Chapter 10

Mortality in Insulin-Dependent Diabetes

Enrico Portuese, MPH, and Trevor Orchard, MD

SUMMARY

Early studies demonstrated a dramatic change in the pattern of mortality from insulin-dependent diabetes mellitus (IDDM) after the introduction of insulin therapy in the 1920s. A major shift occurred as diabetic coma, which predominated as a cause of death in the pre-insulin era, yielded to renal and heart disease after insulin became available. The majority of deaths in people with IDDM now occur in middle and late adulthood rather than soon after diagnosis.

Mortality rates among IDDM patients remain high. For childhood-onset cases, data suggest that >15% will die by age 40 years, at which time the annual mortality will be 20 times that seen in the general population. National data suggest that a downward trend in mortality for patients with IDDM occurred up to the early 1980s but may now be leveling off.

There is marked variation in the cause of death with increasing duration of IDDM. In the early years after diagnosis of IDDM, acute coma is the leading cause of death, while in the middle years renal disease predominates. After 30 years of IDDM, two-thirds of IDDM deaths result from cardiovascular disease. A strong link is seen between renal disease and cardiovascular death. Because death certificate data have many limitations in the examination of cause-specific mortality, more in-depth approaches have been developed to accurately classify cause of death in a standardized manner. These approaches also enable the role of diabetes to be more clearly defined.

Examination of risk factors for IDDM mortality show differences by sex, with female IDDM subjects having a relatively greater increase in mortality, compared with nondiabetic females, than is found for males. In particular, a relatively greater increased risk for ischemic heart disease mortality has been reported for women with IDDM. In IDDM, as in the general U.S. population, African Americans have a higher mortality rate than whites. A familial effect has also been described, wherein premature mortality in diabetic and nondiabetic relatives clusters in families in which there is a deceased IDDM patient. Smoking is an important predictor of all-cause mortality. Many other traditional cardiovascular risk factors, particularly hypertension, appear to be related to mortality in IDDM, but no clear association has been documented between lipids and lipoproteins and cardiovascular mortality. Onset of IDDM before puberty appears to be associated with a lower mortality rate than peripubertal onset.

Comparisons between U.S. populations and other countries reveal considerable differences. For example, a cohort of IDDM subjects from Allegheny County, PA had more than twice the mortality rate of IDDM subjects in Finland. Such findings raise potential concerns with regard to health care in the United States.

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STUDIES OF IDDM MORTALITY PRIOR TO 1980

Although many early studies included individuals with IDDM, a number of these did not differentiate between IDDM and non-insulin-dependent diabetes mellitus (NIDDM). Of the studies that made the differentiation, many were affected by various potential biases, especially selection biases, as in the case of life insurance enrollees[1] or clinic attendees[2,3]. One early study that attempted to avoid such bias was a population-based study in Erie County, NY[4]. Despite these limitations, these early reports provide useful data relevant to the study of IDDM mortality.

Mortality data were reported for individuals with IDDM who attended the Joslin Clinic in Boston, MA during 1897-1961[5]. A dramatic change in death rates

was observed immediately following the introduction of insulin in 1922. For example, in individuals who died at age ≤10 years during the earliest period (1897-1914, called the Naunyn Era[6]), the death rate was 824 per 1,000 diabetic patients, compared with 386.2 per 1,000 in the next period (1914-22, called the Allen Era[6]). During 1950-61, the rate had fallen to 1 per 1,000[5].

Investigators from Toronto, Canada, described clinical data on a cohort of 123 IDDM patients with age at onset of 1-14 years during 1922-31. Total mortality in these patients followed for up to 25 years was 47%. Coma was listed as the leading cause of death (64%)[7]. Another clinic-based study showed a 38% mortality rate for a group of 63 individuals diagnosed with diabetes during 1920-28 and followed for ≥20 years[8]. A group of St. Louis, MO patients diagnosed during 1922-43 also showed the beneficial effects of insulin treatment[9]. In this study, the majority of deaths in the earliest period (1922-33) were from acidosis, whereas deaths from acidosis did not occur in the later study period (1939-43).

In a 1956 study at the Joslin Clinic of 96 insulin-treated patients who survived diabetes for ≥35 years, 45 died during further followup[10]. Cardiovascular disease was the primary cause of death, and hypertension was noted to be twice as high in women as in men. Another study of Joslin patients focused on those diagnosed at age <2 years. Of 118 (58 male) patients diagnosed during 1922-56, 20 individuals had died at the time of followup in 1956-57, with more than a third dying at age <5 years[11]. Infections and coma accounted for more than half of the deaths, but no deaths from coma occurred after 1948.

A later followup found that there was an overall decline in mortality of the Joslin patients. Again, however, an increase in the proportion of deaths due to vascular disease was noted. Whereas diabetic coma accounted for one of every seven deaths in 1922-29, at the time of a more recent followup (1956-62), it was responsible for only 1%[2].

Mortality was examined among purchasers of life insurance. For those with diabetes diagnosed during 1935-63 at age <30 years and who were treated with insulin (and thus likely to have IDDM), mortality was increased sixfold compared to that expected based on the mortality experience of applicants issued standard policies[12]. The presence of both heart disease and cerebrovascular disease was extremely high in those with diabetes.

