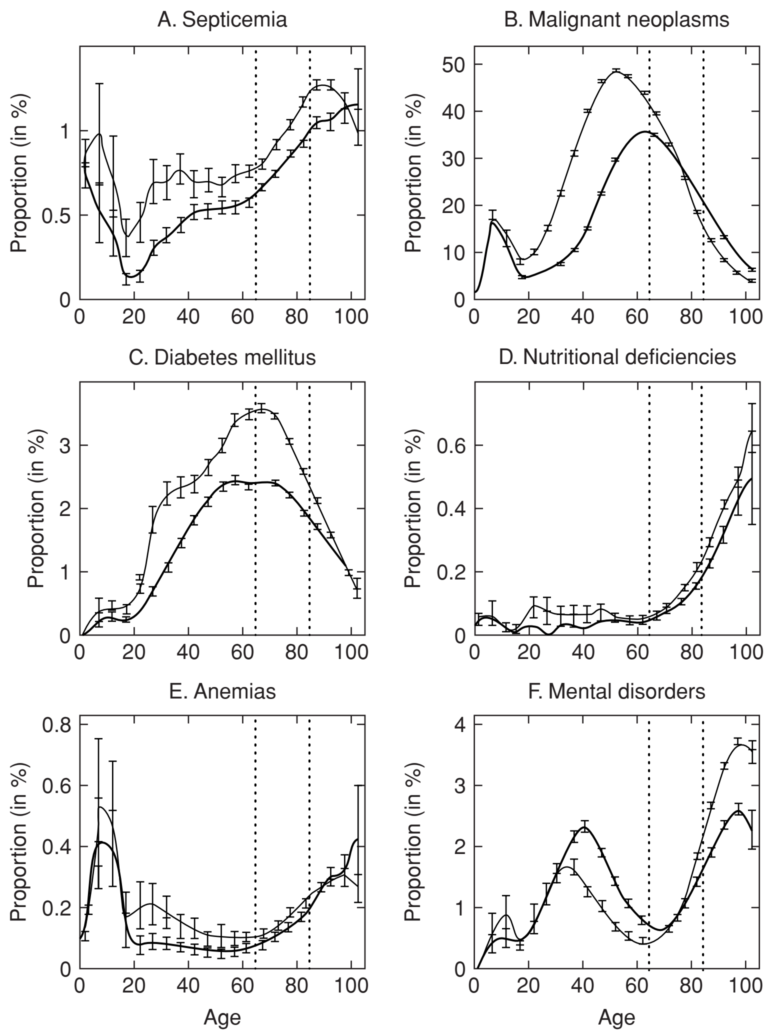

Figure 3. Age-related changes in the distribution of deaths by cause, for selected causes, U.S. White males (thicker line) and females (thinner line), 1991–1994 combined. The vertical axis indicates the proportion of all deaths at the given age that is attributable to the cause of death. The short bars show 95% confidence intervals. The two dotted vertical lines indicate age 65 and age 85.

acute myocardial infarction for females. Thus, most of the curves are classified as upward or downward in old age.

The proportion of deaths due to a given cause rises with age if the death rate from the cause increases with age faster than the total mortality (the death rate for all causes combined).

