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Cause-Specific Mortality Rates in Chronic Disease Populations

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Abstract: Random sample surveys have been used for public health surveillance for about 50 years and have grown in size over that time. Such surveys are sufficiently large to estimate the sizes of relatively small subpopulations, such as patients with chronic diseases, helped by pooling multiple years of the same survey. Survey estimates of population sizes have been used as denominators to estimate death rates from specific causes within specific subpopulations. Since these are ratio estimates, with both numerator and denominator being estimates, additional examination is required to evaluate their reliability. We illustrate these methods for rates using deaths due to diabetes and the estimated population of diabetics to compute death rates due to diabetes among diabetics by age and sex. Substituting the much smaller population of people at risk for the total population yields useful information about the burden of disease.

Keywords: Death rate, chronic disease, diabetes, BRFSS, survey methods.

Modern public health surveillance systems that use random sample surveys of the population have been in use for 50 years and are now large enough to estimate, often with fairly high accuracy, the sizes of small subpopulations of people with a chronic disease. These estimated populations have been used as denominators to compute cause-specific death rates within such subpopulations [1]. In this paper, we illustrate the proper statistical use of such ratio estimates, accounting for random variation in the denominator as well as the numerator, with death rates due to diabetes in the subpopulation of persons with diabetes. Substituting the much smaller diabetic population for the total population to compute death rates better informs our understanding of the burden of disease.

We compute estimated death rates using the Behavioral Risk Factor Surveillance System (BRFSS), a large, nationwide sample, to estimate the population of diabetics and counts of deaths due to diabetes in the United States. The estimated death rates due to diabetes within the diabetic population are ratios estimated as the number of deaths due to diabetes over the survey estimate of the size of the diabetic population.

METHODS

The BRFSS is a random digit dialed (RDD) telephone survey of the U.S. adult population that is conducted by state and territorial health departments under the sponsorship of the Centers for Disease Control (CDC). The BRFSS includes questions on a range of health topics related to chronic diseases and preventive behaviors. A summary description of this surveillance system has been given by Holtzman [2]. States use a small number of design variations so that sampling designs and questionnaires are quite similar. The total number of interviews in 1999 was 159,989, in 2000 it was 184,450, and in 2001 it was 212,510. The public use data files for these years were obtained from http://www.cdc.gov/brfss/ at various dates.

For each year, 1999-2001, we estimated the size of the subpopulation of diabetics in the US by sex and age interval: 25-74 years by 10 year intervals and 75 years and over. These age intervals correspond to standard intervals for compiling counts of deaths in the US. Under age 25 there are very few diabetics or deaths due to diabetes and these were excluded from our analyses. (There were 992 deaths under age 25 with any mention of diabetes in the US in 1999-2001.) We used Stata (http://www.stata.com, March 1, 2008) to compute estimates and standard errors that account for the complex sample design of the BRFSS. The sampling weights were used as supplied with the public use files, states were used for strata and clusters were used in states that had used cluster sampling. We computed the total of the population estimates for all three years and its variance, the sum of the variances for all three years.

The counts of deaths with diabetes for 1999-2001 were obtained from the National Center for Health Statistics, a division of CDC (http://www.cdc.gov/nchs/, March 1, 2008). Separate counts for any mention of diabetes and for diabetes as underlying cause were done by age and sex. We estimated the variance and standard deviation (SD) of each total count as the square root of the count, assuming a Poisson distribution for the number of deaths [3].

Each death rate was estimated as the ratio of the total number of deaths, X, during 1999-2001 to the sum of the estimated populations, Y, for 1999-2001. The estimated variance and standard error of the ratio, X/Y, used a formula based on the Taylor series expansion of the ratio [4]. For two independent random variables, X and Y, both positive, the

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estimated standard error of their ratio is $se(X/Y) = (X/Y)[var(X)/X^2 + var(Y)/Y^2]^{1/2}$. Such ratio estimates require stable estimates, especially for the denominator. Stability for random variables that are non-negative, such as counts of events or estimates of populations, can usually be indicated by low coefficients of variation (CV)–the ratios se(X)/X and se(Y)/Y – preferably under 0.1 [5].

