

Type of Paper: Review Article

Title:

A Primer on Marginal Effects – Part I: Theory and Formulae

Short title: Primer on Marginal Effects

Authors: Onukwugha E¹, Bergtold J², Jain R³

¹220 Arch Street, Department of Pharmaceutical Health Services Research, University of Maryland School of Pharmacy, Baltimore, MD, USA.

²304G Waters Hall, Department of Agricultural Economics, Kansas State University, Manhattan, KS, 66506-4011.

³HealthCore, Inc., 800 Delaware Avenue 5th Floor, Wilmington, DE 19801, USA.

Corresponding author:

Eberechukwu Onukwugha

220 Arch Street, 12th Floor

Baltimore, MD 21201

(410) 706-8981

eonukwug@rx.umaryland.edu

TECHNICAL APPENDIX.

Marginal effect formulas for the linear, logit, multinomial logit, generalized linear model with log link, poisson, negative binomial, two-part, sample selection, and survival models.

1. Linear Regression Model

A typical linear regression equation with two independent variables takes the form:

$$E(y|x_1, x_2) = f(x_1, x_2) = \beta_0 + \beta_1 x_1 + \beta_2 x_2.$$

We examine each of the cases presented above for the linear regression model, showing how marginal and interaction effects changes under different conditions. For each case, assume x_1 and x_2 are continuous unless indicated otherwise.

Case 1: Linearity in the covariates.

Let $E(y|x_1, x_2) = f(x_1, x_2) = \beta_0 + \beta_1 x_1 + \beta_2 x_2$. Then:

$$\text{ME}_2: \frac{\partial f(\cdot)}{\partial x_2} = \beta_2$$

In a linear regression with only linear transformations of variables, *the marginal effect is constant.*

Case 2: Inclusion of nonlinear transformations of the covariates.

Now consider the case where $E(y|x_1, x_2) = f(x_1, x_2) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_2^2$, then

$$\text{ME}_2: \frac{\partial f(\cdot)}{\partial x_2} = \beta_2 + 2\beta_3 x_2.$$

The marginal effect of x_2 , in this case is a function of x_2 . If $\beta_3 \geq 0$ (≤ 0); then the marginal effect of x_2 on y is increasing (decreasing) as x_2 increases (decreases).

Case 3: Inclusion of an interaction term between covariates.

If $E(y|x_1, x_2) = f(x_1, x_2) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 (x_1 * x_2)$, then

$$ME_2: \frac{\partial f(\cdot)}{\partial x_2} = \beta_2 + \beta_3 x_1$$

Now, the marginal effect of x_2 depends on the value of x_1 .

Case 4: Linearity in the covariates with a discrete covariate.

Assume that $E(y|x_1, x_2) = f(x_1, x_2) = \beta_0 + \beta_1 x_1 + \beta_2 x_2$, but now let x_1 be binary. Then:

$$ME_1: f(x_1, x_2)|_{x_1=1} - f(x_1, x_2)|_{x_1=0} = \beta_1.$$

Note that in a linear regression with only linear transformations of variables, *the marginal effect is still constant*.

Case 5: Inclusion of an interaction term with a discrete covariate.

Let $E(y|x_1, x_2) = f(x_1, x_2) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 (x_1 * x_2)$, then:

$$ME_1: f(x_1, x_2)|_{x_1=1} - f(x_1, x_2)|_{x_1=0} = \beta_1 + \beta_3 x_2.$$

The marginal effect of x_1 in this case depends on the value of x_2 .

Case 6: Interaction effects when both covariates are continuous.

Let $E(y|x_1, x_2) = f(x_1, x_2) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 (x_1 * x_2)$. The interaction effect of the marginal effect for x_2 given a change in x_1 is:

$$ME_{21}: \frac{\partial}{\partial x_1} [ME_2] = \beta_3$$

Case 7: Interaction between a continuous and discrete covariate.

Let $E(y|x_1, x_2) = f(x_1, x_2) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 (x_1 * x_2)$, where x_1 is binary.

Then:

$$ME_{21}: \left. \frac{\partial f(\cdot)}{\partial x_2} \right|_{x_1=1} - \left. \frac{\partial f(\cdot)}{\partial x_2} \right|_{x_1=0} = \{\beta_2 + \beta_3 * 1\} - \beta_2 = \beta_3, \text{ and}$$

$$ME_{12}: = \frac{\partial}{\partial x_2} [ME_1] = \beta_3$$

A special case of the linear regression model is the *log-linear*. That is, the regression model:

$$\ln(y) = f(x_1, x_2) + u.$$

For this regression model, if the dependent variable of interest is $\ln(y)$, then the marginal effects derived above apply. That is, the marginal effect of a change in x_k on $\ln(y)$ is the statistic of interest. If instead, the applied modeler is interested in the marginal effect of x_k on y , then the marginal effect formulas will differ. First, let:

$$\overline{ME}_k = \frac{\partial f(x; \beta)}{\partial x_k} = \frac{\partial \ln(y)}{\partial x_k}.$$

To get to the marginal of x_k on y , one will need to transform the above marginal effect. This is

done by incorporating ∂y in the following way: $\frac{\partial \ln(y)}{\partial x_k} = \frac{\partial \ln(y)}{\partial x_k} \times \frac{\partial y}{\partial y} = \frac{\partial \ln(y)}{\partial y} \times \frac{\partial y}{\partial x_k} = \frac{\partial y}{\partial x_k} \times \frac{1}{y}$,

implying that $\frac{\partial y}{\partial x_k} = y \frac{\partial \ln(y)}{\partial x_k}$. Then:

$$ME_k = \overline{ME}_k \times y.$$

Thus, if a log-linear model is estimated, then the marginal effects are those derived above times the value of the dependent variable. This shows that marginal effects can include the dependent variable, as well. The above marginal effect derivations for the log-linear model assume a

homoskedastic retransformation and no need for a ‘smearing estimator’. In the case of heteroskedasticity, the ME functional will include an extra term associated with the derivative of the error term with respect to the independent variable.

