Interaction (Effect Modification) in Regression

CRP 241 Tutorial

Duke University Clinical Research Training Program

2025-11-05

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Introduction

Learning Objectives

After completing this tutorial, you will be able to:

- **Define** interaction (effect modification) in regression
- **Recognize** when an effect differs across subgroups
- **Use** regression with interaction terms to test for effect modification
- **Interpret** stratified analyses and visualizations
- **Apply** clinical reasoning to determine if interactions are meaningful

0.1 What is Interaction (Effect Modification)?

Interaction (also called **effect modification**) occurs when the effect of one variable on an outcome depends on the level of another variable.

! Key Concept

In simple terms: "Does the relationship between X and Y differ across levels of Z?"
Example: Does the effect of smoking on lung function differ by age?

- If younger patients show a small smoking effect but older patients show a large smoking effect, then **age modifies** the smoking effect.
- We say there is **interaction** between smoking and age.

0.2 Why Interaction Matters Clinically

Clinical Relevance

Interactions help us:

- **Personalize treatment:** Identify which patients benefit most (or least) from an intervention
- **Understand mechanisms:** Discover biological or behavioral factors that amplify or reduce effects
- **Avoid misleading conclusions:** A pooled (average) effect may hide important subgroup differences

Example: A drug may be highly effective in younger patients but ineffective (or even harmful) in older patients. Reporting only the average effect across all ages would be misleading.

0.3 How to Detect Interaction

Statistical Approaches

1. **Stratified analysis:** Fit separate models within each subgroup and compare the effect estimates
2. **Regression with interaction term:** Include a product term (e.g., $X \times Z$) in the model; test if the coefficient is significant
3. **Visual inspection:** Plot the relationship for each subgroup; look for different slopes or patterns

Key point: A statistically significant interaction term ($p < 0.05$) provides evidence that the effect differs across subgroups.

---

1 Example 1: FEV1 and Smoking in COPD Patients

1.1 Study Background

A study examined whether smoking status (current/recent/former vs non-smoker) is associated with FEV1 (forced expiratory volume in one second, a measure of lung function) in patients with COPD. Age (65 vs <65 years) was also recorded.

- **Sample:** 200 patients randomly selected from a clinical practice
- **Exposure:** Smoking status (1 = current/recent/former smoker; 0 = non-smoker)
- **Outcome:** FEV1 (liters)
- **Potential effect modifier:** Age (1 = 65 years; 0 = <65 years)

> **Clinical Question**
>
> Does the effect of smoking on lung function differ by age? We expect smokers to have lower FEV1, but is this effect stronger in older or younger COPD patients?

1.2 Data Dictionary

Table 1: FEV1 Study Variables

Variable	Description	Coding
`FEV1`	Forced expiratory volume in 1 second	Liters (continuous); higher = better
`SMOKING`	Patient smoking status	1 = Current/recent/former smoker; 0 = Non-smoker
`AGE65`	Patient age group	1 = Age 65 years; 0 = Age <65 years

1.3 Loading and Examining the Data

```
# Load the FEV1 smoking dataset
load(url("https://www.duke.edu/~sgrambow/crp241data/fev1_smoking.RData"))

# Examine structure
str(fsdata)
```

```
'data.frame':   200 obs. of  3 variables:
 $ FEV1   : num  2.66 4.22 4.8 2.21 3.29 ...
 $ SMOKING: num  0 0 0 0 0 0 0 0 0 0 ...
 $ AGE65  : int  0 1 0 1 0 1 0 1 0 1 ...
```

```r
# Summary statistics
summary(fsdata)
```

```
      FEV1           SMOKING         AGE65
 Min.   :1.335   Min.   :0.0   Min.   :0.0
 1st Qu.:2.760   1st Qu.:0.0   1st Qu.:0.0
 Median :3.569   Median :0.5   Median :0.5
 Mean   :3.577   Mean   :0.5   Mean   :0.5
 3rd Qu.:4.188   3rd Qu.:1.0   3rd Qu.:1.0
 Max.   :6.280   Max.   :1.0   Max.   :1.0
```