We obtained the population of the United States (US) by age and sex for June 1, 2000 (from http://www.census.gov, March 1, 2008) and computed population death rates for diabetes as the average deaths in 1999-2001 divided by the census counts for each age-sex combination.

The ratio estimates of death rates (per 100,000), their 95% confidence intervals, and their coefficients of variation are also reported. These rates are compared with the corresponding rates computed using the US Census. We also report the estimated populations of diabetics overall, by sex, and by age and sex, as well as their standard errors (SE) and coefficients of variation (CV) and the same statistics for counts of deaths. The estimated population pyramid of diabetics aged 25 and up is shown and compared to the US Census.

RESULTS

The estimated average population of diabetics during 1999-2001 was 13.13 million (SE=0.12 million, CV=0.0094), including 6.35 million men (SE=0.09 million, CV=0.0034) and 6.78 million women (SE=0.08 million, CV=0.0025). The number of deaths in three years with any mention of diabetes as a cause was 641 thousand (SE=800.3, CV=0.0012), including 304 thousand men (SE=551.1, CV=0.0018) and 337 thousand women (SE=580.4, CV=0.0017). The number of deaths in three years with diabetes as the underlying cause was 208 thousand (SE=456.6, CV=0.0022), including 95 thousand men (SE=308.7, CV=0.0032) and 112 thousand women (SE=336.5, CV=0.0030).

The ratio estimates of the death rates (per 100,000) were, for all diabetics, 1,626.7 (95% CI: 1,595.8-1,657.6, CV=0.009), for men 1,595.5 (95% CI: 1,548.3-1,642.6, CV=0.015), and for women, 1,656.0 (95% CI: 1,614.9-1,697.0, CV=0.012). The ratio estimates of the death rates (per 100,000) for diabetes as the underlying cause were, for all diabetics, 529.4 (95% CI: 519.2-539.7, CV=0.010), for men, 500.4 (95% CI: 485.4-515.4, CV=0.015), and for women, 556.6 (95% CI: 542.5-570.7, CV=0.013). Note that the difference between men and women is not statistically significant for diabetes as any cause but women have a significantly higher rate for diabetes as the underlying cause, since the confidence intervals for the former overlap, but do not for the latter.

The estimated three year totals of the diabetic population by age and sex are shown in Table **1** and the counts of deaths involving diabetes are shown in Table **2**. The average population estimate for three years is shown in Fig. (**1A**) and the census counts are shown for comparison in Fig. (**1B**). The estimated populations increase across age, except at the oldest age, 75 years and over. All the CVs are below 0.1, so these estimates are sufficiently stable to compute reliable rates. The diabetic population has a substantially older age pattern than the US population as well as being substantially smaller. There are relatively more females at older ages than at younger ages. Some caution might be appropriate for rates computed for the youngest age group of males which has the largest CV at 0.079.

The ratio estimates of death rates, by age and sex, their 95% confidence intervals, and coefficients of variation are shown in Table **3**. All the coefficients of variation are below the recommended limit of 0.1, though those for males aged 25-34 are close at 0.083 and 0.086. The death rates for men are higher than those for women at every age except 75 and over.

The death rates are higher for men than for women both for diabetes as the underlying cause and for any mention of diabetes as a cause, with the single exception of any mention of diabetes at age 75 or over. These differences are statisti-

