

Lesson 10: Interactions

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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.

Learning Objectives

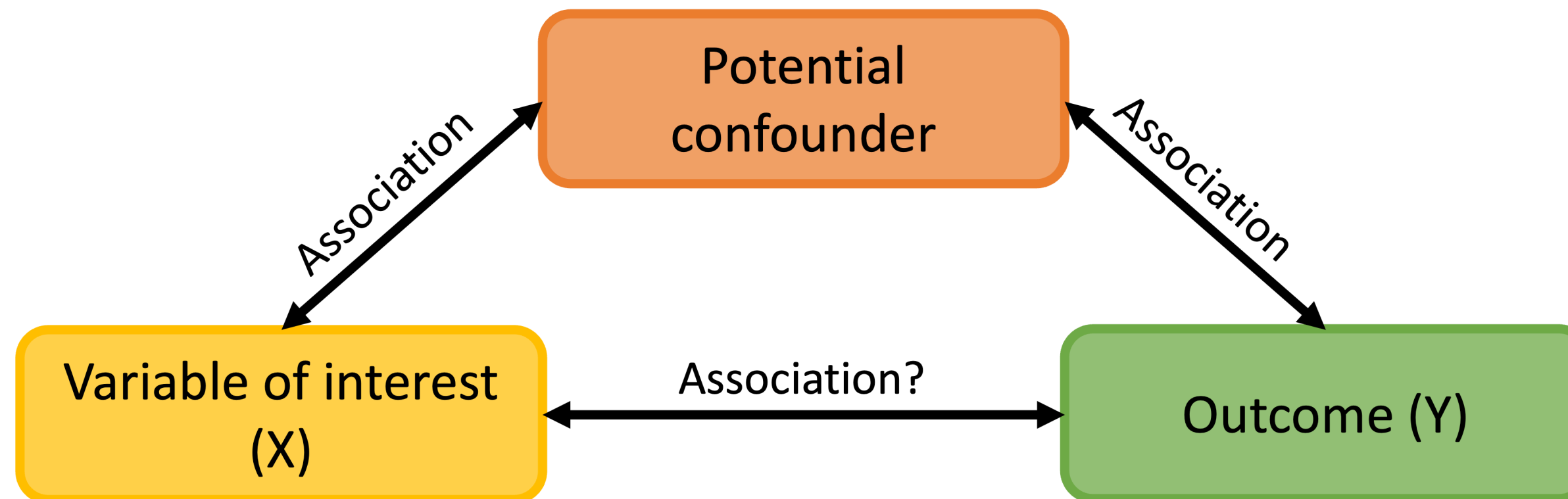
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Reference on slides

- I think these slides from Northwestern do a really good job differentiating between confounders, mediators, and effect modifiers
- <https://www.feinberg.northwestern.edu/sites/bcc/docs/2016lectures/impactofotherfactors.pdf>

Revisit from 512/612: 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
- In study that does not meet causal assumptions (retrospective, observational, case-control)...
 - We need to adjust for **potential** confounders
 - We have no way of proving if a variable is a true confounder



Why do we include a covariate in the model?

- We want our model adjusted for other variables that may alter our estimated relationship between our risk factor/explanatory variable and the outcome
- Cases to include variables in the model:
 - Variable is a potential confounder
 - Variable is not balanced in our explanatory variable
 - Example: mean age is very different in treatment and control group
 - Variable is related to the outcome
- *Hint hint:* This is why we did all those plots in Lab 2
 - To get a sense what might be important to include in the model

Including a confounder in the model

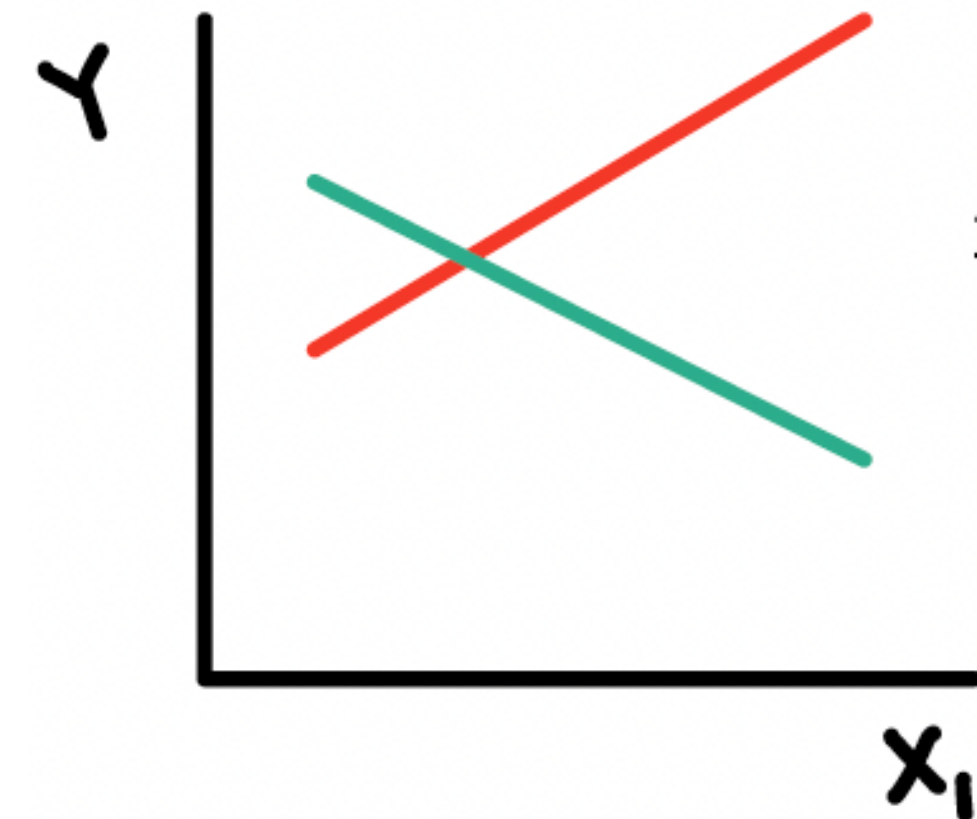
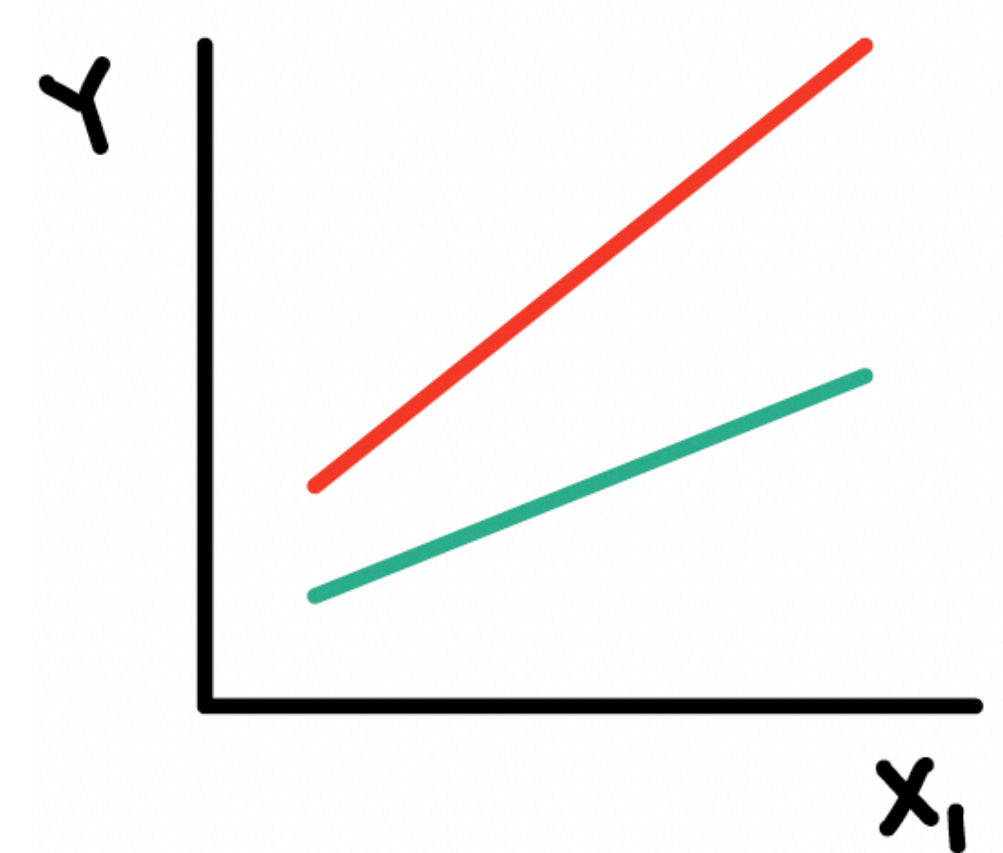
- In the following model we have two variables, X_1 and X_2