2. Logistic Regression Model (or Logit Model)

Let predictor (or index) function of the model be given by $\eta(x_1, x_2; \beta)$, then the Logit model takes the form

$$E(y = 1|x_1, x_2) = \Lambda(\eta(x_1, x_2; \beta)) = \frac{1}{1 + e^{-(\eta(x_1, x_2; \beta))}}$$

where, $\Lambda(\cdot)$ is the cumulative distribution function of the standard logistic distribution. It is important to note that $E(y = 1|x_1, x_2)$ is non-linear in the β 's. Therefore, unlike the linear regression model, the magnitudes of the beta coefficients are **not** the marginal effects of the independent variables.

For the marginal effect derivations below, the following formula will be of use: If

$$\Lambda(z) = \frac{1}{1+e^{-(z)}}, \text{ then}$$

$$\frac{\partial \Lambda(\cdot)}{\partial z} = \frac{e^{-(z)}}{(1+e^{-(z)})^2} = \Lambda(z)(1 - \Lambda(z)).$$

For each case, assume x_1 and x_2 are continuous unless indicated otherwise. In addition, for ease of notation, we may represent $\eta(x_1, x_2; \beta)$ simply as η .

Case 1: Linear in the covariates.

Let $\eta(x_1, x_2; \beta) = \beta_0 + \beta_1 x_1 + \beta_2 x_2$, then:

$$\text{ME}_2: \frac{\partial \Lambda(\cdot)}{\partial x_2} = \frac{\partial \Lambda(\cdot)}{\partial \eta} * \frac{\partial \eta}{\partial x_2} = \Lambda(x_1, x_2)(1 - \Lambda(x_1, x_2))\beta_2$$

For the logit model, (i) *all independent variables* are involved in the calculation of the marginal effect and (ii) the marginal effect depends on the initial value of all the independent variables.

Case 2: Inclusion of nonlinear transformations of the covariates.

Let $\eta(x_1, x_2; \beta) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_2^2$, then:

$$\text{ME}_2: \frac{\partial \Lambda(\cdot)}{\partial x_2} = \frac{\partial \Lambda(\cdot)}{\partial \eta} * \frac{\partial \eta}{\partial x_2} = \Lambda(x_1, x_2)(1 - \Lambda(x_1, x_2))(\beta_2 + 2\beta_3 x_2)$$

As in the case of the linear regression model, we assume that the non-linear transformation of x_2 is a square function. In general, it can be any transformation. For example, if the nonlinear term in the predictor was $\ln(x_2)$ instead of x_2^2 , then:

$$\text{ME}_2: \frac{\partial \Lambda(\cdot)}{\partial x_2} = \frac{\partial \Lambda(\cdot)}{\partial \eta} * \frac{\partial \eta}{\partial x_2} = \Lambda(x_1, x_2)(1 - \Lambda(x_1, x_2))\left(\frac{\beta_2 + 2\ln(x_2)}{x_2}\right).$$

Case 3: Inclusion of an interaction term between covariates.

Consider an interaction term between x_1 and x_2 such that $\eta(x_1, x_2; \beta) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3(x_2 * x_1)$. Then:

$$\text{ME}_2: \frac{\partial \Lambda(\cdot)}{\partial x_2} = \frac{\partial \Lambda(\cdot)}{\partial \eta} * \frac{\partial \eta}{\partial x_2} = \Lambda(x_1, x_2)(1 - \Lambda(x_1, x_2))(\beta_2 + \beta_3 x_1).$$

Case 4: Linearity in the covariates with a discrete covariate.

Let $\eta(x_1, x_2; \beta) = \beta_0 + \beta_1 x_1 + \beta_2 x_2$ and assume that x_1 is binary. Then:

$$\text{ME}_1: \Lambda(x_1, x_2)|_{x_1=1} - \Lambda(x_1, x_2)|_{x_1=0} = \frac{1}{1+e^{-(\beta_0+\beta_1+\beta_2 x_2)}} - \frac{1}{1+e^{-(\beta_0+\beta_2 x_2)}}.$$

Case 5: Inclusion of an interaction term with a discrete covariate

Let $\eta(x_1, x_2; \beta) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3(x_2 * x_1)$ and assume that x_1 is binary. Then:

$$\text{ME}_1: \Lambda(x_1, x_2)|_{x_1=1} - \Lambda(x_1, x_2)|_{x_1=0} = \frac{1}{1+e^{-(\beta_0+\beta_1+\beta_2x_2+\beta_3x_2)}} - \frac{1}{1+e^{-(\beta_0+\beta_2x_2)}}.$$

The remainder of this section (Cases 6, 7, 8) is based on the work by Ai and Norton (2003). For this section, consider the predictor: $\eta(x_1, x_2; \beta) = \beta_0 + \beta_1x_1 + \beta_2x_2 + \beta_3(x_2 * x_1)$.

