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ORIGINAL CONTRIBUTIONS

Logistic Regression Analysis for More than One Characteristic of Exposure

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When more than one characteristic of an exposure is under study, it is easy to misinterpret the results of a logistic regression analysis that incorporates terms for each characteristic. For example, in a study of the risk of endometrial cancer in relation to the duration and the recency of use of estrogen replacement therapy (ERT), simultaneously including terms for duration and recency of exposure to ERT in a logistic model may leave the mistaken impression that it is possible to adjust for recency when a given duration of ERT use is compared with no use. In this article, the authors show why such an adjusted comparison is impossible, and they discuss several pitfalls in the interpretation of logistic regression coefficients when two or more characteristics of exposure are under study. They also suggest a method for avoiding these pitfalls. *Am J Epidemiol* 1999;149:984–92.

confounding factors (epidemiology); epidemiologic methods; logistic models; models, statistical; regression analysis

There are many examples in epidemiology of instances in which we want to evaluate the risks of disease associated with more than one characteristic of exposure. When we assessed the long-term effect of estrogen replacement therapy (ERT) on the risk of endometrial cancer, for example, we were interested in both the recency and the duration of estrogen use (1). Cheng et al. (2) studied the effects of a history of alcohol consumption on the risk of esophageal cancer, and they considered both the cumulative dose and the recency of exposure among former drinkers. A number of studies of reproductive history and the risk of breast cancer have examined the effects of both increasing parity and age at first full-term pregnancy on the risk of breast cancer (3).

In examples such as these, it is tempting to try to adjust the risks associated with one characteristic of exposure relative to unexposed persons for other characteristics of exposure. For example, when estimating the risk of endometrial cancer associated with use of ERT for a given duration relative to never use of estrogen, we might consider adjusting for how recently ERT use stopped, since recency of use has a strong bearing on risk (1). Standard logistic regression analysis may result in the misleading impression that this type of adjustment is possible, since it is easy to create logistic models that simultaneously include terms for duration of use and recency of use and to fit them to data on ever and never users.

However, the coefficients of these terms do *not* give these adjusted log relative risks. In fact, it is not possible to adjust the relative risks associated with one characteristic of exposure for another characteristic when unexposed persons constitute the reference category. In this paper, we propose to 1) explain why this is so, 2) describe the relative risks for each characteristic of exposure that can be estimated from data on both exposed and unexposed persons and show how logistic regression models can be used to make these estimates, 3) show how commonly applied logistic models can be easily misinterpreted and give the correct interpretations for coefficients in several logistic models in which terms are included for more than one characteristic of exposure, and 4) summarize our arguments and recommend how to ensure that logistic regression coefficients are interpreted correctly.

Our discussion is framed in terms of case-control data and logistic models, but the principles we describe

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Abbreviation: ERT, estrogen replacement therapy.

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apply to other designs and other regression models. Our conclusions also generalize to three or more characteristics of exposure (for instance, dose, duration, and recency of exposure to ERT; age when ERT use began; and menopausal status when ERT use began), although all of our examples consider only two.

WHEN IS ADJUSTMENT NOT POSSIBLE?

When we adjust a relative risk for a confounding variable by using either logistic regression or a stratified analysis, the adjusted relative risk obtained is interpreted as a comparison of the risks associated with two levels of the exposure variable among subjects who have a common value of the adjustment variable. For example, in adjusting the relative risk comparing high with low alcohol consumption for smoking in a study of esophageal cancer, we would interpret the adjusted relative risk as comparing high with low alcohol consumption among subjects whose smoking histories were similar. When there is no interaction term, we assume that this relative risk is the same for all smoking histories.

Table 1 shows why this interpretation is not possible when the exposure variable and adjustment variable are characteristics of the same exposure and when the comparison includes subjects who have no exposure. In the table, cells are blank if no data are possible. If the ERT example is used, it is evident that within the stratum defined by last ERT use more than 8 years ago, we cannot compare women in any of the three categories of duration of ERT use with never users, since no unexposed woman belongs to a stratum defined by ERT use more than 8 years ago. Similarly, within the stratum of recency defined by the never users, we cannot compare any of the three duration categories of ERT use with never use of ERT, because no woman with a duration of estrogen use of less than 4 years, 4–8 years, or more than 8 years can belong to the stratum of never users.

