Lesson 11: Interactions

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2024-05-08

Learning Objectives

1. Connect understanding of confounding and interactions from linear regression to logistic regression.
2. Determine if an additional independent variable is a not a confounder nor effect modifier, is a confounder but not effect modifier, or is an effect modifier.
3. Calculate and interpret fitted interactions, including plotting the log-odds, predicted probability, and odds ratios.

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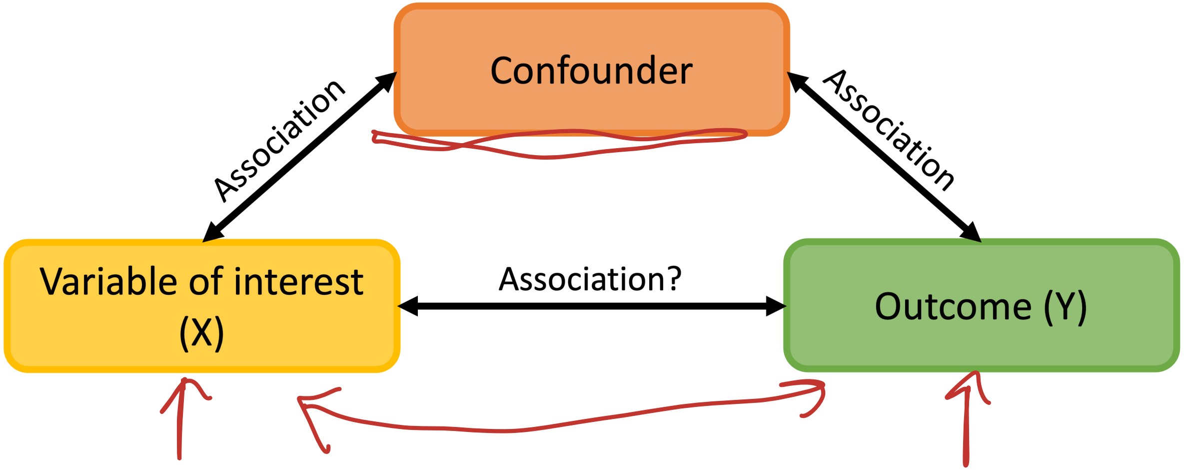
Revisit from 512: What is a confounder?

- A confounding variable, or **confounder**, is a factor/variable that wholly or partially accounts for the observed effect of the risk factor on the outcome
- A confounder must be…
  - Related to the outcome Y, but not a consequence of Y
  - Related to the explanatory variable X, but not a consequence of X



Including a confounder in the model

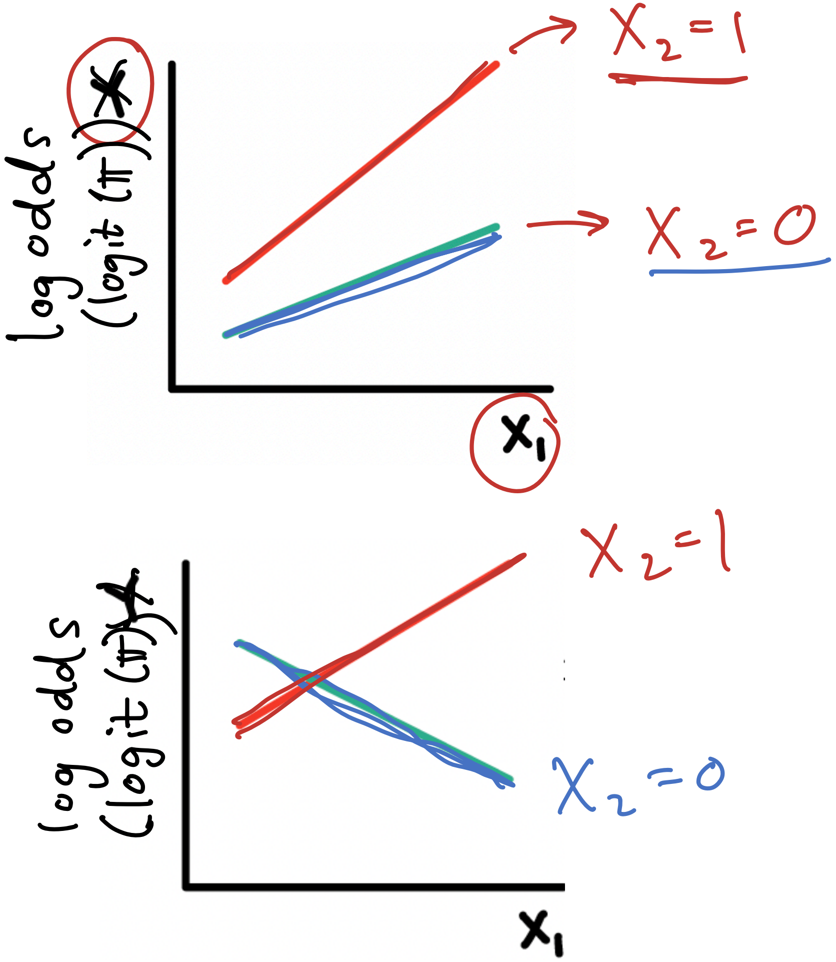
- In the following model we have two variables, $\underline{X_1}$ and $\underline{X_2}$

$$\text{logit}(\pi(X))\,\underline{\cancel{Y}} = \beta_0 + \underline{\beta_1 X_1} + \boxed{\underline{\beta_2 X_2}} + \cancel{\epsilon}$$

- And we assume that every level of the confounder, there is parallel slopes
- Note: to interpret β_1, we did not specify any value of X_2; only specified that it be held constant
  - Implicit assumption: effect of X_1 is equal across all values of X_2
- The above model assumes that X_1 and X_2 do not *interact* (with respect to their effect on Y)
  - epidemiology: no “effect modification”
  - meaning the effect of X_1 is the same regardless of the values of X_2

What is an effect modifier?

- An additional variable in the model
  - Outside of the main relationship between Y and X_1 that we are studying
- An effect modifier will change the effect of X_1 on Y depending on its value
  - Aka: as the effect modifier's values change, so does the association between Y and X_1
  - So the coefficient estimating the relationship between Y and X_1 changes with another variable



Confounding vs. Interaction

- **Confounders:** The adjusted odds ratio for one variable adjusting for confounders can be quite different from unadjusted odds ratio
  - Adjusting for them is called *controlling for confounding*.

- **Interactions:** When odds ratio for one variable is not constant over the levels of another variable, the two variables are said to have a statistical interaction (sometimes also called *effect modification*)
  - i.e.: the log odds of one variable is modified/changed with different values of the other variable
  - A variable is an **effect modifier** if it interacts with a risk factor

Note

Please refer to Lesson 11 from BSTA 512/612 – lots of information about these concepts!

How do we include an effect modifier in the model?

- Interactions!!
- We can incorporate interactions into our model through product terms:

$$\text{logit}(\pi(\mathbf{X}))\cancel{Y} = \underbrace{\beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_1 X_2}_{\text{systematic comp.}} \cancel{+ \epsilon}$$

link fn

- Terminology:
  - main effect parameters: β_1, β_2
    - The main effect models estimate the *average* X_1 and X_2 effects
  - interaction parameter: β_3

Example of interaction

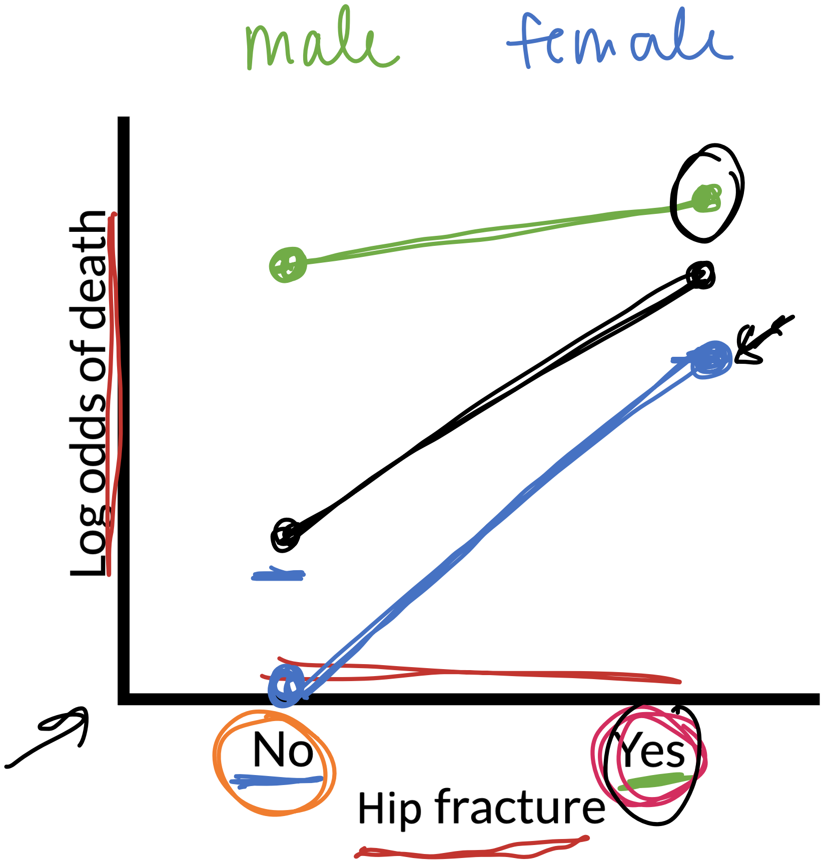
- In a cohort study of elderly people the chance of death (outcome) within 2 years was much higher for those who had previously suffered a hip fracture at the start of these 2 years, but the excess risk associated with a hip fracture was significantly higher for males vs. females

- This is an interaction between hip fracture status (yes/no) and sex (unclear if assigned at birth or no)

$$\frac{\text{yes odds}}{\text{no odds}}$$

- Odds ratio for females > odds ratio for males

odds ratio (of death) comparing hip fracture to NO hip fracture



Types of interactions / non-interactions

No interaction and three potential effects of interaction between two covariates A and B:

- **No interaction** between A and B (confounder with no interaction)

- **Unilateralism:** exposure to A has no effect in the absence of exposure to B, but a considerable effect when B is present.