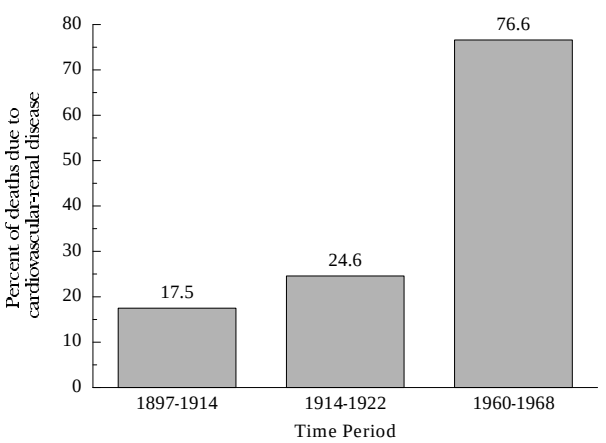
A Cincinnati, OH study whose purpose was to ascertain the effect of an unmeasured diet on the risk of vascular disease in a cohort of patients diagnosed at age <17 years compared cumulative mortality of groups from Boston, MA and Stockholm, Sweden. No major geographic differences were noted: at 25 years duration of diabetes, the cumulative mortality was 19% in Boston, 20% in Cincinnati, and 22% in Stockholm[13].

In 1972, the Joslin group reported that 76.6% of the 5,009 deaths that occurred in its clinical population during 1960-68 were caused by cardiovascular-renal disease[14]. Diabetic coma as a cause of death declined significantly relative to earlier periods, as did infections other than tuberculosis. When comparing the 1960-68 time period with the pre-insulin period, a dramatic increase in the proportion of deaths from cardiovascular and renal diseases was noted (Figure 10.1).

Finally, data comparing the mortality of diabetic to nondiabetic individuals who applied for life insurance at the Equitable Life Assurance Society of the United States during 1950-71 are available[1,15]. For the group with diabetes diagnosed at age <15 years, the mortality ratio was 11.3 (that is, the ratio of deaths in diabetic persons to the expected deaths derived from the nondiabetic population), giving an average life expectancy of only 32 years for individuals with childhood-onset diabetes.

In conclusion, these early studies show that the mortality pattern changed from acute metabolic complications to chronic complications following the introduction of insulin therapy. This raises the issue of how great is the current risk of mortality in IDDM and how does it compare with the general population.

Figure 10.1
Proportional Mortality Due to Cardiovascular-Renal Disease, Joslin Clinic Diabetes Patients, 1897-1968



Source: Reference 14

ABSOLUTE AND RELATIVE MORTALITY IN IDDM

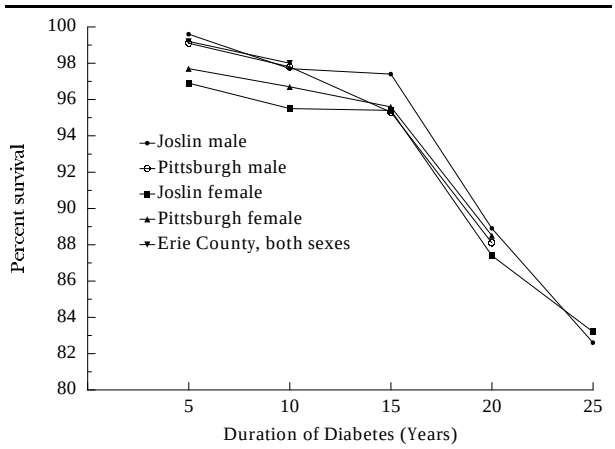
JOSLIN CLINIC STUDIES

Studies of patient mortality at the Joslin Clinic and other groups show a marked difference between mortality in the general U.S. population and the IDDM population[2,16]. A comparison of mortality in Joslin patients during 1931-59 was made using the age- and sex-specific rates of the general population of Massachusetts[17]. Excess mortality in diabetes was noted for all age groups except the 0-9 year category for males. For all males, the observed number of deaths was 3.75-fold higher than the expected number. Figure 10.2 provides a comparison of mortality in the Joslin Clinic, Children's Hospital of Pittsburgh, PA and Erie County, NY. A fairly consistent pattern is seen, wherein >15% of the childhood-onset diabetes cases have died by 25 years duration of IDDM or by age 40 years.

PITTSBURGH, PA STUDIES

A comparison of the mortality of IDDM patients with that of the U.S. population is shown in Figure 10.3[18]. Mortality among diabetic males was 5.4 times higher, and among females it was 11.5 times higher, when compared with the mortality expected based on total U.S. population mortality rates[19]. A 20-fold excess annual mortality was found among diabetic subjects age ≥25 years[19]. Figure 10.4 compares mortality of the Allegheny County, PA cohort, as defined by the Diabetes Epidemiology Research International (DERI) study, with U.S. population mortality obtained from the National Vital Statistics System of the National Center for Health Statistics[20]. Although the declining trend in total mortality over time partly reflects the different duration of followup for the three IDDM cohorts, a dramatic excess in mortality is evident for all groups.

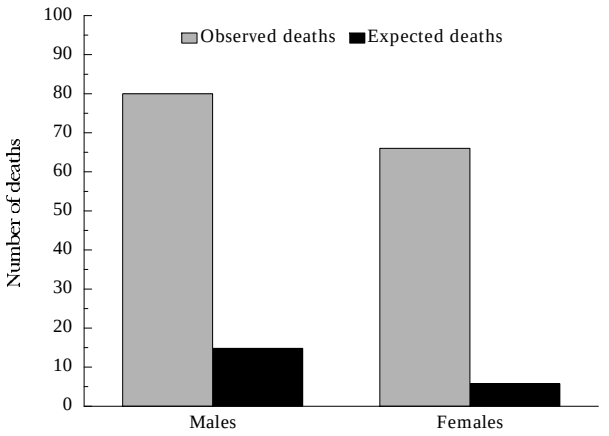
Figure 10.2
Survival in Childhood-Onset IDDM, by Duration of Diabetes



Joslin Clinic, Boston, MA 1939-64, diagnosis <21 years; Children's Hospital of Pittsburgh, 1950-81, diagnosis <17 years; Erie County, NY, 1946-61, diagnosis <15 years.