The same problem occurs when the exposure and adjustment roles of ERT duration and ERT recency are interchanged. In both cases, the problem is due to the logical impossibility of the comparison made by the adjusted relative risks and is not due to missing data or a weakness in any statistical technique. The problem would occur whether we were performing a stratified Mantel-Haenszel or a logistic regression analysis.

TABLE 1. Cross-classification of the duration and recency of estrogen replacement therapy use*

Recency of use	Duration of use			
	Never users	<4 years	4–8 years	>8 years
Never users	✓			
>8 years ago		✓	✓	✓
2–8 years ago		✓	✓	✓
<2 years ago		✓	✓	✓

* Blank cells, no data possible.

WHAT CAN BE ESTIMATED?

Although the "adjusted" comparison of exposed with unexposed persons cannot be made in this setting, two other types of comparisons can be made. The first is the relative risk for exposed persons who have different combinations of the two characteristics of exposure compared with unexposed persons. For example, it makes sense to talk about the relative risks for 1) a duration of less than 4 years and a recency of less than 2 years ago compared with no exposure, 2) a duration of more than 8 years and a recency of less than 2 years ago compared with no exposure, 3) a duration of less than 4 years and a recency of more than 8 years ago compared with no exposure, or 4) a duration of more than 8 years and a recency of more than 8 years ago compared with no exposure, or any other combination of duration and recency among users compared with no exposure. In Codings and Interpretations, we show how the relative risks can be estimated by using logistic models.

The second useful comparison involves calculating the relative risk associated with one characteristic of exposure, adjusted for the other, *among exposed persons*. In the example, it makes sense to compare women who stopped using ERT more than 8 years ago with women who have used ERT within the past 2 years, adjusted for the duration of ERT use. Only when we try to extend these adjusted comparisons to never users do problems occur.

CODINGS AND INTERPRETATIONS

In this section, we consider a number of logistic models that could be fit to data on two characteristics of exposure. We show how the relative risks of interest can be written in terms of model parameters and how naive interpretations of model parameters can be incorrect. For all models, we continue with the example of duration and recency of exposure to ERT. To keep things simple, we consider only the circumstance in which both characteristics of exposure (recency and duration) are divided into three categories for exposed persons, although the similar models and interpretations apply when there are a larger number of categories of either variable or when one or more of the variables are continuous.

In all of the examples, we assume that the data come from a case-control study and that a prospective logistic model is used (4); therefore, the p in logit(p) refers to the probability that a subject in the sample is a case

and not the probability that someone in the population is a case (5). The categories of duration of estrogen use are the same as those shown in table 1.

Indicator variable for ever use and two sets of indicator variables for recency and duration

One way to acknowledge that comparisons among exposed persons are different from comparisons of exposed with unexposed persons is to include an indicator for any exposure whatsoever and then to include indicators for two of the three exposure groups for each of the characteristics of exposure. Let

$$X_E = \begin{cases} 1 & \text{women who ever used ERT} \\ 0 & \text{women who never used ERT,} \end{cases}$$

$$X_{R2} = \begin{cases} 1 & \text{women who stopped using ERT 2–8 years ago} \\ 0 & \text{otherwise,} \end{cases}$$

$$X_{R3} = \begin{cases} 1 & \text{women who have used ERT within the past 2 years} \\ 0 & \text{otherwise,} \end{cases}$$

$$X_{D2} = \begin{cases} 1 & \text{women who used ERT for 4–8 years} \\ 0 & \text{otherwise,} \end{cases}$$

and

$$X_{D3} = \begin{cases} 1 & \text{women who used ERT for more than 8 years} \\ 0 & \text{otherwise.} \end{cases}$$

Then, the model is

$$\text{logit}(p) = \alpha + \beta_E X_E + \beta_{R2} X_{R2} + \beta_{R3} X_{R3} + \beta_{D2} X_{D2} + \beta_{D3} X_{D3}. \quad (1)$$

Unfortunately, although this model provides estimates of all odds ratios of interest discussed in the What Can Be Estimated? section of this paper, it is easy to misinterpret the regression coefficients. For example, it is tempting but incorrect to assume that $\exp(\beta_E)$ is the overall relative risk associated with exposure to ERT. The additional terms in the model indicate that the risk of disease for ERT users depends on both recency and duration of use, so there is no overall relative risk for users compared with nonusers.