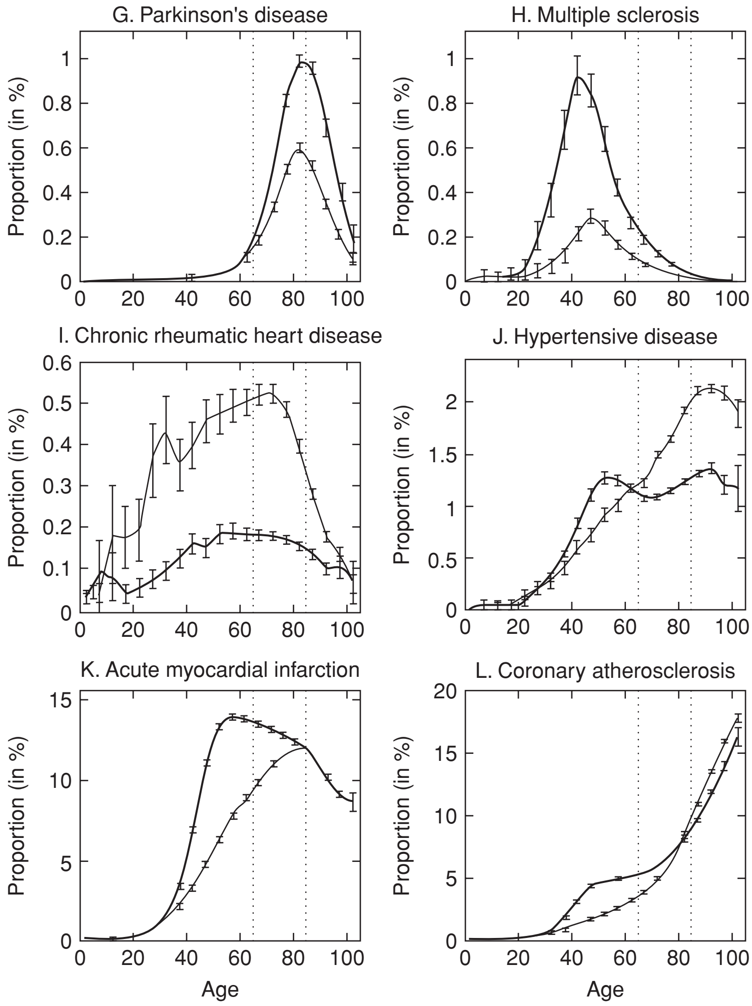

Figure 3. (*Continued*)

The proportion of deaths falls with age if the cause-specific death rate increases with age more slowly than the total mortality, or if the death rate decreases with age.

The age pattern differs notably among major degenerative diseases. The proportion of deaths due to malignant neoplasms declines steeply in old age (Figure 3B). All cancers are grouped together in Figure 3, because their patterns were similar: steep downward curves after peaks in the 40s, 50s or 60s of age, except for the late peak of prostate cancer in 75–79.

The downward patterns of cancers are consistent with the observation that deaths from cancers are infrequent among the oldest-old (Hadley 1992) and rare among centenarians

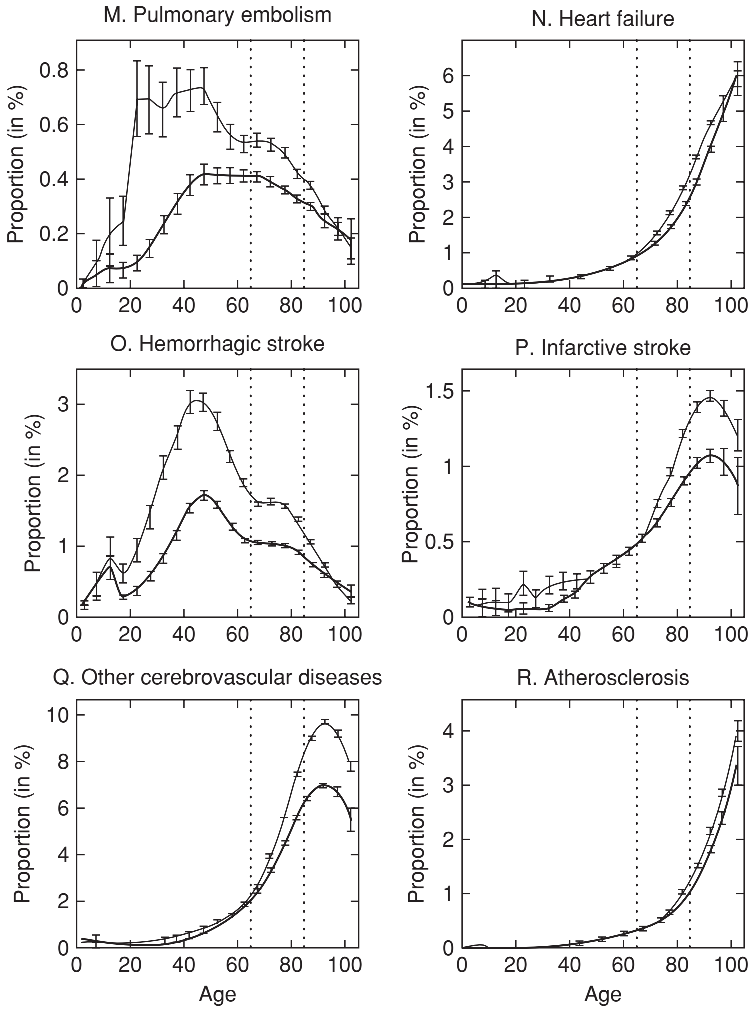

Figure 3. (*Continued*)