$$\text{logit}(\pi(\mathbf{X})) = \beta_0 + \beta_1 \mathbf{X}_1 + \beta_2 \mathbf{X}_2$$

- And we assume that every level of the potential 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
- We need to anchor our X_1 vs Y relationship in a value of X_2
 - Odds ratio for X_1 must be reported for a **specific** X_2



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*.
 - Hard to statistically distinguish between confounders and mediators
- **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?

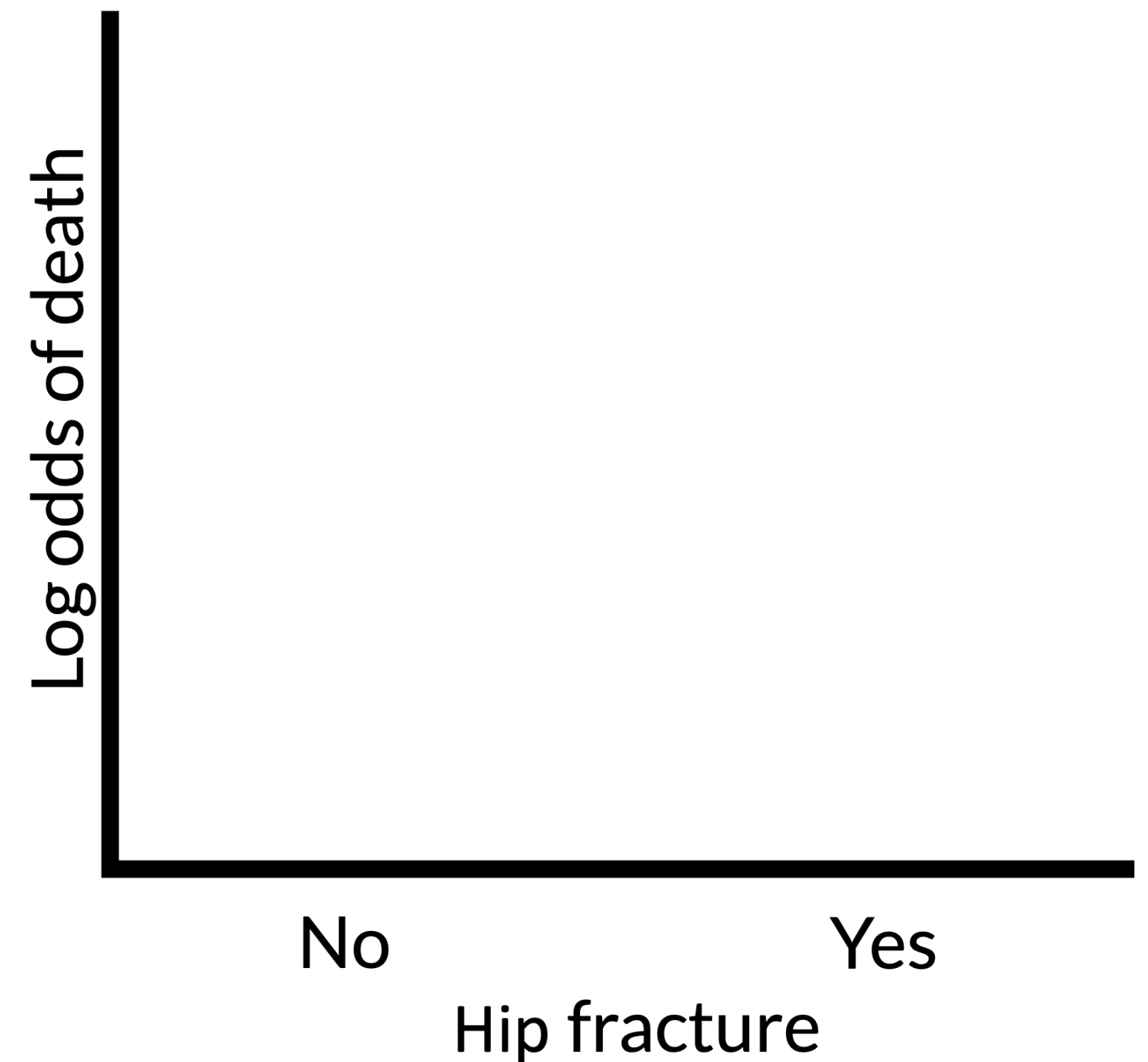
- Interactions!!
- We can incorporate interactions into our model through product terms:

$$\text{logit}(\pi(\mathbf{X})) = \beta_0 + \beta_1\mathbf{X}_1 + \beta_2\mathbf{X}_2 + \beta_3\mathbf{X}_1\mathbf{X}_2$$

- 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)
- Odds ratio for females > odds ratio for males
 - Odds ratio = odds ratio of death, comparing previous hip fracture to no hip fracture