- **Synergism:** the effect of A is in the same direction, but stronger in the presence of B.

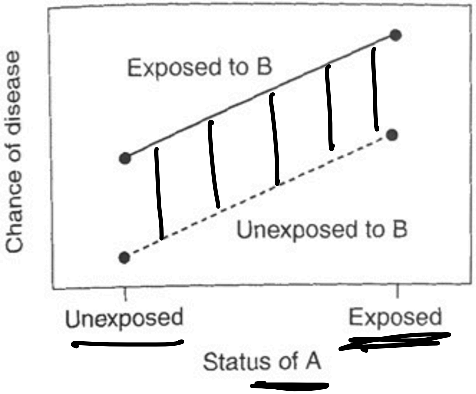
- **Antagonism:** the effect of A works in the opposite direction in the presence of B.

Types of interactions / non-interactions

$$\text{logit}(\pi(x)) = \beta_0 + \beta_1 X_1 + \beta_2 X_2$$

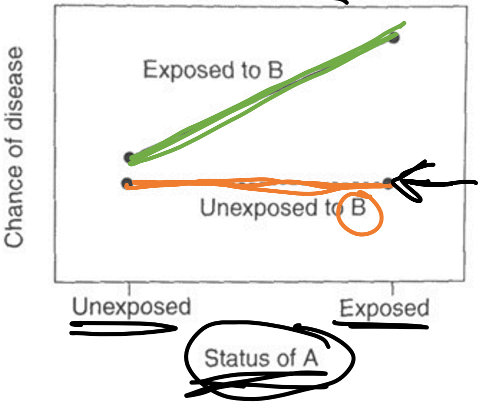
$$= \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \underline{\beta_3} X_1 X_2$$

(a) No interaction



Confounder, but no interaction between A and B

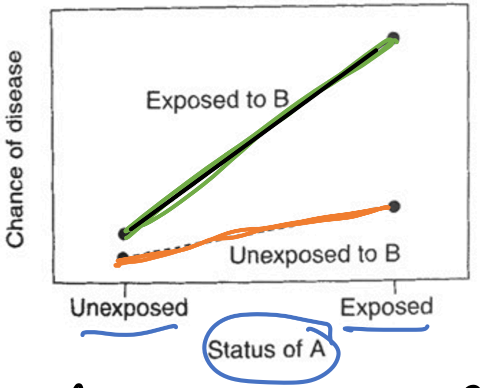
(b) Unilateralism



Exposure to A has no effect in the absence of exposure to B, but a considerable effect when B is present

$\beta_3 > 0 \quad \beta_1 = 0$ OR $\beta_2 = 0$

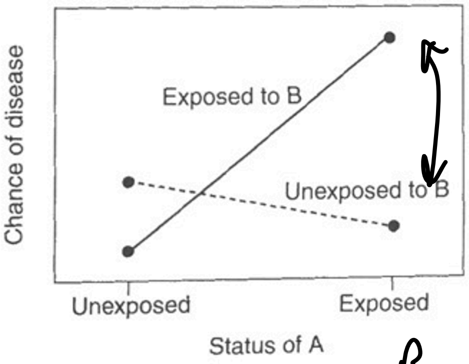
(c) Synergism



Effect of A is in the same direction, but stronger in the presence of B

$\beta_3 > 0, \beta_1 > 0, \beta_2 > 0$

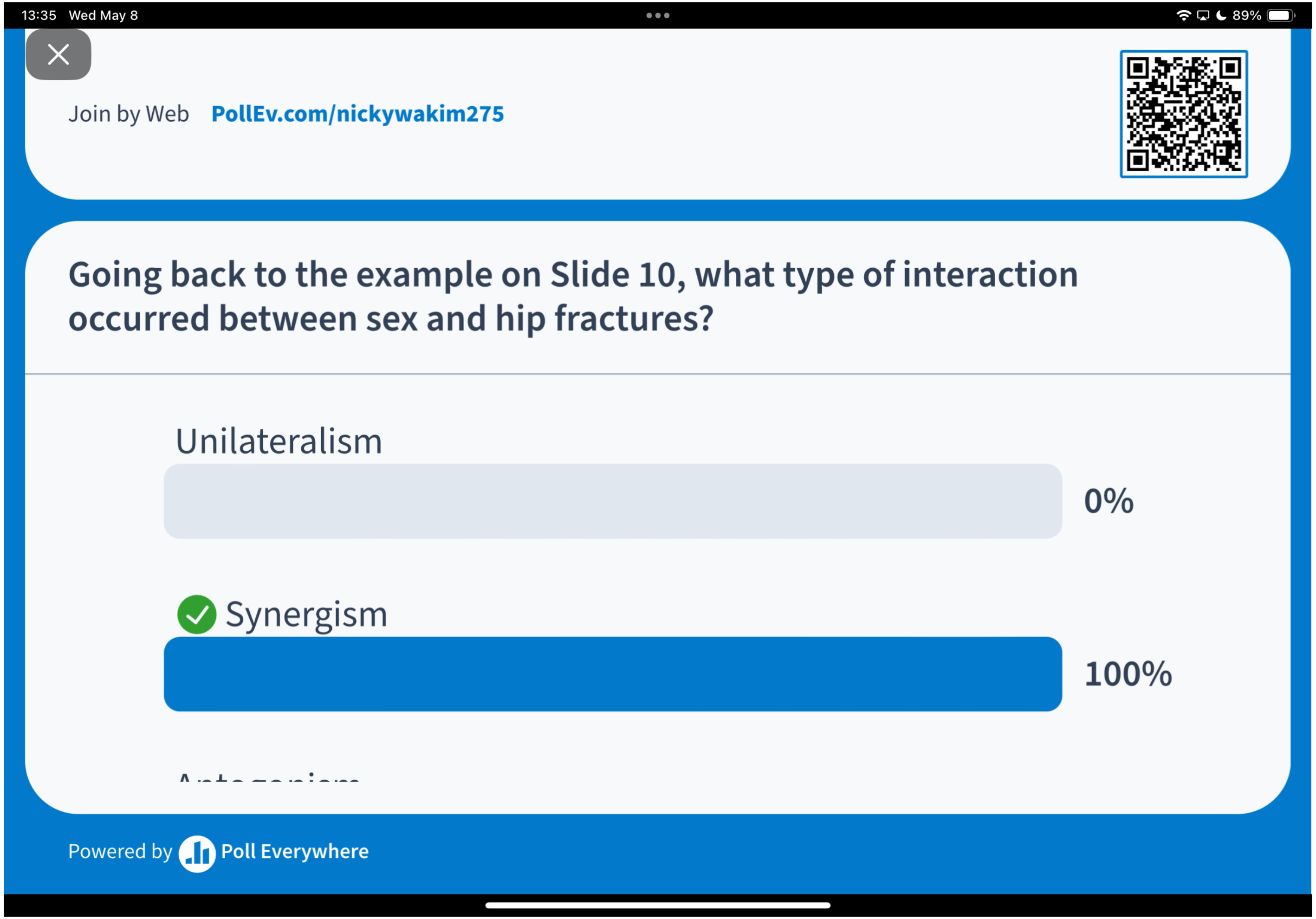
(d) Antagonism



Effect of A works in the opposite direction in the presence of B

$\beta_3 < 0$

Poll Everywhere Question 1



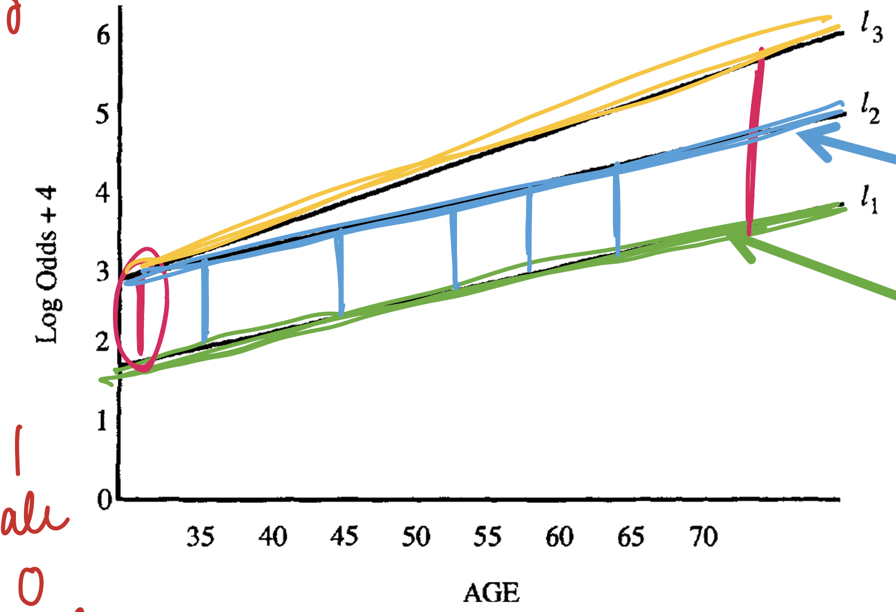
Going back to the example on Slide 10, what type of interaction occurred between sex and hip fractures?

