CHAPTER 25

Standardization

25.1 INTRODUCTION

Death rates and disease incidence rates are usually strongly related to age, and often differ for the two sexes. Population mortality and incidence rates therefore depend critically on the age–sex composition of the population. For example, a relatively older population would have a higher crude mortality rate than a younger population even if, age-for-age, the rates were the same. It is therefore misleading to use overall rates when comparing two different populations unless they have the same age–sex structure. We saw in Chapter 23 how to use Mantel–Haenszel methods and in Chapter 24 how to use Poisson regression to compare rates between different groups after controlling for variables such as age and sex.

We now describe the use of **standardization** and **standardized rates** to produce comparable measures between populations or sub-groups, adjusted for major confounders, such as any age–sex differences in the composition of the different populations or subgroups. **Mantel–Haenszel** or **regression methods** should be used to make formal comparisons between them.

There are two methods of standardization: *direct* and *indirect*, as summarized in Table 25.1. Both use a **standard population**.

Table 25.1 Comparison of direct and indirect methods of standardization.

	Direct standardization	Indirect standardization
Method	Study rates applied to standard population	Standard rates applied to study population
Data required		
Study population(s)	Age–sex specific rates	Age–sex composition + total deaths (or cases)
Standard population	Age–sex composition	Age–sex specific rates (+ overall rate)
Result	Age–sex adjusted rate	Standardized mortality (morbidity) ratio (+ age–sex adjusted rate)

- In **direct standardization**, the age–sex specific rates from each of the populations under study are applied to a *standard* population. The result is a set of **standardized rates**.
- In **indirect standardization**, the age–sex specific rates from a *standard* population are applied to each of the study populations. The result is a set of **standardized mortality (or morbidity) ratios (SMRs)**.

The choice of method is usually governed by the availability of data and by their (relative) accuracy. Thus, direct standardization gives more accurate results when there are small numbers of events in any of the age–sex groups of the study populations. The indirect method will be preferable if it is difficult to obtain national data on age–sex specific rates.

Both methods can be extended to adjust for other factors besides age and sex, such as different ethnic compositions of the study groups. The direct method can also be used to calculate **standardized means**, such as age–sex adjusted mean blood pressure levels for different occupational groups.

25.2 DIRECT STANDARDIZATION

Example 25.1

Table 25.2 shows the number of cases of prostate cancer and number of person-years among men aged $\geq$ 65 living in France between 1979 and 1996. The data are shown separately for six 3-year time periods. Corresponding rates of prostate cancer per 1000 person-years at risk (pyar) are shown in Table 25.3

Table 25.3 shows that the crude rates (those derived from the total number of cases and person-years, ignoring age group) increased to a peak of 2.64/1000 pyar in 1988–90 and then declined. However Table 25.2 shows that the age-distribution of the population was also changing during this time: the number of person-years in the oldest ($\geq$ 85 year) age group more than doubled between 1979–81 and 1994–96, while increases in other age groups were more modest. The oldest age group also experienced the highest rate of prostate cancer, in all time periods.

Table 25.2 Cases of prostate cancer/1000 person-years among men aged $\geq$ 65 living in France between 1979 and 1996.

	Time period					
Age group	1979–81	1982–84	1985–87	1988–90	1991–93	1994–96
65–69	2021/2970	1555/2197	1930/2686	2651/3589	2551/3666	2442/3764
70–74	3924/2640	3946/2674	3634/2272	2842/1860	3863/2703	4158/3177
75–79	5297/1886	5638/1946	6018/1980	6211/2028	4640/1598	4253/1659
80–84	4611/985	5400/1134	6199/1189	6844/1294	6926/1393	6412/1347
$\geq$ 85	3273/478	3812/539	4946/616	6581/764	7680/878	8819/1003
Total	19126/8959	20351/8490	22727/8743	25129/9535	25660/10238	26084/10950

Table 25.3 Rates of prostate cancer (per 1000 person-years) in men aged $\geq$ 65 living in France between 1979 and 1996.

	Time period					
Age group	1979–81	1982–84	1985–87	1988–90	1991–93	1994–96
65–69	0.68	0.71	0.72	0.74	0.70	0.65
70–74	1.49	1.48	1.60	1.53	1.43	1.31
75–79	2.81	2.90	3.04	3.06	2.90	2.56
80–84	4.68	4.76	5.21	5.29	4.97	4.76
$\geq$ 85	6.85	7.07	8.03	8.61	8.75	8.79
Crude rate	2.13	2.40	2.60	2.64	2.51	2.38
Standardized rate	2.35	2.40	2.60	2.64	2.54	2.39

This means that the overall rates in each time period need to be adjusted for the age distribution of the corresponding population before they can meaningfully be compared. We will do this using the method of direct standardization.