Source: References 4, 16, 19, and 23

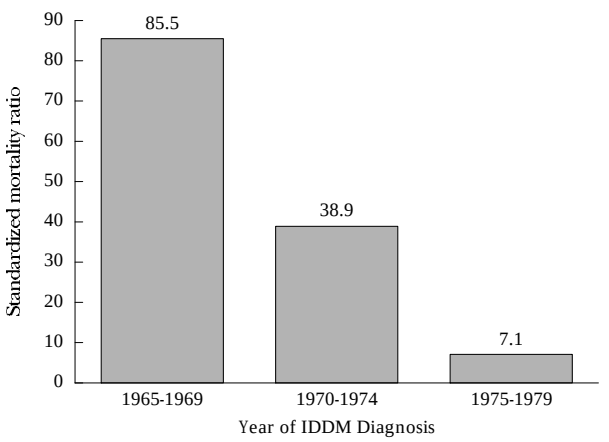
Figure 10.3
Mortality of IDDM Patients at Children's Hospital, Pittsburgh, PA, Compared with U.S. Population Mortality, 1950-81



Number of IDDM patients: 1,984 total, 951 male, 943 female; ratio of observed to expected deaths: 5.4 male, 11.5 female.

Source: References 18 and 19

Figure 10.4
Mortality of the Allegheny County, PA DERI Cohort Compared with 1980 U.S. Population Mortality



DERI, Diabetes Epidemiology Research International; data are age-standardized all-cause mortality ratios; mortality in IDDM patients was determined as of January 1, 1990.

Source: Reference 20

WISCONSIN STUDY

In the population-based Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR), age- and sex-standardized mortality ratios were calculated[21]. Males with diabetes diagnosed at age <30 years who were on insulin therapy (and therefore likely to have IDDM) had a 6.8-fold greater mortality risk compared with the general Wisconsin population, and females had an 8.9-fold increased risk. For ischemic heart disease, mortality rates were 9.1 times higher in the diabetic males and 13.5 times higher in the diabetic females.

REDUCTION IN LIFE EXPECTANCY

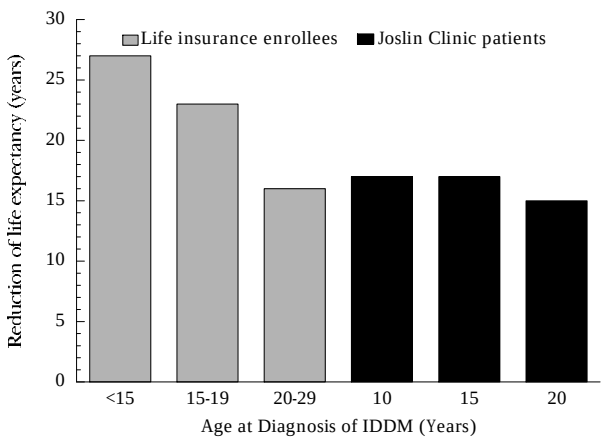
Another approach to examining the relative impact of diabetes on mortality is the calculation of life expectancy. Panzram compiled an analysis of reduction of life expectancy in diabetic persons from various sources[22]. Figure 10.5 is an abridged version dealing with IDDM only and presents data from the Joslin Clinic[5] and life insurance enrollees[1]. The data indicate that, irrespective of age at diagnosis, life expectancy is reduced by at least 15 years. The life expectancy of diabetic subjects enrolled in life insurance is lower than that of the Joslin IDDM patients, perhaps reflecting different health care and selection factors.

TEMPORAL TRENDS IN IDDM MORTALITY

Difficulties arise when trends in mortality in IDDM populations in the United States are examined. Limitations of death certificate data, described later in this chapter, hinder efforts to monitor national changes in mortality trends of IDDM. Data from the Joslin Clinic provide dramatic evidence of the decline in mortality in IDDM since the introduction of insulin[5,23] (Figure 10.6). Another analysis showed that 74% of deaths in the pre-insulin era were due to ketoacidosis, whereas cardiovascular disease became the main cause of death in the post-insulin era[24]. Death rates in diabetic patients, excluding deaths occurring within 1 week of first observation or hospital discharge, fell by 96% in those age <20 years between 1914-22 and 1926-29[5,23]. Using U.S. death certificates with diabetes coded as the cause of death for young age groups as a proxy for IDDM mortality[25-27], the diabetes death rate per 100,000 population can be estimated. Figure 10.7 shows this death rate during 1950-88 for deaths at age 1-4 years, 5-14 years, and 15-24 years. As with the Joslin Clinic data, there has been a marked downward trend in IDDM mortality, which appears to have leveled off during the 1980s. This may reflect improved care for diabetes rather than decreased incidence of IDDM.

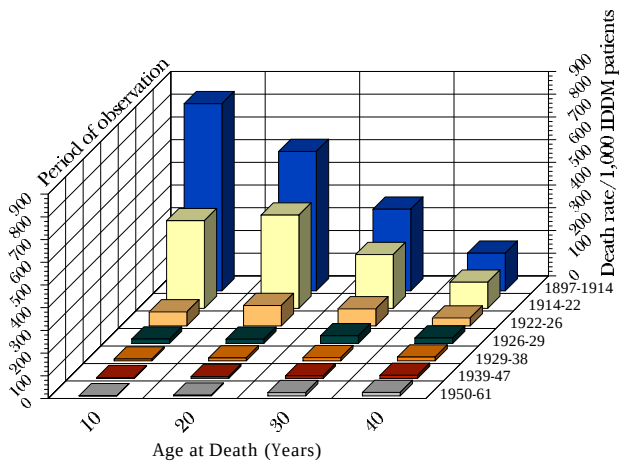
Another approach to examining temporal trends is to identify groups based on age and year of IDDM diagnosis from a well-defined cohort and to compare mortality across diagnosis years. Mortality as of January 1, 1982, of the Pittsburgh Children's Hospital cohort for diagnosis years 1950-71 is shown in relation to year of diagnosis and duration of diabetes in Figure 10.8. There is a trend for a reduced mortality within 10