Case 6: Interaction effects with continuous covariates.

$$\begin{aligned} \text{ME}_{21}: \frac{\partial}{\partial x_1} [\text{ME}_2] &= \left[\frac{\partial \Lambda(x_1, x_2)}{\partial x_1} - \frac{\partial \Lambda(x_1, x_2)^2}{\partial x_1} \right] \frac{\partial z}{\partial x_2} + \Lambda(x_1, x_2)(1 - \Lambda(x_1, x_2)) \frac{\partial^2 z}{\partial x_2 \partial x_1} = \\ &= [\text{ME}_1(1 - 2\Lambda(x_1, x_2))](\beta_2 + \beta_3x_1) + \Lambda(x_1, x_2)(1 - \Lambda(x_1, x_2))\beta_3. \end{aligned}$$

Case 7: Interaction effects with a continuous and discrete covariate.

Let x_1 be binary again, making $\eta_1 = \beta_0 + \beta_1 + \beta_2x_2 + \beta_3x_2$ and $\eta_0 = \beta_0 + \beta_2x_2$. Then:

$$\text{ME}_{21}: [\text{ME}_2]|_{x_1=1} - [\text{ME}_2]|_{x_1=0} = \Lambda(\eta_1)(1 - \Lambda(\eta_1))(\beta_2 + \beta_3) - \Lambda(\eta_0)(1 - \Lambda(\eta_0))\beta_2.$$

It should be emphasized that $\text{ME}_{21} = \text{ME}_{12}$, as well.

Case 8: Interaction effects for predictor linear in the coefficients and covariates.

An interesting case is when there are no nonlinear transformations or interaction terms, i.e:

$\eta(x_1, x_2; \beta) = \beta_0 + \beta_1x_1 + \beta_2x_2$. Now let $\eta_1 = \beta_0 + \beta_1 + \beta_2x_2$ and $\eta_0 = \beta_0 + \beta_2x_2$. Then:

$$\text{ME}_{21}: [\text{ME}_2]|_{x_1=1} - [\text{ME}_2]|_{x_1=0} = \Lambda(\eta_1)(1 - \Lambda(\eta_1))\beta_2 - \Lambda(\eta_0)(1 - \Lambda(\eta_0))\beta_2.$$

3. Multinomial Logistic Regression Model

There exists a separate set of marginal effects for each outcome in the multinomial logistic regression model. These will be designated $\text{ME}_{i,j}$ for the marginal effect of variable i for

outcome j and $ME_{ik,j}$ for the interaction marginal effect of variable i and variable k for outcome j .

For each case, assume x_1 and x_2 continuous unless indicated otherwise. In addition, for ease of notation, we may represent $\eta_j(x_1, x_2; \beta)$ simply as η_j . In addition, we will assume that:

$$E(y = j | x_1, x_2, x_3) = \frac{\exp(\eta_j)}{1 + \sum_{k=1}^J \exp(\eta_k)} = h_j(x_1, x_2)$$

Case 1: Linearity in the covariates.

Let $\eta_j(x_1, x_2; \beta) = \beta_{0,j} + \beta_{1,j}x_1 + \beta_{2,j}x_2$ for $j = 1, \dots, J$. Then:

$$ME_{2,j}: \frac{\partial h(\cdot)}{\partial x_2} = \mathbf{h}_j(\mathbf{x}_1, \mathbf{x}_2) [\boldsymbol{\beta}_{2,j} - \sum_{k=0}^J \mathbf{h}_k(\mathbf{x}_1, \mathbf{x}_2) \boldsymbol{\beta}_{2,k}].$$

As was with the logit model, for the multinomial logit model (i) *all independent variables* are involved in the calculation of the marginal effect and (ii) the marginal effect depends on the initial value of the independent variables.

Case 2: Inclusion of nonlinear transformations of the covariates.

Consider the predictor $\eta_j(x_1, x_2; \beta) = \beta_{0,j} + \beta_{1,j}x_1 + \beta_{2,j}x_2 + \beta_{3,j}x_2^2$ for $j = 1, \dots, J$. Then:

$$ME_{2,j}: \frac{\partial h(\cdot)}{\partial x_2} = \mathbf{h}_j(\mathbf{x}_1, \mathbf{x}_2) [(\boldsymbol{\beta}_{2,j} + 2\boldsymbol{\beta}_{3,j}x_2) - \sum_{k=0}^J \mathbf{h}_k(\mathbf{x}_1, \mathbf{x}_2) (\boldsymbol{\beta}_{2,k} + 2\boldsymbol{\beta}_{3,k}x_2)].$$

Case 3: Inclusion of interaction terms between the covariates.

Let $\eta_j(x_1, x_2; \beta) = \beta_{0,j} + \beta_{1,j}x_1 + \beta_{2,j}x_2 + \beta_{3,j}(x_2 * x_1)$ for $j = 1, \dots, J$. Then:

$$ME_{2,j}: \frac{\partial h(\cdot)}{\partial x_2} = \mathbf{h}_j(\mathbf{x}_1, \mathbf{x}_2) [(\boldsymbol{\beta}_{2,j} + \boldsymbol{\beta}_{3,j}x_1) - \sum_{k=0}^J \mathbf{h}_k(\mathbf{x}_1, \mathbf{x}_2) (\boldsymbol{\beta}_{2,k} + \boldsymbol{\beta}_{3,k}x_1)].$$

Case 4: Linearity in the covariates with a discrete covariate.

Let x_1 be binary and $\eta_j(x_1, x_2; \beta) = \beta_{0,j} + \beta_{1,j}x_1 + \beta_{2,j}x_2$ for $j = 1, \dots, J$. Now let $\eta_{j,1} = \beta_{0,j} + \beta_{1,j} + \beta_{2,j}x_2$ and $\eta_{j,0} = \beta_{0,j} + \beta_{2,j}x_2$ for $j = 1, \dots, J$. Then:

$$ME_{1,j}: h_j(x_1, x_2) \Big|_{x_1=1} - h_j(x_1, x_2) \Big|_{x_1=0} = \frac{\exp(\eta_{j,1})}{1 + \sum_{k=1}^J \exp(\eta_{k,1})} - \frac{\exp(\eta_{j,0})}{1 + \sum_{k=1}^J \exp(\eta_{k,0})}.$$

Case 5: Inclusion of an interaction term with a discrete covariate.