> **Quick Check**
>
> - 200 observations
> - FEV1 is continuous (liters)
> - SMOKING and AGE65 are binary (0/1)
> - No missing values (if all variables show 200 obs)

```r
# Create subsets by age group for stratified analyses
old   <- subset(fsdata, AGE65 == 1)
young <- subset(fsdata, AGE65 == 0)
```

1.4 Exploratory Summaries

```r
# FEV1 by age group
by(fsdata$FEV1, fsdata$AGE65, summary)
```

```
fsdata$AGE65: 0
   Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
  1.479   2.984   3.729   3.783   4.682   6.280
------------------------------------------------------------
fsdata$AGE65: 1
   Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
  1.335   2.704   3.444   3.371   4.011   5.547
```

Clinical Interpretation

Compare mean FEV1 for age <65 vs 65. Expect older patients to have lower FEV1 due to age-related lung function decline.

```
# FEV1 by smoking status
by(fsdata$FEV1, fsdata$SMOKING, summary)
```

```
fsdata$SMOKING: 0
   Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
  1.745   3.323   3.860   3.921   4.633   6.280
------------------------------------------------------------
fsdata$SMOKING: 1
   Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
  1.335   2.442   3.170   3.233   3.923   5.573
```

Clinical Interpretation

Compare mean FEV1 for smokers vs non-smokers. Expect smokers to have lower FEV1 because smoking damages airways and lung tissue.

1.5 Analysis 1: Overall Smoking Effect (Ignoring Age)

First, let's test if FEV1 differs by smoking status in the entire cohort, ignoring age.

```
# Two-sample t-test
t.test(fsdata$FEV1 ~ fsdata$SMOKING, var.equal = TRUE)
```

```
    Two Sample t-test

data:  fsdata$FEV1 by fsdata$SMOKING
t = 4.7934, df = 198, p-value = 3.215e-06
alternative hypothesis: true difference in means between group 0 and group 1 is not equal to
95 percent confidence interval:
 0.4045320 0.9700351
sample estimates:
mean in group 0 mean in group 1
       3.920575        3.233291
```

```r
# Difference in means
3.233291 - 3.920575
```

```
[1] -0.687284
```

> **Interpretation**
>
> - **Mean FEV1:** Non-smokers ~3.92 L; Smokers ~3.23 L
> - **Difference:** Non-smokers have ~0.69 L higher FEV1
> - **p-value:** Check if difference is statistically significant ($p < 0.05$)
>
> **Clinical takeaway:** Smoking is associated with reduced lung function in COPD patients. However, this pooled analysis does not tell us if the effect differs by age.

1.6 Analysis 2: Stratified t-Tests by Age

Now let's examine the smoking effect separately in each age group.

1.6.1 Among Age <65 Years

```r
# Summary by smoking status in younger patients
by(young$FEV1, young$SMOKING, summary)
```

```
young$SMOKING: 0
   Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
  1.745   3.298   3.859   3.962   4.704   6.280
------------------------------------------------------------
young$SMOKING: 1
   Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
  1.479   2.680   3.510   3.604   4.642   5.573
```

```r
# Two-sample t-test among younger patients
t.test(young$FEV1 ~ young$SMOKING, var.equal = TRUE)
```

```
    Two Sample t-test

data:  young$FEV1 by young$SMOKING
```

```
t = 1.64, df = 98, p-value = 0.1042
alternative hypothesis: true difference in means between group 0 and group 1 is not equal to
95 percent confidence interval:
 -0.07517284  0.79089874
sample estimates:
mean in group 0 mean in group 1
       3.961962        3.604099
```

```r
# Difference in means
3.604099 - 3.961962
```

```
[1] -0.357863
```

> **Interpretation**
>
> - **Difference in means:** ~0.36 L (non-smokers higher)
> - **Clinical takeaway:** Among younger COPD patients, smoking is associated with a modest reduction in FEV1.