Figure 10.5
Reduction of Life Expectancy, by Age at Diagnosis of IDDM



Source: References 1, 22, and 53

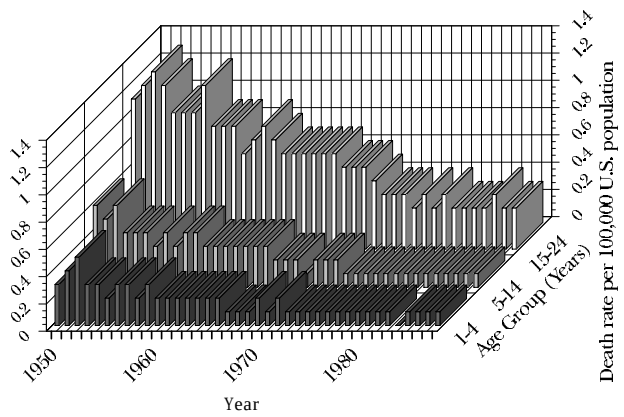
Figure 10.6
Death Rate of Patients with IDDM, Joslin Clinic, 1897-1961



Joslin Clinic, Boston, MA; deaths that occurred within 1 week of first observation or hospital discharge are excluded.

Source: References 5 and 23

Figure 10.7
Death Rate for Deaths Coded to Diabetes on U.S. Death Certificates, 1950-88

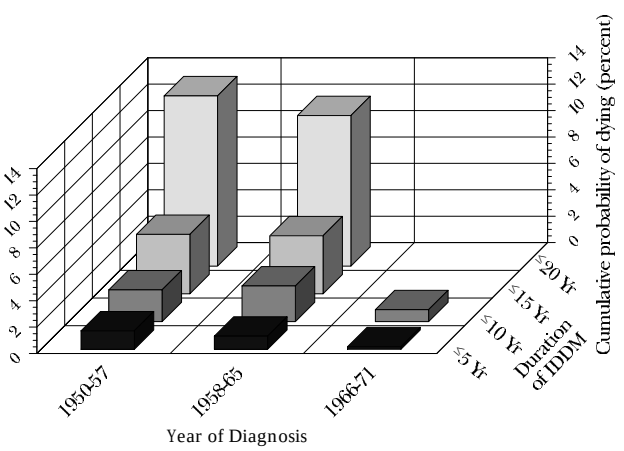


Denominator for death rate is the number of people in the U.S. in the specified age group.

Source: References 25-27

years of diagnosis for those diagnosed after 1966, compared with those diagnosed earlier[19]. Using the Allegheny County, PA population-based DERI cohort[28], the 10-year mortality for those diagnosed during 1965-79 has been determined. As shown in Figure 10.9, there is a decrease in overall mortality for those diagnosed during 1975-79, compared with the earlier diagnosis years.

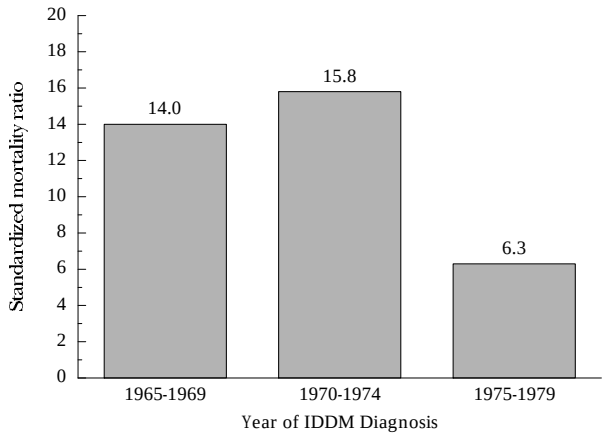
Figure 10.8
Cumulative Probability of Dying for IDDM Patients at Children's Hospital, Pittsburgh, PA as of January 1, 1982



For duration ≤5 years and ≤10 years, the difference across year of diagnosis groups approached significance (p=0.06 and 0.07, respectively). For duration ≤20 years in 1958-65, mortality was calculated only for 1958-61 and excluded all deaths within 1 year of onset of IDDM.

Source: Reference 19

Figure 10.9
Standardized Mortality Ratio, Allegheny County, PA DERI Registry Patients, Compared with 1980 U.S. Population



DERI, Diabetes Epidemiology Research International; diabetes deaths are for IDDM patients with ≤10 years diabetes duration; mortality was determined as of January 1, 1990.

Source: Reference 28

CAUSES OF DEATH IN IDDM

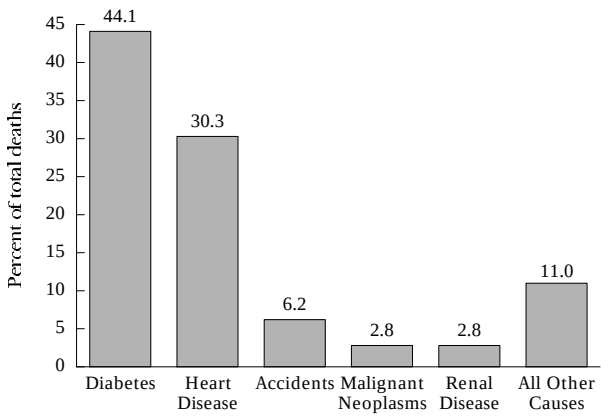
CAUSE-SPECIFIC MORTALITY

In the population-based WESDR[21], diabetes was the underlying cause listed on death certificates for 44.1% of deaths in individuals with diabetes diagnosed at age <30 years, followed by heart disease (30.3%) and accidents (6.2%) (Figure 10.10).