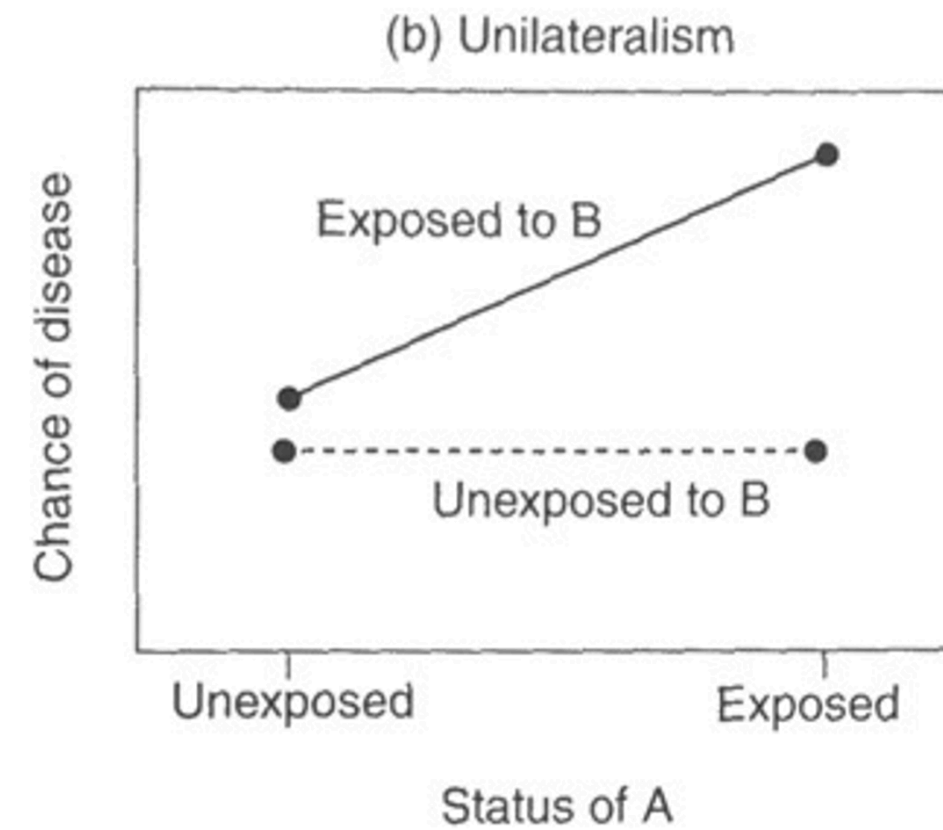
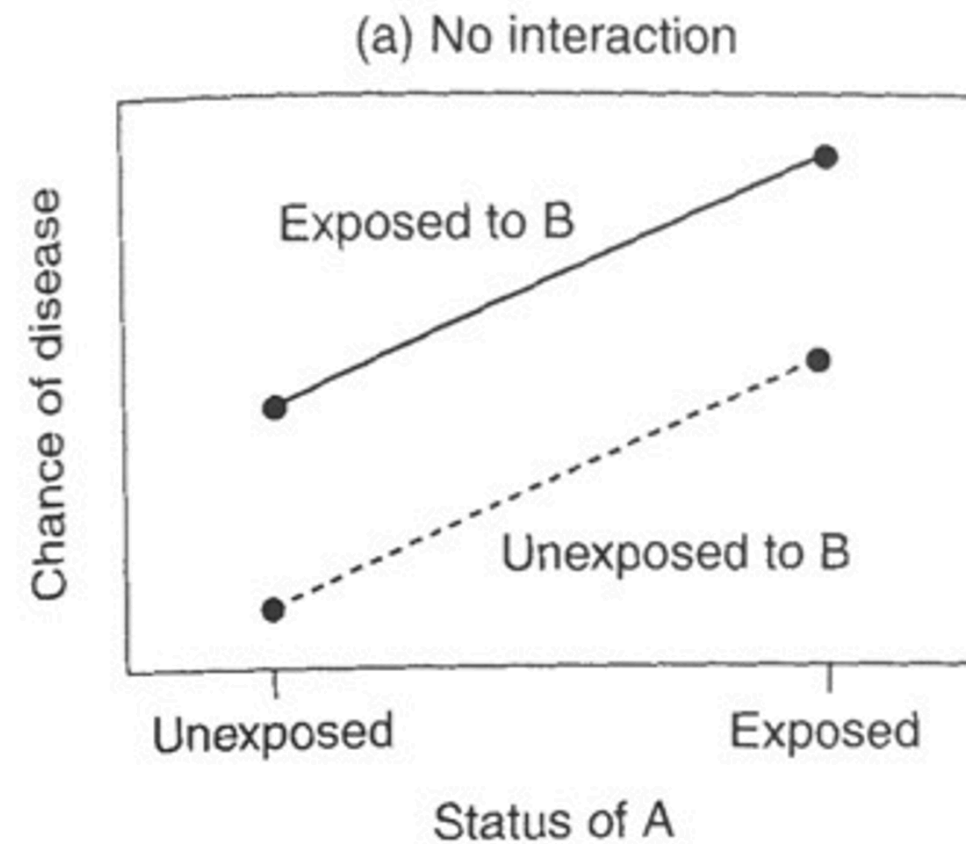
Types of interactions / non-interactions

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.

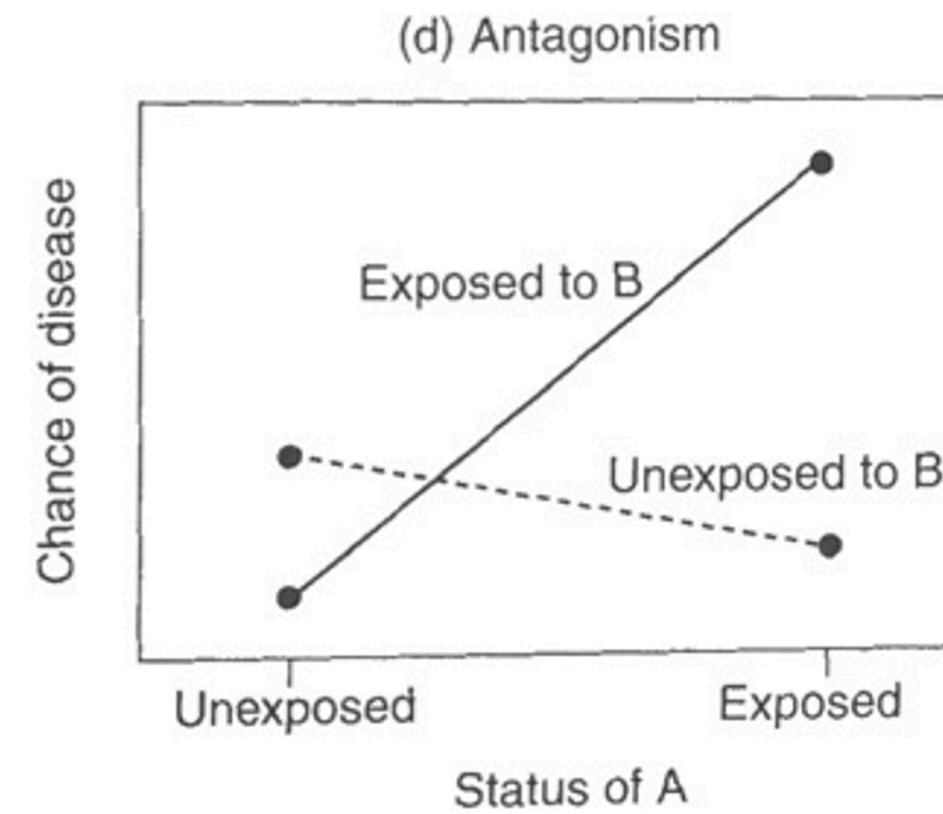
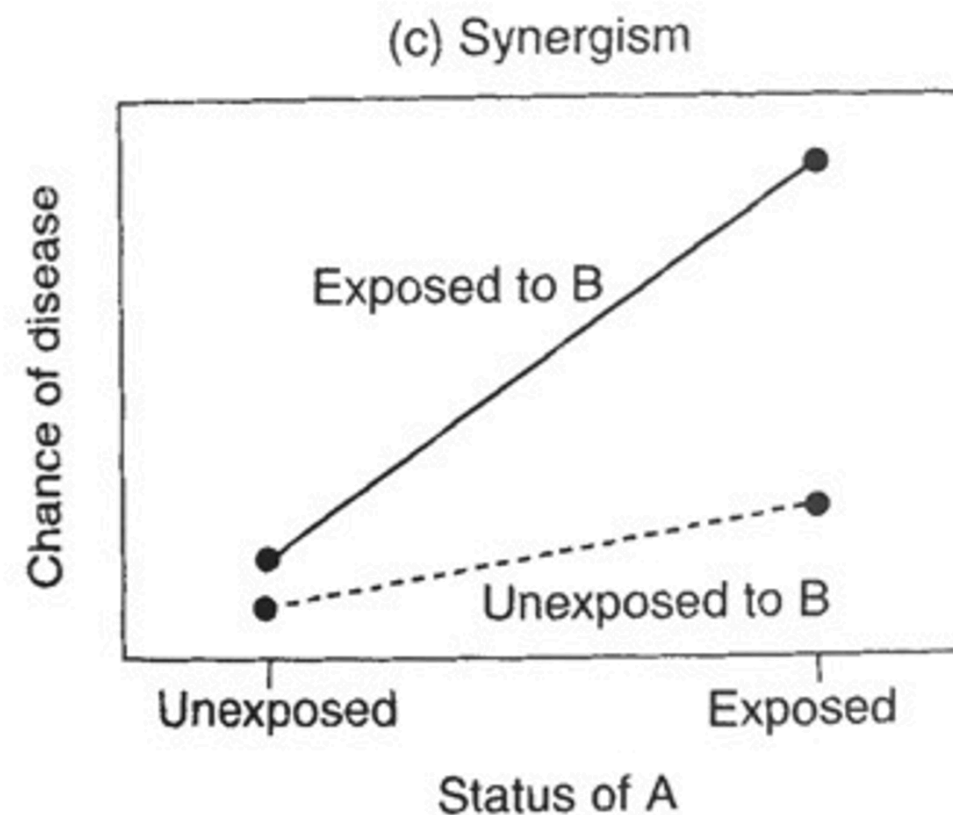
Types of interactions / non-interactions