1.6.2 Among Age 65 Years

```r
# Summary by smoking status in older patients
by(old$FEV1, old$SMOKING, summary)
```

```
old$SMOKING: 0
   Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
  1.883   3.348   3.860   3.879   4.485   5.547
------------------------------------------------------------
old$SMOKING: 1
   Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
  1.335   2.180   2.803   2.862   3.644   4.243
```

```r
# Two-sample t-test among older patients
t.test(old$FEV1 ~ old$SMOKING, var.equal = TRUE)
```

```
    Two Sample t-test

data:  old$FEV1 by old$SMOKING
```

```
t = 5.8922, df = 98, p-value = 5.388e-08
alternative hypothesis: true difference in means between group 0 and group 1 is not equal to
95 percent confidence interval:
 0.674283 1.359125
sample estimates:
mean in group 0 mean in group 1
       3.879188        2.862483
```

```r
# Difference in means
2.862483 - 3.879188
```

```
[1] -1.016705
```

Interpretation

- **Difference in means:** ~1.02 L (non-smokers higher)
- **Clinical takeaway:** Among older COPD patients, smoking is associated with a much larger reduction in FEV1 (nearly 3× the effect seen in younger patients).

Key Finding: Evidence of Interaction

The smoking effect differs substantially by age:

- **Younger patients:** ~0.36 L difference
- **Older patients:** ~1.02 L difference

This suggests **age modifies** the smoking effect. Let's test this formally with a regression interaction term.

1.7 Analysis 3: Regression with Interaction Term

We can formally test for interaction by including a product term (`SMOKING × AGE65`) in the regression model.

```r
# Fit model with interaction term
ifit <- lm(FEV1 ~ SMOKING + AGE65 + SMOKING*AGE65, data = fsdata)
summary(ifit)
```

```
Call:
lm(formula = FEV1 ~ SMOKING + AGE65 + SMOKING * AGE65, data = fsdata)
```

```
Residuals:
     Min       1Q   Median       3Q      Max
-2.21667 -0.66888 -0.06022  0.77311  2.31807

Coefficients:
              Estimate Std. Error t value Pr(>|t|)
(Intercept)    3.96196    0.13910  28.484   <2e-16 ***
SMOKING       -0.35786    0.19671  -1.819   0.0704 .
AGE65         -0.08277    0.19671  -0.421   0.6744
SMOKING:AGE65 -0.65884    0.27819  -2.368   0.0188 *
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 0.9836 on 196 degrees of freedom
Multiple R-squared:  0.1653,    Adjusted R-squared:  0.1525
F-statistic: 12.93 on 3 and 196 DF,  p-value: 9.579e-08
```

Interpreting the Interaction Model

Key coefficient: `SMOKING:AGE65` (the interaction term)

- **If p $<$ 0.05:** The smoking effect differs significantly by age (interaction is present)
- **If p 0.05:** No strong evidence that the smoking effect differs by age

Coefficients interpretation:

- **Intercept:** Mean FEV1 for non-smokers age <65
- **SMOKING:** Smoking effect among younger patients (age <65)
- **AGE65:** Age effect among non-smokers
- **SMOKING:AGE65:** Additional smoking effect in older patients (how much larger the smoking effect is in age 65 compared to age <65)

Clinical Interpretation

If the interaction is significant:

- **Report stratified results:** Present smoking effects separately for each age group (as we did in Analysis 2)
- **Avoid pooled estimates:** The overall effect (Analysis 1) masks important age differences
- **Clinical implication:** Smoking's impact on lung function is particularly severe in

older COPD patients. Smoking cessation interventions may be especially beneficial for this subgroup.

1.8 Analysis 4: Stratified Regressions

Let's fit separate regressions within each age group. This mirrors the t-tests but provides regression output (coefficients, confidence intervals, R-squared).