If interest centers on duration of use and recency is considered an adjustment variable, it is also tempting to interpret $\exp(\beta_E)$ in this model as the odds ratio comparing a duration of less than 4 years with never use, adjusted for recency. As discussed in the When Is Adjustment Not Possible? section, this interpretation also must be incorrect.

To enable the parameters in model 1 to be interpreted correctly, the model formula for logit(p) can be written for each cell for which data are possible. These are presented in table 2. Relative risks that compare any two categories of data can be obtained by subtracting logit(p)'s for the two categories and exponentiating. Thus, it is easy to understand that $\exp(\beta_E)$ is the odds ratio that compares a subset of ERT users: those women who used ERT for less than 4 years but more than 8 years ago with never users. The odds ratio that compares women who used ERT for less than 4 years and stopped using it 2–8 years ago with never users is given by $\exp(\beta_E + \beta_{R2})$, and the odds ratio that compares women who used ERT for less than 4 years and have used it within the past 2 years with those who never used it is given by $\exp(\beta_E + \beta_{R3})$. In general, any comparison of exposed with unexposed women depends on the categories of both recency and duration of use.

Among women exposed to ERT use, adjusted comparisons are possible. The adjusted odds ratio comparing 4–8 years of use with less than 4 years of use, adjusted for recency, is given by $\exp(\beta_{D2})$; β_{D3}, β_{R2}, and β_{R3} are inter-

TABLE 2. Values for logit(p) under model 1 for the duration and recency of estrogen replacement therapy use*

Recency of use	Duration of use			
	Never users	<4 years	4–8 years	>8 years
Never users	α			
>8 years ago		$\alpha + \beta_E$	$\alpha + \beta_E + \beta_{D2}$	$\alpha + \beta_E + \beta_{D3}$
2–8 years ago		$\alpha + \beta_E + \beta_{R2}$	$\alpha + \beta_E + \beta_{D2} + \beta_{R2}$	$\alpha + \beta_E + \beta_{D3} + \beta_{R2}$
<2 years ago		$\alpha + \beta_E + \beta_{R3}$	$\alpha + \beta_E + \beta_{D2} + \beta_{R3}$	$\alpha + \beta_E + \beta_{D3} + \beta_{R3}$

* Blank cells, no data possible.

preted similarly. Model 1 assumes that these adjusted odds ratios are constant across levels of the adjustment variable. This is known as a multiplicative model, since the odds ratio associated with differences in each of two exposure characteristics is the product of the odds ratios associated with the same changes in each characteristic individually. If we wanted the odds ratios associated with different durations of use among women exposed to ERT to differ from one recency category to the next, which is a departure from the multiplicative model, we could include interaction terms between the X_D and X_R terms. To determine whether the multiplicative model described the data adequately, we would perform a score or likelihood ratio test for the simultaneous inclusion of all interaction terms.

Several of the odds ratios of interest in this model are obtained by estimating sums of coefficients in the model. Some statistical software automatically computes confidence intervals for any linear combination of logistic regression coefficients that the user specifies. However, in many statistical packages, the confidence interval must be computed by using the estimated variances and covariances of the coefficient estimates, which is done by using the standard error (SE) of the linear combination. For a linear combination of coefficients, $\beta_1 x_1 + \cdots + \beta_k x_k$:

$$\widehat{\text{Var}}(\hat{\beta}_1 x_1 + \cdots + \hat{\beta}_k x_k) = \Sigma_{i=1}^{k} x_i^2 \widehat{\text{Var}}(\hat{\beta}_i) + 2\Sigma_{i<j} x_i x_j \widehat{\text{Cov}}(\hat{\beta}_i, \hat{\beta}_j),$$

$$\text{SE}(\hat{\beta}_1 x_1 + \cdots + \hat{\beta}_k x_k) = \sqrt{(\widehat{\text{Var}}(\hat{\beta}_1 x_1 + \cdots + \hat{\beta}_k x_k))},$$

