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Interpretation of the Pattern in Rate Ratios Across Strata*

Paul F. Visintainer, PhD,[†] and Suzanne Havstad, MA[†]

The pattern in the ratio of disease rates over strata is a summary statistic used to describe the changing risk of disease in one group relative to another. While patterns of the ratios of disease rates over strata appear to correspond to specific changes in disease rates, plots of the disease rates over strata seem to contradict the information yielded by the ratios. For example, if disease rates from populations A and B have identical rates of decline (parallel lines), the difference in the rates (A - B) at each strata remains constant, while the ratio of the rates (A/B) increases over strata. Through simple algebraic manipulation, one can show that the pattern of the rate ratio is a function of the rate difference relative to the endemic disease rate. Thus, rather than describing the behavior of the disease rates, ratio patterns reflect the importance of exposure relative to the disease rate in the unexposed population. (Henry Ford Hosp Med J 1992;40:139-43)

The use of summary statistics offers a convenient way of conveying complex information, yet use of summary statistics heightens the potential for misinterpretation if the user or audience is unaware of the limitations of the statistic. Plotting the rate ratio over strata (e.g., time or age) is one method used for describing changes in the risk of disease over strata. A rate ratio, such as the relative risk, is computed by dividing the disease rate of one population by the disease rate of another. To examine evidence of trends, stratum-specific ratios, such as ratios over time periods or age groups, are plotted and compared across strata (1,2). Rate ratio patterns are usually presented along with patterns in the rate differences (e.g., attributable risk) over strata in order to display both the relative and absolute changes over strata. However, plots of rate ratios and rate differences yield different patterns and the interpretations of each can be difficult to reconcile.

The confusion in the interpretation of patterns in rate ratios and rate differences arises from two areas. The first deals with the apparent contradiction in the information between rate ratios and rate differences. For instance, Satariano and Swanson (1) examined racial differences in cancer incidence by comparing the age-specific incidence for stomach cancer among black and white females (Fig 1). The incidence rate for black females increased from 1.59 cases per 100,000 in the youngest age group to 106.73 cases per 100,000 in the oldest age group. Corresponding incidence rates for white females were 0.58 and 95.80 cases per 100,000. The black/white incidence ratio declines with advancing age from 2.74 at the youngest age group to 1.11 at the oldest age group. This suggests that the risk of stomach cancer due to being black declines with age. However, the difference in the incidence rates increases from 1.01 cases per 100,000 at the youngest age group to 10.93 cases per 100,000 at the oldest age group. The contradiction can be stated simply: why does the risk of stomach cancer (due to being black) decline with advancing age, while the difference in the number of cases between blacks

and whites increases? Statisticians will recognize that this seeming contradiction results from data being described using two different mathematical models. However, to practicing health professionals, the resolution may not be clear.

The second area that leads to confusion in examining these data is how to interpret rate ratios relative to rate differences. For those who are familiar with them, the mathematical models associated with each measure can guide interpretations. Some have attempted to provide textual guidelines for use. In comparing the sex differential in mortality rates, Wingard and Verbrugge (2,3) have suggested that ratios should be used when assessing changes in the sex differentials in mortality over time, since differences will reflect both changes in sex differentials in mortality and changes in the overall risk of disease. We suspect that many will find this explanation vague and of little help in using rate ratios and rate differences.

In view of the problems in the application and interpretation of the rate ratio, we will explain the behavior of the pattern of the rate ratio over strata in light of changes in the disease rates of two populations. First, with a simple algebraic manipulation, we will show how the rate ratio relates to the rate difference. Second, we will clarify the interpretation of the pattern of the rate ratio relative to the rate difference.

Explanation and Interpretation of the Models

To demonstrate the problem, consider the following illustration. Fig 2 shows the general patterns of the disease ratio relative

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to the disease rates for imaginary populations A and B. (For simplicity, the patterns in the disease rates over age for populations A and B are presented as straight lines. This pattern would result if disease rates were linearly related to time and represented by a simple linear regression.) In Fig 2A, the disease rates for both populations increase with advancing age in parallel fashion (i.e., slopes are equal). The difference in the rates (A - B) at each age stratum is constant. However, the ratio of the disease rates (A/B) at each age strata *decreases* with advancing age. If the plot of the rate ratio were the only information given to represent the disease experience of population A compared to population B, one might interpret this pattern as evidence that the disease rates of populations A and B were becoming more similar with advancing age. That is, one might conclude that the disease rates were converging as age increased. However, this is not the case.