1 The first step in direct standardization is to identify a standard population. This is usually one of the following:
   - one of the study populations
   - the total of the study populations
   - the census population from the local area or country

   The choice is to some extent arbitrary. Different choices lead to different summary rates but this is unlikely to affect the interpretation of the results unless the patterns of change are different in the different age group strata (see point 5). Here we will use the number of person-years for the period 1985–87.

2 Second, for *each of the time periods of interest*, we calculate what would be the overall rate of prostate cancer in our standard population if the age-specific rates equalled those of the time period of interest. This is called the *age standardized survival rate* for that time period.

$$\text{Age standardized rate} = \begin{array}{l}\text{Overall rate in standard population}\\ \text{if the age-specific rates were the same}\\ \text{as those of the population of interest}\end{array} = \frac{\Sigma(w_i \times \lambda_i)}{\Sigma w_i}$$

In the above definition, w_i is the person-years at risk in age group i in the standard population, $\lambda_i = d_i/pyar_i$ is the rate in age group i in the time period of interest and the summation is over all age groups. Note that this is simply a **weighted average** (see Section 18.3) of the rates in the different age groups in the time period of interest, weighted by the person-years at risk in each age group in the standard population.

Table 25.4 Calculating the age standardized rate of prostate cancer for 1979–81, using direct standardization with the person-years during 1985–87 as the standard population.

Age group	Standard population: thousands of person-years in 1985–87, w_i	Study population: Rates in 1979–81, λ_i	Estimated number of cases in standard population, $w_i \times \lambda_i$
65–69	2686	0.6805	1827.8
70–74	2272	1.4864	3377.1
75–79	1980	2.8086	5561.0
80–84	1189	4.6812	5565.9
$\geq$ 85	616	6.8473	4217.9
All ages	$\Sigma w_i = 8743$	Age adjusted rate = 2.35	$\Sigma(w_i \times \lambda_i) = 20549.8$

For example, Table 25.4 shows the details of the calculations for the age-standardized rate for 1979–81, using the person-years in 1985–87 as the standard population. In the 65 to 69-year age group, applying the rate of 0.6805 per 1000 person-years to the 2686 person-years in that age group in the standard population gives an estimated number of cases in this age group of $0.6805 \times 2686 = 1827.8$. Repeating the same procedure for each age group, and then summing the numbers obtained, gives an overall estimate of 20549.8 cases out of the total of 8743 thousand person-years in the *standard* population: an age-standardized rate for the *study* population of 2.35 per 1000 person-years.

3 The results for all the time periods are shown in the bottom row of Table 25.3. The crude and standardized rates of prostate cancer in the different time periods are plotted in Figure 25.1(a). This shows that the crude rate was lower than the directly standardized rate in the 1979–81 period, but similar thereafter. This is because, as can be seen in Table 25.2, in the 1979–81 period there were proportionally fewer person-years in the oldest age groups, in which prostate cancer death rates were highest.

4 The standard error for the standardized rate is calculated as:

Standard error of standardized rate	Standard error of standardized proportion
$\dfrac{1}{\Sigma w_i}\sqrt{\left(\sum \dfrac{w_i^2 d_i}{(pyar_i)^2}\right)}$	$\dfrac{1}{\Sigma w_i}\sqrt{\left(\sum \dfrac{w_i^2 p_i(1-p_i)}{n_i}\right)}$

where the left hand formula is used for standardized rates and the right hand formula for standardized proportions. In these formulae the weights w_i are the person-years or number of individuals in the standard population. Using this formula, the standard error of the standardized rate in 1979–81 is 0.017 per 1000 person-years, so that the 95% confidence interval for the standardized rate in 1979–81 is:

$$\begin{aligned}95\%\ \text{CI} &= 2.35 - 1.96 \times 0.017 \text{ to } 2.35 + 1.96 \times 0.017\\ &= 2.32 \text{ to } 2.38 \text{ per 1000 person-years}\end{aligned}$$

5 Finally, it is important to inspect the patterns of rates in the individual strata before standardizing, because when we standardize we assume *that the patterns of change in the rates are similar in each stratum*. If this is not the case then the choice of standard population will influence the observed pattern of change in the standardized rates. For example, in Figure 25.1(b) it can be seen that the rate in the ≥ 85 year age group increased more sharply than the rates in the other age groups. This means that the greater the proportion of individuals in the ≥ 85 year age group in the standard population, the sharper will be the increase in the standardized rate over time.