Unilateralism	0%
✓ Synergism	100%
Antagonism	

Both log odds increasing w/ hip fracture but @ diff rates

Understand the interaction (1/3)

- Figure plots the logits (log-odds) under ~~three~~ two different models showing the presence and absence of interaction.
- Response variable: CHD
- Risk factor: sex → sex=1 Male, sex=0 female
- Covariate to be controlled: age



Logit for males (with interaction)

Logit for males (w/o interaction)

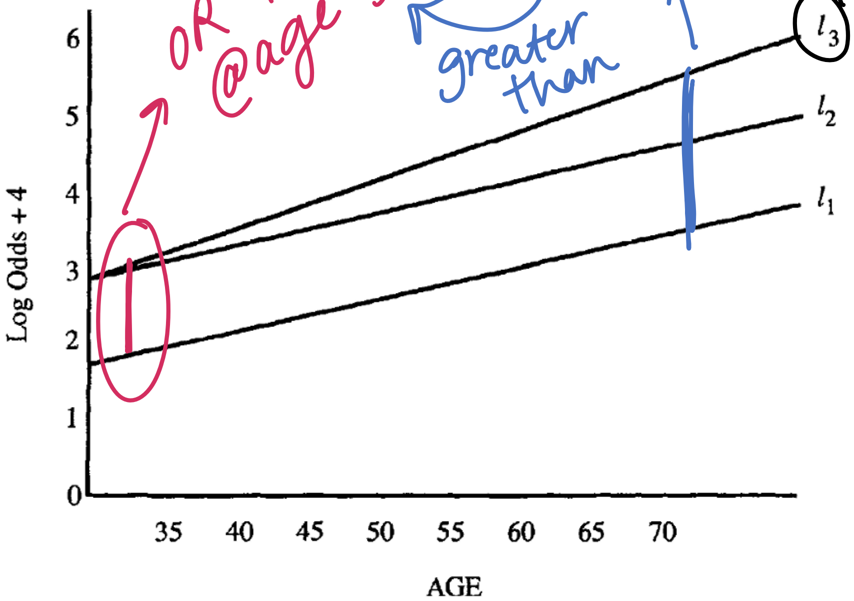
Logit for females

$$\text{logit}(\pi(x)) = \beta_0 + \beta_1 \text{Sex} + \beta_2 \text{Age}$$

$$\cancel{+ \beta_3 \text{Age} \times \text{Sex}}$$

Understand the interaction (2/3)

- **If age does not interact with sex**, the distance between l_2 and l_1 is the log odds ratio for sex, controlling for age ($l_2 - l_1$) stays the same for all values of age.
- **If age interacts with sex**, the distance between l_3 and l_1 is the log odds ratio for sex, controlling for age.
  - Age values need to be specified because ($l_3 - l_1$) differs for different values of age.
  - Must specify age when reporting odds ratio comparing sex



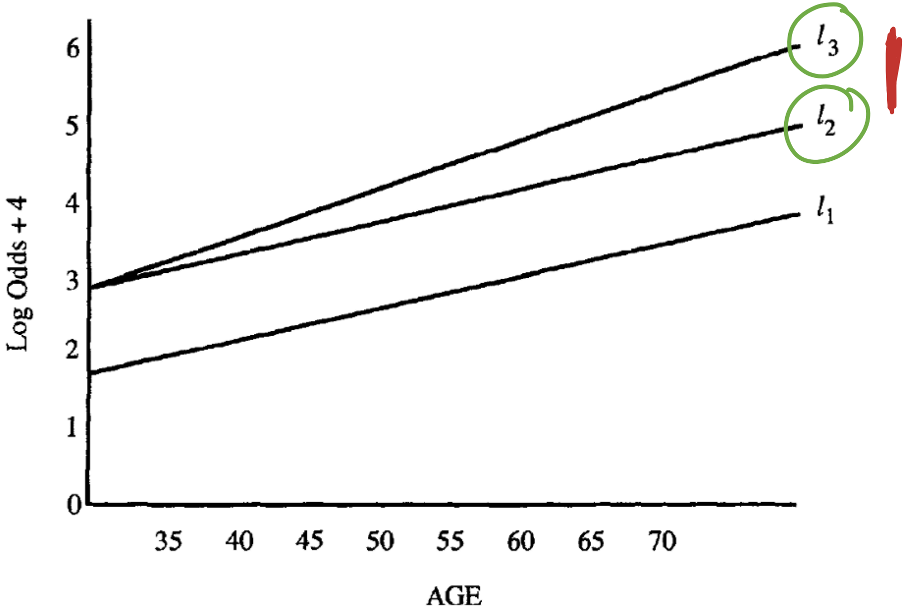
OR for sex @age 30

OR for sex @ age 70

greater than

Understand the interaction (3/3)

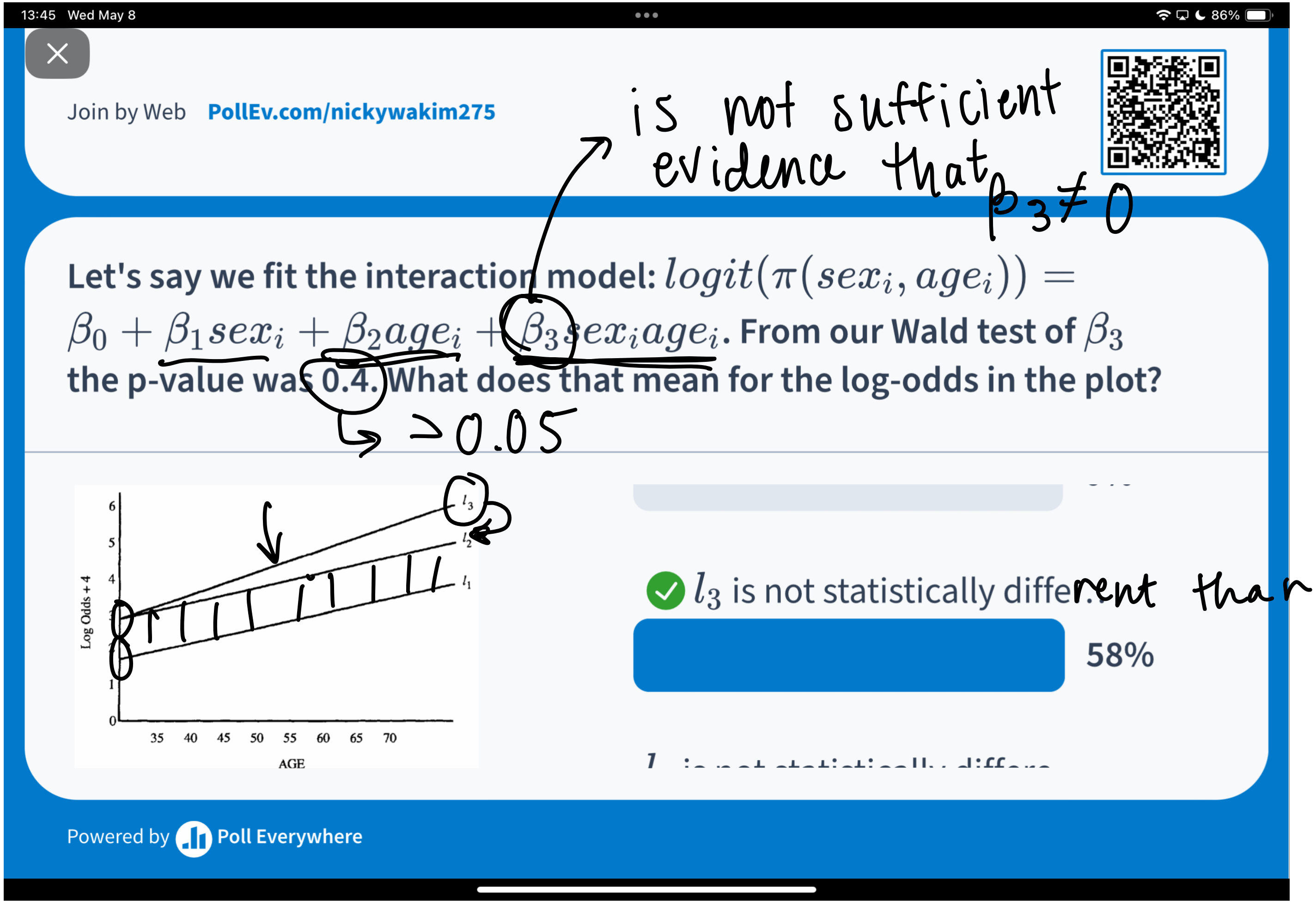
- In the real world, it is rare to see two completely parallel logit plots as we see l_2 and l_1
    - But we need to determine if the difference between l_2 and l_3 is important in the model
- We may not want to include the interaction term unless it is statistically significant and/or clinically meaningful
- Likelihood ratio test (or Wald test) may be used to test the significance of coefficients for variables of the interaction term



testing $\beta_3 = 0$ vs. $\beta_3 \neq 0$

if multi level cat involved: need to test multiple coeff (w/ LRT)

Poll Everywhere Question 2



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is not sufficient evidence that $\beta_3 \neq 0$

Let's say we fit the interaction model: $logit(\pi(sex_i, age_i)) = \beta_0 + \beta_1 sex_i + \beta_2 age_i + \beta_3 sex_i age_i$**. From our Wald test of** β_3 **the p-value was 0.4. What does that mean for the log-odds in the plot?**

> 0.05

✓ l_3 is not statistically different than l_3

58%

l is not statistically differe

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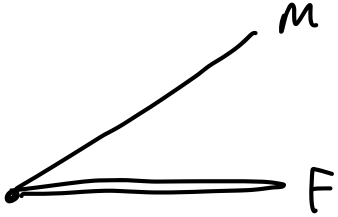

