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Visualizing interaction effects: a proposal for presentation and interpretation

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Abstract

Objective: Interaction terms are often included in regression models to test whether the impact of one variable on the outcome is modified by another variable. However, the interpretation of these models is often not clear. We propose several graphical presentations and corresponding statistical tests alleviating the interpretation of interaction effects.

Study Design and Setting: We implemented functions in the statistical program R that can be used on interaction terms in linear, logistic, and Cox Proportional Hazards models. Survival data were simulated to show the functionalities of our proposed graphical visualization methods.

Results: The mutual modifying effect of the interaction term is grasped by our presented figures and methods: the combined effect of both continuous variables is shown by a two-dimensional surface mimicking a 3D-Plot. Furthermore, significance regions were calculated for the two variables involved in the interaction term, answering the question for which values of one variable the effect of the other variable significantly differs from zero and vice versa.

Conclusion: We propose several graphical visualization methods to ease the interpretation of interaction effects making arbitrary categorizations unnecessary. With these approaches, researchers and clinicians are equipped with the necessary information to assess the clinical relevance and implications of interaction effects.

Keywords: Interaction; Visualization; Categorization; Cox models; Linear models; Logistic models

1. Background

In epidemiology, interaction terms are often incorporated into multivariable regression models to test whether the impact of one variable on the outcome is modified by another variable. However, the interpretation of interaction effects is often not clear. It depends on the scale of the variables included in the interaction term (continuous and/or categorical) and the scale of the model (linear regression, logistic regression, Cox Proportional Hazards model). The interpretation is rather straightforward, if interaction effects between the two categorical variables or between one continuous and one categorical variable are considered. One such example would be an effect that can only be seen in men, but not in women, in Europeans but not in Asians etc. For such situations, there are also graphical solutions implemented in standard statistical programs [1]. If researchers are interested in interaction between two continuous variables, the interpretation is less clear. It seems that interaction terms between continuous variables are avoided or continuous variables are categorized beforehand. If significant *P*-values of continuous interaction terms are reported, most authors switch to categorizations of these former continuous variables for interpretation purposes. In general, categorizations of continuous variables are often done rather arbitrarily by choosing percentiles of the respective interacting variables, for example, by dichotomizing using the median [2]. Categorization of continuous variables leads to significant loss of information and power, though [3]. Sometimes, clinically recognized and predefined cutpoints are chosen, such as a body mass index of >30 kg/m^2 for the definition of obesity. Even in this case, information is lost because the definition of these cutpoints has been designed for a totally different purpose. This approach can lead to considerable bias. The problem even worsens, if both continuous variables that constitute to an interaction term are categorized [4].

In other cases, regression coefficients and *P*-values of interaction terms are shown, but the reader is left alone with the

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What is new?

1. Epidemiological publications on interaction effects in survival analyses mostly use categorizations of variables for the ease of interpretation. This approach might lead to considerable bias, though.
2. To ease the interpretation of interaction effects between two continuous variables, we propose a graphical visualization approach which we implemented in functions in the statistical program R. They can be used on Generalized Linear Models and Cox Proportional Hazards models.
3. The mutual modifying effect of both variables constituting the interaction effect can be shown by a two-dimensional twisted surface and interaction plots showing the effect estimator of one variable for varying values of the other variable.

interpretation. The effects and *P*-values of the main effects are also not interpretable without taking into account the concurrent levels of the other constituting variable [5].

By including multiplicative interaction terms, conditional hypotheses are tested: An increase in one variable is associated with an increase in the outcome variable, when the second interacting variable is equal to a specific value. Inevitably, all constitutive terms of an interaction term should be included in the regression model also individually. With the inclusion of an interaction term, these former average effects are conditional effects then and change just by definition. Therefore, changes in effects and/or *P*-values after including interaction terms cannot be interpreted usefully. The conditional nature also applies for the *P*-values of the conditional effects, which are given in the output tables of statistical programs: they test, whether the slope of one variable is significantly different from zero, if the other constituting variable is zero. In most cases, this test is not very useful, depending on the scale of the variable.

The typical reader will not make the necessary linear combinations to calculate the effect of the first variable for specific values of the second variable. It would be possible, though, given the typical output table of a regression model, including effect estimates, standard errors, and *P*-values. However, it is not possible to conclude on the statistical significance of such a linear combination.

Therefore, it is hardly possible to interpret interaction effects simply by looking at the output table from regression models. The results of interaction terms have to be presented in a different, more reader-friendly way.

Such examples can only rarely be found. We conducted a literature search on survival analyses publications including interaction terms between two continuous variables (see Appendix on the journal's Web site at www.jclinepi.com). It revealed that only one study group used the complete range of both continuous variables to interpret the interaction effects: The authors presented interaction plots, showing the modifying effect of waist circumference on the relationship between several parameters (cholesterol, leptin, and adiponectin) and mortality [6,7].

The lack of such forms of presentations is certainly because of unfamiliarity with the methodological background and lack of easy to use methods. Therefore, such methods are required in the clinical epidemiological setting to avoid common misinterpretations in interaction models.

To ease the interpretation of interaction effects between two continuous variables, we propose several possibilities for graphical presentation, which we implemented in functions in the statistical program R: These functions have been implemented for linear regression, logistic regression, and Cox Proportional Hazards models. To demonstrate the functionalities, one data set including survival data has been simulated and analyzed in Cox models including linear interaction effects between two continuous predictors.

2. Methods

2.1. Formulating and interpreting multiplicative interaction terms in linear, logistic, and Cox models

For explanatory purposes, a linear regression model is assumed first. Interaction terms between two continuous variables x_1 and x_2 on the continuous outcome variable Y can be modeled in the following way:

$$E(Y|x_1,x_2) = X\beta = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 (x_1 * x_2) \tag{1}$$

with β_0 being the intercept, β_1 and β_2 the conditional effects of x_1 and x_2 and β_3 being the interaction effect on the outcome Y. The linear combination on the right side of the equation is the linear predictor $X\beta$, to which further covariates can be added. The regression coefficients for x_1 and x_2 are conditional effects because they depend on the values of the other constituting variable:

A one unit change of x_1 corresponds to a change of $\beta_1 + \beta_3 x_2$ on Y.

A one unit change of x_2 corresponds to a change of $\beta_2 + \beta_3 x_1$ on Y.

This means that β_1 itself is the effect of x_1 on Y, if x_2 is equal to zero and vice versa. Thus, the interpretation of regression coefficients cannot be done without taking the levels of the interacting variable into account. According to Rothman [8], the statistical term " interaction" is used to refer to departure from the underlying form of a statistical model. For a linear model, a significant interaction term thus implies deviation from additivity, meaning the additive effect of the individual effects $\beta_1 x_1 + \beta_2 x_2$ on the outcome.