1.8.1 Among Age <65 Years

```
# Regression among younger patients
yfit <- lm(FEV1 ~ SMOKING, data = young)
summary(yfit)
```

```
Call:
lm(formula = FEV1 ~ SMOKING, data = young)

Residuals:
     Min       1Q   Median       3Q      Max
-2.21667 -0.73090 -0.09361  0.85583  2.31807

Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept)   3.9620     0.1543   25.68   <2e-16 ***
SMOKING      -0.3579     0.2182   -1.64    0.104
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 1.091 on 98 degrees of freedom
Multiple R-squared:  0.02671,   Adjusted R-squared:  0.01678
F-statistic:  2.69 on 1 and 98 DF,  p-value: 0.1042
```

```
confint(yfit)
```

```
                2.5 %     97.5 %
(Intercept)  3.6557595 4.26816455
SMOKING     -0.7908987 0.07517284
```

Interpretation

- **Slope (SMOKING):** Change in mean FEV1 for smokers vs non-smokers
- **95% CI:** Uncertainty around the estimate
- **Should match:** t-test result from Analysis 2a

1.8.2 Among Age 65 Years

```
# Regression among older patients
ofit <- lm(FEV1 ~ SMOKING, data = old)
summary(ofit)
```

```
Call:
lm(formula = FEV1 ~ SMOKING, data = old)

Residuals:
     Min       1Q   Median       3Q      Max
-1.99650 -0.60340 -0.04252  0.66335  1.66817

Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept)   3.8792     0.1220  31.794  < 2e-16 ***
SMOKING      -1.0167     0.1726  -5.892 5.39e-08 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 0.8628 on 98 degrees of freedom
Multiple R-squared:  0.2616,    Adjusted R-squared:  0.2541
F-statistic: 34.72 on 1 and 98 DF,  p-value: 5.388e-08
```

```
confint(ofit)
```

```
                2.5 %    97.5 %
(Intercept)  3.637059  4.121316
SMOKING     -1.359125 -0.674283
```

Interpretation

- **Slope (SMOKING):** Change in mean FEV1 for smokers vs non-smokers in older patients
- **Compare to younger patients:** This slope should be about 3× larger, confirming the interaction

1.9 Analysis 5: Pooled Regression (No Age Adjustment)

For comparison, here's the overall smoking effect ignoring age (matches Analysis 1).

```
# Regression ignoring age
ufit <- lm(FEV1 ~ SMOKING, data = fsdata)
summary(ufit)
```

```
Call:
lm(formula = FEV1 ~ SMOKING, data = fsdata)

Residuals:
     Min       1Q   Median       3Q      Max
-2.17528 -0.67376 -0.06018  0.69897  2.35946

Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept)   3.9206     0.1014  38.670  < 2e-16 ***
SMOKING      -0.6873     0.1434  -4.793 3.21e-06 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 1.014 on 198 degrees of freedom
Multiple R-squared:  0.104, Adjusted R-squared:  0.09945
F-statistic: 22.98 on 1 and 198 DF,  p-value: 3.215e-06
```

```
confint(ufit)
```

```
                2.5 %    97.5 %
(Intercept)  3.7206393  4.120510
SMOKING     -0.9700351 -0.404532
```

Important Note

This pooled estimate averages the smoking effect across age groups. If interaction is present, this average can be misleading. Always check for interaction before reporting a pooled effect!

---

2 Example 2: Birth Weight and Mother's Age

2.1 Study Background

A study at Baystate Medical Center, Springfield, Massachusetts, examined variables related to the likelihood of a mother giving birth to a low birth weight baby (defined as <2500 grams). Low birth weight is a risk factor for infant morbidity and mortality.

- **Sample:** 189 mothers randomly selected
- **Exposure:** Mother's age during pregnancy (years)
- **Outcome:** Baby's birth weight (grams)
- **Potential effect modifier:** Maternal smoking during pregnancy (1 = smoker; 0 = non-smoker)

Clinical Question

Does maternal age affect birth weight? And does this relationship differ between mothers who smoke and those who do not?

2.2 Data Dictionary

Table 2: Birth Weight Study Variables

Variable	Description	Coding
`bwt`	Birth weight of baby	Grams (continuous); higher = better
`age`	Age of mother during pregnancy	Years (continuous)
`smoke`	Smoking status of mother during pregnancy	1 = Smoker; 0 = Non-smoker

2.3 Loading the Data

```r
# Load the birth weight dataset
load(url("https://www.duke.edu/~sgrambow/crp241data/bwdata.RData"))
```

2.4 Question 1: Association Between Age and Birth Weight?

Is there evidence that maternal age is associated with birth weight (ignoring smoking status)?