(Allard *et al*. 1996; Gessert *et al*. 2002). This seems partly due to selection: persons who are less likely to have cancers tend to survive to older ages. It may also be due to age-related changes in cancer development. Generally, cancers at older ages are slower, less aggressive/virulent, and less metastatic (Sarma 1987; reviewed in Bordin *et al*. 1999). It is difficult to determine which one of the two effects is the more dominant reason for the downward patterns of cancers.

For heart diseases, a sharp contrast is observed between acute myocardial infarction (Figure 3K)—which is downward for males and bell-shaped for females—and coronary atherosclerosis (Figure 3) and heart failure (Figure 3N), both of which are steeply upward. Another

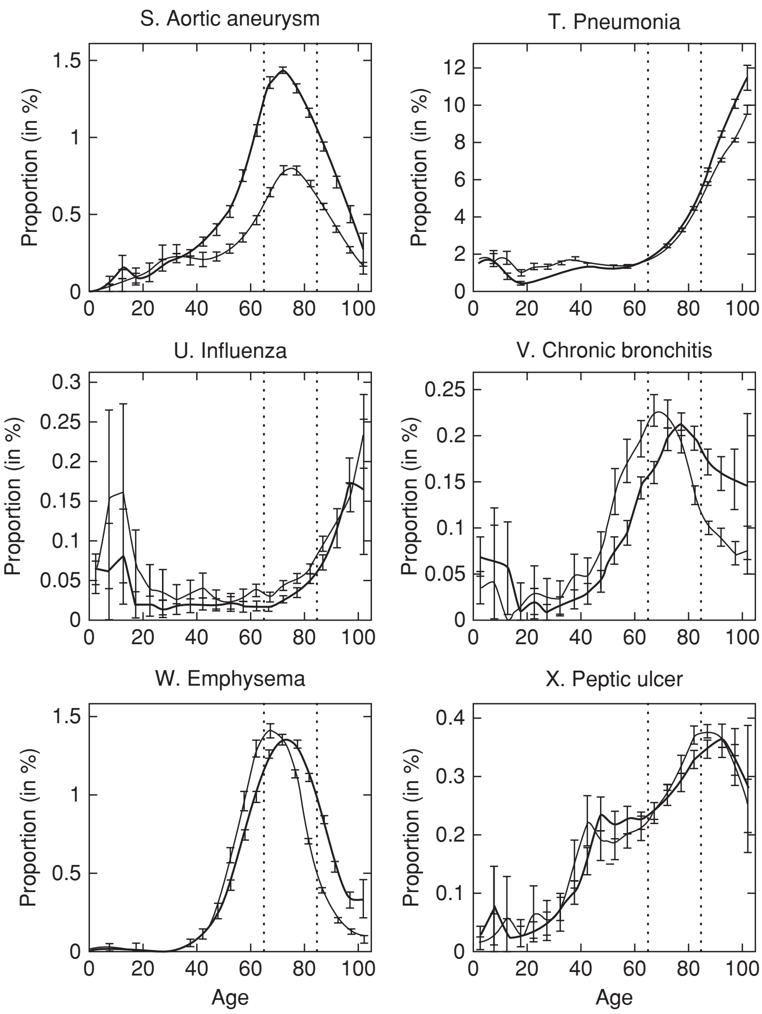

Figure 3. (*Continued***)**

sharp contrast is observed for cerebrovascular diseases, between the downward pattern of haemorrhagic stroke (Figure 3O) and the upward pattern (with a peak in oldest-old age) of infarctive stroke (Figure 3P). Although the majority of deaths due to stroke fall in the "other cerebrovascular diseases" category, their collective pattern (Figure 3Q) is similar to that of infarctive stroke. Thus, deaths classified in "other cerebrovascular diseases" may be predominantly infarctive.