Let x_1 be binary and $\eta_j(x_1, x_2; \beta) = \beta_{0,j} + \beta_{1,j}x_1 + \beta_{2,j}x_2 + \beta_{3,j}(x_2 * x_1)$ for $j = 1, \dots, J$. Now let $\eta_{j,1} = \beta_{0,j} + \beta_{1,j} + \beta_{2,j}x_2 + \beta_{3,j}x_2$ and $\eta_{j,0} = \beta_{0,j} + \beta_{2,j}x_2$ for $j = 1, \dots, J$. Then:

$$ME_{1,j}: h_j(x_1, x_2) \Big|_{x_1=1} - h_j(x_1, x_2) \Big|_{x_1=0} = \frac{\exp(\eta_{j,1})}{1 + \sum_{k=1}^J \exp(\eta_{k,1})} - \frac{\exp(\eta_{j,0})}{1 + \sum_{k=1}^J \exp(\eta_{k,0})}.$$

For the next two cases, consider the predictor: $\eta_j(x_1, x_2; \beta) = \beta_{0,j} + \beta_{1,j}x_1 + \beta_{2,j}x_2 + \beta_{3,j}(x_2 * x_1)$ for $j = 1, \dots, J$. The derivations here are based on work by Bergtold and Onukwugha[1].

Case 6: Interaction effects when the covariates are both continuous.

$$\begin{aligned} ME_{21,j}: \frac{\partial}{\partial x_1} [ME_{2,j}] \\ = h_j(x_1, x_2) [\beta_{3,j} - \sum_{k=1}^J (ME_{1,k}(\beta_{2,k} + \beta_{3,k}x_1) + h_k(x_1, x_2)\beta_{3,k})] \\ + \frac{(ME_2)(ME_1)}{h_j(x_1, x_2)} \end{aligned}$$

Case 7: Interaction effects with a continuous and discrete covariate.

Let $\eta_{j,1} = \beta_{0,j} + \beta_{1,j} + \beta_{2,j}x_2 + \beta_{3,j}x_2$ and $\eta_{j,0} = \beta_{0,j} + \beta_{2,j}x_2$ for $j = 1, \dots, J$. Then:

$$\begin{aligned} \text{ME}_{21,j}: [ME_{2,j}]|_{x_1=1} - [ME_{2,j}]|_{x_1=0} = \\ h_j(\eta_{j,1})[(\beta_{2,j} + \beta_{3,j}) - \sum_{k=0}^J h_k(\eta_{j,1})(\beta_{2,k} + \beta_{3,k})] - h_j(\eta_{j,0})[\beta_{2,j} - \\ \sum_{k=0}^J h_k(\eta_{j,0})\beta_{2,k}]. \end{aligned}$$

Case 8: Interaction effects for predictor linear in the coefficients and covariates.

An interesting case is when there are no nonlinear transformations or interaction terms, i.e:

$\eta_j(x_1, x_2; \beta) = \beta_{0,j} + \beta_{1,j}x_1 + \beta_{2,j}x_2$ for $j = 1, \dots, J$. Let $\eta_{j,1} = \beta_{0,j} + \beta_{1,j} + \beta_{2,j}x_2$ and $\eta_{j,0} = \beta_{0,j} + \beta_{2,j}x_2$ for $j = 1, \dots, J$. Then:

$$\begin{aligned} \text{ME}_{21}: [ME_2]|_{x_1=1} - [ME_2]|_{x_1=0} = \\ h_j(\eta_{j,1})[\beta_{2,j} - \sum_{k=0}^J h_k(\eta_{j,1})\beta_{2,k}] - h_j(\eta_{j,0})[\beta_{2,j} - \sum_{k=0}^J h_k(\eta_{j,0})\beta_{2,k}]. \end{aligned}$$

4. Generalized Linear Model (GLM) with Log Link Function

The conditional mean for the GLM model with log link takes the form:

$$E(y|x_1, x_2) = \exp(\eta_j(x_1, x_2; \beta)),$$

where $\eta_j(x_1, x_2; \beta)$ is the predictor function. For each case, assume x_1 and x_2 are continuous unless indicated otherwise. In addition, for ease of notation, we represent $\eta(x_1, x_2; \beta)$ simply as η .

Case 1: Linear in the covariates.

Let $\eta(x_1, x_2; \beta) = \beta_0 + \beta_1x_1 + \beta_2x_2$, then:

$$\text{ME}_2: \frac{\partial \exp(\eta)}{\partial x_2} = \exp(\eta) \beta_2$$

Case 2: Inclusion of nonlinear transformations of the covariates.

Let $\eta(x_1, x_2; \beta) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_2^2$, then:

$$\text{ME}_2: \frac{\partial \exp(\eta)}{\partial x_2} = \exp(\eta) (\beta_2 + 2\beta_3 x_2)$$

Case 3: Inclusion of an interaction term between covariates.

Consider an interaction term between x_1 and x_2 such that $\eta(x_1, x_2; \beta) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 (x_2 * x_1)$. Then:

$$\text{ME}_2: \frac{\partial \exp(\eta)}{\partial x_2} = \exp(\eta) (\beta_2 + \beta_3 x_1).$$

Case 4: Linearity in the covariates with a discrete covariate.