and a $(1 - \alpha)$ 100 percent confidence interval for $\exp(\beta_1 x_1 + \cdots + \beta_k x_k)$ is given by

$$(\exp(\hat{\beta}_1 x_1 + \cdots + \hat{\beta}_k x_k - z_{\alpha/2}\text{SE}(\hat{\beta}_1 x_1 + \cdots + \hat{\beta}_k x_k)), \exp(\hat{\beta}_1 x_1 + \cdots + \hat{\beta}_k x_k + z_{\alpha/2}\text{SE}(\hat{\beta}_1 x_1 + \cdots + \hat{\beta}_k x_k))).$$

For the odds ratio given by $\exp(\hat{\beta}_E + \hat{\beta}_{R2})$, the standard error is

$$\sqrt{(\widehat{\text{Var}}(\hat{\beta}_E) + \widehat{\text{Var}}(\hat{\beta}_{R2}) + 2\widehat{\text{Cov}}(\hat{\beta}_E, \hat{\beta}_{R2}))}$$

and a 95 percent confidence interval is given by

$$(\exp(\hat{\beta}_E + \hat{\beta}_{R2} - 1.96\text{SE}(\hat{\beta}_E + \hat{\beta}_{R2})), \exp(\hat{\beta}_E + \hat{\beta}_{R2} + 1.96\text{SE}(\hat{\beta}_E + \hat{\beta}_{R2}))).$$

Indicator variables for recency and duration

A more naive use of indicator variables for these data might omit the indicator of any exposure, X_E, and include dummy variables for all three of the exposure categories for each of the two characteristics of exposure. Let

$$X_{R1} = \begin{cases} 1 & \text{women who stopped using ERT more than 8 years ago} \\ 0 & \text{otherwise,} \end{cases}$$

and let

$$X_{D1} = \begin{cases} 1 & \text{women who used ERT for less than 4 years} \\ 0 & \text{otherwise.} \end{cases}$$

A model that contained all six indicator variables would be

$$\text{logit}(p) = \alpha + \beta_{R1}X_{R1} + \beta_{R2}X_{R2} + \beta_{R3}X_{R3} + \beta_{D1}X_{D1} + \beta_{D2}X_{D2} + \beta_{D3}X_{D3}. \quad (2)$$

Unfortunately, this model cannot be fit. Some statistical software will not fit it at all; other programs will drop one of the variables in the model to arrive at a model that can be fit. To understand why the model cannot be fit, consider how the coefficients would be interpreted if it were possible for all cells shown in table 1 to contain data. Table 3 shows model values for logit(p) in all of the possible and impossible (values in parentheses) cells. When table 3 is studied without noting the impossibility of some of the cells, β_{R1} would be interpreted as the log odds ratio comparing women who last used ERT more than 8 years ago with never users, among women in the same category of duration (in the same column of table 3). Similarly, β_{R2} would be interpreted as comparing women who last used ERT 2–8 years ago with never users, among women included in the same column of table 3, and β_{R3} would be interpreted as comparing women who used ERT within the past 2 years with never users, among women included in the same column of table 3. The parameters β_{D1}, β_{D2}, and β_{D3} would be interpreted as log odds ratios comparing women in each of the three categories of duration with never users, among women in the same recency category (same row of table 3).

As explained previously, data from at least one of the impossible cells in the tables would be needed to make *every one* of these comparisons. Stated in another way, we do not have information in the data about any of these adjusted log odds ratios. Thus, the data do not provide a way to estimate any of the β coefficients in model 2, and the model cannot be fit.

Grouped linear variables for recency and duration

To test whether the risk of endometrial cancer increases with the duration or the recency of ERT use among users, we can fit a model that requires the log odds ratios associated with duration or recency to increase linearly with increasing categories of duration or recency and then test whether the slopes of these linear increases differ from 0. The model assumes that the odds ratio comparing any two adjacent categories of a characteristic of exposure is the same but permits the odds ratio to be greater or less than 1, so the model is also useful when risk is expected to decrease as recency or duration of exposure increases. Even when the linear model does not fit exactly, hypothesis tests about the linear slope parameter have reasonable power (6). However, if a test for trend is not of interest, it may be preferable to estimate odds ratios by using model 1 because it does not make the linearity assumption.