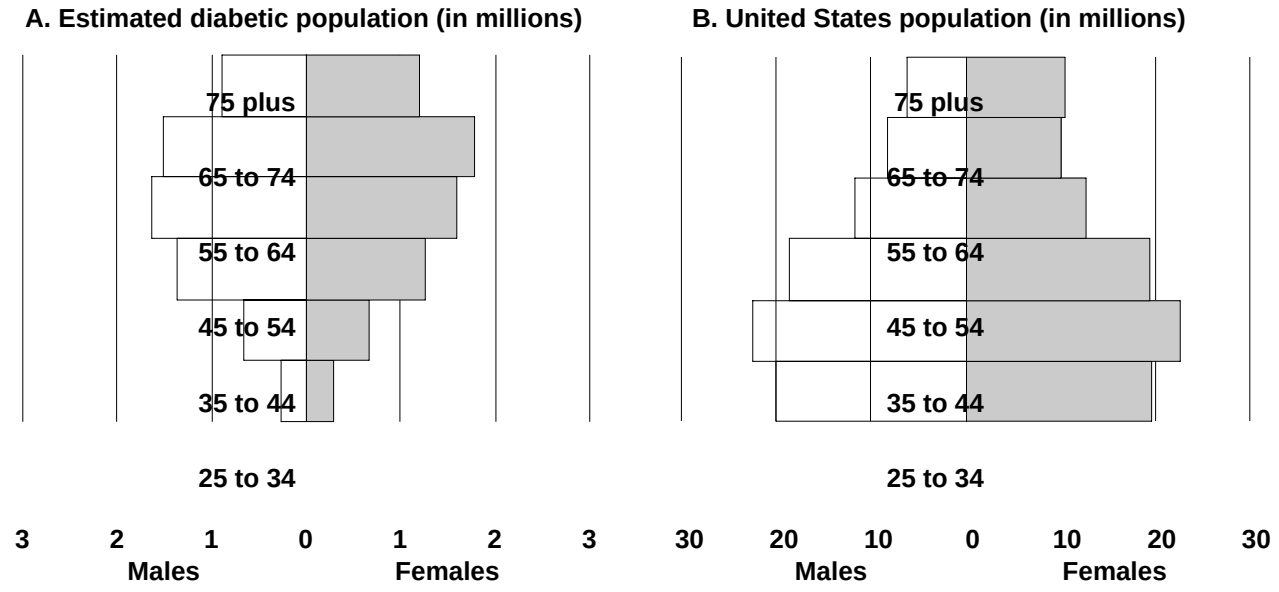

Fig. (1). Estimated diabetic population in the United States, by age and sex. Estimates are the average of three years, 1999-2001, from the BRFSS and the US Census population for June 1, 2000, by age and sex.

cally significant since the corresponding confidence intervals do not overlap.

Table 1. Sum Over Three Years of the Estimated Population of Persons with Diabetes by Sex and Age Group with Standard Errors (SE) and Coefficients of Variation (CV) for the United States, 1999-2001

Age Group	Estimated Diabetic Population	SE	CV
Males			
25 to 34	818,857	65,045	0.079
35 to 44	2,009,592	112,894	0.056
45 to 54	4,109,962	134,461	0.033
55 to 64	4,894,422	137,563	0.028
65 to 74	4,548,130	125,824	0.028
75 plus	2,657,165	96,332	0.036
Females			
25 to 34	876,732	48,445	0.055
35 to 44	1,978,480	77,722	0.039
45 to 54	3,794,971	113,496	0.030
55 to 64	4,770,598	130,102	0.027
65 to 74	5,311,484	125,861	0.024
75 plus	3,607,295	98,139	0.027

The death rates due to diabetes in the US population are shown in Table **4** for comparison with the estimated rates in Table **3**. The pattern of death rates is quite different. The US death rates are much lower at younger ages than at older ages, for both males and females., both for any mention of diabetes and for diabetes as the underlying cause. Comparison of these rates at younger ages, in particular, indicates that deaths among young diabetics is a more substantial problem than one might conclude from the US rates.

Table 2. Sum Over Three Years of The Total Deaths with Diabetes as an Underlying Cause and with Any Mention of Diabetes as a Cause by Sex and Age Group with Standard Errors (SE) and Coefficients of Variation (CV) for the United States, 1999-2001

Age Group	Deaths with Diabetes as an Underlying Cause			Deaths with Diabetes as Any Cause		
	Deaths	SE	CV	Deaths	SE	CV
Males						
25to34	1,036	32.2	0.031	1,799	42.4	0.024
35to44	3,471	58.9	0.017	7,466	86.4	0.012
45to54	8,766	93.6	0.011	22,615	150.4	0.007
55to64	15,040	122.6	0.008	44,786	211.6	0.005
65to74	24,942	157.9	0.006	82,083	286.5	0.003
75plus	42,011	205.0	0.005	144,995	380.8	0.003
Females						
25to34	764	27.6	0.036	1,429	37.8	0.026
35to44	2,355	48.5	0.021	5,041	71.0	0.014
45to54	6,266	79.2	0.013	15,689	125.3	0.008
55to64	12,813	113.2	0.009	35,498	188.4	0.005
65to74	25,371	159.3	0.006	74,842	273.6	0.004
75plus	65,640	256.2	0.004	204,319	452.0	0.002