Let $\eta(x_1, x_2; \beta) = \beta_0 + \beta_1 x_1 + \beta_2 x_2$ and assume that x_1 is binary. Then:

$$\text{ME}_1: \exp(\eta)|_{x_1=1} - \exp(\eta)|_{x_1=0} = \exp(\beta_0 + \beta_1 + \beta_2 x_2) - \exp(\beta_0 + \beta_2 x_2).$$

Case 5: Inclusion of an interaction term with a discrete covariate

Let $\eta(x_1, x_2; \beta) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 (x_2 * x_1)$ and assume that x_1 is binary. Then:

$$\text{ME}_1: \exp(\eta)|_{x_1=1} - \exp(\eta)|_{x_1=0} = \exp(\beta_0 + \beta_1 + \beta_2 x_2 + \beta_3 x_2) - \exp(\beta_0 + \beta_2 x_2).$$

For the next two cases (cases 6 and 7), let the predictor be given by:

$$\eta(x_1, x_2; \beta) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 (x_2 * x_1).$$

Case 6: Interaction effects with continuous covariates.

$$\mathbf{ME}_{21}: \frac{\partial}{\partial x_1} [\mathbf{ME}_2] = \exp(\boldsymbol{\eta}) (\boldsymbol{\beta}_1 + \boldsymbol{\beta}_3 x_2)(\boldsymbol{\beta}_2 + \boldsymbol{\beta}_3 x_1) + \exp(\boldsymbol{\eta}) \boldsymbol{\beta}_3.$$

Case 7: Interaction effects with a continuous and discrete covariate.

Let x_1 be binary again, making $\eta_1 = \beta_0 + \beta_1 + \beta_2 x_2 + \beta_3 x_2$ and $\eta_0 = \beta_0 + \beta_2 x_2$. Then:

$$\mathbf{ME}_{21}: [\mathbf{ME}_2]|_{x_1=1} - [\mathbf{ME}_2]|_{x_1=0} = \exp(\boldsymbol{\eta}_1)(\boldsymbol{\beta}_2 + \boldsymbol{\beta}_3) - \exp(\boldsymbol{\eta}_0)\boldsymbol{\beta}_2.$$

It should be emphasized that $\mathbf{ME}_{21} = \mathbf{ME}_{12}$ in this case, as well.

Case 8: Interaction effects for predictor linear in the coefficients and covariates.

An interesting case is when there are no nonlinear transformations or interaction terms, i.e.:

$\eta(x_1, x_2; \boldsymbol{\beta}) = \beta_0 + \beta_1 x_1 + \beta_2 x_2$. Again let x_1 be binary, $\eta_1 = \beta_0 + \beta_1 + \beta_2 x_2$, and $\eta_0 = \beta_0 + \beta_2 x_2$. Then:

$$\mathbf{ME}_{21}: [ME_2]|_{x_1=1} - [ME_2]|_{x_1=0} = \exp(\boldsymbol{\eta}_1)\boldsymbol{\beta}_2 - \exp(\boldsymbol{\eta}_0)\boldsymbol{\beta}_2.$$

5. Count Models

The conditional mean function for both Poisson and Negative Binomial models (as well as a number of other count data models) is:

$$E(y|x_1, x_2) = \exp(\eta(x_1, x_2; \boldsymbol{\beta})).$$

For each case, assume x_1 and x_2 are continuous unless indicated otherwise. In addition, for ease of notation, we represent $\eta(x_1, x_2; \boldsymbol{\beta})$ simply as η . The marginal effects for the count models presented below are similar in derivation to those for the GLM model with log link function

presented earlier, but it should be emphasized that the parameter estimates will not be the same in both models as the underlying distributions are different.

Case 1: Linear in the covariates.

Let $\eta(x_1, x_2; \beta) = \beta_0 + \beta_1 x_1 + \beta_2 x_2$, then:

$$\text{ME}_2: \frac{\partial \exp(\eta)}{\partial x_2} = \mathbf{exp}(\eta) \beta_2$$

Case 2: Inclusion of nonlinear transformations of the covariates.

Let $\eta(x_1, x_2; \beta) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_2^2$, then:

$$\text{ME}_2: \frac{\partial \exp(\eta)}{\partial x_2} = \mathbf{exp}(\eta) (\beta_2 + 2\beta_3 x_2)$$

Case 3: Inclusion of an interaction term between covariates.

Consider an interaction term between x_1 and x_2 such that $\eta(x_1, x_2; \beta) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 (x_2 * x_1)$. Then:

$$\text{ME}_2: \frac{\partial \exp(\eta)}{\partial x_2} = \mathbf{exp}(\eta) (\beta_2 + 2\beta_3 x_1).$$

Case 4: Linearity in the covariates with a discrete covariate.

Let $\eta(x_1, x_2; \beta) = \beta_0 + \beta_1 x_1 + \beta_2 x_2$ and assume that x_1 is binary. Then:

$$\text{ME}_1: \mathbf{exp}(\eta)|_{x_1=1} - \mathbf{exp}(\eta)|_{x_1=0} = \mathbf{exp}(\beta_0 + \beta_1 + \beta_2 x_2) - \mathbf{exp}(\beta_0 + \beta_2 x_2).$$

Case 5: Inclusion of an interaction term with a discrete covariate

Let $\eta(x_1, x_2; \beta) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 (x_2 * x_1)$ and assume that x_1 is binary. Then:

$$\text{ME}_1: \exp(\eta)|_{x_1=1} - \exp(\eta)|_{x_1=0} = \exp(\beta_0 + \beta_1 + \beta_2 x_2 + \beta_3 x_2) - \exp(\beta_0 + \beta_2 x_2).$$

For the next two cases (cases 6 and 7), let the predictor be given by:

$$\eta(x_1, x_2; \beta) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 (x_2 * x_1).$$

Case 6: Interaction effects with continuous covariates.

$$\text{ME}_{21}: \frac{\partial}{\partial x_1} [\text{ME}_2] = \exp(\eta) (\beta_1 + \beta_3 x_2) (\beta_2 + \beta_3 x_1) + \exp(\eta) \beta_3.$$

Case 7: Interaction effects with a continuous and discrete covariate.