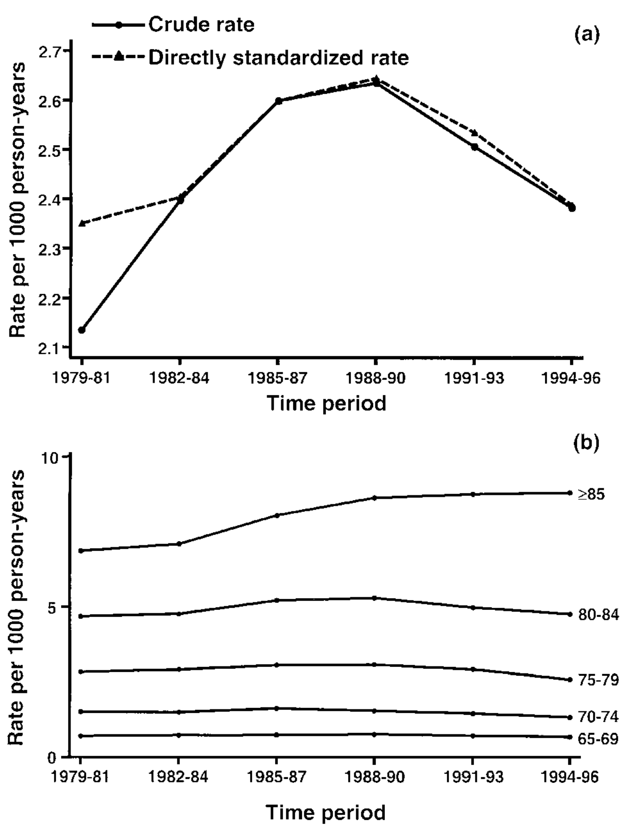

Fig. 25.1 (a) Crude and directly standardized rates of prostate cancer among men aged $\geq$ 65 years living in France between 1979 and 1986, with the population in 1985–87 chosen as the standard population. (b) Time trends in age-specific rates of prostate cancer, among men aged $\geq$ 65 years living in France between 1979 and 1986.

25.3 INDIRECT STANDARDIZATION

Example 25.2

Table 25.5 shows mortality rates from a large one-year study in an area endemic for onchocerciasis. One feature of interest was to assess whether blindness, the severest consequence of onchocerciasis, leads to increased death rates. From the results presented in Table 25.5 it can be seen that:

- not only does mortality increase with age and differ slightly between males and females, but
- the prevalence of blindness also increases with age and is higher for males than for females.

The blind sub-population is therefore on average older, with a higher proportion of males, than the non-blind sub-population. This means that it would have a higher crude mortality rate than the non-blind sub-population, even if the individual age–sex specific rates were the same. An overall comparison between the blind and non-blind will be obtained using the method of indirect standardization.

1 As for direct standardization, the *first* step is to identify a standard population. The usual choices are as before, with the restrictions that age–sex specific mortality rates are needed for the standard population and that the population chosen for this should therefore be large enough to have reliable estimates of these rates. In this example the rates among the non-blind will be used.

2 These standard rates are then applied to the population of interest to calculate the *number of deaths* that would have been *expected* in this population if the mortality experience were the same as that in the standard population.

For example, in stratum 1 (males aged 30–39 years) one would expect a proportion of 19/2400 of the 120 blind to die, if their risk of dying was the same as that of the non-blind males of similar age. This gives an expected 0.95 deaths for this age group. In total, 22.55 deaths would have been expected among the blind compared to a total observed number of 69.

3 The ratio of the observed to the expected number of deaths is called the **standardized mortality ratio (SMR)**. It equals 3.1 (69/22.55) in this case. Overall, blind persons were 3.1 times more likely to die during the year than non-blind persons.

$$\text{Standardized mortality ratio (SMR)} = \frac{\text{observed number of deaths}}{\text{expected number of deaths if the age–sex specific rates were the same as those of the } \textit{standard} \text{ population}} = \frac{\Sigma d_i}{\Sigma E_i}$$

The SMR measures how much more (or less) likely a person is to die in the study population compared to someone of the same age and sex in the standard population. A value of 1 means that they are equally likely to die, a value larger

Table 25.5 Use of indirect standardization to compare mortality rates between the blind and non-blind, collected as part of a one-year study in an area endemic for onchocerciasis. The mortality rates among the non-blind have been used as the standard rates.