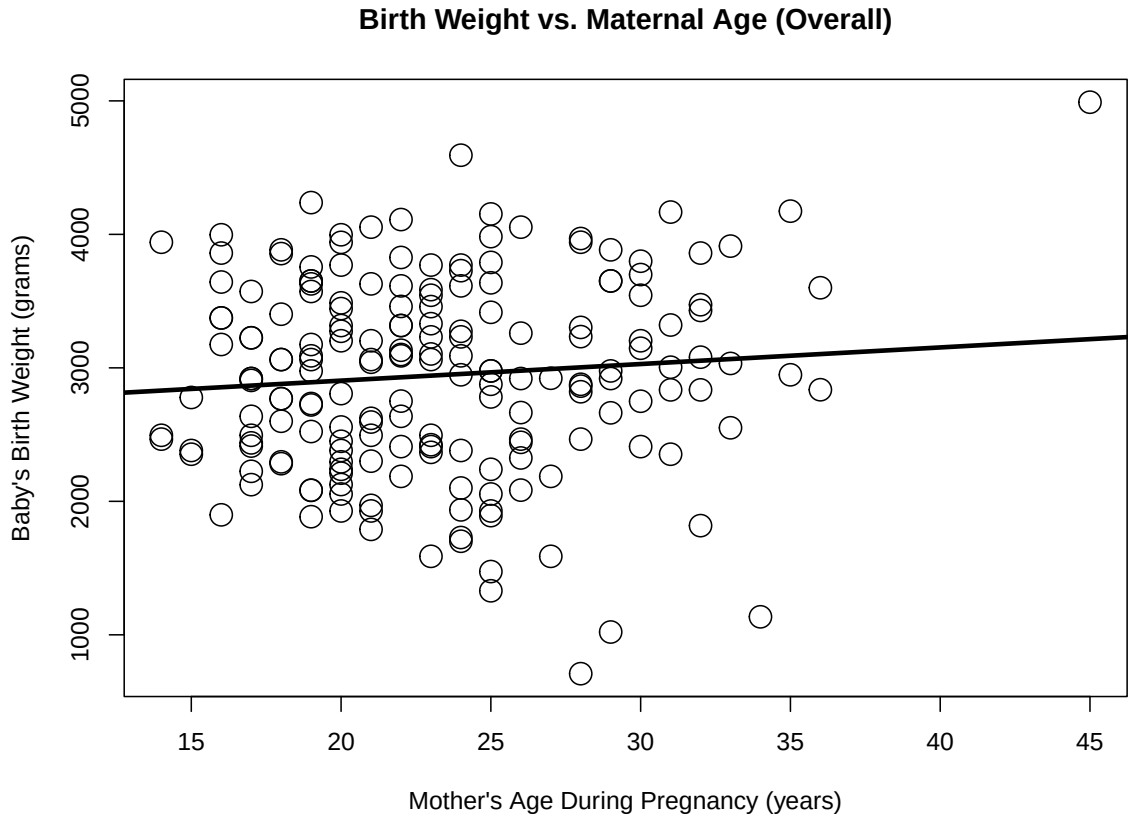
```r
# Simple linear regression: birth weight ~ age
fit1 <- lm(bwt ~ age, data = bwdata)
summary(fit1)
```

```
Call:
lm(formula = bwt ~ age, data = bwdata)

Residuals:
     Min       1Q   Median       3Q      Max
-2294.78  -517.63    10.51   530.80  1774.92

Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept)  2655.74     238.86   11.12   <2e-16 ***
age            12.43      10.02    1.24    0.216
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 728.2 on 187 degrees of freedom
Multiple R-squared:  0.008157,  Adjusted R-squared:  0.002853
F-statistic: 1.538 on 1 and 187 DF,  p-value: 0.2165
```

> **Interpretation**
>
> - **Slope (age):** Change in birth weight (grams) per 1-year increase in maternal age
> - **p-value:** Is this association statistically significant?
> - **Clinical context:** Biological plausibility? Older mothers may have more resources and prenatal care, or conversely, may face age-related pregnancy complications.