Summary

- In a logistic model with two covariates : X_1 (the risk factor, a binary variable) and X_2 (potential confounder/effect modifier)
- The role of X_2 can be one of the three possibilities:

1. **Not a confounder nor effect modifier**, and not significantly associated with Y
    - No need to include X_2 in the model (for your dataset)
    - May still be nice to include if other literature in the field includes it

2. It is a **confounder but not an effect modifier**. There is statistical adjustment but no statistical interaction
    - Should include X_2 in the model as main effect

3. It is an **effect modifier**. There is statistical interaction.
    - Should include X_2 in the model as main effect and interaction term

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Deciding between confounder and effect modifier

- This is more of a model selection question (in coming lectures)
- But if we had a model with **only TWO covariates**, we could step through the following process:

1. Test the interaction (of potential effect modifier): use a ~~partial F-test~~ to test if interaction term(s) explain enough variation compared to model without interaction LRT (Wald)
    - Recall that for two continuous covariates, we will **test a single coefficient**
    - For a binary and continuous covariate, we will **test a single coefficient**
    - For two binary categorical covariates, we will **test a single coefficient**
    - **For a multi-level categorical covariate (with any other type of covariate), we must test a group of coefficients!!**
2. Then look at the main effect (or potential confounder)
    - If interaction already included, then automatically included as main effect (and thus not checked for confounding)
    - For variables that are not included in any interactions:
        - Check to see if they are confounders by seeing whether exclusion of the variable changes any of the main effect of the primary explanatory variable by more than 10%

Step 1: Testing the interaction

- We test with $\alpha = 0.10$ from 513
- Follow the LRT procedure in Lesson 6, slide 38
- Use the hypothesis tests for the specific covariate combo:

Binary & continuous variable

Testing a **single coefficient** for the interaction term using LRT comparing full model (with interaction) to reduced model (without interaction)

Binary & continuous variables

Testing a **group of coefficients** for the interaction term using LRT comparing full model (with interaction) to reduced model (without interaction)

Binary & multi-level variable

Testing a **group of coefficients** for the interaction term using LRT comparing full model (with interaction) to reduced model (without interaction)

Two continuous variables

Testing a **single coefficient** for the interaction term using LRT comparing full model (with interaction) to reduced model (without interaction)

Poll Everywhere Question 2

Step 2: Testing a confounder

- If interaction already included:
  - Meaning: LRT showed evidence for alternative/full model
  - Then the variable is an effect modifier and we don't need to consider it as a confounder
  - Then automatically included as main effect (and thus not checked for confounding)
- For variables that are not included in any interactions:
  - Check to see if they are confounders
  - One way to do this is by seeing whether exclusion of the variable changes any of the main effect of the primary explanatory variable by more than 10%
- If the main effect of the primary explanatory variable changes by less than 10%, then the additional variable is neither an effect modifier nor a confounder
  - We leave the variable out of the model

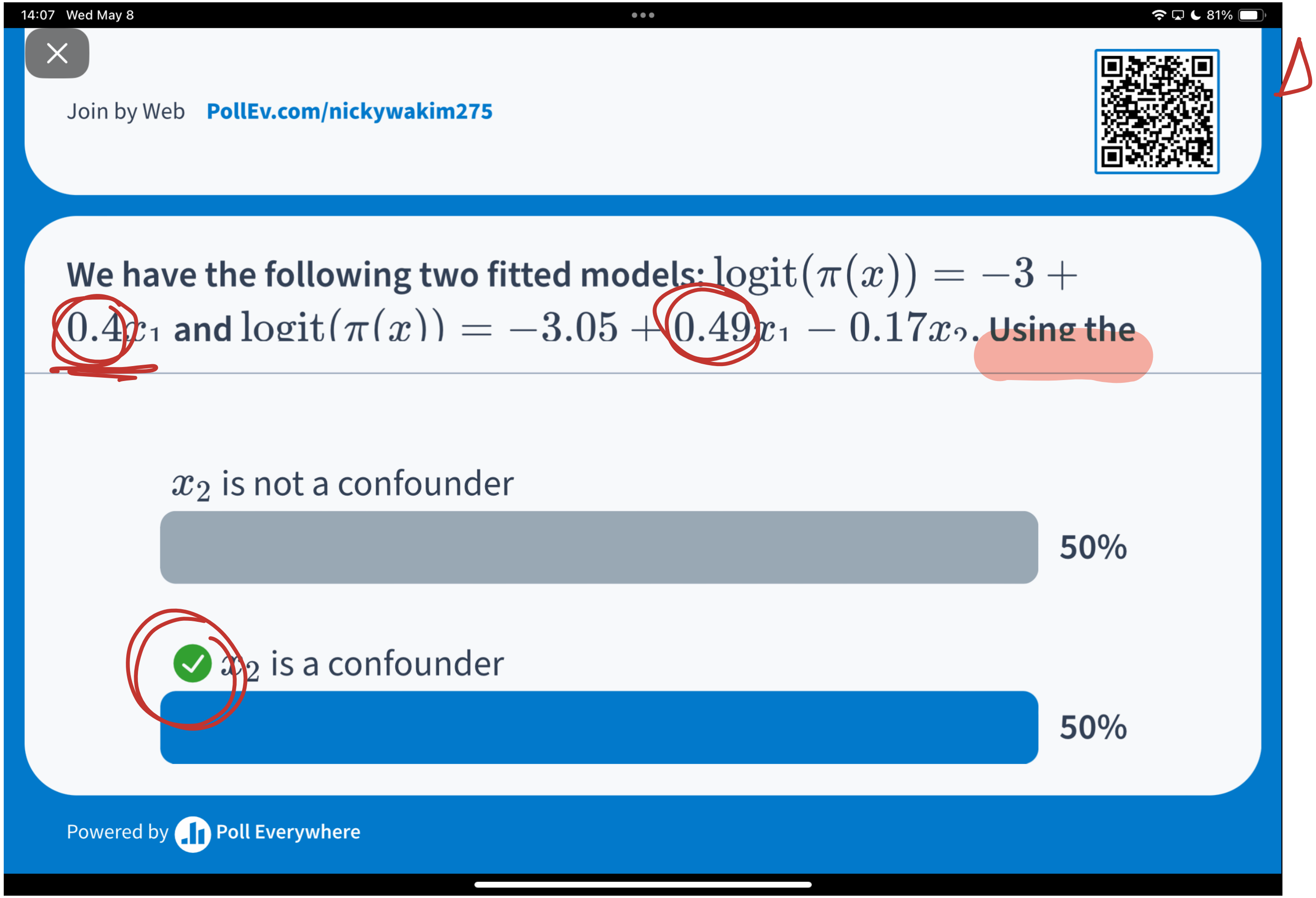
Testing for percent change ($\Delta\%$) in a coefficient

- Let's say we have X_1 and X_2, and we specifically want to see if X_2 is a confounder for X_1 (the explanatory variable or variable of interest)
- If we are only considering X_1 and X_2, then we need to run the following two models:
  - **Fitted model 1 / reduced model (`mod1`):** $\text{logit}\left(\widehat{\pi}(\mathbf{X})\right) = \widehat{\beta}_0 + \widehat{\beta}_1 X_1$
    - We call the above $\widehat{\beta}_1$ the reduced model coefficient: $\widehat{\beta}_{1,\text{mod1}}$ or $\widehat{\beta}_{1,\text{red}}$
  - **Fitted model 2 / full model (`mod2`):** $\text{logit}\left(\widehat{\pi}(\mathbf{X})\right) = \widehat{\beta}_0 + \widehat{\beta}_1 X_1 + \underline{\widehat{\beta}_2 X_2}$
    - We call this $\widehat{\beta}_1$ the full model coefficient: $\widehat{\beta}_{1,\text{mod2}}$ or $\widehat{\beta}_{1,\text{full}}$

Calculation for % change in coefficient

$$\Delta\% = 100\% \cdot \left|\frac{\widehat{\beta}_{1,\text{mod1}} - \widehat{\beta}_{1,\text{mod2}}}{\widehat{\beta}_{1,\text{mod2}}}\right| = 100\% \cdot \left|\frac{\widehat{\beta}_{1,\text{red}} - \widehat{\beta}_{1,\text{full}}}{\widehat{\beta}_{1,\text{full}}}\right|$$

Poll Everywhere Question 3



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We have the following two fitted models: $\text{logit}(\pi(x)) = -3 + 0.4x_1$ **and** $\text{logit}(\pi(x)) = -3.05 + 0.49x_1 - 0.17x_2$**. Using the**

x_2 is not a confounder 50%

✓ x_2 is a confounder 50%

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$$\Delta\% = \frac{\overbrace{0.4-0.49}^{-0.09}}{0.49} \times 100\%$$

$$= \frac{-0.09}{0.49} \times 100\%$$

$$= -18\%$$

Example: GLOW Study

- From GLOW (Global Longitudinal Study of Osteoporosis in Women) study

- **Outcome variable:** any fracture in the first year of follow up (FRACTURE: 0 or 1)

- **Risk factor/variable of interest:** history of prior fracture (PRIORFRAC: 0 or 1)

- **Potential confounder or effect modifier:** age (AGE, a continuous variable)
  - Center age will be used! We will center around the rounded mean age of 69 years old

