

## Summative Quiz 4 (Confounding and Effect Modification) Solutions

1. A randomized trial with 5,000 male and female participants was conducted and about half of the subjects were randomized to receive a new flu vaccine and the other half received a placebo. The patients were observed for the development of flu symptoms within three months after receiving the vaccine or placebo. The unadjusted relative risk of flu symptoms in the vaccine group relative to the placebo was 0.90 (95% CI 0.83, 1.02). Similarly, the sex adjusted relative risk of flu symptoms in the vaccine group relative to the placebo was 0.91 (95% CI 0.81, 1.03). However, among the females, the relative risk of flu symptoms in the vaccine group relative to the placebo group was 0.60 (95% CI 0.51, 0.67). Among the males, the relative risk of flu symptoms in the vaccine group relative to the placebo group was 1.7 (95% CI 1.59, 1.84). The best explanation for these results is:

**Answer:** There is an interaction between sex and the vaccine - in other words sex modifies the association between having flu symptoms and the vaccine

**Reasoning:** The magnitude of the overall flu/treatment (vaccine) association (as measured by the relative risk) is the same whether this estimate is adjusted for sex differences between the vaccine and placebo groups or not. This suggests that the flu/vaccine association is not confounded by gender. This makes sense, as patients were randomized to vaccine or placebo arms, there should not be any major differences in the sex composition between the two groups, and hence gender should not confound the flu/vaccine associations. However, when males and females are analyzed separately, the magnitude (and direction) of the flu/vaccine association is different. (and the confidence intervals do not overlap at all) This result is consistent with effect modification: ie the flu/treatment association is modified by sex.

2. A randomized study has an outcome Y, and a predictor X (treatment or control groups). How does randomization minimize the potential that the relationship between Y and X will be confounded by some other factor Z?

**Answer:** Randomization minimized the potential for an association between X and Z.

**The following information is relevant to questions 3-4:**

In a study published in the American Journal of Public Health<sup>1</sup>, researchers the results of analyses based on data from the National Health and Nutrition Examination Survey (NHANES), a nationally representative sample of U.S. residents.

The study authors “sought to determine the association between Medicaid coverage (versus being uninsured) and the receipt of appropriate clinical care “.

The primary study outcome was whether a person had seen a primary physician at least one in the prior year. (and hence, *had an annual outpatient visit*). The primary predictor of interest was whether a person had Medicaid (government sponsored insurance) or had no insurance.

Odds ratios comparing the odds of having an annual outpatient visit for persons with Medicaid to persons without insurance are as follows:

*Unadjusted* odds ratio and 95% CI: 8.4 (6.4, 10.8).

*Adjusted* odds ratio and 95% CI : 5.0 (3.8, 6.1)

(The adjusted comparison was adjusted for differences in personal characteristics between the Medicaid and uninsured groups)

3. The authors claim that both the unadjusted and adjusted odds ratios are statistically significant ( $\alpha=0.05$ ). Which of the following supports this claim?

**Answer:** The 95% confidence interval for each odds ratio does not include 1.

**Reasoning:** : the null value for ratios is 1: as the 95% CIs for both the unadjusted and adjusted odds ratio do not include 1, the null hypothesis ( $H_0: OR=1$ ) is rejected at the  $\alpha=0.05$  level.

---

<sup>1</sup> Christopher et al. Access to Care and Chronic Disease Outcomes Among Medicaid-Insured Persons Versus the Uninsured (2016). *American Journal of Public Health*. Vol 106 (1) pps 63 – 69.

4. Of the following choices, the conclusion most consistent with the results presented is:

**Answer:** Persons with Medicaid had higher odds of an annual outpatient visit (when compared to those without insurance), even after adjusting for personal characteristics. However, there is evidence of some confounding by these personal characteristics.

**Reasoning:** The adjusted odds ratio showed a positive, statistically significant association between being having an annual outpatient visit and Medicaid, but is lower in value than the unadjusted odds ratio (and the confidence intervals for the unadjusted and adjusted odds ratios do not overlap)

FYI: in the actual reported study results the two confidence interval overlap slightly:

*Unadjusted* odds ratio and 95% CI: 8.4 (6.4, 10.8).

*Adjusted* odds ratio and 95% CI : 5.0 (3.8, 6.6)

For quiz use, I altered the upper bound in the adjusted OR 95% CI to 6.1 so there was no potential ambiguity. Even given the reported CI, I would strongly argue that d is the best answer, but did not want the slight crossover to be a distraction or water down the “big picture”.

In a study published in the *American Journal of Public Health*, researchers presented the results of analyses based on data from the National Health and Nutrition Examination Survey (NHANES), a nationally representative sample of U.S. residents.

The study authors “sought to determine the association between Medicaid coverage (versus being uninsured) and the receipt of appropriate clinical care “. The primary study outcome was whether a person had seen a primary physician at least one in the prior year (and hence, had an annual outpatient visit). The primary predictor of interest was whether a person had Medicaid (government sponsored insurance) or had no insurance. Odds ratios comparing the odds of having an annual outpatient visit for persons with Medicaid to persons without insurance are as follows:

Unadjusted odds ratio and 95% CI: 8.4 (6.4, 10.8)

.Adjusted odds ratio and 95% CI : 5.0 (3.8, 6.1)

(The adjusted comparison was adjusted for differences in personal characteristics between the Medicaid and uninsured groups.)

The unadjusted odds ratio presented in the above table was computed via simple logistic regression. The model results are as follows:

$\ln(\text{odds of an annual outpatient visit}) = -2.63 + 2.13x_1$ , where  $x_1 = 1$  if the person has Medicaid, 0 person has no insurance

5. Based on the results of this logistic regression, what is the (approximate) estimated proportion of persons with Medicaid who had an annual outpatient visit?

**Answer:** 0.07

**Reasoning:** The estimated  $\ln(\text{odds})$  for without insurance is:

$$\ln(\text{odds of an annual outpatient visit}) = -2.63 + 2.13(1) = 0.5$$

Hence, the estimated odds is  $e^{-0.5} \approx 0.61$  and the resulting probability estimate is

$$\hat{p} = \frac{ODDS}{1+ODDS} = \frac{0.61}{1.61} = 0.378 \approx 0.38$$

6. Suppose the researchers are interested in whether the association between having Medicaid (versus no insurance) and having an annual outpatient visit is modified by whether the state has a governor who is a member of the Republican Party or has a governor who is a member of the Democratic Party. How should the researchers proceed?

**Answer:** Estimate separate odds ratios of having an annual outpatient visit for persons with Medicaid to persons without insurance for persons from states with a Republican governor and persons from states with a Democratic governor. Compare these political-party specific associations to each other.