The Pittsburgh Epidemiology of Diabetes Complications Study has identified the causes of death based on death certificate data by duration of diabetes in a childhood-onset cohort of IDDM subjects[29]. As the cohort aged and experienced diabetes for a longer period, changes in the cause of death occurred. Deaths from acute IDDM complications predominated in the shorter-duration group compared with renal disease in the 10-19 year duration group and cardiovascular disease in those with ≥20 years duration of IDDM (Figure 10.11).

These findings are consistent with a report on the Steno Memorial Hospital population in Denmark. All individuals with IDDM diagnosed at age ≤30 years prior to 1943 were followed until death or January 1, 1984; patients dying within 35 years of IDDM onset were compared with those with ≥40 years of IDDM[30]. The cause of death in 54% of those who died within 35 years of onset was renal failure due to diabetic neph-

Figure 10.10
Distribution of Cause of Deaths in Younger-Onset Diabetic Persons, WESDR, 1980-88



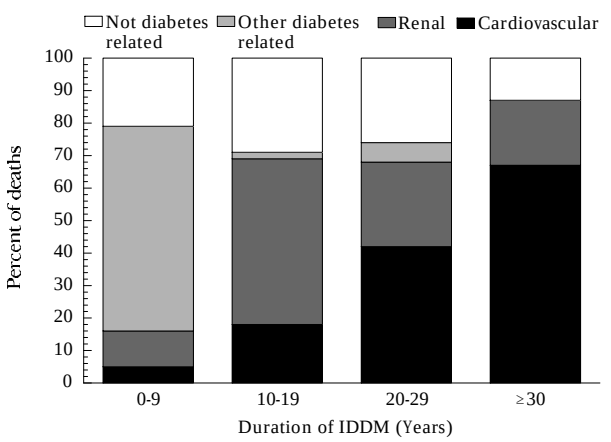
Younger-onset, diabetes diagnosed at age <30 years; WESDR, Wisconsin Epidemiologic Study of Diabetic Retinopathy; cause of death was determined from death certificate information.

Source: Reference 21

ropathy, compared with 5% of those who survived ≥40 years. Cardiovascular diseases accounted for 27% of deaths within 35 years, compared with 67% of deaths for patients that survived ≥40 years (Figure 10.12).

Another study targeting a specific subset of IDDM patients, i.e., individuals who were waiting for renal transplants, found a high prevalence of coronary artery disease (42.9%)[31]. These data support the close link between renal disease and heart disease mortality

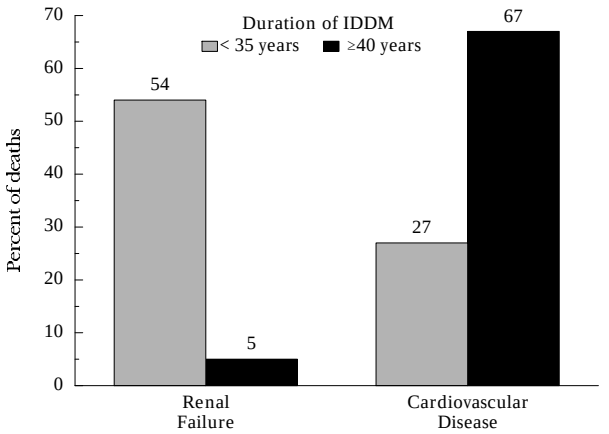
Figure 10.11
Causes of Death by Duration of IDDM, Pittsburgh,PA Epidemiology of Diabetes Complications Study



Other diabetes-related causes are primarily acute diabetic coma.

Source: Reference 29

Figure 10.12
Cause of Death by Duration of IDDM, Steno Memorial Hospital, Denmark



Data are based on patients with IDDM diagnosed at age ≤30 years prior to 1943 and followed to death or January 1, 1984. Renal failure deaths were due to diabetic nephropathy.

Source: Reference 30

in the Steno Hospital data, wherein the excess coronary heart disease mortality was largely limited to those with renal disease[32]. Indeed, the cardiovascular disease mortality was increased ninefold in those with proteinuria compared with those without[32]. Data from the Joslin clinic also support this link between renal disease and coronary heart disease and suggest that, in the absence of renal disease, coronary artery disease mortality by age 55 years would be reduced by half[33].

LIMITATIONS OF DEATH CERTIFICATE DATA

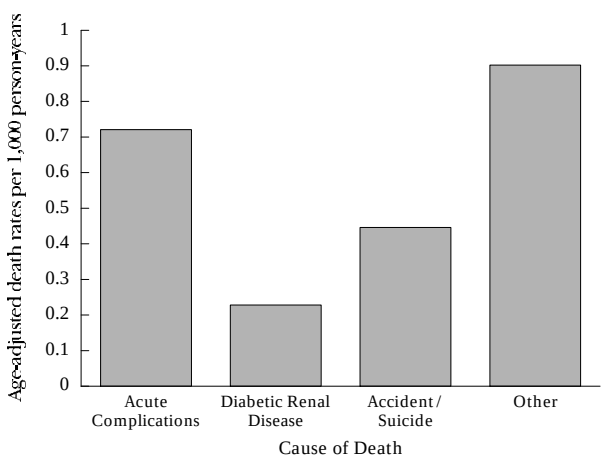
In *Epidemiology of Diabetes and Its Vascular Lesions*, West illustrated problems with sensitivity and specificity in using death certificates not only in the United States but worldwide[26]. Another estimate suggests that only 25% of death certificates of people with diabetes list diabetes as an underlying cause of death[34]. A study based on the population of King County, WA also found that diabetes was underreported on certificates, with only 41% of certificates mentioning diabetes for known diabetic persons dying from heart disease[35]. Thus, death certificates clearly do not fully represent the total contribution of diabetes to mortality. This underreporting is further complicated by the variable degree to which diabetes contributes to many causes of death and the variation with which death certificates are completed and coded to represent these influences.