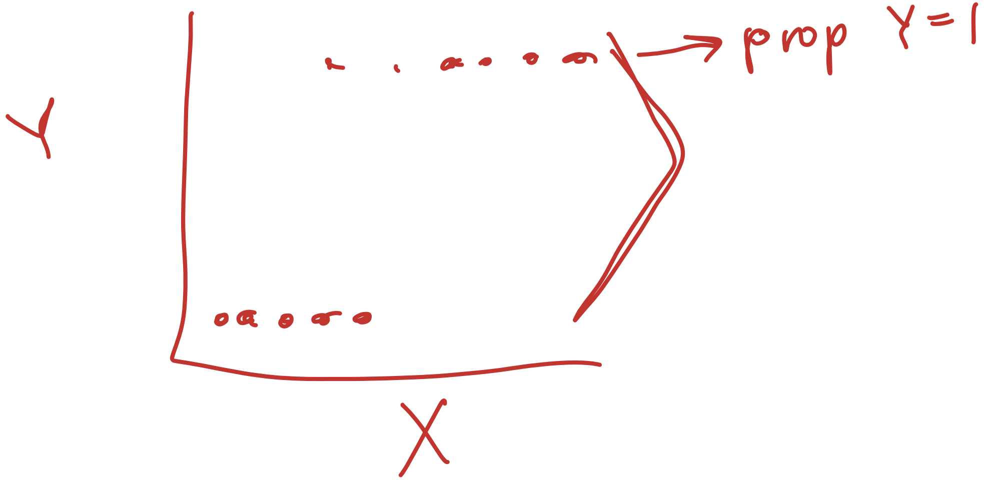
```r
library(aplore3)
mean_age = mean(glow500$age) %>% round()
glow = glow500 %>% mutate(age_c = age - mean_age)
```

↳ aid us w/ interp of coefficients

Example: GLOW Study: Try to visual the sample proportions

- Back in BSTA 512/612, we could visual the data to get a sense if there was an interaction before fitting a model

- With a binary outcome, this is a little harder
    - We could use a contingency table or plot proportions of the outcome
    - Hard to do this when our potential confounder or effect modifier is continuous



Example: GLOW Study: Calculate the proportions

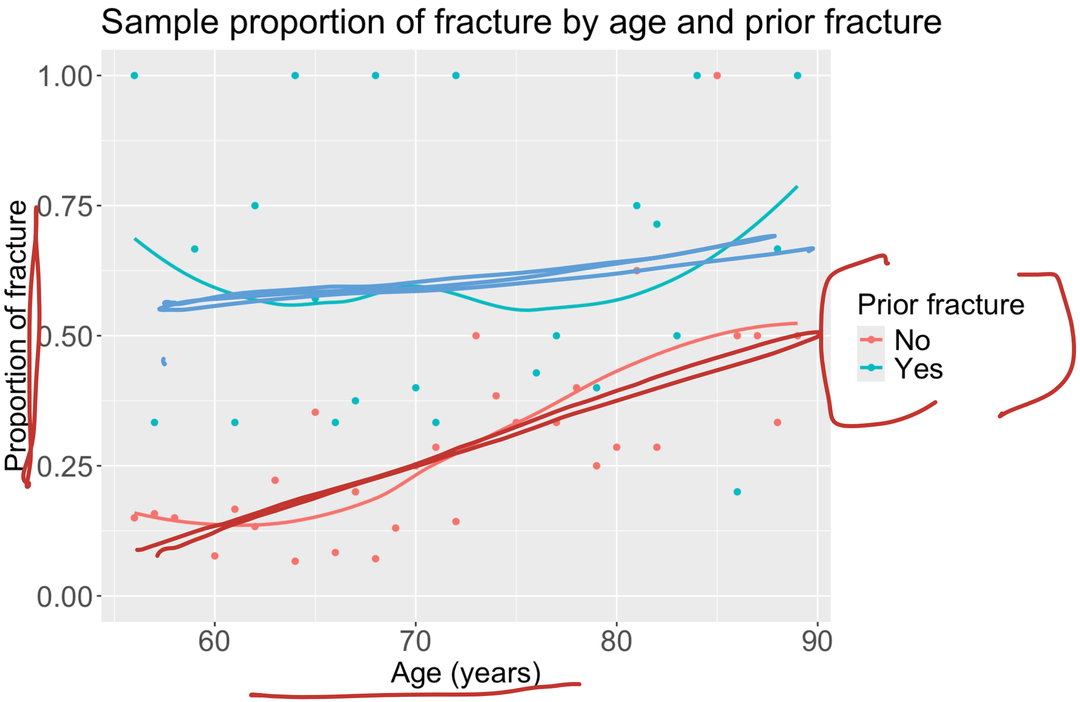
```r
glow2 = glow %>%
  group_by(age, priorfrac, fracture) %>% # last one needs to be outcome
  summarise(n = n()) %>%
  mutate(freq = n / sum(n)) %>% # takes the proportion of yes/no
  filter(fracture == "Yes") # Filtering so only "success" shown
  #filter(freq != 1 | n != 1)

head(glow2)
```

```
# A tibble: 6 × 5
# Groups:   age, priorfrac [6]
    age priorfrac fracture     n  freq
  <int> <fct>     <fct>    <int> <dbl>
1    56 No        Yes          3 0.15 
2    56 Yes       Yes          1 1    
3    57 No        Yes          3 0.158
4    57 Yes       Yes          1 0.333
5    58 No        Yes          3 0.15 
6    59 Yes       Yes          2 0.667
```

Example: GLOW Study: Plot the proportions

```
ggplot(data = glow2, aes(y = freq, x = age, color = priorfrac)) +
  geom_point() + ylim(0, 1) + geom_smooth(se = F) +
  labs(x = "Age (years)", y = "Proportion of fracture",
       color = "Prior fracture", title = "Sample proportion of fracture by age and prior fracture") +
  theme(axis.title = element_text(size = 18), axis.text = element_text(size = 18),
        title = element_text(size = 18), legend.text=element_text(size=18))
```



- From sample proportions, looks like age and prior fracture may have an interaction!

Example: GLOW Study

We also *could jump right into model fitting* (connecting to the three possible roles of Age):

- **Model 1:** Age not included

determine confounding

$$\text{logit}\left(\pi(\mathbf{X})\right) = \beta_0 + \beta_1 \boxed{\cdot\, I(\text{PF})}$$

indicator for prior fracture

- **Model 2:** Age as main effect (age as potential confounder)

determine int

$$\text{logit}\left(\pi(\mathbf{X})\right) = \beta_0 + \underline{\beta_1 \cdot I(\text{PF})} + \underline{\beta_2 \cdot Age}$$

- **Model 3:** Age and Prior Fracture interaction (age as potential effect modifier)

$$\text{logit}\left(\pi(\mathbf{X})\right) = \beta_0 + \underline{\beta_1 \cdot I(\text{PF})} + \underline{\beta_2 \cdot Age} + \underline{\beta_3 \cdot I(\text{PF}) \cdot Age}$$

Example: GLOW Study

We also *could jump right into model fitting* (connecting to the three possible roles of Age):

- **Model 1:** Age not included

```
glow_m1 = glm(fracture ~ priorfrac,
              data = glow, family = binomial)
```

- **Model 2:** Age as main effect (age as potential confounder)

```
glow_m2 = glm(fracture ~ priorfrac + age_c,
              data = glow, family = binomial)
```

- **Model 3:** Age and Prior Fracture interaction (age as potential effect modifier)

```
glow_m3 = glm(fracture ~ priorfrac + age_c + priorfrac*age_c,
              data = glow, family = binomial)
```

Example: GLOW Study: Age an effect modifier or confounder?

- **Model 1:** Age not included

term	estimate	std.error	statistic	p.value	conf.low	conf.high
(Intercept)	−1.417	0.130	−10.859	0.000	−1.679	−1.167
priorfracYes	1.064	0.223	4.769	0.000	0.626	1.502

- **Model 2:** Age as main effect (age as potential confounder)

term	estimate	std.error	statistic	p.value	conf.low	conf.high
(Intercept)	−1.372	0.132	−10.407	0.000	−1.637	−1.120
priorfracYes	0.839	0.234	3.582	0.000	0.378	1.297
age_c	0.041	0.012	3.382	0.001	0.017	0.065

- **Model 3:** Age and Prior Fracture interaction (age as potential effect modifier)

term	estimate	std.error	statistic	p.value	conf.low	conf.high
(Intercept)	−1.376	0.134	−10.270	0.000	−1.646	−1.120
priorfracYes	1.002	0.240	4.184	0.000	0.530	1.471
age_c	0.063	0.015	4.043	0.000	0.032	0.093
priorfracYes:age_c	−0.057	0.025	−2.294	0.022	−0.107	−0.008

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- Is age an effect modifier?
  - Test the significance of the interaction term in Model 3
  - We can use the Wald test or LRT

- If not an effect modifier, check the change in coefficient for prior fracture between Model 1 and Model 2

Example: GLOW Study: Age an effect modifier or confounder?