Fig 2B shows that parallel decreasing rates can produce an increasing trend in the rate ratio. Figs 2C and 2D show that disease rates that either diverge or converge can yield a constant rate ratio. While the initial encounter with these illustrations appears to yield contradictory information, resolution lies in distinguishing between the rate difference and rate ratio and the models associated with each.

First, the rate difference is defined by the additive model as the difference between the two rates for each stratum. This can be expressed as:

$$d_i = w_{Ai} - w_{Bi} \quad (1)$$

where w_{Ai} represents the disease rate in the exposed population for the i -th strata, and w_{Bi} represents the disease rate in the unexposed population for the i -th strata. If population A represents the exposed group and population B the unexposed group, and the two groups are similar with respect to other covariates affecting outcome, the difference between the two rates (d_i) is attributed to exposure. In the absence of exposure, population A would be expected to have the same endemic disease rate as B (4). The difference in rates also has been referred to as "excess risk," "risk difference," or "attributable risk" (4,5).

If the rate of change over strata (i.e., slope) of the disease rates is identical for the two populations, then the subscript i can be dropped from the left side of equation (1) and the rate difference can be stated as:

$$d = w_{Ai} - w_{Bi} \quad (2)$$

where w_{Ai} and w_{Bi} are defined as above. The rate difference due to exposure is represented by d , which is constant over strata.

In comparison, the rate ratio is defined by the multiplicative model and is represented by:

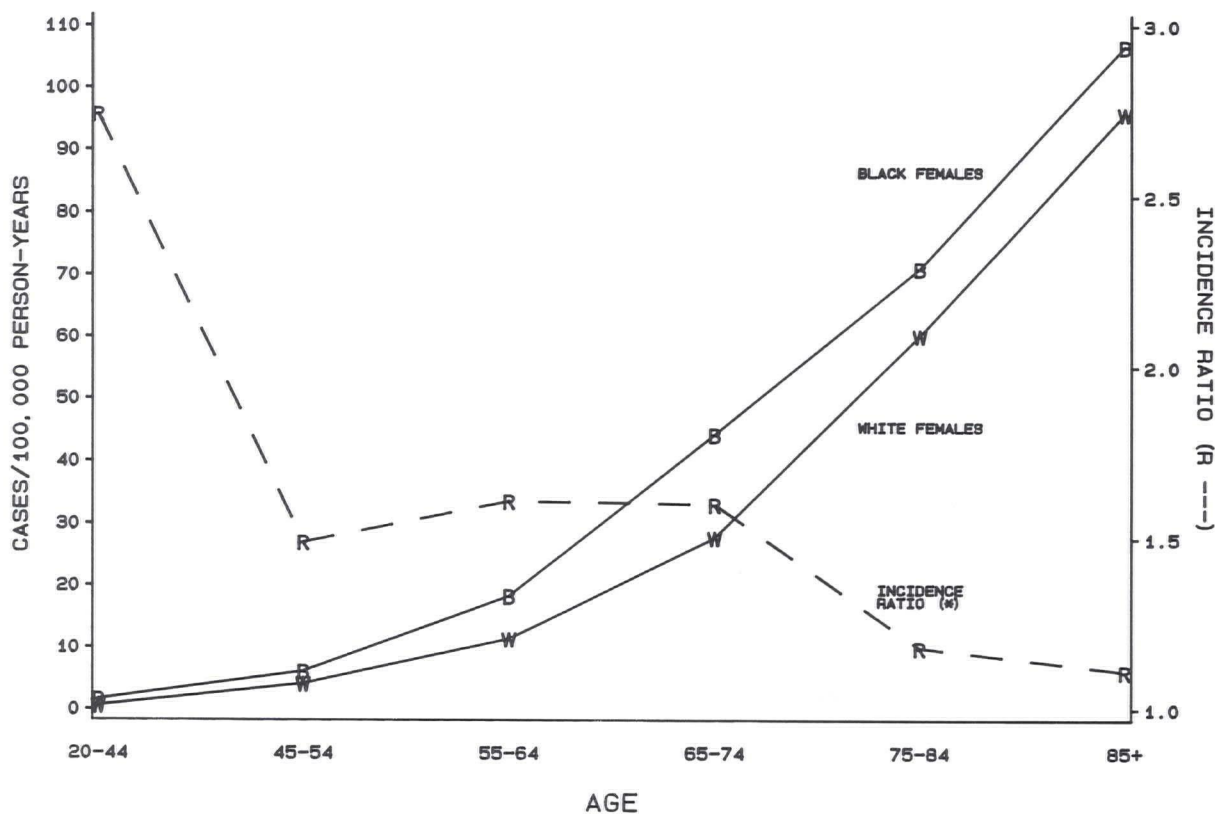


Fig 1—Incidence rates and the corresponding incidence ratio for cancer of the stomach for females, 1973-1982, by race and age (1). (*) Incidence ratio (R) = (incidence rate for blacks [B])/(incidence rate for whites [W]).

$$r_i = w_{Ai}/w_{Bi} \quad (3)$$

where r_i represents the proportional increase or decrease in risk due to exposure for the i -th strata. The term rate ratio has been used interchangeably with "risk ratio" and "relative risk" (4,5).

With the above notation, it is possible to demonstrate why the rate ratio changes over strata when the rate difference remains constant. In Fig 2A, the increasing disease rates of populations A and B are represented by two parallel lines with positive slopes. Parallel lines reflect the constant difference in disease rates across strata, in this case age strata (i.e., $d_i = d$). Using equation (2), we can substitute for w_{Ai} in equation (3), and the rate ratio can be expressed as:

$$r_i = (w_{Bi} + d)/w_{Bi} \quad (4)$$

which reduces to:

$$r_i = 1 + d/w_{Bi} \quad (5)$$

Therefore, if the slopes of the disease rates of populations A and B are parallel, whether increasing or decreasing over strata, the rate ratio (r_i) must change as a function of the change in the disease rate of the reference population (w_{Bi}).

Equation (5) also provides the basis for interpreting the changing rate ratios over strata. To show this, assume that the disease rate in an exposed population and unexposed population increases with advancing age. In addition, assume that the rate difference is greater than zero and is constant over strata (i.e., slopes are equal as in Fig 2A). In this situation, the rate ratio will decline with advancing age, indicating that the relative risk of disease due to exposure is greater at younger ages than at older ages. From equation (5), one can see that the rate ratio will approach 1.0 as the quantity (d/w_{Bi}) approaches zero. Thus, the declining rate ratio with advancing age reflects the declining contribution of the disease rate difference *relative* to the changes in the endemic disease rate.

The pattern in the rate ratios may also indicate the possibility of interaction between exposure and strata. A relatively stable pattern (i.e., slope of the rate ratios over strata is zero) in the rate ratios over strata suggests that the risk of disease due to exposure is independent of strata. Thus there is no interaction between exposure and strata. A consistent increasing or decreasing pattern in the rate ratios suggests that the risk of disease due to exposure is influenced by the strata.

To demonstrate this, we present the output of an analysis as it might be conducted in investigating changes in mortality rates over strata. We examined the pattern of mortality rates by gender for major diseases of the heart, for the age group 45 to 54