Let x_1 be binary again, making $\eta_1 = \beta_0 + \beta_1 + \beta_2 x_2 + \beta_3 x_2$ and $\eta_0 = \beta_0 + \beta_2 x_2$. Then:

$$\text{ME}_{21}: [\text{ME}_2]|_{x_1=1} - [\text{ME}_2]|_{x_1=0} = \exp(\eta_1) (\beta_2 + \beta_3) - \exp(\eta_0) \beta_2.$$

It should be emphasized that $\text{ME}_{21} = \text{ME}_{12}$ in this case, as well.

Case 8: Interaction effects for predictor linear in the coefficients and covariates.

An interesting case is when there are no nonlinear transformations or interaction terms, i.e:

$\eta(x_1, x_2; \beta) = \beta_0 + \beta_1 x_1 + \beta_2 x_2$. Again let x_1 be binary, $\eta_1 = \beta_0 + \beta_1 + \beta_2 x_2$, and $\eta_0 = \beta_0 + \beta_2 x_2$. Then:

$$\text{ME}_{21}: [\text{ME}_2]|_{x_1=1} - [\text{ME}_2]|_{x_1=0} = \exp(\eta_1) \beta_2 - \exp(\eta_0) \beta_2.$$

6. Survival models

To incorporate conditioning factors, a common approach is the use of proportional hazard models. The proportional hazards model takes the form:

$$\lambda(t; \mathbf{x}) = \kappa(\mathbf{x})\lambda_0(t),$$

where $\lambda_0(t)$ is the baseline hazard. A common parameterization is to let $\kappa(\mathbf{x}) = \exp(\eta(x_1, x_2; \beta))$, where $\eta(x_1, x_2; \beta)$ is a predictor function. The ME of interest is the marginal change in $\mathbf{x}$ on the conditional hazard function. That is:

$$\frac{\partial \lambda(t; \mathbf{x})}{\partial \mathbf{x}} = \exp(\eta(x_1, x_2; \beta)) \frac{\partial \eta(x_1, x_2; \beta)}{\partial \mathbf{x}} \times \lambda_0(t).$$

In this case, the ME formula will follow those derived for the Gamma (or log linear) regression model and the Count Data models presented earlier, except the corresponding ME will be multiplied by $\lambda_0(t)$ [2]. Despite the similarity in the ME formulae, the estimated ME will differ due to the difference in the underlying distribution.

For time-varying factors or covariates, the proportional hazards model takes the form:

$$\lambda(t; \mathbf{x}(t)) = \kappa(\mathbf{x}(t))\lambda_0(t).$$

If $\lambda(t; \mathbf{x}(t))$ is the Weibull hazard function[3], then the ME will be similar to the ME presented above for the time-invariant case. If $\lambda(t; \mathbf{x}(t))$ is the log-logistic hazard then:

$$\lambda(t; \mathbf{x}(t)) = \left[\frac{\exp(\eta(x_1, x_2; \beta)) \alpha t^{\alpha-1}}{1 + \exp(\eta(x_1, x_2; \beta)) t^\alpha} \right],$$

where $\eta(x_1, x_2; \beta)$ is a predictor function[2]. The ME is:

$$\frac{\partial \lambda(t; \mathbf{x})}{\partial \mathbf{x}} = \left[\frac{\exp(\eta(x_1, x_2; \beta)) \alpha t^{\alpha-1}}{(1 + \exp(\eta(x_1, x_2; \beta)) t^\alpha)^2} \right] \times \frac{\partial \eta(x_1, x_2; \beta)}{\partial \mathbf{x}}$$

The interaction (marginal) effect of x_1 given a change in x_2 is given by:

$$\begin{aligned} ME_{12} = & \left[\frac{\exp(\eta(x_1, x_2; \beta)) \alpha t^{\alpha-1} (1 - \exp(\eta(x_1, x_2; \beta)) t^\alpha)}{(1 + \exp(\eta(x_1, x_2; \beta)) t^\alpha)^3} \right] \times \frac{\partial \eta(x_1, x_2; \beta)}{\partial x_1} \times \frac{\partial \eta(x_1, x_2; \beta)}{\partial x_2} \\ & + \left[\frac{\exp(\eta(x_1, x_2; \beta)) \alpha t^{\alpha-1}}{(1 + \exp(\eta(x_1, x_2; \beta)) t^\alpha)^2} \right] \times \frac{\partial^2 \eta(x_1, x_2; \beta)}{\partial x_1 \partial x_2} \end{aligned}$$

7. Two-Part Regression Model

Consider a two part model that consists of a probability model and distribution involving strictly positive values, i.e.

$$H(.) = \Pr(y = 1) \times E(y|y > 0)$$

where $\Pr(y = 1) = \frac{\exp(\eta)}{1+\exp(\eta)}$ and $E(y|y > 0) = \exp(\eta)$. The regression function is then given

by: $f(x_1, x_2; \beta) = \frac{\exp(\eta)}{1+\exp(\eta)} \times \exp(\eta) = \frac{\exp(\eta)}{1+\exp(-\eta)}$, where $\eta = \eta(x_1, x_2; \beta)$ is the predictor

function. For each case, assume x_1 and x_2 are continuous unless indicated otherwise.