Confounder, but
no interaction
between A and B



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

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



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

Poll Everywhere Question 1

Understand the interaction (1/3)

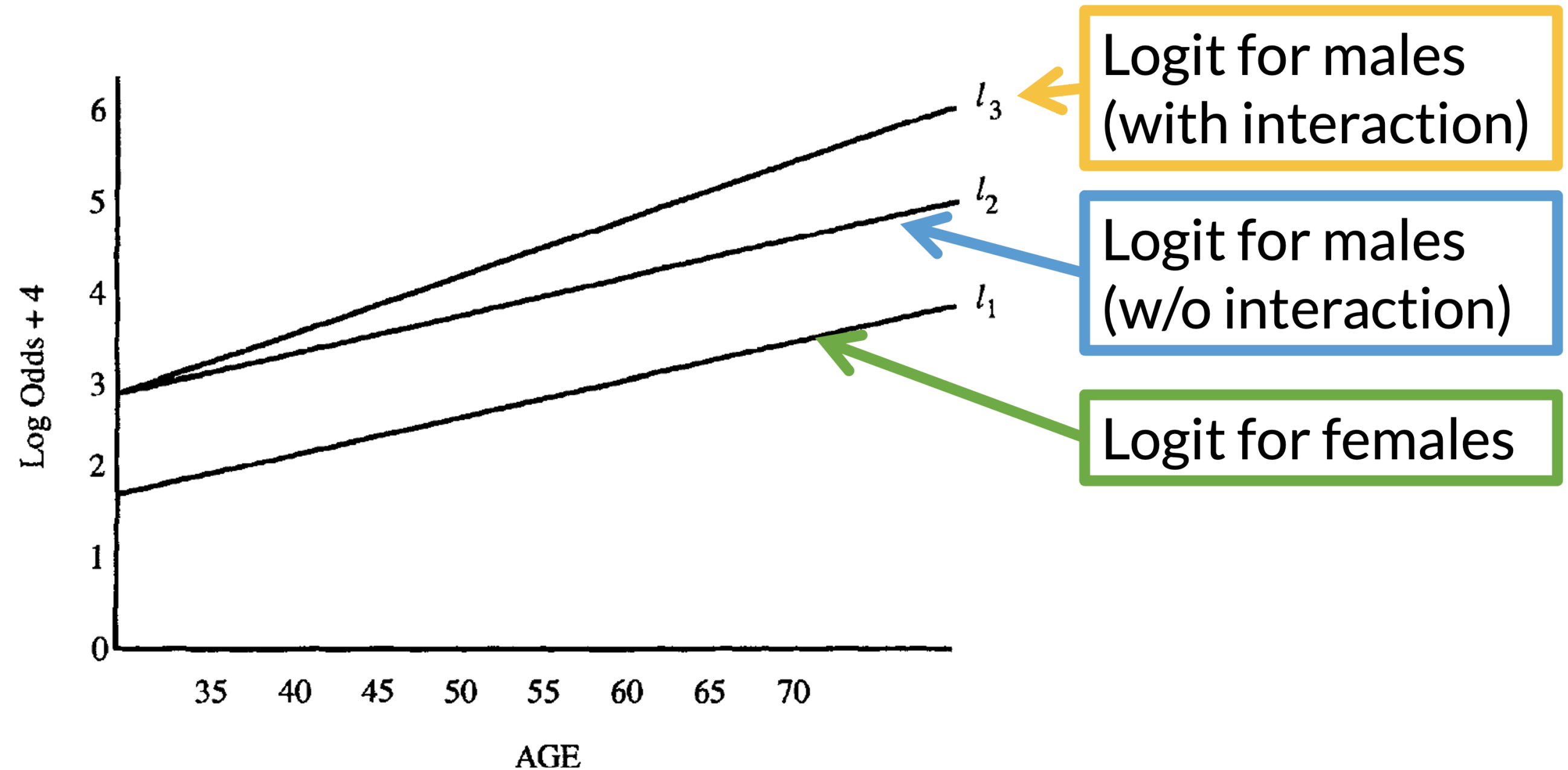
- Figure plots the logits (log-odds) under two different models:

- Model 1: No interaction between sex and age
- Model 2: Interaction between sex and age