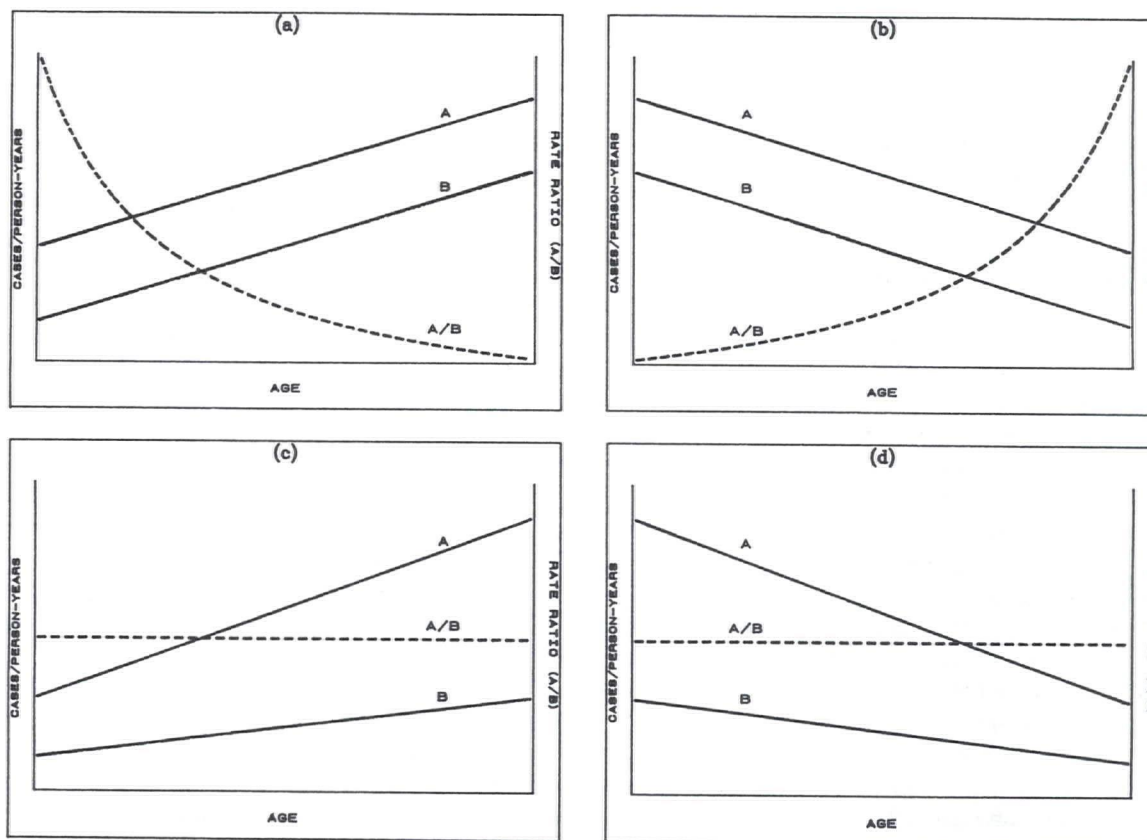


Fig 2—Incidence rate patterns for two hypothetical populations (A and B) and the corresponding pattern in the rate ratio (A/B). A = disease rate in the exposed population, B = disease rate in the unexposed population, A/B = rate ratio (relative risk).

Table 1
Mortality Rates, Rate Difference, and Rate Ratios
for Major Diseases of the Heart for Persons
Aged 45 to 54, for 1950 to 1986, by Gender

Year	Mortality Rates*		Rate Difference (M - F)	Rate Ratio (M/F)
	Males	Females		
1950	423.6	141.9	281.7	2.99
1960	413.2	103.4	309.8	3.99
1970	365.7	91.4	274.3	4.00
1980	269.8	71.2	198.6	3.80
1983	243.0	67.4	175.6	3.61
1984	231.2	63.1	168.1	3.66
1985	224.4	62.1	162.3	3.61
1986	208.8	59.8	149.0	3.49

*Deaths per 100,000.

Table 2
Linear Regression of Death Rates
for Major Diseases of the Heart, 45 to 54 Year Age
Group, on Time (1950 to 1986) and Gender:
The Additive Model

Variable	b	SE	P-Value
Time	-6.41	0.481	0.0001
Gender	-567.34	51.566	0.0001
Time × Gender	4.31	0.680	0.0001

years, from 1950 through 1986 (6). Table 1 shows the rate differences and rate ratios by gender at each year. Inspection of the rate difference shows a fairly consistent decline over time. On the other hand, the rate ratios do not show any increasing or decreasing trend across strata. If the data are fitted to a linear regression model (additive model), a significant interaction term (Time × Gender) emerges, as shown in Table 2 (see Kleinbaum and Kupper [7] for a general discussion of multiple variable methods). The regression coefficient of the interaction term represents the disparity over time in the slopes of the male and female death rates. The significant interaction term verifies that the rate difference (M - F) declines as time advances. Thus, the attributable risk changes over time.

If the multiplicative model (8) is fitted to the data (i.e., log $[w_{Ai}/w_{Bi}] = a + B_1[\text{time}] + B_2[\text{gender}] + B_3[\text{time} \times \text{gender}] + e$) as in Table 3, regression analysis of the transformed data shows that only the main effects of Time and Gender are significant. The absence of a significant interaction term indicates that the rate ratio (M/F) does not vary over time. In other words, the *relative risk* does not change over time.