The proportion of deaths due to pneumonia rises sharply from about 2 percent around age 60 to about 10 percent among centenarians (Figure 3T). Influenza, though less prevalent as a cause of death than pneumonia, follows a similar trajectory of steep increase (Figure 3U). **Au: Insertion O.K.? Ed.**

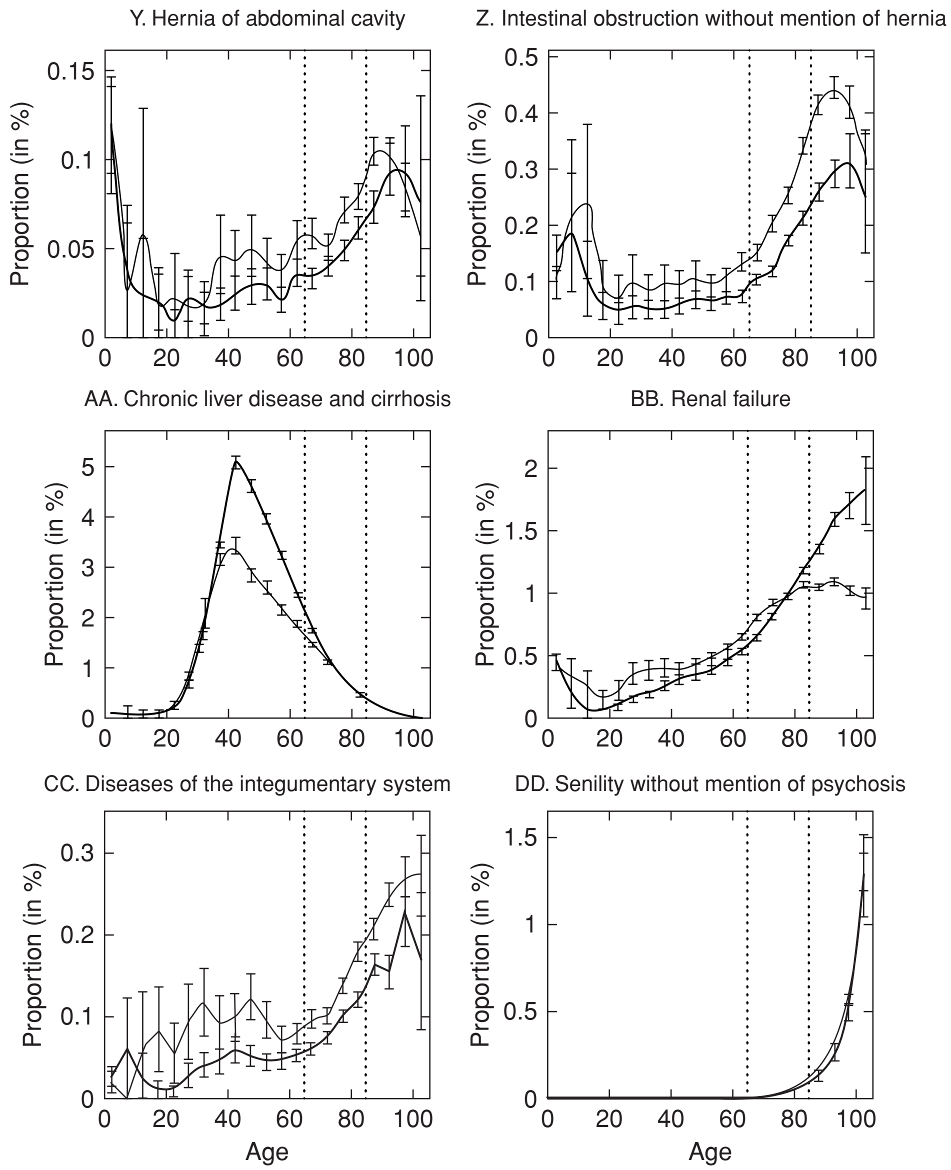

Figure 3. (*Continued*)

Most “infectious and parasitic diseases” (which, as described earlier, do not include many infectious diseases that are common among the elderly) have a very small number of deaths at old ages in the U.S. White population. The notable exception is septicemia, which constitutes about 70 percent of all deaths in this group and shows a clear upward pattern (Figure 3A).