DERI MORTALITY CLASSIFICATION

To overcome the above problems with death certificate data, an ongoing international study involving registries from four countries—Finland, Israel, Japan, and the United States (Allegheny County, PA)—has carefully reviewed deaths in IDDM patients in a standardized manner. In addition to death certificates, the DERI researchers collected other records, including autopsy reports, coroner and police reports, and hospital records. A committee of physicians, after reviewing all data, assigned underlying causes of death and ranked other causes according to their contribution to causing death. In this way, it is possible to systematically study the roles of secondary causes. The underlying causes of death for Allegheny County, PA are shown in Figure 10.13[28] .

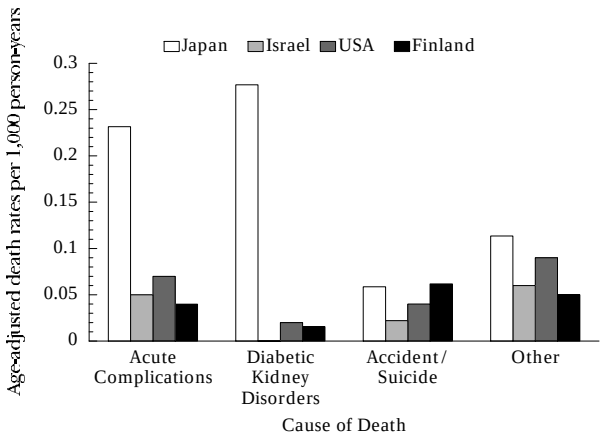
The DERI group also established three separate levels of contribution of diabetes to death: Level 1—diabetes caused the death regardless of other conditions present; Level 2—diabetes contributed significantly to the death; and Level 3—diabetes contributed marginally to the death, that is, diabetes played a role in the death but was not essential for an explanation of the death[28]. In this manner, a more clearly defined analysis of death within an IDDM population was developed. The DERI study shows that an underestimation of the proportion of deaths due to acute complications and kidney disease would have occurred without the review and classification system[28]. Cross-country differences were found in the DERI study when cause-specific mortality was examined. Individuals with IDDM in Japan were more likely to die than those in the other countries, with the elevated mortality resulting from acute diabetes-related complications and kidney disease (Figure 10.14). More than 25% of the deaths in each country were from acute diabetes-related complications[28]. Also, there was a high rate of accidents and suicide in the Finnish IDDM population[28]. In Japan, virtually all deaths (96%) were in some way related to diabetes. In Allegheny County, PA this proportion was 75%, while in Finland less than two-thirds were related to diabetes. Thus, it seems that where overall mortality is lowest (Finland), fewer deaths are attributable to diabetes itself, while the opposite pattern is seen where mortality is highest (Japan). These data suggest a considerable potential to reduce diabetes-related mortality in Japan and the United States.

Figure 10.13
Age-Adjusted Death Rates for Patients with IDDM, Allegheny County, PA



Source: Reference 28

Figure 10.14
Age-Adjusted Death Rates for Patients with IDDM, by Cause and Country



Source: Reference 28

HYPOGLYCEMIA AS A CAUSE OF DEATH

With the increased focus on better glycemic control and concern that human insulin may reduce awareness of hypoglycemia, an important current concern is whether hypoglycemia is an increasingly significant cause of death in IDDM. Unfortunately, national data based on underlying cause of death are inadequate to address this question, because such deaths are coded only as "diabetic coma" for lack of a specific subgroup for hypoglycemia. However, based on investigation of deaths from the Allegheny County, PA registry, no deaths during the 23 years of followup were thought to be primarily due to hypoglycemia, although many were ascribed to acute diabetes complications[36]. When comparing the Allegheny County data with other countries participating in the DERI study, the fre-

quency of hypoglycemia as a cause of death ranged from 0 in Israel and Allegheny County to 0.81 per 1,000 person-years in Japan[36].

RISK FACTORS FOR MORTALITY

NATURE AND EFFECTS OF RISK FACTORS

A number of risk factors have been examined and/or identified in relation to mortality of individuals with IDDM. The study methods used have varied from case-control to prospective cohort studies.

Sex

Based on a followup of 1,966 patients in the Pittsburgh Children's Hospital registry, a similar age-adjusted total mortality rate for males and females (6.5 per 1,000 and 5.7 per 1,000, respectively) was found[19]. However, females had higher mortality rates than males in the younger age groups, whereas males had a twofold excess mortality in the older age groups. For the 1-4 year age group, females had a mortality rate of 19.0 per 1,000 compared with 2.4 per 1,000 for males; for the 30-34 year age group, males had a mortality rate of 29.6 per 1,000 compared with 14.6 per 1,000 for females[19]. Relative to the nondiabetic population, the rates are particularly high for females: the mortality ratio is 11.5 for females and 5.4 for males.

The WESDR found that the excess mortality for ischemic heart disease was significantly different between females and males, with mortality ratios compared with nondiabetic persons of 13.5 and 9.1, respectively[21]. However, the excess mortality was higher in males than females for other heart diseases (ratios of 7.3 and 4.5, respectively). A difference was also found when examining deaths from accidents: females had a significantly higher mortality ratio than males[21].