- Response variable: CHD

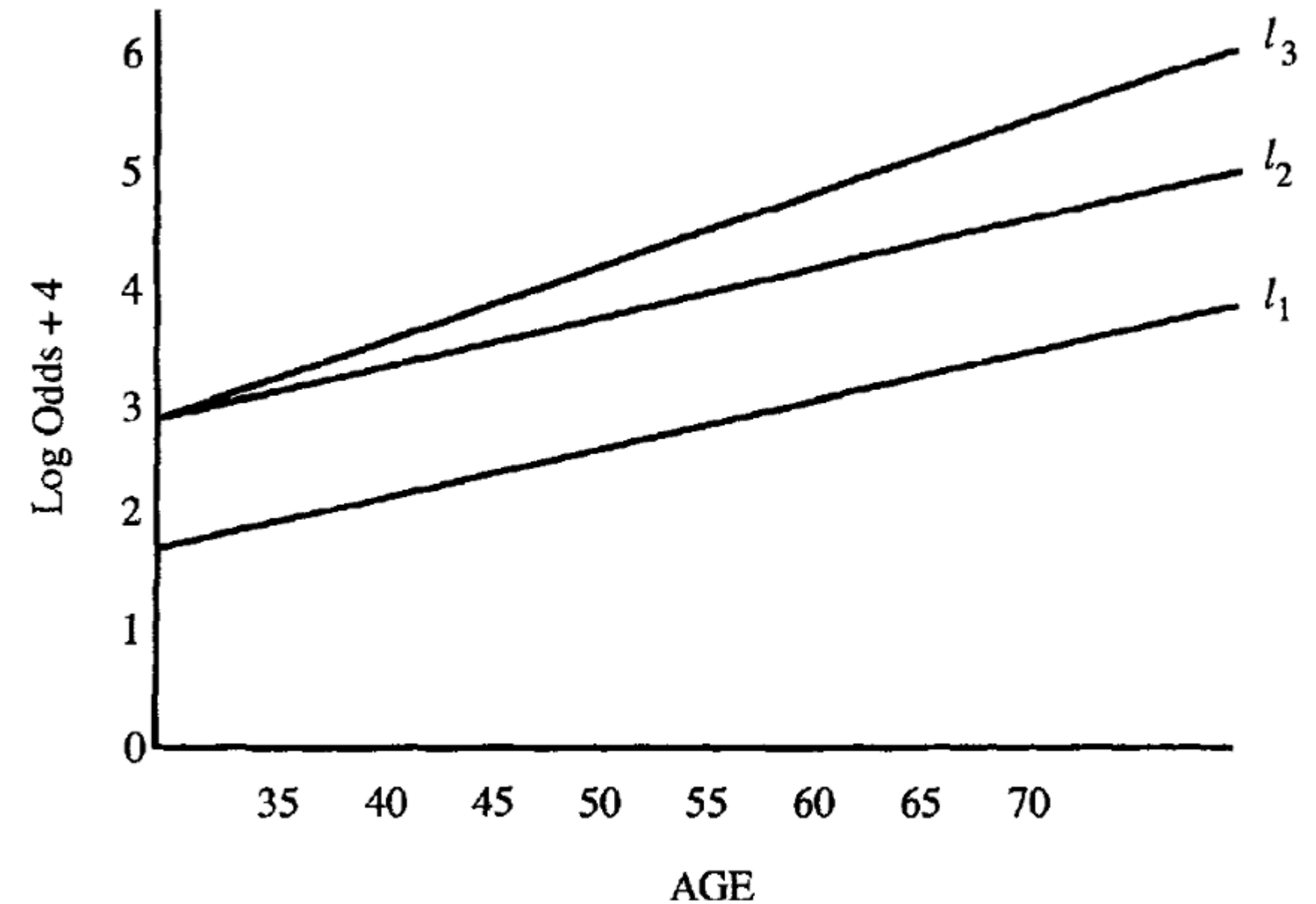
- Risk factor: sex

- Covariate to be controlled: age



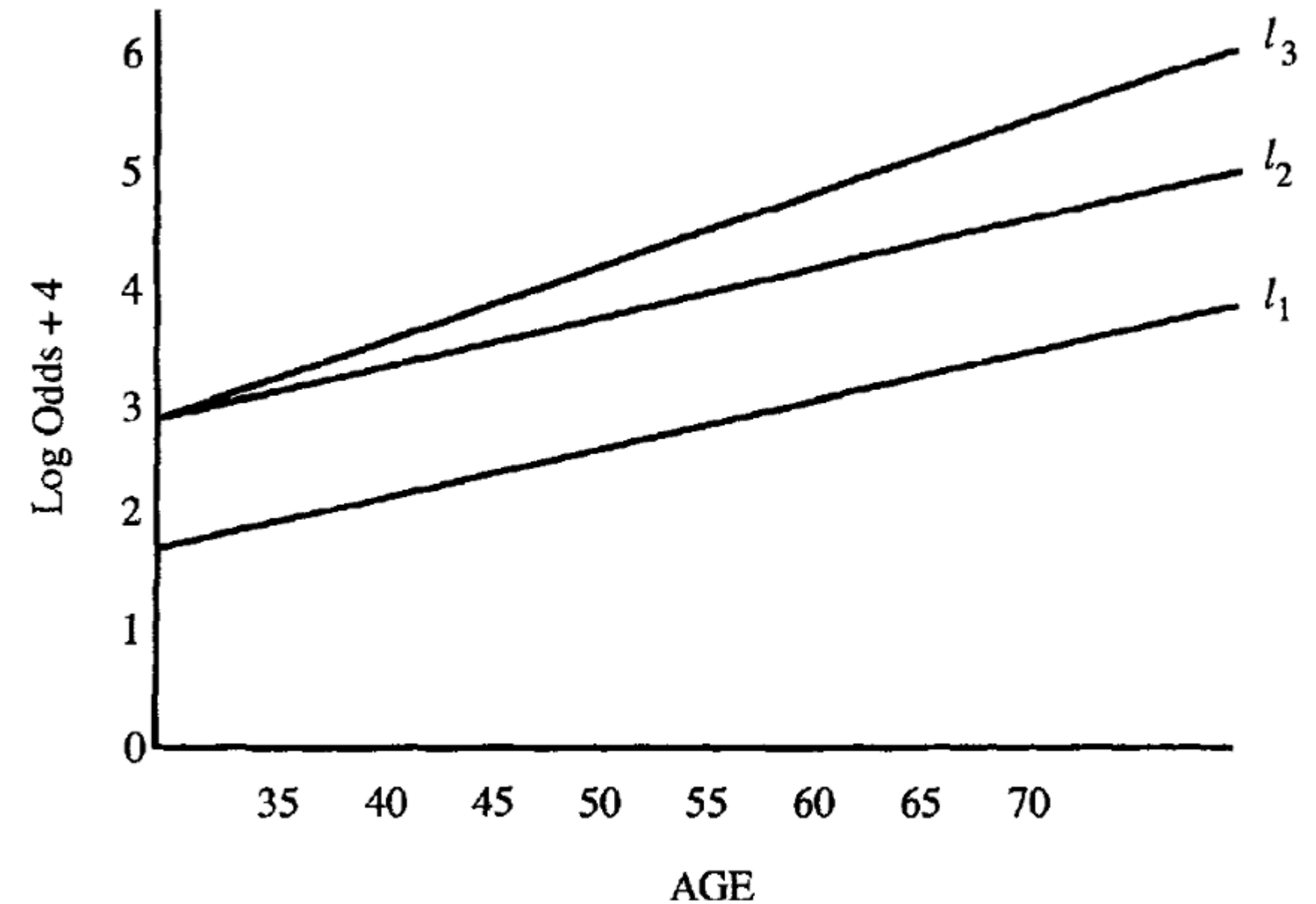
Understand the interaction (2/3)

- **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 at specific values of 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



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 sometimes) may be used to test the significance of an interaction term
 - Compare model **with** interaction to model **without** interaction



Poll Everywhere Question 2

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
 - 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 $\alpha = 0.10$
- 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)

Multi-level categorical & 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):** $\text{logit}(\hat{\pi}(\mathbf{X})) = \hat{\beta}_0 + \hat{\beta}_1 X_1$
 - We call the above $\hat{\beta}_1$ the reduced model coefficient: $\hat{\beta}_{1,\text{mod1}}$ or $\hat{\beta}_{1,\text{red}}$
 - **Fitted model 2 / full model (mod2):** $\text{logit}(\hat{\pi}(\mathbf{X})) = \hat{\beta}_0 + \hat{\beta}_1 X_1 + \hat{\beta}_2 X_2$
 - We call this $\hat{\beta}_1$ the full model coefficient: $\hat{\beta}_{1,\text{mod2}}$ or $\hat{\beta}_{1,\text{full}}$

Calculation for % change in coefficient

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

Poll Everywhere Question 3

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

```
1 library(aplcore3)
2 mean_age = mean(glow500$age) %>% round()
3 glow = glow500 %>% mutate(age_c = age - mean_age)
```

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

```
1 glow2 = glow %>%
2   group_by(age, priorfrac, fracture) %>% # last one needs to be outcome
3   summarise(n = n()) %>%
4   mutate(freq = n / sum(n)) %>% # takes the proportion of yes/no
5   filter(fracture == "Yes") # Filtering so only "success" shown
6   #filter(freq != 1 | n != 1)
7
8 head(glow2)
```