Let

$$X_R = \begin{cases} 0 & \text{women who never used ERT} \\ 1 & \text{women who last used ERT more than 8 years ago} \\ 2 & \text{women who last used ERT 2–8 years ago} \\ 3 & \text{women who have used ERT within the past 2 years,} \end{cases}$$

TABLE 3. Values for logit(p) under model 2 for the duration and recency of estrogen replacement therapy use*

Recency of use	Duration of use			
	Never users	<4 years	4–8 years	>8 years
Never users	α	$(\alpha + \beta_{D1})$	$(\alpha + \beta_{D2})$	$(\alpha + \beta_{D3})$
>8 years ago	$(\alpha + \beta_{R1})$	$\alpha + \beta_{D1} + \beta_{R1}$	$\alpha + \beta_{D2} + \beta_{R1}$	$\alpha + \beta_{D3} + \beta_{R1}$
2–8 years ago	$(\alpha + \beta_{R2})$	$\alpha + \beta_{D1} + \beta_{R2}$	$\alpha + \beta_{D2} + \beta_{R2}$	$\alpha + \beta_{D3} + \beta_{R2}$
<2 years ago	$(\alpha + \beta_{R3})$	$\alpha + \beta_{D1} + \beta_{R3}$	$\alpha + \beta_{D2} + \beta_{R3}$	$\alpha + \beta_{D3} + \beta_{R3}$

* Parentheses, logit(p) in impossible cells (no information in the data to estimate these values).

and let

$$X_D = \begin{cases} 0 & \text{women who never used ERT} \\ 1 & \text{women who used ERT for less than 4 years} \\ 2 & \text{women who used ERT for 4–8 years} \\ 3 & \text{women who used ERT for more than 8 years.} \end{cases}$$

The logistic model with grouped linear variables for both recency and duration would be given by

$$\text{logit}(p) = \alpha + \beta_R X_R + \beta_D X_D. \quad (3)$$

This model is similar to model 2 in that no indicator variable separates the women exposed to ERT use from those unexposed. However, unlike model 2, model 3 can be fit. The difficulty with model 3 is in interpreting the coefficients correctly. The best way to be sure that this is done is to write model formulas for logit(p) in the cells as shown in table 4.

The naive user of logistic regression analysis might assume that since model 3 contains both X_R and X_D, $\exp(\beta_R)$ is the relative risk associated with a difference of one category of recency of ERT use adjusted for duration of ERT use and that $\exp(\beta_D)$ is the relative risk associated with a difference of one category of duration of ERT use adjusted for recency. As long as this comparison is made among estrogen users, table 4 shows that this assumption is correct. However, as stated previously, when the comparison categories include nonusers, these relative risks make impossible comparisons. We can compare only *combinations* of duration and recency among users with nonusers.

As shown in table 4, for example, the risk for a woman who used ERT for less than 4 years and stopped using it more than 8 years ago relative to the risk for a woman who never used ERT is given by $\exp(\beta_D + \beta_R)$, and the risk for a woman who used ERT for 4–8 years and stopped using it 2–8 years ago relative to a woman who never used ERT is given by $\exp(2\beta_D + 2\beta_R)$. The relative risk that compares 4–8 years of ERT use with less than 4 years of ERT use, adjusted for recency, is given by $\exp(\beta_D)$, and the relative risk that compares more than 8 years of ERT use with less than 4 years of use, adjusted for recency, is given by $\exp(2\beta_D)$. As we did with model 1, we can relax the assumption that among users, the relative risks associated with different categories of duration of use are the same for all categories of recency by including an interaction term between X_D and X_R. However, when interaction terms are added to this model, it is still assumed that the odds ratios comparing any two adjacent categories of one characteristic of exposure will be the same as long as the other characteristic of exposure is held constant.