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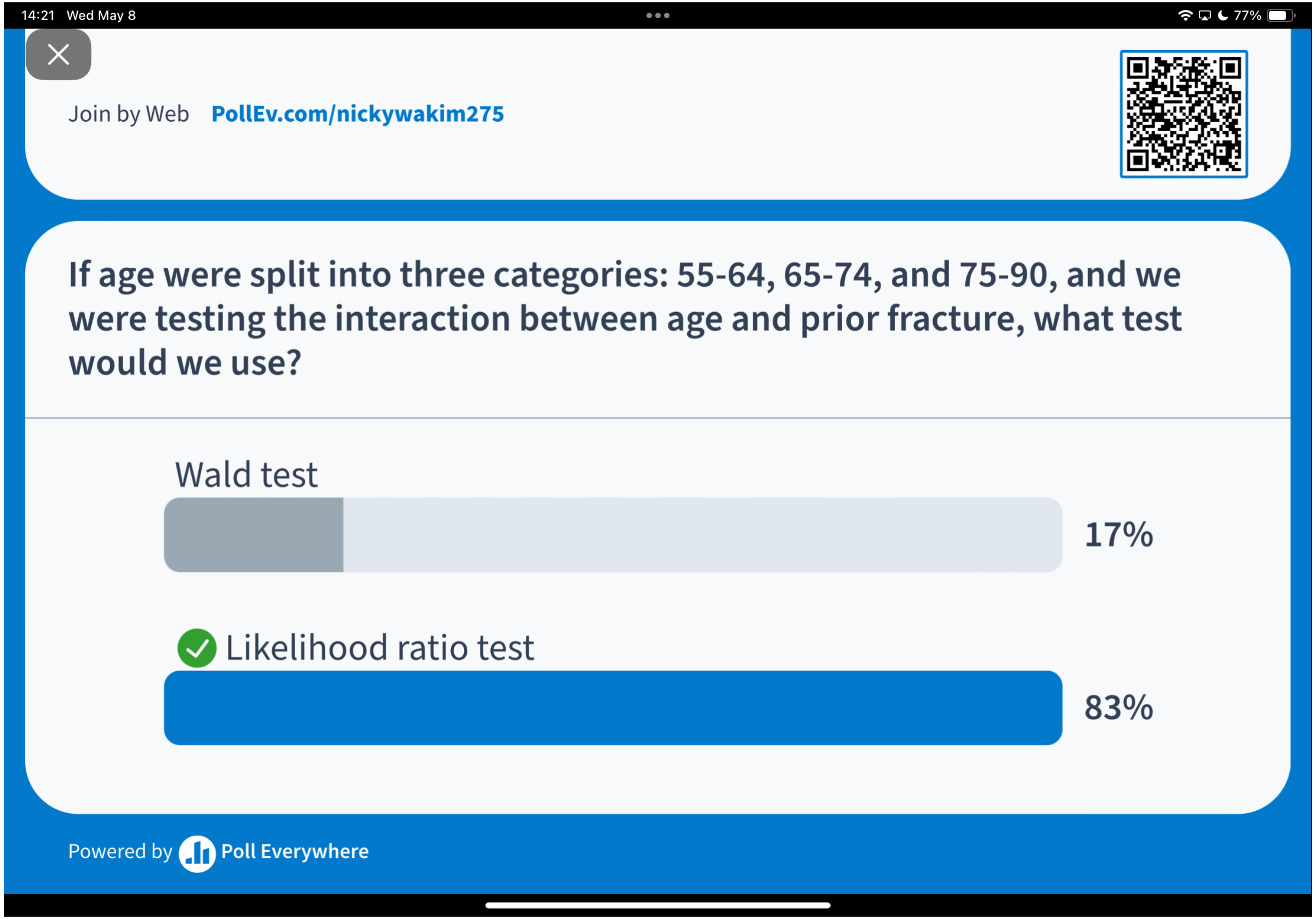
Short version of testing the interaction: Wald statistic for the interaction coefficient, $\widehat{\beta}_3$, is statistically significant with $p = 0.022$. Thus, there is evidence of a statistical interaction between these age and prior fracture.

Poll Everywhere Question 4



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77%

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If age were split into three categories: 55-64, 65-74, and 75-90, and we were testing the interaction between age and prior fracture, what test would we use?

Wald test 17%

✓ Likelihood ratio test 83%

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$$
\begin{aligned}
\operatorname{logit}(\pi(X)) = \; & \beta_0 + \beta_1 I(PF) \\
& + \beta_2 \text{Age}55\text{-}64 \\
& + \beta_3 \text{Age}65\text{-}74 \\
& + \beta_4 \text{Age}75\text{-}90 \\
& \boxed{\begin{aligned} & + \beta_5 I(PF) \times \text{Age}55\text{-}64 \\ & + \beta_6 I(PF) \times \text{Age}65\text{-}74 \\ & + \beta_7 I(PF) \times \text{Age}75\text{-}90 \end{aligned}}
\end{aligned}
$$

Please please please reference your work from BSTA 512/612

- We had lessons and homeworks dedicated to this process!
- The process will be the same!
    - Only differences are t-test and F-test are replaced by Wald test and Likelihood ratio test, respectively!!

Learning Objectives

1. Connect understanding of confounding and interactions from linear regression to logistic regression.
2. Determine if an additional independent variable is a not a confounder nor effect modifier, is a confounder but not effect modifier, or is an effect modifier.
3. Calculate and interpret fitted interactions, including plotting the log-odds, predicted probability, and odds ratios.

Example: GLOW Study

- Age is an **effect modifier** of prior fracture

- When a covariate is an **effect modifier**, its status as a confounder is of secondary importance since the estimate of the effect of the risk factor depends on the specific value of the covariate

- Must summarize the effect of prior fracture on current fracture *by age*
  - Cannot summarize as a single (log) odds ratio

Example: GLOW – Interaction interpretation

- **Model 3:**

$$\text{logit}\left(\widehat{\pi}(\mathbf{X})\right) = \widehat{\beta}_0 \quad + \widehat{\beta}_1 \cdot I(\text{PF}) \quad + \widehat{\beta}_2 \cdot Age \quad + \widehat{\beta}_3 \cdot I(\text{PF}) \cdot Age$$

$$\text{logit}\left(\widehat{\pi}(\mathbf{X})\right) = -1.376 \quad \underline{+1.002 \cdot I(\text{PF})} \quad +0.063 \cdot \underbrace{Age}_{=0} \quad -0.057 \cdot I(\text{PF}) \cdot \underbrace{Age}_{=0}$$

term	estimate	std.error	statistic	p.value	conf.low	conf.high
(Intercept)	−1.376	0.134	−10.270	0.000	−1.646	−1.120
priorfracYes	1.002	0.240	4.184	0.000	0.530	1.471
age_c	0.063	0.015	4.043	0.000	0.032	0.093
priorfracYes:age_c	−0.057	0.025	−2.294	0.022	−0.107	−0.008

Example: GLOW – Interaction interpretation

- **Model 3:**

term	estimate	p.value	conf.low	conf.high
(Intercept)	−1.376	0.000	−1.646	−1.120
priorfracYes	1.002	0.000	0.530	1.471
age_c	0.063	0.000	0.032	0.093
priorfracYes:age_c	−0.057	0.022	−0.107	−0.008

- Estimated odds ratios table:

term	estimate	p.value	conf.low	conf.high
(Intercept)	0.25	0.00	0.19	0.33
priorfracYes	2.72	0.00	1.70	4.35
age_c	1.06	0.00	1.03	1.10
~~priorfracYes:age_c~~	~~0.94~~	~~0.02~~	~~0.90~~	~~0.99~~