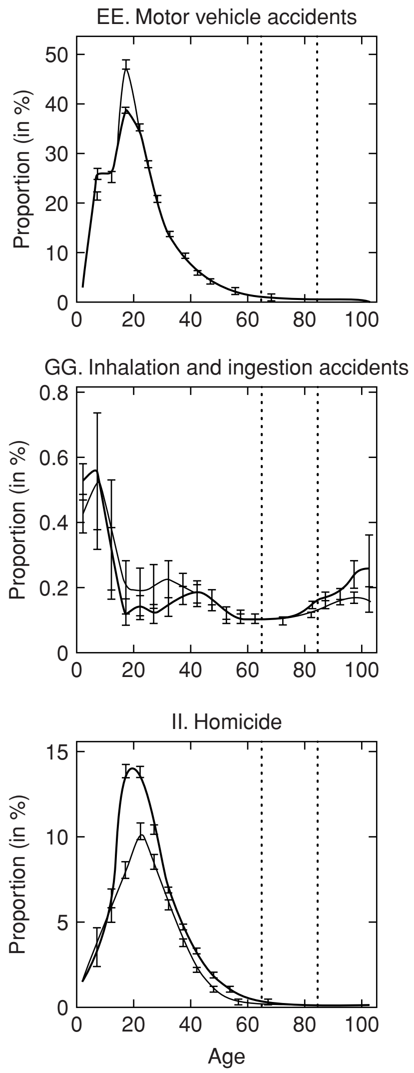

Figure 4. (*Continued*)

The trajectory of Parkinson's disease is bell-shaped (Figure 3G). Although some effects on Parkinson's disease of heredity, estrogen and folate levels, and exposure to insecticides and herbicides were found, risk factors of the disease have not been well established yet. However, its steep downward slope at oldest-old ages seem to suggest that the disease may be highly selective, too.

The proportions of deaths due to motor vehicle accidents, suicide, and homicide are substantially smaller at old ages than at young adult ages (Figures 3EE, 3HH and 3II). The

Table 3. Selected list of causes of death that characterize the oldest-old population.

More prevalent in 85+ than in 65–84[a]
septicemia
nutritional deficiencies
anemias
mental disorders
hypertensive disease (females)
coronary atherosclerosis
heart failure
infarctive stroke
other cerebrovascular diseases
atherosclerosis
pneumonia
influenza
peptic ulcer
hernia of abdominal cavity
intestinal obstruction without mention of hernia
renal failure
diseases of the integumentary system
senility without mention of psychosis
accidental falls
inhalation and ingestion accidents
Less prevalent in 85+ than in 65–84[b]
malignant neoplasms
diabetes mellitus
multiple sclerosis
chronic rheumatic heart disease
acute myocardial infarction (males)
pulmonary embolism
haemorrhagic stroke
aortic aneurysm
chronic bronchitis
emphysema
chronic liver disease and cirrhosis

[a] The proportion of deaths in 85+ due to the cause is higher than in 65–84.
[b] The proportion of deaths in 85+ due to the cause is lower than in 65–84.

downward patterns of motor vehicle accidents and homicide seem attributable to the declining exposure to risk, although older drivers have high risks when they drive (Bilban 1997; Dulisse 1997; Sjogren *et al*. 1993). In spite of the age-related increase of the death rate from suicide, the proportion of suicidal deaths declines notably in old age, because death rates from many diseases rise faster with age than the suicide death rate.

Table 3 shows two groups of causes of death: those for which the proportion of deaths is significantly higher among the oldest-old (85+) than among the younger-old (65–84), and those for which the order is reversed. As for the causes that are relatively more prevalent among the oldest-old, the following points seem noteworthy. First, the group includes some common diseases and injuries that seldom cause deaths at younger adult ages but become serious threats at very old ages (anemia, influenza, hernia of abdominal cavity, other types of intestinal obstruction, skin diseases, and inhalation and ingestion accidents). Secondly, a few diseases in the group are always or usually caused by infection (septicemia, pneumonia, and influenza). Thirdly, some are related to a frail musculoskeletal system and/or inappropriate neural control (accidental falls, inhalation and ingestion accidents, intestinal obstruction). Fourthly, debilitation and weakening of two major organs (heart failure and renal failure) are included. Lastly, the group seems pathologically more diverse than the other group, including diseases of the urinary, integumentary, and musculoskeletal systems as well as such causes as nutritional deficiencies and mental disorders.