Equation (5) provides some insight for interpreting the results. While the rate difference (d_i) declines over strata, the change in d_i remains proportional to the declining mortality rate of the reference population (w_{Bi}). Thus the quantity (d_i/w_{Bi}) remains constant. Therefore, relative to changes in the female rate, the rate difference maintains its contribution in explaining the gender effect.

Table 3
Log-Linear Regression of Death Rates
for Major Diseases of the Heart, 45 to 54 Year Age
Group, on Time (1950 to 1986) and Gender:
The Multiplicative Model

Variable	b	SE	P-Value
Time	-0.02	0.002	0.0001
Gender	-1.13	0.211	0.0002
Time × Gender	-0.002	0.003	0.4525

Clinical Relevance and Discussion

Patterns in the ratios of disease rates may provide useful information in explaining disease etiology. However, we have demonstrated that the pattern in the rate ratio over strata requires careful examination. Not surprisingly, the interpretation of the pattern in the rate ratio is an extension of the stratum-specific point estimate (e.g., the relative risk). While both show the proportional increase (or decrease) in risk due to a specific exposure, neither provides any information about the actual disease rates of the two populations being compared. Consequently, rate ratio patterns do not necessarily correspond to simple trends in the population disease rates. An increasing pattern in the rate ratio does not necessarily indicate diverging disease rates, nor does a decreasing rate ratio pattern always correspond to converging disease rates. A stable pattern in the rate ratio can be generated by disease rates that are quite dynamic, either converging or diverging. Thus, the precise interpretation of rate ratio variations over strata should consider the changing contribution of the difference in disease rates due to exposure relative to changes in the endemic disease rate.

Interpreting rate ratio patterns as changes in the risk difference relative to changes in the endemic disease rate provides a way to reconcile the seemingly contradictory patterns in the rate ratios and rate differences. Recall in the example of racial differences in stomach cancer that the incidence rate differences increased with advancing age while the incidence rate ratio decreased. Using the definition provided above, the difference in the cancer incidence rates due to exposure (i.e., being black) did not increase as rapidly over age strata as did the cancer incidence rate in the endemic group (white females). In other words, even though the rate difference increased over strata due to race, this increase became less important relative to the large changes in the incidence rate of white females. Thus, the relative risk of stomach cancer due to race declines with age.

Deciding which mathematical model, either rate ratio or rate difference, to apply to the data requires comment. Some advocate using the model that provides the simplest fit; that is, a fit without a significant interaction term. We feel that this approach to model selection is limited because each model yields different information. In addition to simplicity, model selection should be guided by the question that one wishes to address.

The additive model is generally considered most appropriate when addressing public health issues, such as disease frequency

reduction (5,9-11) or individual decision-making (11). For instance, as shown previously, a relative risk that declines with age suggests that the risk of disease that can be attributed to the exposure grows less with age. Yet, intervening on the risk factor at older ages may prevent as many *cases* of the disease as interventions targeted at younger groups. When addressing changes in disease frequency over strata, one should apply the additive model and examine changes in the rate difference. As we have demonstrated, one cannot rely on the pattern of the rate ratio to provide information on changes in frequency since there is no simple correspondence between patterns of the rate difference and the rate ratios.

Rate ratios, such as the relative risk, are considered to be more useful in describing disease etiology (5,10,11). For example, Pollack and others (12) found a significant threefold increase in the risk of rectal cancer among heavy beer drinkers compared to non-beer drinkers. This significant increase in the relative risk implicates alcohol consumption in the etiology of rectal cancer. However, the relative risk alone provides no information on the incidence of rectal cancer in the exposed and unexposed groups or on the prevalence of the exposure. Without these data, the practitioner would not know whether this increased risk represents a substantial increase in the number of *cases* of rectal cancer. As Breslow and Day (4) point out, relative risk is important in evaluating the extent to which a relationship is causal. They note that the relative risk as a summary statistic requires little qualification in describing the point estimate of disease risk due to exposure in a population. Similarly, the pattern in the rate ra-

tios over strata can be useful in investigating disease etiology. One must caution, though, against misinterpreting the patterns in the disease rates.

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