2.5 Question 2: Visualize the Relationship

```r
# Scatterplot with fitted regression line
plot(bwdata$age, bwdata$bwt,
     xlab = 'Mother\'s Age During Pregnancy (years)',
     ylab = 'Baby\'s Birth Weight (grams)',
     cex = 2,
     main = 'Birth Weight vs. Maternal Age (Overall)')
abline(fit1, lwd = 3)
```



Visual Interpretation

- **Scatter:** Shows variability in birth weight at each age
- **Line slope:** Direction and strength of the association
- **Clinical check:** Does the relationship look linear? Any outliers?

2.6 Question 3: Does Smoking Modify the Age-Birth Weight Relationship?

Test for interaction by including a product term (`age × smoke`).

```
# Regression with interaction term
fit2 <- lm(bwt ~ age + smoke + age*smoke, data = bwdata)
summary(fit2)
```

```
Call:
lm(formula = bwt ~ age + smoke + age * smoke, data = bwdata)

Residuals:
     Min       1Q   Median       3Q      Max
-2189.27  -458.46    51.46   527.26  1521.39

Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept)  2406.06     292.19   8.235 3.18e-14 ***
age            27.73      12.15   2.283   0.0236 *
smoke         798.17     484.34   1.648   0.1011
age:smoke     -46.57      20.45  -2.278   0.0239 *
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 709.3 on 185 degrees of freedom
Multiple R-squared:  0.06909,   Adjusted R-squared:  0.054
F-statistic: 4.577 on 3 and 185 DF,  p-value: 0.004068
```

! Interpreting the Interaction

Key coefficient: `age:smoke` (the interaction term)

- **If $p < 0.05$:** The effect of maternal age on birth weight differs significantly between smokers and non-smokers
- **If p 0.05:** No strong evidence of effect modification by smoking

Clinical interpretation: If significant, maternal age affects birth weight differently in mothers who smoke vs those who do not. We should report age-specific slopes for each smoking group.

2.7 Question 4: Visualize Effect Modification

Create separate regression lines for smokers and non-smokers to show how the relationship differs.

```
# Subset by smoking status
smoker    <- subset(bwdata, smoke == 1)
nonsmoker <- subset(bwdata, smoke == 0)
```

```
# Regression among smokers
fit3 <- lm(bwt ~ age, data = smoker)
summary(fit3)
```

```

Call:
lm(formula = bwt ~ age, data = smoker)

Residuals:
    Min      1Q  Median      3Q     Max
-1967.7  -464.1    13.6   498.8  1391.7

Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept)  3204.23     357.96   8.951 2.57e-13 ***
age           -18.84      15.24  -1.236     0.22
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 657.3 on 72 degrees of freedom
Multiple R-squared:  0.02078,   Adjusted R-squared:  0.007183
F-statistic: 1.528 on 1 and 72 DF,  p-value: 0.2204
```

```
confint(fit3)
```

```
                2.5 %     97.5 %
(Intercept) 2490.64656 3917.81914
age          -49.22246   11.54138
```

Interpretation (Smokers)

- **Slope (age):** Change in birth weight per 1-year increase in maternal age **among mothers who smoke**

```r
# Regression among non-smokers
fit4 <- lm(bwt ~ age, data = nonsmoker)
summary(fit4)
```

```
Call:
lm(formula = bwt ~ age, data = nonsmoker)

Residuals:
     Min       1Q   Median       3Q      Max
-2189.27  -449.75    73.58   542.25  1521.39

Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept)  2406.06     305.05   7.887 2.14e-12 ***
age            27.73      12.68   2.186   0.0309 *
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 740.5 on 113 degrees of freedom
Multiple R-squared:  0.04058,   Adjusted R-squared:  0.03209
F-statistic:  4.78 on 1 and 113 DF,  p-value: 0.03085
```