Race

Although data on racial differences for IDDM mortality are scant, some studies have indicated that there are differences. In the Children's Hospital of Pittsburgh (PA) cohort, the overall age-adjusted mortality rate was 12.3 per 1,000 person-years for African Americans, compared with 6.1 per 1,000 person-years for whites[19]. Mortality ratios were calculated comparing the white IDDM population with the white U.S. population and the African-American IDDM population with the African-American U.S. population and excluding deaths within 1 year of IDDM onset. The relative excess mortality was higher in African-American than in white IDDM patients (mortality ratios of 9.7 and 7.1, respectively)[19].

Familial Effect

Clustering of premature mortality was investigated in 1,761 IDDM individuals from Children's Hospital of Pittsburgh and their family members[37]. Life-table analysis showed that fathers of individuals with diabetes who died were more likely to die prematurely than fathers of living individuals with diabetes, suggesting a familial effect on mortality beyond that of diabetes per se[37]. In addition, diabetic siblings of deceased diabetic subjects were also more likely to die prematurely.

Smoking

A prospective study examining the relation between mortality and cigarette smoking in the Children's Hospital of Pittsburgh cohort diagnosed during 1950-64 found that heavy smoking was a significant independent predictor of all-cause mortality among females but not among males[38]. These data also showed an excess mortality in females that was explained by an excess risk of coronary heart disease mortality[38].

Lipoproteins

Very little data exist relating lipoproteins to subsequent mortality in IDDM. The significance of lipoproteins in diabetes and the relationship to cardiovascular morbidity, however, have been described[39] and reviewed[40]. A lack of association between lipoprotein(a) and coronary heart disease in IDDM has been reported, unlike the relationship seen in the general population[41]. Two case-control analyses using the Epidemiology of Diabetes Complications study have also found no association between lipoprotein(a) and mortality[42] nor between lipoprotein(a) and coronary heart disease[43].

Blood Pressure

As part of the WESDR, mortality was examined 6 years after the baseline examination[44]. Those diagnosed with IDDM at age <30 years who had died (9.5% of the 996 insulin-taking individuals) were compared with those who survived; it was found that higher blood pressure was associated with mortality. This relationship had previously been reported for Joslin Clinic IDDM patients[16].

Metabolic Regulation

A study of the Steno Memorial Hospital population in Denmark to identify factors associated with long-term survival showed that metabolic regulation was the strongest predictor of survival[45]. A subset analysis of individuals diagnosed at age <15 years found that long-term survivors were younger at diagnosis, attended out-patient clinics more often, and had better metabolic regulation[45].

Diuretics

Excess mortality has been associated with the use of diuretics in individuals with IDDM. Among IDDM patients in southern Wisconsin diagnosed at age <30 years, an approximate fourfold increase in mortality was found in those who had used diuretics[44]. Another cohort study found similar results, although the population examined included some people with NIDDM[46].

Other Factors

The prevalence of physician-diagnosed hypertension, retinopathy, blindness, laser therapy, and renal disease were significantly higher among those who died compared with a control population of survivors[18]. Physical activity levels have been shown to be inversely related to mortality among males but not females in a Pittsburgh, PA cohort study that examined mortality through January 1, 1988[47].

A retrospective case-control analysis of mortality in the Children's Hospital of Pittsburgh IDDM registry revealed a difference in risk between males and females[18]. A total of 48 males and 36 females who had died as of January 1, 1982, were matched by age, sex, age at onset, and race. For males, short relative height at onset of IDDM, frequent diabetes-related hospitalizations, presence of diabetes complications (renal disease), alcohol consumption, premature familial mortality, and no participation in school team sports were associated with mortality. For females, shorter duration of diabetes clinic attendance and presence of diabetes complications (renal disease) were associated with mortality[18].

EFFECT OF PREPUBERTAL YEARS ON MORTALITY

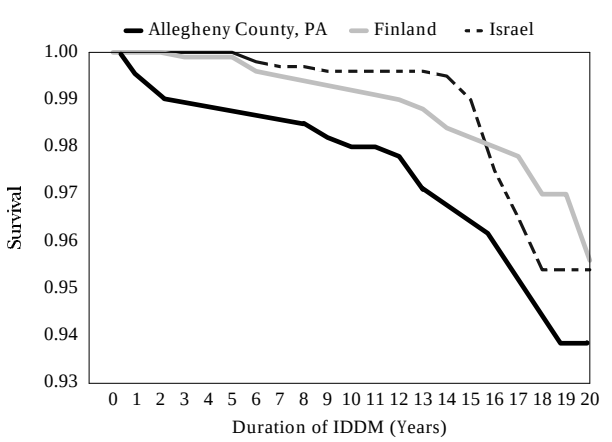
The effect on mortality of a prepubertal (age <11 years in girls and <12 years in boys) or peripubertal age at IDDM onset was examined in the Children's Hospital of Pittsburgh cohort[48]. Using proportional hazard models, individuals with a peripubertal onset of diabetes had a higher risk of mortality than those with a prepubertal onset. This confirms earlier work suggesting that the prepubertal years are relatively benign[49].

UNITED STATES VERSUS OTHER COUNTRIES: DERI STUDIES

The DERI study of four countries has shown that for patients with a 20-year duration of IDDM, 5.5% of the Allegheny County, PA cohort, 4.6% of the Israeli cohort, and 3.1% of the Finnish cohort died (Japan was not included because of the method used to establish the cohort)[50] (Figure 10.15). Intercountry differences are particularly striking for the groups with older age at diagnosis (Figure 10.16). Age-adjusted death rates for the four countries are presented in Figure 10.14.