Case 1: Linear in the covariates.

Let $\eta(x_1, x_2; \beta) = \beta_0 + \beta_1 x_1 + \beta_2 x_2$, then:

$$\begin{aligned} \text{ME}_2: \left(\frac{\partial f(\cdot)}{\partial x_2} \right) &= \frac{\exp(\eta)}{1+\exp(-\eta)} (\beta_2) - \frac{\exp(\eta)}{[1+\exp(-\eta)]^2} \exp(-\eta) (\beta_2) \\ &= f(x_1, x_2; \beta) \beta_2 \left[1 + \frac{1}{1 + \exp(\eta)} \right], \end{aligned}$$

because $\frac{\exp(-\eta)}{1+\exp(-\eta)} = \frac{1}{1+\exp(\eta)}$.

Case 2: Inclusion of nonlinear transformations of the covariates.

Let $\eta(x_1, x_2; \beta) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_2^2$, then:

$$\begin{aligned} \text{ME}_2: \left(\frac{\partial f(\cdot)}{\partial x_2} \right) &= \frac{\exp(\eta)}{1+\exp(-\eta)} (\beta_2 + 2\beta_3 x_2) + \frac{\exp(\eta)}{[1+\exp(-\eta)]^2} \exp(-\eta) (\beta_2 + 2\beta_3 x_2) \\ &= f(x_1, x_2; \beta) (\beta_2 + 2\beta_3 x_2) \left[1 + \frac{1}{1 + \exp(\eta)} \right]. \end{aligned}$$

Case 3: Inclusion of an interaction term between covariates.

Consider an interaction term between x_1 and x_2 such that $\eta(x_1, x_2; \beta) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3(x_2 * x_1)$. Then:

$$\begin{aligned} \text{ME}_2: \left(\frac{\partial f(\cdot)}{\partial x_2} \right) &= \frac{\exp(\eta)}{1+\exp(-\eta)} (\beta_2 + \beta_3 x_1) + \frac{\exp(\eta)}{[1+\exp(-\eta)]^2} \exp(-\eta) (\beta_2 + \beta_3 x_1) \\ &= f(x_1, x_2; \beta) (\beta_2 + \beta_3 x_1) \left[1 + \frac{1}{1+\exp(\eta)} \right]. \end{aligned}$$

Case 4: Linearity in the covariates with a discrete covariate.

Let $\eta(x_1, x_2; \beta) = \beta_0 + \beta_1 x_1 + \beta_2 x_2$ and assume that x_1 is binary. Then:

$$\begin{aligned} \text{ME}_1: f(x_1, x_2; \beta)|_{x_1=1} - f(x_1, x_2; \beta)|_{x_1=0} \\ = \frac{\exp(\beta_0 + \beta_1 + \beta_2 x_2)}{1+\exp(-\beta_0 - \beta_1 - \beta_2 x_2)} - \frac{\exp(\beta_0 + \beta_2 x_2)}{1+\exp(-\beta_0 - \beta_2 x_2)}. \end{aligned}$$

Case 5: Inclusion of an interaction term with a discrete covariate

Let $\eta(x_1, x_2; \beta) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3(x_2 * x_1)$ and assume that x_1 is binary. Then:

$$\begin{aligned} \text{ME}_1: f(x_1, x_2; \beta)|_{x_1=1} - f(x_1, x_2; \beta)|_{x_1=0} \\ = \frac{\exp(\beta_0 + \beta_1 + \beta_2 x_2 + \beta_3 x_2)}{1+\exp(-\beta_0 - \beta_1 - \beta_2 x_2 - \beta_3 x_2)} - \frac{\exp(\beta_0 + \beta_2 x_2)}{1+\exp(-\beta_0 - \beta_2 x_2)}. \end{aligned}$$

For the next two cases (cases 6 and 7), let the predictor be given by:

$$\eta(x_1, x_2; \beta) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3(x_2 * x_1).$$

Case 6: Interaction effects with continuous covariates.

$$\text{ME}_{21}: \frac{\partial}{\partial x_1} [\text{ME}_2] = [\text{ME}_1(\beta_2 + \beta_3 x_1) + f(x_1, x_2; \beta) \beta_3] \times \left[1 + \frac{1}{1 + \exp(\eta)} \right]$$

$$-\frac{f(x_1, x_2; \beta)(\beta_2 + \beta_3 x_1)}{[1 + \exp(\eta)]^2} \exp(\eta)(\beta_1 + \beta_3 x_2),$$

where ME₁: $\left(\frac{\partial f(\cdot)}{\partial x_1}\right) = f(x_1, x_2; \beta)(\beta_1 + \beta_3 x_2) \left[1 + \frac{1}{1 + \exp(\eta)}\right]$.

Case 7: Interaction effects with a continuous and discrete covariate.

Let x_1 be binary again, making $\eta_1 = \beta_0 + \beta_1 + \beta_2 x_2 + \beta_3 x_2$ and $\eta_0 = \beta_0 + \beta_2 x_2$. Then:

$$\begin{aligned} \text{ME}_{21}: [\text{ME}_2]|_{x_1=1} - [\text{ME}_2]|_{x_1=0} \\ = \frac{\exp(\eta_1)}{1 + \exp(-\eta_1)} (\beta_2 + \beta_3) \left[1 + \frac{1}{1 + \exp(\eta_1)}\right] - \frac{\exp(\eta_0)}{1 + \exp(-\eta_0)} (\beta_2) \left[1 + \frac{1}{1 + \exp(\eta_0)}\right]. \end{aligned}$$

Case 8: Interaction effects for predictor linear in the coefficients and covariates.