$Age\_c = 0$

↳ age is 69

$Age\text{-}c = 1$

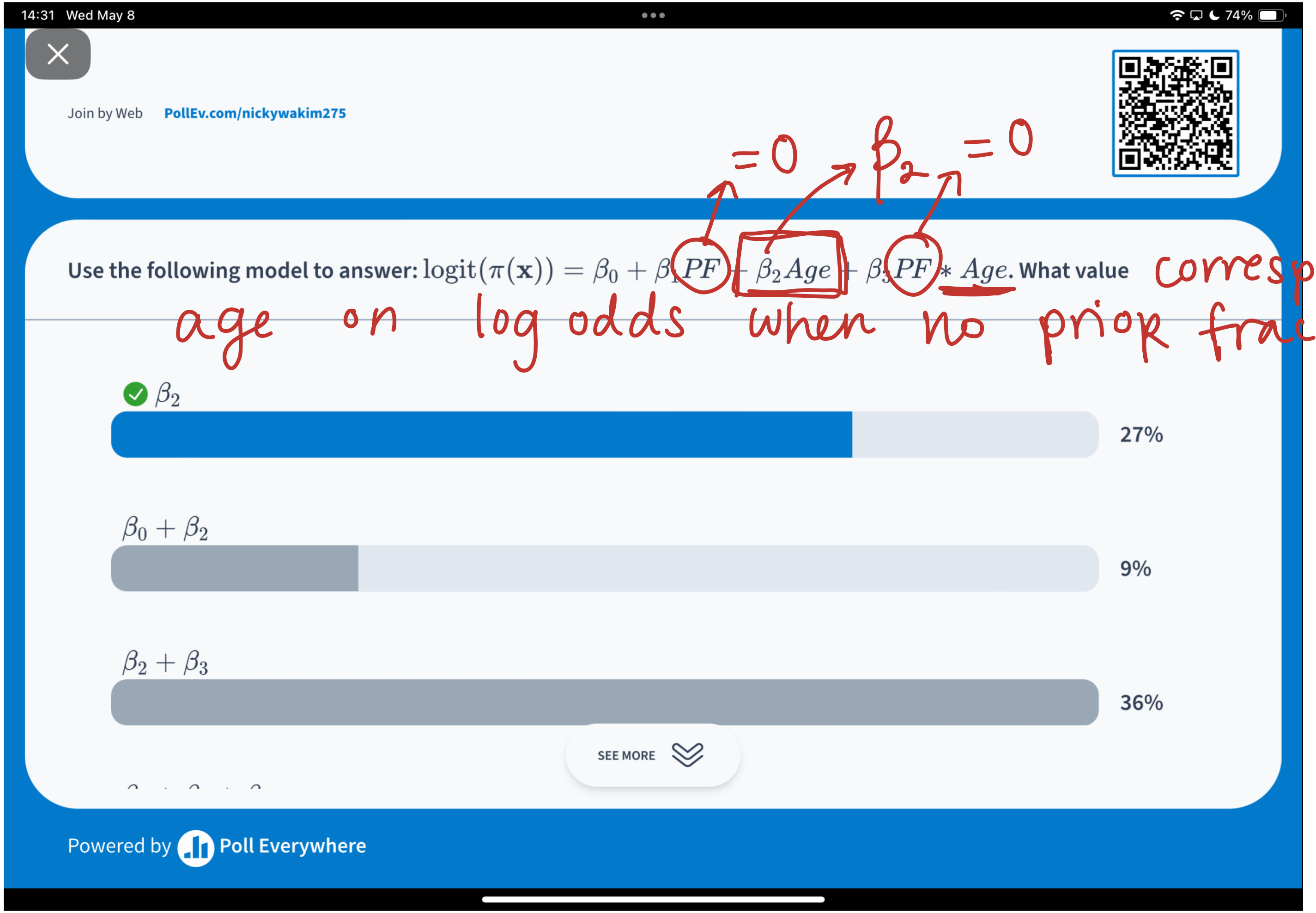
age 70

$70-69$

$=1$

- $\widehat{\beta}_3 = -0.057$
- The effect of having a prior fracture on the log odds of having a new fracture decreases by an estimated 0.057 for every one year increase in age (95% CI: 0.008, 0.107).
  - Aka the *log odds of a new fracture* comparing prior fracture to no prior fracture gets closer to one another as age increases
- $\widehat{\beta}_1 = 1.002$
- For individuals 69 years old, the estimated difference in log odds for a new fracture is 1.002 comparing individuals with a prior fracture to individuals with no prior fracture (95% CI: 0.530, 1.471).
- $\exp(\widehat{\beta}_1) = 2.72$ $\boxed{OR}$
- For individuals 69 years old, the estimated odds of a new fracture for individuals with prior fracture is 2.72 times the estimated odds of a new fracture for individuals with no prior fracture (95% CI: 1.70, 4.35).

Poll Everywhere Question 5



Join by Web **PollEv.com/nickywakim275**

=0 β_2 =0

Use the following model to answer: $\text{logit}(\pi(\mathbf{x})) = \beta_0 + \beta_1 PF + \boxed{\beta_2 Age} + \beta_3 PF * \underline{Age}$. **What value** corresponds to effect of age on log odds when no prior fracture?

✓ β_2 27%

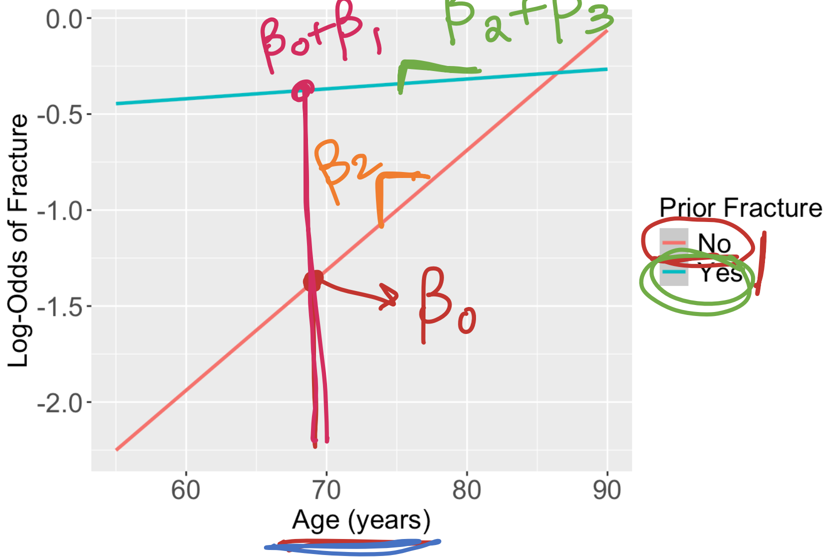
$\beta_0 + \beta_2$ 9%

$\beta_2 + \beta_3$ 36%

Plot of estimated log odds

```r
prior_age = expand_grid(priorfrac = c("No", "Yes"), age_c = (55:90)-69)
frac_pred_log = predict(glow_m3, prior_age, se.fit = T, type="link")
pred_glow2 = prior_age %>% mutate(frac_pred_log = frac_pred_log$fit,
                                  age = age_c + mean_age)

ggplot(pred_glow2) + #geom_point(aes(x = age, y = frac_pred, color = priorfrac)) +
  geom_smooth(method = "loess", aes(x = age, y = frac_pred_log, color = priorfrac))
  theme(text = element_text(size=20), title = element_text(size=16)) +
  labs(color = "Prior Fracture", x = "Age (years)", y = "Log-Odds of Fracture")
```

$$\text{logit}(\pi(X)) = \beta_0 + \beta_1 \underset{=0}{PF} + \beta_2 \underset{=0}{Age} + \beta_3 \underset{=0}{PF} \times \underset{=0}{Age}$$

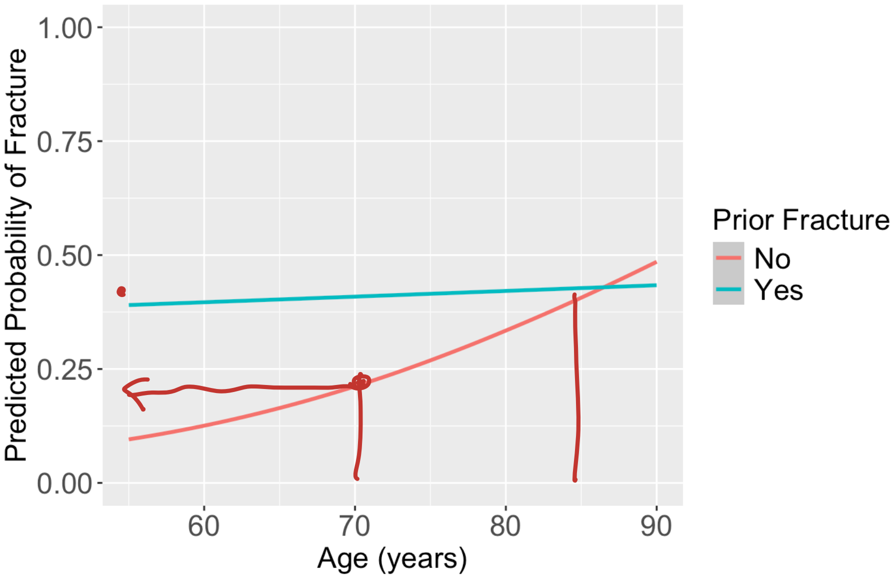


Poll Everywhere Question 6 (Bonus q if we're feeling it)

Plot the predicted probability of fracture

probability

```
frac_pred = predict(glow_m3, prior_age, se.fit = T, type="response")
pred_glow = prior_age %>% mutate(frac_pred = frac_pred$fit,
                                  age = age_c + mean_age)

ggplot(pred_glow) + #geom_point(aes(x = age, y = frac_pred, color = priorfrac)) +
  geom_smooth(method = "loess", aes(x = age, y = frac_pred, color = priorfrac)) +
  theme(text = element_text(size=20), title = element_text(size=16)) + ylim(0,1) +
  labs(color = "Prior Fracture", x = "Age (years)", y = "Predicted Probability of F
```



Odds Ratio in the Presence of Interaction (1/2)

- When interaction exists between a risk factor (F) and another variable (X), the estimate of the odds ratio for F depends on the value of X

- When an interaction term (F*X) exists in the model
  - $\widehat{OR}_F \neq \exp(\widehat{\beta}_F)$ in general

- Assume we want to compute the odds ratio for $(F = f_1$ and $F = f_0$, the correct model-based estimate is

$$\widehat{OR}_F = \exp\left(\hat{g}\left(F = f_1, X = x\right) - \hat{g}\left(F = f_0, X = x\right)\right)$$

  - Let's work this out on the next slide!

Odds Ratio in the Presence of Interaction (2/2) ← look @ lesson 5 simple logistic regress

- We may write the two logits (log-odds) for given x as below:

$$\hat{g}\left(F=f_1, X=x\right)=\hat{\beta}_0+\hat{\beta}_1 f_1+\hat{\beta}_2 x+\hat{\beta}_3 f_1 \cdot\ x$$
$$\hat{g}\left(F=f_0, X=x\right)=\hat{\beta}_0+\hat{\beta}_1 f_0+\hat{\beta}_2 x+\hat{\beta}_3 f_0 \cdot\ x$$

- The difference in two logits (log-odds) is: diff b/w log odds

$$\hat{g}\left(f_1, x\right)-\hat{g}\left(f_0, x\right)=\left[\hat{\beta}_0+\hat{\beta}_1 f_1+\hat{\beta}_2 x+\hat{\beta}_3 f_1 \cdot\ x\right]-\left[\hat{\beta}_0+\hat{\beta}_1 f_0+\hat{\beta}_2 x+\hat{\beta}_3 f_0 \cdot\ x\right]$$
$$\hat{g}\left(f_1, x\right)-\hat{g}\left(f_0, x\right)=\hat{\beta}_1 f_1-\hat{\beta}_1 f_0+\hat{\beta}_3 x f_1-\hat{\beta}_3 x f_0$$
$$\hat{g}\left(f_1, x\right)-\hat{g}\left(f_0, x\right)=\hat{\beta}_1\left(f_1-f_0\right)+\hat{\beta}_3 x\left(f_1-f_0\right)$$

- Therefore,

$$\widehat{OR}(F=f-1, F=f_0, X=x)=\widehat{OR}_F=\exp\left[\hat{\beta}_1\left(f_1-f_0\right)+\hat{\beta}_3 x\left(f_1-f_0\right)\right]$$

Steps to compute OR under interation

- Note: You don't need to know the math itself, but I think it's helpful to think of it this way