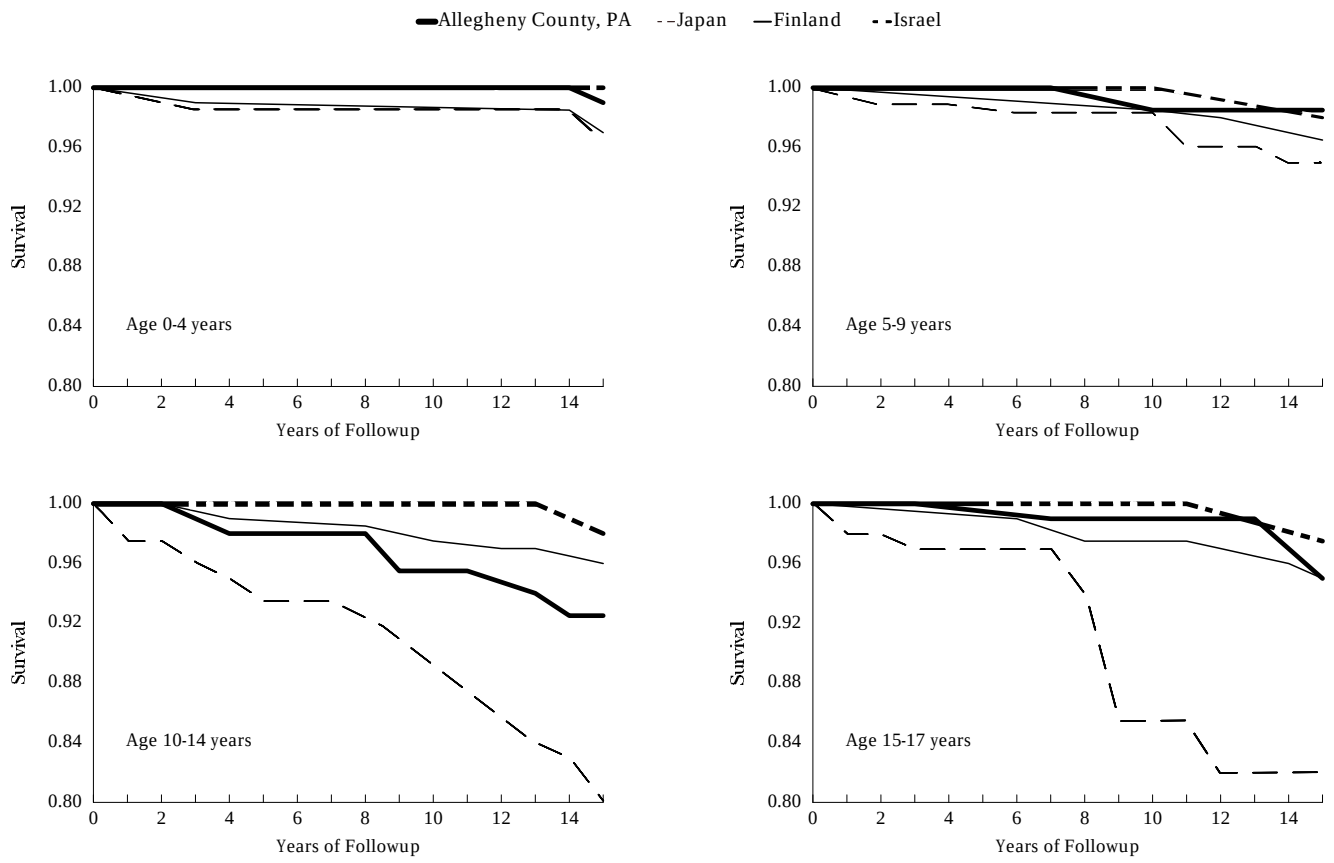
For individuals age 25-37 years in the DERI mortality study, the overall mortality rate in Allegheny County, PA was more than twice the rate in Finland (812 deaths per 100,000 person-years versus 405 deaths per 100,000 person-years, respectively)[51]. Figure 10.17 shows the distribution of primary causes of death in Allegheny County and Finland[28]. By comparing the Finnish mortality rate with that of the Allegheny County cohort, it was suggested that ~50% of the deaths in Allegheny County were theoretically preventable, and the possibility was raised that a discrepancy in the availability of health care due to cost may be responsible[51].

Figure 10.15
Life-Table Analysis of IDDM Mortality, by Duration of Diabetes



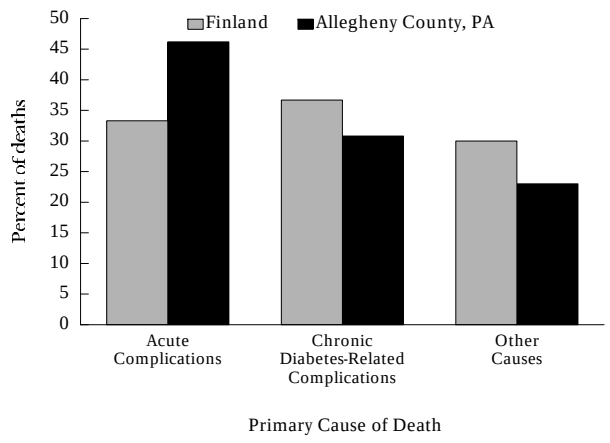
Source: Reference 50

Figure 10.16
Life-Table Analysis of IDDM Mortality, by Age at Diagnosis



Source: Reference 50

Figure 10.17
Distribution of Primary Cause of Death in IDDM, Finland Versus Allegheny County, PA



Source: Reference 28

Sex differences in the mortality of IDDM within the four population groups were examined. In Finland, males had a significantly greater premature death rate compared with females, mainly due to accidents and suicides, although the same sex-specific rate differences were not seen in the other countries[52]. Also, there was little difference between absolute mortality rates for females and males across all countries, which confirms previous reports that IDDM largely eliminates the mortality protection seen in women in the general population[52].

Mr. Enrico Portuese is Research Assistant, and Dr. Trevor Orchard is Professor, Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA.

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