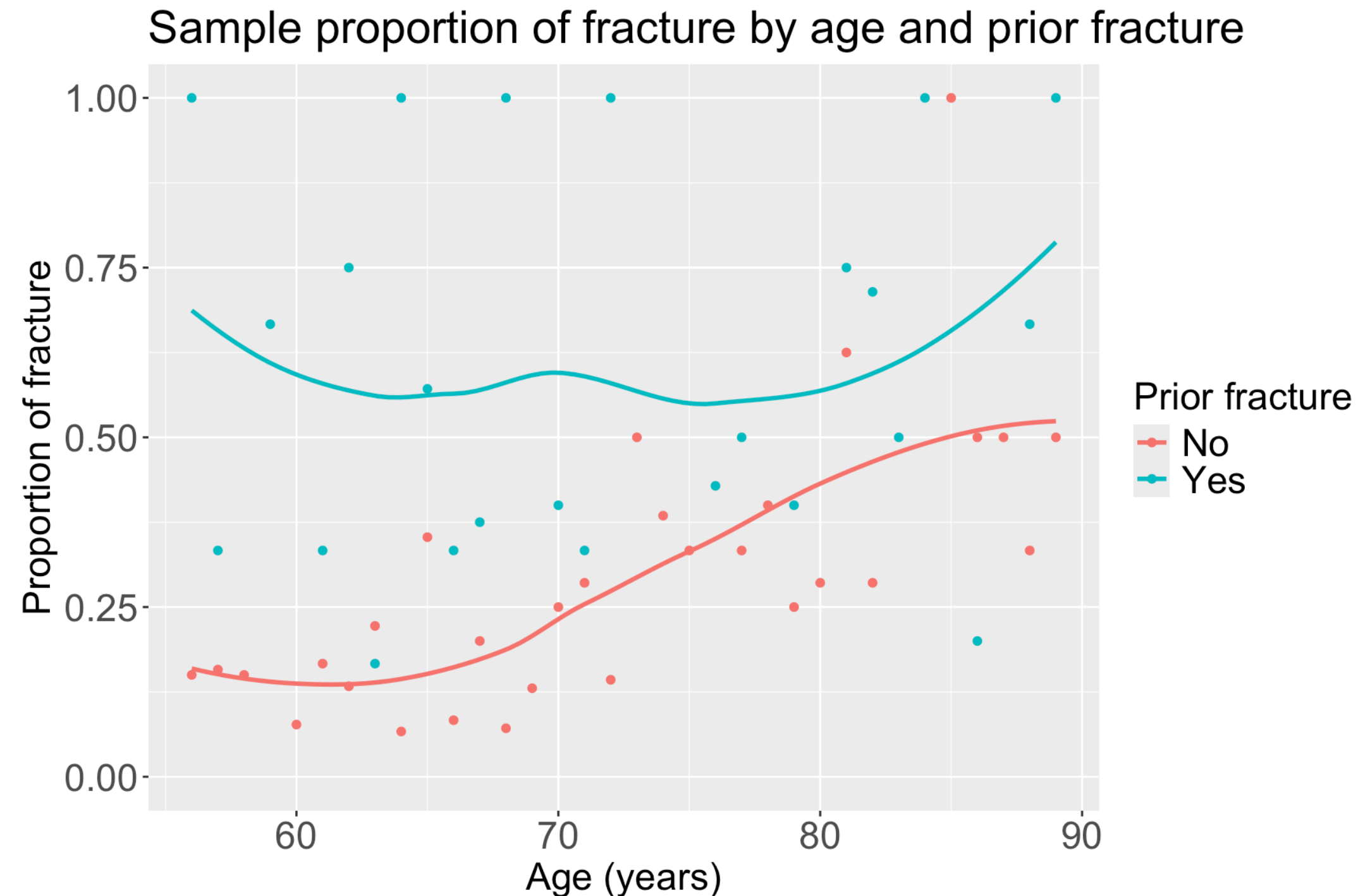
A tibble: 6 × 5

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

```
1 ggplot(data = glow2, aes(y = freq, x = age, color = priorfrac)) +  
2   geom_point() + ylim(0, 1) + geom_smooth(se = F) +  
3   labs(x = "Age (years)", y = "Proportion of fracture",  
4         color = "Prior fracture", title = "Sample proportion of fracture by age and prior fracture") +  
5   theme(axis.title = element_text(size = 18), axis.text = element_text(size = 18),  
6         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

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

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

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

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

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

Example: GLOW Study

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- **Model 1:** Age not included

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

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

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

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

```
1 glow_m3 = glm(fracture ~ priorfrac + age_c + priorfrac*age_c,  
2               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 LRT (or Wald test bc only one coefficient for interaction)
- 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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 - We can use LRT (or Wald test bc only one coefficient for interaction)
- If not an effect modifier, check the change in coefficient for prior fracture between Model 1 and Model 2

Short version of testing the interaction:
Wald statistic for the interaction coefficient, $\hat{\beta}_3$, 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

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!!

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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:

$$\text{logit}(\hat{\pi}(\mathbf{X})) = \hat{\beta}_0 + \hat{\beta}_1 \cdot I(\text{PF}) + \hat{\beta}_2 \cdot \text{Age} + \hat{\beta}_3 \cdot I(\text{PF}) \cdot \text{Age}$$
$$\text{logit}(\hat{\pi}(\mathbf{X})) = -1.376 + 1.002 \cdot I(\text{PF}) + 0.063 \cdot \text{Age} - 0.057 \cdot I(\text{PF}) \cdot \text{Age}$$

term	estimate	std.error	statistic	p.value	conf.low	conf.high
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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
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Example: GLOW – Interaction interpretation

- Model 3 estimated **coefficients**:

term	estimate	p.value	conf.low	conf
(Intercept)	-1.376	0.000	-1.646	-1
priorfracYes	1.002	0.000	0.530	1
age_c	0.063	0.000	0.032	0
priorfracYes:age_c	-0.057	0.022	-0.107	-0

- Model 3 estimated **odds ratios**:

term	estimate	p.value	conf.low	conf
(Intercept)	0.25	0.00	0.19	
priorfracYes	2.72	0.00	1.70	
age_c	1.06	0.00	1.03	
priorfracYes:age_c	0.94	0.02	0.90	

- $\hat{\beta}_3 = -0.057$

- 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

- $\hat{\beta}_1 = 1.002$

- 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).