Indicator variable for ever use and two grouped linear variables for recency and duration

Another way to write a model for the joint effects of recency and duration is to include a dummy variable for ever use of ERT and then use grouped linear variables to model the effects of duration and recency among users. This method can be helpful when the analyst wants to test for trend among exposed persons only, so that the trend test is not influenced by differences between exposed and unexposed persons. Define

$$X'_R = \begin{cases} 0 & \text{women who never used ERT or last used ERT more than 8 years ago} \\ 1 & \text{women who last used ERT 2–8 years ago} \\ 2 & \text{women who last used ERT less than 2 years ago,} \end{cases}$$

TABLE 4. Values for logit(p) under model 3 for the duration and recency of estrogen replacement therapy use*

Recency of use	Duration of use			
	Never users	<4 years	4–8 years	>8 years
Never users	α			
>8 years ago		$\alpha + \beta_D + \beta_R$	$\alpha + 2\beta_D + \beta_R$	$\alpha + 3\beta_D + \beta_R$
2–8 years ago		$\alpha + \beta_D + 2\beta_R$	$\alpha + 2\beta_D + 2\beta_R$	$\alpha + 3\beta_D + 2\beta_R$
<2 years ago		$\alpha + \beta_D + 3\beta_R$	$\alpha + 2\beta_D + 3\beta_R$	$\alpha + 3\beta_D + 3\beta_R$

* Blank cells, no data possible.

and define

$$X'_D = \begin{cases} 0 & \text{women who never used ERT or used ERT for less than 4 years} \\ 1 & \text{women who used ERT for 4–8 years} \\ 2 & \text{women who used ERT for more than 8 years.} \end{cases}$$

Then, a logistic model incorporating these three variables would be written as

$$\text{logit}(p) = \alpha + \beta_E X_E + \beta_R X'_R + \beta_D X'_D. \quad (4)$$

As in model 1, if interest centers on duration of use and recency is considered an adjustment variable, it is tempting to interpret $\exp(\beta_E)$ in this model as the odds ratio comparing a duration of less than 4 years with never use, adjusted for recency. This interpretation is again incorrect. As in model 1, $\exp(\beta_E)$ is the relative risk comparing women who used ERT for less than 4 years *and* more than 8 years ago with never users. However, the odds ratio comparing women who used ERT for less than 4 years and stopped using it 2–8 years earlier with never users is given by $\exp(\beta_E + \beta_R)$, and the odds ratio comparing women who used ERT for less than 4 years and have used it within the past 2 years is given by $\exp(\beta_E + 2\beta_R)$. Other relative risks can be obtained by exponentiating differences between cells in table 5. Note that although the variables X'_R and X'_D aggregate exposed and unexposed persons, the model permits unexposed persons to have a risk different from that of every exposed person. In contrast with model 3, tests of $H_0 : \beta_R = 0$ and $H_0 : \beta_D = 0$ test for trend with increasing recency and duration among exposed persons only.

Indicator variables for combinations of recency and duration

When interest centers on comparing different combinations of the recency and duration of exposure to ERT with no exposure, a simple way to model this with few constraints is to include one dummy variable for each combination of recency and duration. This model makes no assumptions about how odds ratios that compare different pairs of exposure configurations are related, so it is more general than multiplicative model 1 and trend models 3 and 4. It is useful when there is no interest in measuring the odds ratio associated with either characteristic of exposure adjusted for the other among exposed persons or when a statistical test indicates that interaction terms are required in multiplicative model 1. Let

$$X_{D1R1} = \begin{cases} 1 & \text{women who used ERT for less than 4 years and stopped using ERT more than 8 years ago} \\ 0 & \text{otherwise,} \end{cases}$$

$$X_{D2R1} = \begin{cases} 1 & \text{women who used ERT for 4–8 years and stopped using ERT more than 8 years ago} \\ 0 & \text{otherwise,} \end{cases}$$

$$X_{D3R1} = \begin{cases} 1 & \text{women who used ERT for more than 8 years and stopped using ERT more than 8 years ago} \\ 0 & \text{otherwise,} \end{cases}$$

TABLE 5. Values for logit(p) under model 4 for the duration and recency of estrogen replacement therapy use*