These characteristics seem to reflect senescent processes that eventually make almost all individuals vulnerable to multiple pathologies. At middle ages and younger-old ages, deaths are largely limited to certain diseases such as malignant neoplasm, acute myocardial infarction, stroke, and liver cirrhosis. However, with the advancing age, various causes of death that are uncommon at younger ages become increasingly common. The resulting diversification of causes of death seems to reflect the long-term accumulation of unrepaired damage, leading to simultaneous deterioration of many physiological functions. The general ability to maintain homeostasis declines, making the person vulnerable to various kinds of physiological stress (Gavrilov and Gavrilova 1991). Particularly notable are the weakening of immune functions as well as the frail musculoskeletal system and the compromised ability to control physical movements of internal organs. Some major organs (such as the heart and the kidney) that have been severely debilitated by previous diseases and/or chronic problems may become too weak to function properly. The increasing proportion of deaths reported as "senility" (Figure 3DD) indicates the difficulty of determining the primary cause of death for a very old person with multiple weaknesses and limited reserve capacities.

Most causes of death that are relatively more prevalent among the younger-old than among the oldest-old seem to be diseases that tend to develop selectively and prematurely in some high-risk individuals at middle ages and younger-old ages. These diseases are known to be strongly associated with certain risk factors. They include malignant neoplasms (heredity, smoking, exposure to toxic materials), diabetes mellitus (heredity, diet, obesity, inactivity), multiple sclerosis (heredity), chronic rheumatic heart disease (acute rheumatic fever earlier in life), acute myocardial infarction (diet, smoking, heavy drinking, mental stress), haemorrhagic stroke (hypertension), chronic bronchitis (smoking), emphysema (smoking), and chronic liver disease and cirrhosis (chronic hepatitis and heavy alcohol consumption). Causes of death that are dominant at oldest-old ages have risk factors as well; but overall, their risk factor effects do not seem as strong as those of the diseases that are dominant at younger old ages. **Au: Sense ?**

Death rates from those diseases increase with age, partly because the diseases or conditions leading to the diseases tend to develop over decades. However, the proportions of deaths from those diseases decrease with age, probably because senescent processes do not necessarily make all individuals highly vulnerable to those diseases; and persons who have the risk factors are less likely to survive to older ages. Thus, the causes of death that are more prevalent among the younger-old do not seem to be associated with senescent processes as strongly as those that are more prevalent among the oldest-old.

Conclusion

In summary, causes of death that are more prevalent among the oldest-old than among the younger-old include heart failure, pneumonia, influenza, coronary atherosclerosis, infarctive stroke, septicemia, mental disorder, nutritional deficiency, and accidental fall. They seem to be strongly associated with senescent processes that eventually raise the general vulnerability of almost all individuals to multiple pathologies. Causes of death that are more prevalent among the younger-old than among the oldest-old include malignant neoplasms, acute myocardial infarction (particularly for males), haemorrhagic stroke, chronic liver disease and cirrhosis, diabetes mellitus, and multiple sclerosis. These diseases tend to develop selectively and prematurely in some high-risk individuals at middle ages and younger-old ages.

In textbooks of pathology and epidemiology, many degenerative diseases and some types of external injuries have been described, fairly uniformly, as having age-associated increases in incidence, prevalence, and mortality. Because death rates from most degenerative diseases increase with age, their age trajectories may appear similar. However, death rates from some diseases and injuries rise significantly faster with age than others, and those differences are clearly reflected in age variations of the proportional cause-of-death distribution. The simple analysis of the age variations in this study helps us to unambiguously distinguish major causes of death that are more prevalent among the oldest-old and those that are more prevalent among the younger-old and demonstrates the usefulness of information on age-related changes in the cause-of-death structure for gerontological research.

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