Models In Epidemiology And Biostatistics
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Session 8 : Exposure

Measured Exposure

Two Dichotomous Exposures

Exposure With More Than Two Levels

Measured Exposure

Let us now suppose that exposure (E) is measured and we will suppose that age is also measured in years (A). We will see in this section, that the issues addressing dichotomous exposure translate over with minor changes in terminology.

If the log of odds of disease varies linearly with age and the log odds of disease varies linearly with exposure:

We get a familiar looking model

Indeed, we could start with:

$$\log(p/(1-p)) = \beta_0 + \beta_1 \mathrm{G} + \beta_2 \mathrm{A} + \beta_3 \mathrm{GA} + \beta_4 \mathrm{E} + \beta_5 \mathrm{GE} + \beta_6 \mathrm{AE} + \beta_7 \mathrm{GAE}$$

This can also be rewritten as:

$$\log(p/(1-p)) = \beta_0 + \beta_1 \mathrm{G} + \beta_2 \mathrm{A} + \beta_3 \mathrm{GA} + (\beta_4 + \beta_5 \mathrm{G} + \beta_6 \mathrm{A} + \beta_7 \mathrm{GA}) \mathrm{E}$$

With this writing, we can see how age and gender change the rate of change of log of odds of disease per unit of exposure.

Indeed:

$$\log(p/(1-p)) = \beta_0 + \beta_1 G + (\beta_2 + \beta_3 G) A + (\beta_4 + \beta_5 G + (\beta_6 + \beta_7 G) A) E$$

This slope (the rate of change of log of odds of disease per unit of exposure) is now:

From the coefficient of E:

$$\beta_4 + \beta_5 G + (\beta_6 + \beta_7 G) A$$

Viewed as a function of age, we again get a line and so the rate of change of the slope per year of age is (from the coefficient of A for this line):

$$\beta_6 + \beta_7 G$$

Interpretation begins:

Here, again, we can see that, if $\beta_7 \neq 0$, then gender modifies the age modification, in that the rate of change of this slope depends on gender.

There are, of course, all the other scenarios starting with $\beta_7 = 0$ as before.

Two Dichotomous Exposures

Now let us consider the assessment of 2 exposures with indicators E_1 and E_2. The probabilities $p_{E_1 E_2}$ or the log odds $\log\left(p_{E_1 E_2}/(1-p_{E_1 E_2})\right)$ can be functions of the exposures and age and gender as before. An assessment of 2 exposures would typically begin with the study of the potential interaction. Does the disease exposure 1 relationship depend on the presence or absence of exposure 2? How is such a relationship modified by age and/or gender? If there is no modification of this form, is this interaction confounded by age and/or gender? This assessment is based on the consideration of:

...a difference between 2 differences:

The log odds ratio (exposure 1) in the presence of exposure 2 – the log odds ratio (exposure 1) in the absence of exposure 2

$$\log(p_{11}/(1-p_{11}))-\log(p_{01}/(1-p_{01}))$$
$$-(\log(p_{10}/(1-p_{10}))-\log(p_{00}/(1-p_{00})))$$

$$=\log(p_{11}/(1-p_{11}))-\log(p_{01}/(1-p_{01}))$$
$$-\log(p_{10}/(1-p_{10}))+\log(p_{00}/(1-p_{00}))$$

Notice

This is the same measure of:

The log odds ratio (exposure 2) in the presence of exposure 1 – the log odds ratio (exposure 2) in the absence of exposure 1

i.e. Does the disease exposure 2 relationship depend on the presence or absence of exposure 1?

Modeling

We now must explore how this function depends on age and gender using the strategies detailed in earlier sections.

Modeling might begin with:

$$\begin{aligned}\log(p/(1-p)) = {} & \beta_0 + \beta_1 \mathrm{G} + \beta_2 \mathrm{A} + \beta_3 \mathrm{GA} \\ & + [\beta_4 + \beta_5 \mathrm{G} + \beta_6 \mathrm{A} + \beta_7 \mathrm{GA}]\mathrm{E}_1 \\ & + [\beta_8 + \beta_9 \mathrm{G} + \beta_{10} \mathrm{A} + \beta_{11} \mathrm{GA}]\mathrm{E}_2 \\ & + [\beta_{12} + \beta_{13} \mathrm{G} + \beta_{14} \mathrm{A} + \beta_{15} \mathrm{GA}]\mathrm{E}_1 \mathrm{E}_2\end{aligned}$$

The interaction is then readily seen as:

[an exercise]

$$\beta_{12} + \beta_{13} G + \beta_{14} A + \beta_{15} GA$$

For the males: $\beta_{12} + \beta_{13} + (\beta_{14} + \beta_{15}) A$

For the females: $\beta_{12} + \beta_{14} A$

The difference is: $\beta_{13} + \beta_{15} A$

Interpretation

If $\beta_{14} \neq 0$, then, for the females, the interaction between the 2 exposures depends on age.

If $\beta_{14} + \beta_{15} \neq 0$, then, for the males, the interaction between the 2 exposures depends on age.

If $\beta_{15} \neq 0$, then the dependency on age for the males is different from the dependency on age for the females.

Just as age and/or gender can modify any individual exposure, age and/or gender can modify an interaction of 2 exposures.

Confounding

Similarly, models such as:

$$\log(p/(1-p)) = \beta_0 + \beta_1 \mathrm{G} + \beta_2 \mathrm{A} + \beta_3 \mathrm{GA}$$
$$+ \beta_4 \mathrm{E}_1 + \beta_8 \mathrm{E}_2 + \beta_{12} \mathrm{E}_1 E_2$$

could be considered to address the potential confounding of age and/or gender on the interaction through a consideration of changes to β_{12} in the models with and without A and G.

There are many other options...

For example, if the interaction of the 2 exposures is ruled out, it may still be warranted to consider both exposures in a single model starting with:

$$\log(p/(1-p)) = \beta_0 + \beta_1 G + \beta_2 A + \beta_3 GA$$
$$+ [\beta_4 + \beta_5 G + \beta_6 A + \beta_7 GA] E_1$$
$$+ [\beta_8 + \beta_9 G + \beta_{10} A + \beta_{11} GA] E_2$$

More Than 2 Levels of Exposure

The previous model could also be considered if there is a single exposure recorded at 3 levels with indicators: E_0, E_1 and E_2