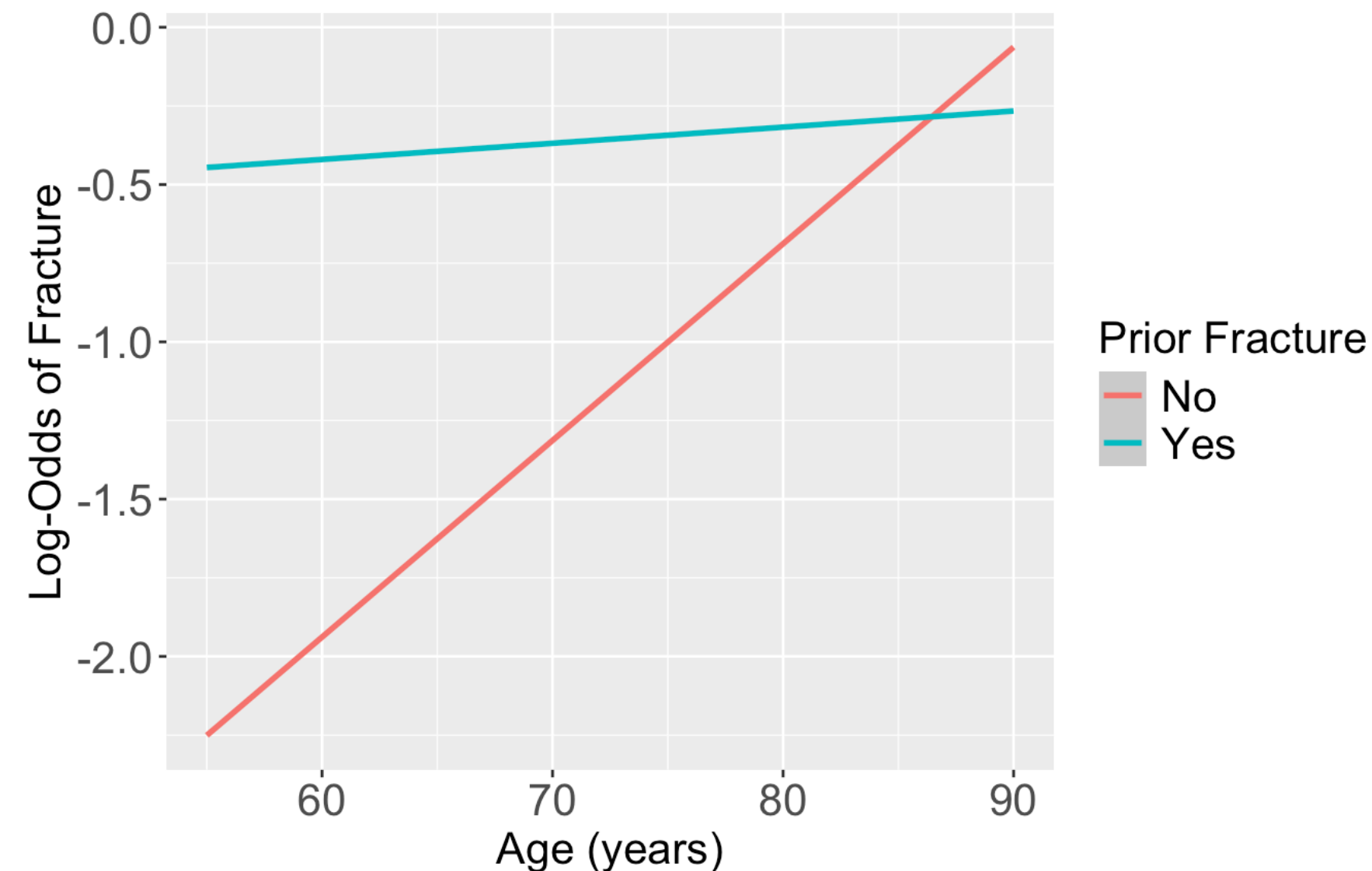
- $\exp(\hat{\beta}_1) = 2.72$

- 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

Plot of estimated log odds

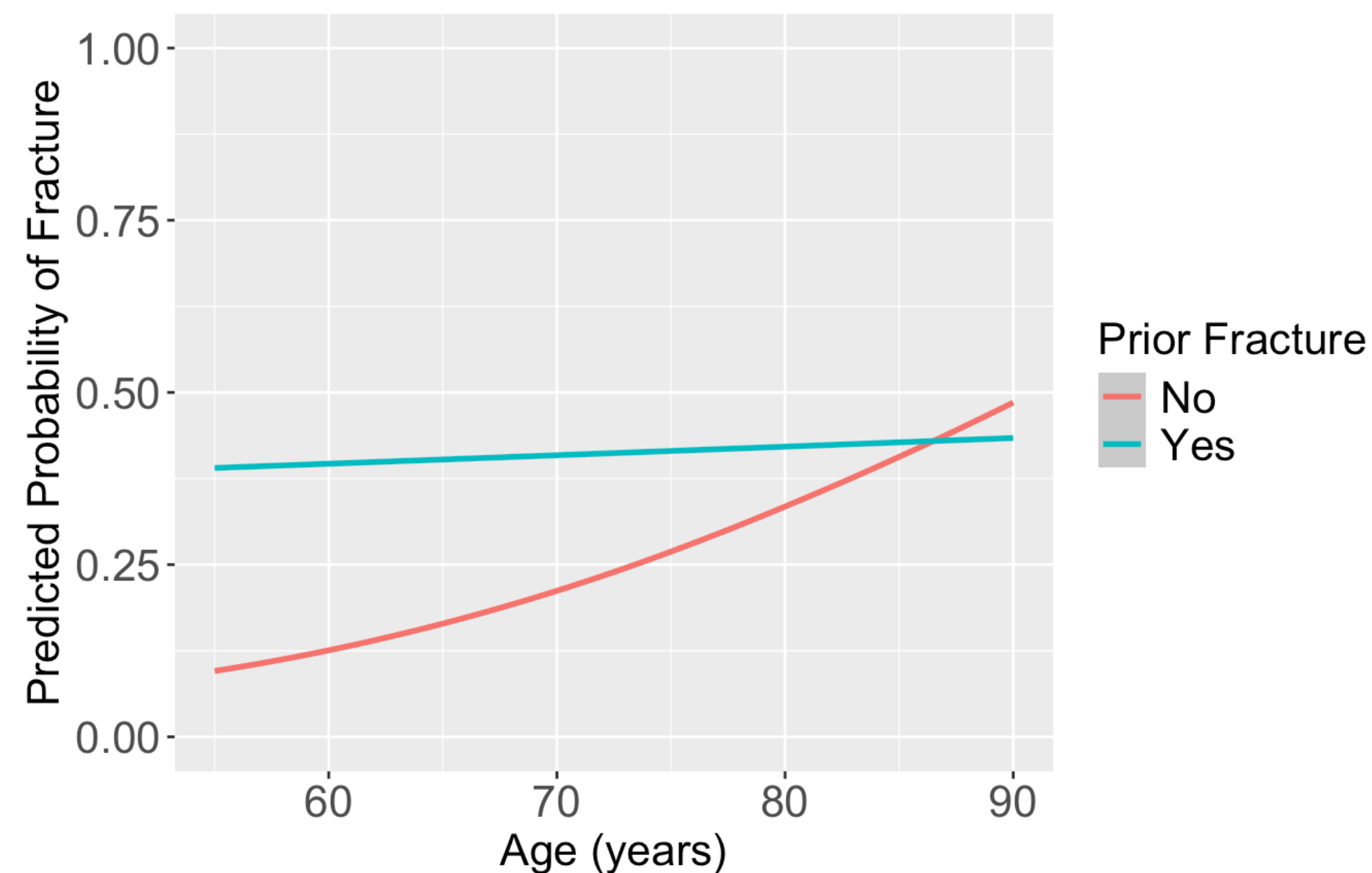
```
1 prior_age = expand_grid(priorfrac = c("No", "Yes"), age_c = (55:90)-69)
2 frac_pred_log = predict(glow_m3, prior_age, se.fit = T, type="link")
3 pred_glow2 = prior_age %>% mutate(frac_pred_log = frac_pred_log$fit,
4                                   age = age_c + mean_age)
5
6 ggplot(pred_glow2) + #geom_point(aes(x = age, y = frac_pred, color = priorfrac)) +
7   geom_smooth(method = "loess", aes(x = age, y = frac_pred_log, color = priorfrac)) +
8   theme(text = element_text(size=20), title = element_text(size=16)) +
9   labs(color = "Prior Fracture", x = "Age (years)", y = "Log-Odds of Fracture")
```



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

Plot the predicted probability of fracture

```
1 frac_pred = predict(glow_m3, prior_age, se.fit = T, type="response")
2 pred_glow = prior_age %>% mutate(frac_pred = frac_pred$fit,
3                                age = age_c + mean_age)
4
5 ggplot(pred_glow) + #geom_point(aes(x = age, y = frac_pred, color = priorfrac)) +
6   geom_smooth(method = "loess", aes(x = age, y = frac_pred, color = priorfrac)) +
7   theme(text = element_text(size=20), title = element_text(size=16)) + ylim(0,1) +
8   labs(color = "Prior Fracture", x = "Age (years)", y = "Predicted Probability of Fracture")
```



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
 - $\widehat{OR}_F \neq \exp(\hat{\beta}_F)$ in general
- Assume we want to compute the odds ratio for ($F = f_1$ and $F = f_0$), the correct model-based estimate is

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

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

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

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

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

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

- The difference in two logits (log-odds) is:

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

$$\hat{g}(f_1, x) - \hat{g}(f_0, x) = \hat{\beta}_1 f_1 - \hat{\beta}_1 f_0 + \hat{\beta}_3 x f_1 - \hat{\beta}_3 x f_0$$

$$\hat{g}(f_1, x) - \hat{g}(f_0, x) = \hat{\beta}_1 (f_1 - f_0) + \hat{\beta}_3 x (f_1 - f_0)$$

- Therefore,

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

Steps to compute OR under interaction

- 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: $PF = 0, Age = a$

2. Substitute values in the fitted log-odds model

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

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

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

Example: GLOW Study

3. Take the difference of the two log-odds

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

4. Exponentiate the resulting difference

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

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 (`estimable()`)