Recency of use	Duration of use			
	Never users	<4 years	4–8 years	>8 years
Never users	α			
>8 years ago		$\alpha + \beta_E$	$\alpha + \beta_E + \beta_D$	$\alpha + \beta_E + 2\beta_D$
2–8 years ago		$\alpha + \beta_E + \beta_R$	$\alpha + \beta_E + \beta_D + \beta_R$	$\alpha + \beta_E + 2\beta_D + \beta_R$
<2 years ago		$\alpha + \beta_E + 2\beta_R$	$\alpha + \beta_E + \beta_D + 2\beta_R$	$\alpha + \beta_E + 2\beta_D + 2\beta_R$

* Blank cells, no data possible.

$$X_{D1R2} = \begin{cases} 1 & \text{women who used ERT for less than 4 years and stopped using ERT 2–8 years ago} \\ 0 & \text{otherwise,} \end{cases}$$

$$X_{D2R2} = \begin{cases} 1 & \text{women who used ERT for 4–8 years and stopped using ERT 2–8 years ago} \\ 0 & \text{otherwise,} \end{cases}$$

$$X_{D3R2} = \begin{cases} 1 & \text{women who used ERT for more than 8 years and stopped using ERT 2–8 years ago} \\ 0 & \text{otherwise,} \end{cases}$$

$$X_{D1R3} = \begin{cases} 1 & \text{women who used ERT for less than 4 years and used ERT within the past 2 years} \\ 0 & \text{otherwise,} \end{cases}$$

$$X_{D2R3} = \begin{cases} 1 & \text{women who used ERT for 4–8 years and used ERT within the past 2 years} \\ 0 & \text{otherwise,} \end{cases}$$

and

$$X_{D3R3} = \begin{cases} 1 & \text{women who used ERT for more than 8 years and used ERT within the past 2 years} \\ 0 & \text{otherwise.} \end{cases}$$

Then, in the model

$$\text{logit}(p) = \alpha + \beta_{D1R1}X_{D1R1} + \beta_{D2R1}X_{D2R1} + \beta_{D3R1}X_{D3R1} + \beta_{D1R2}X_{D1R2} + \beta_{D2R2}X_{D2R2} + \beta_{D3R2}X_{D3R2} + \beta_{D1R3}X_{D1R3} + \beta_{D2R3}X_{D2R3} + \beta_{D3R3}X_{D3R3} \quad (5)$$

the odds ratio comparing, for example, women who used ERT for 4–8 years and used it within the past 2 years with the reference category of never users is given by $\exp(\beta_{D2R3})$. Model 5 is a reparameterization of the model that adds all interaction terms between recency and duration variables to model 1. Unlike the parameterization that includes interaction terms, model 5 provides odds ratios that compare different combinations of exposure with no exposure as the exponentials of single coefficients, as shown in table 6. This can make presentation simpler when software is used that readily exponentiates and provides confidence intervals for single coefficients only.

CONCLUSIONS

It is common to encounter exposures with more than one characteristic that may be related to the risk of disease. As these examples have demonstrated, logistic models can be useful in analyzing these data, but the

TABLE 6. Values for logit(p) under model 5 for the duration and recency of estrogen replacement therapy use*

Recency of use	Duration of use			
	Never users	<4 years	4–8 years	>8 years
Never users	α			
>8 years ago		$\alpha + \beta_{D1R1}$	$\alpha + \beta_{D2R1}$	$\alpha + \beta_{D3R1}$
2–8 years ago		$\alpha + \beta_{D1R2}$	$\alpha + \beta_{D2R2}$	$\alpha + \beta_{D3R2}$
<2 years ago		$\alpha + \beta_{D1R3}$	$\alpha + \beta_{D2R3}$	$\alpha + \beta_{D3R3}$

* Blank cells, no data possible.

data analyst must be careful to interpret logistic regression coefficients correctly. Although in many contexts the coefficient of a logistic regression model term is a log odds ratio that has been adjusted for all other terms in the model, this is not always true, and we have provided several examples in which this interpretation is incorrect. When more than one characteristic of exposure is examined, it is impossible to estimate relative risk by comparing one characteristic of exposure among exposed persons with unexposed persons, adjusting for the other characteristic of exposure, even though at first it may seem as if this were possible when examining the regression equation or the repression output. We recommend that whenever the interpretation of logistic regression coefficients is in doubt, tables similar to tables 2–6 should be constructed to verify the interpretation.

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