An interesting case is when there are no nonlinear transformations or interaction terms, i.e:

$\eta(x_1, x_2; \beta) = \beta_0 + \beta_1 x_1 + \beta_2 x_2$. Again let x_1 be binary, $\eta_1 = \beta_0 + \beta_1 + \beta_2 x_2$, and $\eta_0 = \beta_0 + \beta_2 x_2$. Then:

$$\begin{aligned} \text{ME}_{21} = [\text{ME}_2]|_{x_1=1} - [\text{ME}_2]|_{x_1=0} \\ = \frac{\exp(\eta_1)}{1 + \exp(-\eta_1)} (\beta_2) \left[1 + \frac{1}{1 + \exp(\eta_1)}\right] - \frac{\exp(\eta_0)}{1 + \exp(-\eta_0)} (\beta_2) \left[1 + \frac{1}{1 + \exp(\eta_0)}\right]. \end{aligned}$$

8. Sample Selection Model

The Heckman model with a log linear dependent variable[4, 5] is specified below:

$$\ln y = X' \beta + \beta_\lambda \lambda(W' \gamma) + \varepsilon$$

$$\varepsilon_i \sim \text{distr. (iid)}, E(\varepsilon_i) = 0, \text{var}(\varepsilon_i) = \sigma^2, W \ni X$$

$$y = \exp(X' \beta + \beta_\lambda \lambda(\cdot) + \varepsilon)$$

$$E(y) = E(e^{X'\beta + \beta_\lambda \lambda(\cdot) + \varepsilon})$$

$$E(y) = e^{X'\beta} e^{\beta_\lambda \lambda(\cdot)} E(e^\varepsilon | x)$$

The general case of the marginal effect of the log linear formulation is derived as follows[6, 7]:

$$\begin{aligned} \frac{\partial E(y)}{\partial x_k} &= \frac{\partial (e^{X'\beta} e^{\beta_\lambda \lambda(\cdot)} E(e^\varepsilon | x))}{\partial x_k} \\ \frac{\partial E(y)}{\partial x_k} &= e^{X'\beta} e^{\beta_\lambda \lambda(\cdot)} \left(\beta_k E(e^\varepsilon | x) + \gamma_k \beta_\lambda (-\lambda(\cdot)^2 - \gamma x_k \lambda(\cdot) E(e^\varepsilon | x)) + \frac{\partial E(e^\varepsilon | x)}{\partial x_k} \right) \end{aligned}$$

The formulation above is for the general case in which x_k is a continuous variable and appears in both the main regression model and the IMR function. The ME function will differ according to the scenarios represented by the cases defined in the main article.

If homoskedastic in x_k , as assumed in the specification above, then

$$\frac{\partial E(y)}{\partial x_k} = e^{X'\beta} e^{\beta_\lambda \lambda(\cdot)} (\beta_k E(e^\varepsilon | x) + \gamma_k \beta_\lambda (-\lambda(\cdot)^2 - \gamma x_k \lambda(\cdot) E(e^\varepsilon | x)))$$

If heteroskedastic in x_k , then

$$\frac{\partial E(y)}{\partial x_k} = e^{X'\beta} e^{\beta_\lambda \lambda(\cdot)} \left(\beta_k \cdot E(e^\varepsilon | x) + \gamma_k \beta_\lambda (-\lambda(\cdot)^2 - \gamma x_k \lambda(\cdot) E(e^\varepsilon | x)) + \frac{\partial E(e^\varepsilon | x)}{\partial x_k} \right)$$

The ‘naïve’ estimate is appropriate to use in retransformation when the error structure is homoskedastic (log normal distribution is appropriate). Duan proposed a smearing estimator that does not require a log normality assumption[8] . Of note, the smearing estimator may differ across patient subgroups and in this case would require a subgroup-specific smearing estimator[4].

- Naïve estimate (normal distribution of ϵ_i is assumed)

$$\hat{E}(y) = \exp \left(X' \beta + \beta_{\lambda} \lambda(\cdot) + \frac{\sigma^2}{2} \right)$$

- Smearing estimate (normal distribution of ϵ_i is not needed)

$$\hat{E}(y) = e^{X' \hat{\beta}} \times \frac{1}{n} \sum_{i=1}^n e^{\hat{\epsilon}_i}$$

References (Technical Appendix)

1. Bergtold JS, Onukwugha E. The probabilistic reduction approach to specifying multinomial logistic regression models in health outcomes research. *Journal of Applied Statistics*. 2014;41(10):2206-21.
2. Wooldridge J. *Econometric analysis of cross section and panel data* Cambridge: MIT Press; 2002.
3. Ishak KJ, Kreif N, Benedict A, Muszbek N. Overview of parametric survival analysis for health-economic applications. *Pharmacoeconomics*. Aug;31(8):663-75.
4. Manning WG. The logged dependent variable, heteroscedasticity, and the retransformation problem. *Journal of Health Economics*. 1998;17(3):283-95.
5. Dow WH, Norton EC. Choosing Between and Interpreting the Heckit and Two-part models for corner solutions. *Health Services and Outcomes Research Methodology*. 2003;4(1):5-18.
6. Greene W. *Econometric Analysis*. 7th edition ed. Upper Saddle River, NJ: Prentice Hall; 2012.
7. Vance C. Marginal effects and significance testing with Heckman's sample selection model: a methodological note. *Applied Economics Letters*. 2009;16(14):1415-9.
8. Duan N. Smearing estimate: A nonparametric retransformation method. *Journal of the American Statistical Association*. 1983;78(383):605-10.