- We could use `estimable()` to calculate this linear combination of coefficients ([see BSTA 512 Lesson](#))

```
1 library(gmodels)
2 glow_m3 %>% estimable(
3     cbind("(Intercept)"           = 0,    # beta0
4         "priorfracYes"           = 1,    # beta1
5         "age_c"                  = 0,    # beta2
6         "priorfracYes:age_c"     = (55:90)-69),
7     conf.int = 0.95) %>%
8     exp(.) %>%
9     head(5)
```

	Estimate	Std. Error	X^2 value	DF	Pr(> X^2)	Lower.CI	Upper.CI
(0 1 0 -14)	6.081961	1.613392	1535383	2.718282	1.000161	2.354473	15.71063
(0 1 0 -13)	5.742790	1.578600	2324162	2.718282	1.000129	2.321435	14.20657
(0 1 0 -12)	5.422533	1.545094	3605103	2.718282	1.000102	2.287290	12.85533
(0 1 0 -11)	5.120136	1.512903	5721950	2.718282	1.000080	2.251861	11.64184
(0 1 0 -10)	4.834603	1.482070	9262667	2.718282	1.000062	2.214941	10.55260

Calculate odds ratios across values (`predict()`)

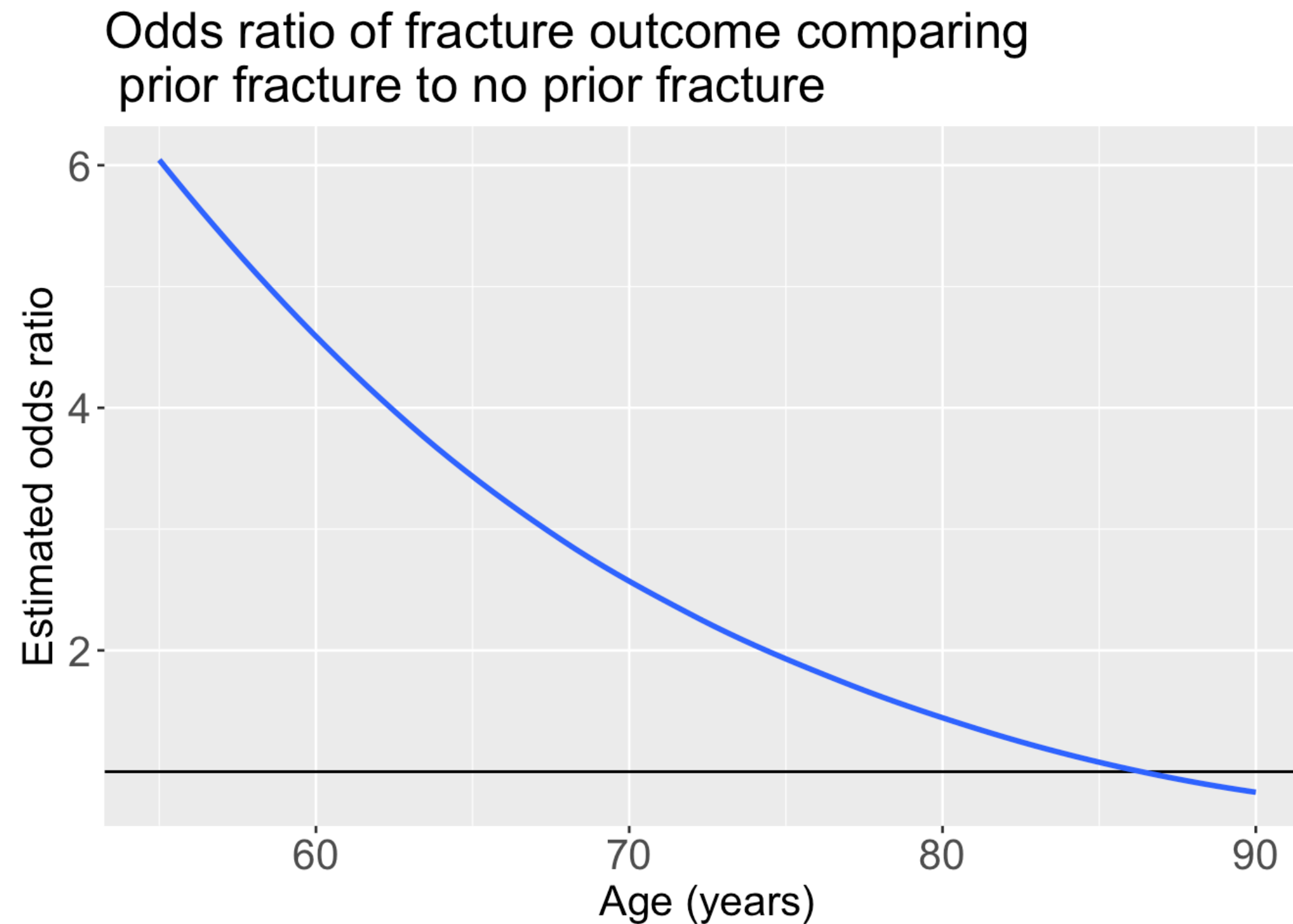
```
1 prior_age = expand_grid(priorfrac = c("No", "Yes"), age_c = (55:90)-69)
2 frac_pred_logit = predict(glow_m3, prior_age, se.fit = T, type="link")
3 pred_glow2 = prior_age %>% mutate(frac_pred = frac_pred_logit$fit,
4                                   age = age_c + mean_age) %>%
5
6     pivot_wider(names_from = priorfrac, values_from = frac_pred) %>%
7
8     mutate(OR_YN = exp(Yes - No))
9 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

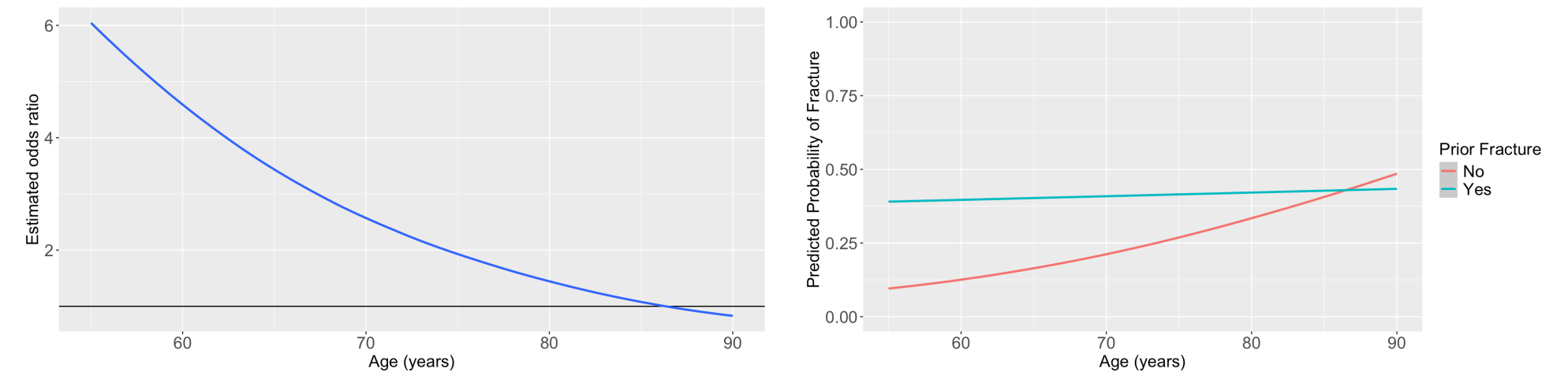
```
1 ggplot(pred_glow2) +  
2   geom_hline(yintercept = 1) +  
3   geom_smooth(method = "loess", aes(x = age, y = OR_YN)) +  
4   theme(text = element_text(size=20), title = element_text(size=16)) +  
5   labs(x = "Age (years)", y = "Estimated odds ratio", title = "Odds ratio of fracture outcome comparing  
prior fracture to no prior fracture")
```



How would I report these results?

- Remember our main covariate is prior fracture, so we want to focus 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 estimated 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 predicted 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