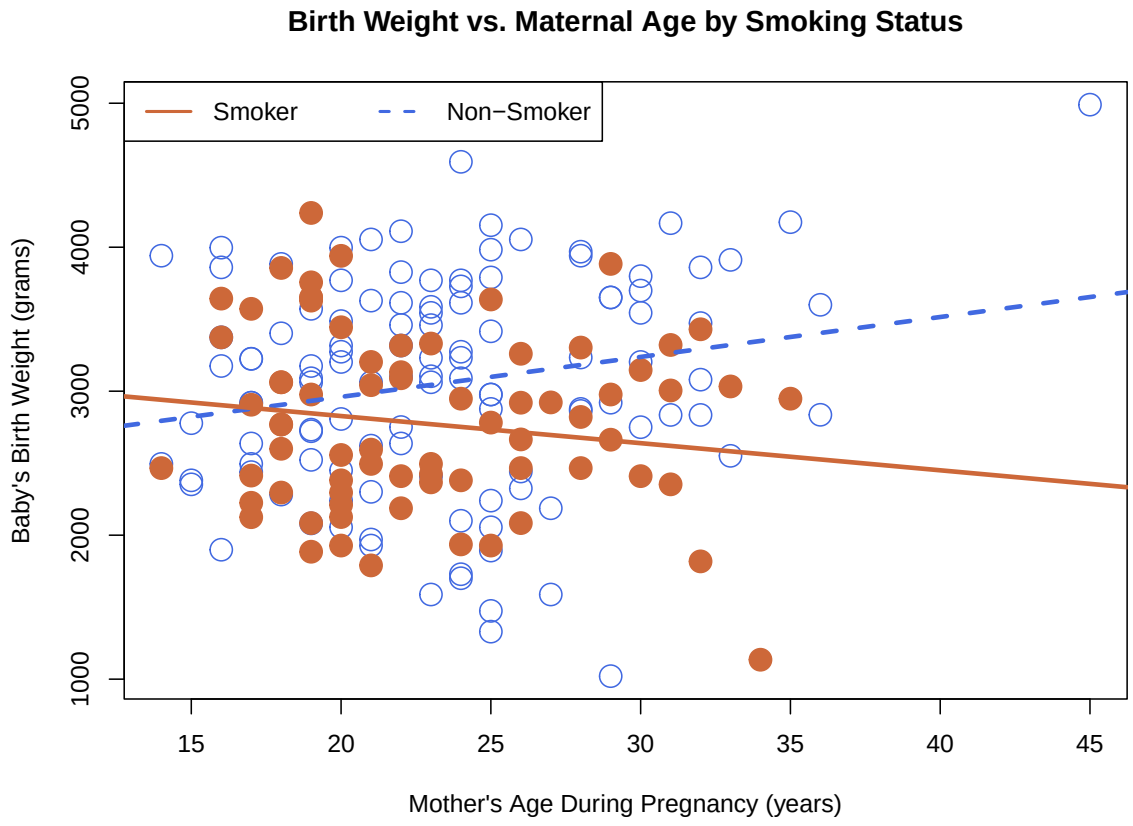
```r
confint(fit4)
```

```
                 2.5 %     97.5 %
(Intercept) 1801.691173 3010.42478
age            2.602105   52.86065
```

Interpretation (Non-Smokers)

- **Slope (age):** Change in birth weight per 1-year increase in maternal age **among mothers who do not smoke**
- **Compare slopes:** Are they similar or different?

```r
# Scatterplot with separate lines for smokers and non-smokers
plot(nonsmoker$age, nonsmoker$bwt,
     xlab = 'Mother\'s Age During Pregnancy (years)',
     ylab = 'Baby\'s Birth Weight (grams)',
     col = 'royalblue', cex = 2,
     main = 'Birth Weight vs. Maternal Age by Smoking Status')
points(smoker$age, smoker$bwt,
       col = 'sienna3', pch = 19, cex = 2)
abline(fit4, col = 'royalblue', lty = 2, lwd = 3)
abline(fit3, col = 'sienna3', lwd = 3)
legend('topleft', c('Smoker', 'Non-Smoker'),
       col = c('sienna3', 'royalblue'),
       lty = c(1, 2), lwd = 2, horiz = TRUE)
```



Visual Interpretation

- **Different slopes:** Evidence of interaction (effect modification)
- **Parallel lines:** No interaction (same age effect in both groups)

Clinical example: If the slope is steeper in non-smokers, older non-smoking mothers have heavier babies, but this benefit is reduced or absent in mothers who smoke. Smoking may blunt the positive effect of maternal age on fetal growth.