		Non-blind persons			Blind persons				
Age (yrs)	Stratum (i)	Number of person-years	Number of deaths	Deaths/1000/yr (λ_i)	% blind	Number of person-years (T_i)	Number of deaths (d_i)	Deaths/1000/yr	Expected number of deaths among blind if rates were the same as those of the non-blind ($E_i = \lambda_i \times T_i$)
Males									
30–39	1	2400	19	7.9	4.8	120	3	25.0	0.95
40–49	2	1590	21	13.2	9.7	171	7	40.9	2.26
50–59	3	1120	20	17.9	17.9	244	13	53.3	4.36
60+	4	610	20	32.8	28.0	237	24	101.3	7.77
Females									
30–39	5	3100	23	7.4	2.6	84	2	23.8	0.62
40–49	6	1610	22	13.7	4.1	69	3	43.5	0.94
50–59	7	930	16	17.2	15.3	168	8	47.6	2.89
60+	8	270	8	29.6	25.6	93	9	96.8	2.76
Total		11630	149	12.8	9.3		69	58.2	22.55
SMR				1.0				3.1 (69/22.5)	
Age–sex adjusted mortality rate				12.8				39.7 (3.1 × 12.8)	

than 1 that they are more likely to die, and a value smaller than 1 that they are less likely to do so. The SMR is sometimes multiplied by 100 and expressed as a percentage. Since the non-blind population was used as the standard, its expected and observed numbers of deaths are equal, resulting in an SMR of 1.

4 The 95% confidence interval for the SMR is derived using an error factor (EF) in the same way as that for a rate ratio (see Section 23.2):

$$95\%\ \text{CI} = \text{SMR}/\text{EF to SMR} \times \text{EF, where}$$
$$\text{EF} = \exp(1.96/\sqrt{\text{d}_\text{i}})$$

In this example, $\text{EF} = \exp(1.96/\sqrt{69}) = 1.266$, and the 95% confidence interval for the SMR is:

$$95\%\ \text{CI} = \frac{\text{SMR}}{\text{EF}} \text{ to SMR} \times \text{EF} = 3.06/1.266 \text{ to } 3.06 \times 1.266 = 2.42 \text{ to } 3.87$$

5 **Age–sex adjusted mortality rates** may be obtained by multiplying the SMRs by the crude mortality rate of the standard population, when this is known. This gives age–sex adjusted mortality rates of 12.8 and 39.7/1000/year for the non-blind and blind populations respectively.

$$\begin{array}{c} \text{Age–sex adjusted} \\ \text{mortality rate} \end{array} = \text{SMR} \times \begin{array}{c} \text{crude mortality rate of} \\ \text{standard population} \end{array}$$

25.4 USE OF POISSON REGRESSION FOR INDIRECT STANDARDIZATION

We may use Poisson regression to derive the SMR, by fitting a model with:

- each row of data corresponding to the strata in the study population;
- the number of events in the study population as the outcome. In Example 25.2 this would be the number of deaths in the blind population;
- *no* exposure variables (a 'constant-only' model);
- specifying the *expected number* of events in each stratum (each row of the data), instead of the number of person-years, as the offset in the model. In Example 25.2, these are the expected number of deaths given in the right hand column of Table 25.5.

Table 25.6 shows the output from fitting such a model to the data in Example 25.2. The output is on the log scale, so the SMR is calculated by antilogging the

Table 25.6 Poisson regression output (log scale), using the expected number of deaths in the blind population as the offset.

	Coefficient	s.e.	z	$P > \lvert z \rvert$	95% CI
Constant	1.1185	0.1204	9.29	0.000	0.8825 to 1.3544

coefficient for the constant term. It equals exp(1.1185) = 3.1, the same as the value calculated above.

SMR = exp(regression coefficient for constant term)

The 95% CI for the SMR is derived by antilogging the confidence interval for the constant term. It is exp(0.8825) to exp(1.3544) = 2.42 to 3.87. It should be noted that indirect standardization assumes that the age–sex specific rates in the standard population are known without error. Clearly this is not true in the example we have used: the consequence of this is that confidence intervals for the SMR derived in this way will be somewhat too narrow. For comparison, a standard Poisson regression analysis of the association between blindness and death rates for the data in Table 25.5 gives a rate ratio of 3.05, and a 95% CI of 2.24 to 4.15.

Extension to several SMRs

It is fairly straightforward to extend this procedure to estimate, for example, the SMRs for each area in a geographical region by calculating the observed and expected number of deaths in each age–sex stratum in each area, and fitting a Poisson regression model including indicator variables for each area, and *omitting* the constant term. The SMRs would then be the antilogs of the coefficients for the different area indicator variables.