1. Identify two sets of values that you want to compare with only one variable changed
   - In previous slides, one set was $(F = f_1, X = x)$ and the other was $(F = f_0, X = x)$
2. Substitute values in the fitted log-odds model
   - You should have two equations, one for each set of values
3. Take the difference of the two log-odds
4. Exponentiate the resulting difference

Example: GLOW Study

1. Identify two sets of values that you want to compare with only one variable changed
   - Set 1: $PF = 1, Age = a$
   - Set 2: $PF = 0, Age = a$

↳ odds ratio for prior fracture

2. Substitute values in the fitted log-odds model

$$\text{logit}\left(\widehat{\pi}(\mathbf{X})\right) = \widehat{\beta}_0 + \widehat{\beta}_1 \cdot I(\text{PF}) + \widehat{\beta}_2 \cdot Age + \widehat{\beta}_3 \cdot I(\text{PF}) \cdot Age$$

$$\begin{aligned}\text{logit}\left(\widehat{\pi}(PF = 1, Age = a)\right) &= \widehat{\beta}_0 + \widehat{\beta}_1 \cdot 1 + \widehat{\beta}_2 \cdot a + \widehat{\beta}_3 \cdot 1 \cdot Age \\ &= \widehat{\beta}_0 + \widehat{\beta}_1 + \widehat{\beta}_2 \cdot a + \widehat{\beta}_3 \cdot a\end{aligned}$$

$$\begin{aligned}\text{logit}\left(\widehat{\pi}(PF = 0, Age = a)\right) &= \widehat{\beta}_0 + \widehat{\beta}_1 \cdot 0 + \widehat{\beta}_2 \cdot a + \widehat{\beta}_3 \cdot 0 \cdot Age \\ &= \widehat{\beta}_0 + \widehat{\beta}_2 \cdot a\end{aligned}$$

Example: GLOW Study

3. Take the difference of the two log-odds

$$\begin{aligned}
\left[logit\left(\pi\left(PF=1,\ Age=a\right)\right)\right]-\left[logit\left(\pi\left(PF=0,\ Age=a\right)\right)\right] \\
&= \left[\hat{\beta}_0+\hat{\beta}_1+\hat{\beta}_2 a+\hat{\beta}_3 a\right]-\left[\hat{\beta}_0+\hat{\beta}_2 a\right] \\
&\boxed{= \hat{\beta}_1+\hat{\beta}_3 a}
\end{aligned}$$

4. Exponentiate the resulting difference

$$\widehat{OR}\left[\left(PF=1,\ Age=a\right),\left(PF=0,\ Age=a\right)\right] = \underline{exp\ \left(\hat{\beta}_1+\hat{\beta}_3 a\right)}$$

We can put in values for age to see how the OR changes

- If we let $a = 60$, i.e., compute OR for age = 60, then

$$\widehat{OR}_{a=60} = \exp(1.002 - 0.057 \cdot (60 - 69)) \ = 4.55$$

- If we let $a = 70$, i.e., compute OR for age = 70, then

$$\widehat{OR}_{a=70} = \exp(1.002 - 0.057 \cdot (70 - 69)) \ = 2.57$$

Calculate odds ratios across values

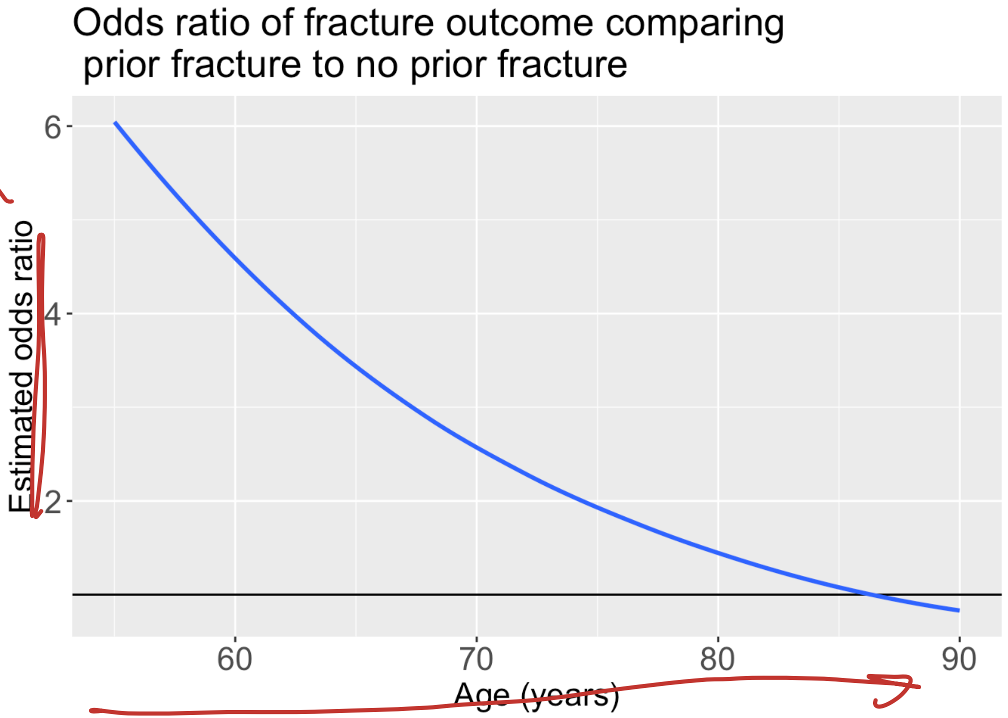
```r
prior_age = expand_grid(priorfrac = c("No", "Yes"), age_c = (55:90)-69)
frac_pred_logit = predict(glow_m3, prior_age, se.fit = T, type="link")
pred_glow2 = prior_age %>% mutate(frac_pred = frac_pred_logit$fit,
                                  age = age_c + mean_age) %>%

                pivot_wider(names_from = priorfrac, values_from = frac_pred) %>%

                mutate(OR_YN = exp(Yes - No))
head(pred_glow2)
```

```
# A tibble: 6 × 5
  age_c   age    No    Yes OR_YN
  <dbl> <dbl> <dbl>  <dbl> <dbl>
1   -14    55 -2.25 -0.446  6.08
2   -13    56 -2.19 -0.441  5.74
3   -12    57 -2.13 -0.436  5.42
4   -11    58 -2.06 -0.430  5.12
5   -10    59 -2.00 -0.425  4.83
6    -9    60 -1.94 -0.420  4.56
```

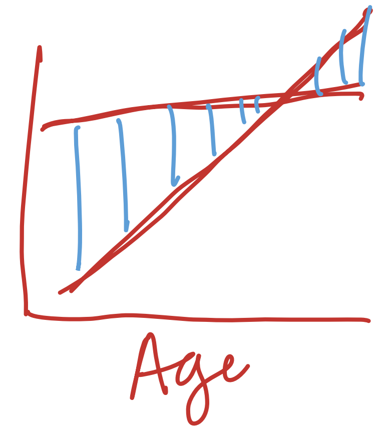
Plotting the odds ratio for an interaction

```r
ggplot(pred_glow2) +
  geom_hline(yintercept = 1) +
  geom_smooth(method = "loess", aes(x = age, y = OR_YN)) +
  theme(text = element_text(size=20), title = element_text(size=16)) +
  labs(x = "Age (years)", y = "Estimated odds ratio", title = "Odds ratio of fractu
```

$$OR = \frac{\text{odds for prior frac}}{\text{odds for no prior frac}}$$


Odds ratio of fracture outcome comparing prior fracture to no prior fracture

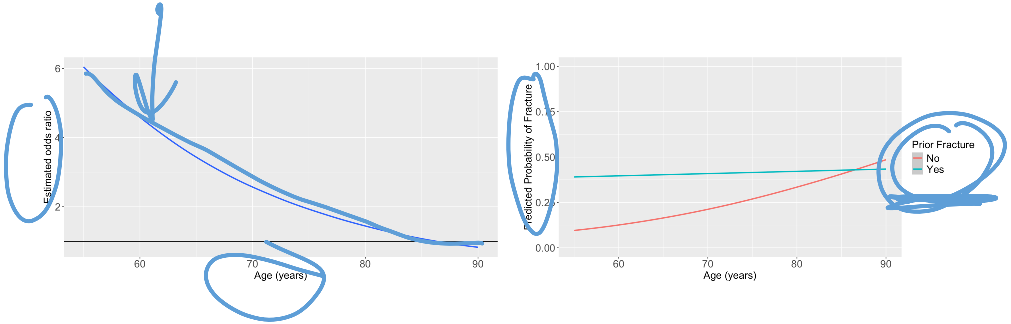
$$e^{\hat{\beta}_1 + \hat{\beta}_3 age}$$



How would I report these results?

- Remember our main covariate is prior fracture, so we want to focuse on how age changes the relationship between prior fracture and a new fracture!

For individuals 69 years old, the estimated odds of a new fracture for individuals with prior fracture is 2.72 times the estimated odds of a new fracture for individuals with no prior fracture (95% CI: 1.70, 4.35). As seen in Figure 1 (a), the odds ratio of a new fracture when comparing prior fracture status decreases with age, indicating that the effect of prior fractures on new fractures decreases as individuals get older. In Figure 1 (b), it is evident that for both prior fracture statuses, the predict probability of a new fracture increases as age increases. However, the predicted probability of new fracture for those without a prior fracture increases at a higher rate than that of individuals with a prior fracture. Thus, the predicted probabilities of a new fracture converge at age [insert age here].



(a) Odds ratio of fracture outcome comparing prior fracture to no prior fracture

(b) Predicted probability of fracture

Figure 1: Plots of odds ratio and predicted probability from fitted interaction model