Summary and Key Takeaways

2.1 What is Interaction?

Key Points

- **Interaction (effect modification):** The effect of one variable on an outcome depends on the level of another variable
- **Example:** Smoking's effect on lung function differs by age; maternal age's effect on birth weight differs by smoking status
- **Why it matters:** Pooled (average) effects can mask important subgroup differences

2.2 How to Detect Interaction

Key Points

1. **Stratified analysis:** Fit separate models in each subgroup and compare effect estimates
2. **Regression with interaction term:** Include a product term (X $\times$ Z); test if the coefficient is significant ($p < 0.05$)
3. **Visualization:** Plot the relationship for each subgroup; look for different slopes

Rule of thumb: If the interaction term is significant, report stratified results. Do not rely on the pooled estimate.

2.3 Clinical Interpretation

Key Points

Example 1: FEV1 and Smoking in COPD

- Smoking's impact on lung function is much larger in older patients (~1.02 L) than younger patients (~0.36 L)
- **Clinical implication:** Smoking cessation is especially critical for older COPD patients

Example 2: Birth Weight and Maternal Age

- The effect of maternal age on birth weight may differ by smoking status
- **Clinical implication:** Smoking may reduce the benefit of older maternal age on fetal growth. Smoking cessation during pregnancy is vital.

2.4 When to Report Interaction

Best Practices

- **Always test for interaction** when you have a plausible effect modifier
- **If interaction is significant ($p < 0.05$):**
  - Report stratified results (group-specific effects)
  - Visualize with separate lines or subgroup analyses
  - Discuss clinical implications (which patients benefit most?)
- **If interaction is not significant:**
  - Report the main effect (pooled estimate)
  - Mention that you tested for interaction and found no evidence
- **Consider biological plausibility:** Not all statistical interactions are clinically meaningful. Use clinical knowledge to interpret findings.

Glossary

- **Interaction (Effect Modification):** When the effect of one variable on an outcome depends on the level of another variable.

- **Stratified Analysis:** Analyzing the relationship separately within levels of a third variable (e.g., age groups, smoking status).
- **Interaction Term:** A product of two variables (e.g., X × Z) included in a regression model to test for interaction.
- **Main Effect:** The effect of a variable on the outcome, averaged across levels of other variables (ignoring interaction).
- **Subgroup Analysis:** Examining effects within specific patient subgroups to identify who benefits most (or least) from an exposure or treatment.

Session Information

This document was created using Quarto and R. Here's the session information for reproducibility:

```
sessionInfo()
```

```
R version 4.4.2 (2024-10-31)
Platform: aarch64-apple-darwin20
Running under: macOS Sequoia 15.7.1

Matrix products: default
BLAS:   /Library/Frameworks/R.framework/Versions/4.4-arm64/Resources/lib/libRblas.0.dylib
LAPACK: /Library/Frameworks/R.framework/Versions/4.4-arm64/Resources/lib/libRlapack.dylib;

locale:
[1] en_US.UTF-8/en_US.UTF-8/en_US.UTF-8/C/en_US.UTF-8/en_US.UTF-8

time zone: America/New_York
tzcode source: internal

attached base packages:
[1] stats     graphics  grDevices utils     datasets  methods   base

other attached packages:
[1] ellmer_0.1.1

loaded via a namespace (and not attached):
 [1] digest_0.6.37     coro_1.1.0        R6_2.5.1          fastmap_1.2.0
 [5] xfun_0.50         magrittr_2.0.3    rappdirs_0.3.3    glue_1.8.0
 [9] knitr_1.49        htmltools_0.5.8.1 rmarkdown_2.29    lifecycle_1.0.4
[13] cli_3.6.3         S7_0.2.0          compiler_4.4.2    tools_4.4.2
```

```
[17] evaluate_1.0.3    yaml_2.3.10       httr2_1.1.0       jsonlite_1.8.9
[21] rlang_1.1.5
```