Table 3. Estimated Death Rates with Diabetes as an Underlying Cause and with any Mention of Diabetes as a Cause Among Persons with Diabetes with 95% Confidence Intervals and Coefficients of Variation (CV) for the United States, 1999-2001

Age Group	Death Rates with Diabetes as an Underlying Cause			Death Rates with Diabetes as Any Cause		
	Death Rate (Per 100,000)	95% Confidence Interval	CV	Death Rate (Per 100,000)	95% Confidence Interval	CV
Males						
25 to 34	126.5	(104.9, 148.1)	0.085	219.7	(183.3, 256.1)	0.083
35 to 44	172.7	(152.4, 193.0)	0.059	371.5	(328.9, 414.1)	0.057
45 to 54	213.3	(198.6, 228.0)	0.034	550.2	(513.5, 587.0)	0.033
55 to 64	307.3	(289.3, 325.3)	0.029	915.0	(862.9, 967.2)	0.029
65 to 74	548.4	(517.3, 579.5	0.028	1,804.8	(1,704.1, 1,905.4)	0.028
75 plus	1,581.0	(1,465.4, 1,696.7)	0.037	5,456.8	(5,060.1, 5,853.4)	0.036
Females						
25 to 34	87.1	(75.6, 98.7)	0.066	163.0	(143.0, 183.0)	0.061
35 to 44	119.0	(108.5, 129.6)	0.044	254.8	(233.5, 276.1)	0.042
45 to 54	165.1	(154.4, 175.8)	0.032	413.4	(387.8, 439.0)	0.031
55 to 64	268.6	(253.2, 284.0)	0.029	744.1	(702.8, 785.4)	0.028
65 to 74	477.7	(454.2, 501.1)	0.025	1,409.1	(1,341.5, 1,476.6)	0.024
75 plus	1,819.6	(1,719.6, 1,919.7)	0.027	5,664.1	(5,354.8, 5,973.3)	0.027

Table 4. Death Rates Due to Diabetes as an Underlying Cause and with any Mention of Diabetes in the United States, 2000

Age Group	Death Rates (Per 100,000)	
	Diabetes as the Underlying Cause	Any Mention of Diabetes
Male		
25 to 34	5.2	9.0
35 to 44	15.5	33.3
45 to 54	46.9	121.1
55 to 64	128.3	382.0
65 to 74	300.5	988.8
75 plus	682.9	2,357.0
Female		
25 to 34	3.9	7.2
35 to 44	10.4	22.2
45 to 54	32.4	81.0
55 to 64	100.8	279.2
65 to 74	251.9	743.0
75 plus	622.5	1,937.6

DISCUSSION

Estimation of death rates due to diabetes among the population of diabetics provides useful information by restricting the population to the people at risk from the specific cause. Most importantly, the age pattern of death rates is quite different, with much higher death rates among diabetics at younger ages than at older ages than we see with diabetic death rates in the US population. This is a result of the relatively much smaller estimated population of diabetics at younger ages, compared with the size of the US population. Among these younger diabetics, deaths due to diabetes are more frequent than the US rates show. Also, the age-specific death rates among diabetics are lower for men than for women over age 74, whereas the US death rates are higher. These patterns suggest that the burden of diabetes is higher among young diabetics than is indicated by death rates in the US population.

There are more diabetic men at each age interval from 35 to 64 and men had higher death rates except over age 74. These indicate that the burden of disease is systematically greater among men.

Large sample surveys used for public health surveillance can be used to compute reliable denominators, the population estimates of the rates. These are ratio estimators, that is, the denominator as well as the numerator is a random variable and this must be accounted for not only in estimating the variance of the ratio but the reliability of such a ratio must also be evaluated, most simply but only approximately, with the coefficient of variation of the denominator. Such rates can yield valuable perspectives on the burden of chronic diseases. Careful design of survey questionnaires to obtain chronic disease status that correspond to causes of death would strengthen this sources of information.

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