**Instructions**

Please complete the following lab assignment. You may work on the assignment in groups or on your own. However, to get credit, you must submit your own answers in Canvas. This lab is open note and open book. You may also ask the instructor and the TA questions. Please note that in most cases we will try to guide you towards answering your own question rather than directly providing you with an answer.

# Calculations

[R calculations are available here](https://www.dropbox.com/s/gn19tm3657bf9i5/lab_effect_modification.Rmd?dl=0).

[Google sheet calculations are available here](https://docs.google.com/spreadsheets/d/1QK2ZH9YAopJ-YBWL3E_MbjZnNFBP4Taks2WPbqHesvs/edit#gid=961627830).

# Q1. Calculate RR and RD

[Fill in Multiple Blanks]

In a prospective study of the relationship of hepatitis C virus (HCV) to newly developed hepatocellular carcinoma, the authors were interested in a potential modifying effect of alcohol consumption. The following table is based on this study’s results:

| Alcohol drinking | HCV | No. of persons | Incidence rates/100,000 |
| --- | --- | --- | --- |
| Absent | Negative | 8968 | 78.7 |
| Positive | 2352 | 127.1 |
| Present | Negative | 461 | 309.7 |
| Positive | 90 | 384.9 |

Using the category “absent–negative” as the reference, calculate the risk ratios and risk differences (in the exposed) for those with positive antibodies to HCV only, for those who consumed alcohol only, and for those exposed to both. Please round your answers to two decimal places.

| Alcohol drinking | HCV | No. of persons | Incidence rates/100,000 | RR | RD |
| --- | --- | --- | --- | --- | --- |
| Absent | Negative | 8968 | 78.7 | [rr1] | [rd1] |
| Positive | 2352 | 127.1 | [rr2] | [rd2] |
| Present | Negative | 461 | 309.7 | [rr3] | [rd3] |
| Positive | 90 | 384.9 | [rr4] | [rd4] |

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# Q1. Feedback

| Alcohol drinking | HCV | No. of persons | Incidence rates/100,000 | RR | RD |
| --- | --- | --- | --- | --- | --- |
| Absent | Negative | 8968 | 78.7 | Reference | Reference |
| Positive | 2352 | 127.1 | 1.61 | 48.40 |
| Present | Negative | 461 | 309.7 | 3.94 | 231.00 |
| Positive | 90 | 384.9 | 4.89 | 306.20 |

Please make sure you understand why this is the correct answer. You may use the "Previous" button below to update your answer if your original answer was incorrect.

Click the "Next" button below to move on to the next question.

# Q2. Calculate expected joint RR

[Numerical Answer]

Calculate the expected joint risk ratio (multiplicative model) in the exposed. The table from the previous question is provided below. Please round your answers to two decimal places.

| Alcohol drinking | HCV | No. of persons | Incidence rates/100,000 | RR | RD |
| --- | --- | --- | --- | --- | --- |
| Absent | Negative | 8968 | 78.7 | Reference | Reference |
| Positive | 2352 | 127.1 | 1.61 | 48.40 |
| Present | Negative | 461 | 309.7 | 3.94 | 231.00 |
| Positive | 90 | 384.9 | 4.89 | 306.20 |

# Q2. Feedback

| Alcohol drinking | HCV | No. of persons | Incidence rates/100,000 | RR | RD |
| --- | --- | --- | --- | --- | --- |
| Absent | Negative | 8968 | 78.7 | Reference | Reference |
| Positive | 2352 | 127.1 | 1.61 | 48.40 |
| Present | Negative | 461 | 309.7 | 3.94 | 231.00 |
| Positive | 90 | 384.9 | 4.89 | 306.20 |

Expected joint risk ratio = (RR in HCV alone) \* (RR in alcohol alone)

Expected joint risk ratio = 1.61 \* 3.94

Expected joint risk ratio = 6.34

Please make sure you understand why this is the correct answer. You may use the "Previous" button below to update your answer if your original answer was incorrect.

Click the "Next" button below to move on to the next question.

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# Q3. Multiplicative effect modification?

[Multiple Choice]

Based on your previous knowledge of alcohol consumption, HCV, and hepatocellular carcinoma, a difference of 1 point or more on the risk ratio scale would constitute a meaningful difference. Assuming there is no random variability, is there evidence in this sample that alcohol consumption modifies the relationship between hepatitis C virus and newly developed hepatocellular carcinoma on the multiplicative scale? The table from the previous question is provided below.

| Alcohol drinking | HCV | No. of persons | Incidence rates/100,000 | RR | RD |
| --- | --- | --- | --- | --- | --- |
| Absent | Negative | 8968 | 78.7 | Reference | Reference |
| Positive | 2352 | 127.1 | 1.61 | 48.40 |
| Present | Negative | 461 | 309.7 | 3.94 | 231.00 |
| Positive | 90 | 384.9 | 4.89 | 306.20 |

| ✅ | Yes | |
| --- | --- | --- |
|  | No | |

# Q3. Feedback

| Alcohol drinking | HCV | No. of persons | Incidence rates/100,000 | RR | RD |
| --- | --- | --- | --- | --- | --- |
| Absent | Negative | 8968 | 78.7 | Reference | Reference |
| Positive | 2352 | 127.1 | 1.61 | 48.40 |
| Present | Negative | 461 | 309.7 | 3.94 | 231.00 |
| Positive | 90 | 384.9 | 4.89 | 306.20 |

Yes, there is evidence of effect modification on the multiplicative scale because the expected joint risk ratio (6.34) is different from the observed joint risk ratio (4.89) by 1.45 points. Based on our previous knowledge of alcohol consumption, HCV, and hepatocellular carcinoma, we know that a difference of 1 point or more on the risk ratio scale constitutes a meaningful difference.

Please make sure you understand why this is the correct answer. You may use the "Previous" button below to update your answer if your original answer was incorrect.

# Click the "Next" button below to move on to the next question.

# Q4. Positive or negative?

[Multiple Choice]

We previously determined that the expected joint risk ratio was 6.34 and the observed joint risk ratio was 4.89, and therefore, there was evidence of effect modification on a multiplicative scale. Is that effect modification positive or negative?

|  | Positive | |
| --- | --- | --- |
| ✅ | Negative | |

# Q4. Feedback

“If interaction exists and the presence of the effect modifier strengthens (accentuates) the effect of the exposure of interest, the variable and exposure are said to be synergistic (positive interaction); if the presence of the effect modifier diminishes or eliminates the effect of the exposure of interest, it can be said that the effect modifier and the exposure are antagonistic (negative interaction).”

Szklo, Moyses, Nieto, F. Javier. Epidemiology (pg. 209).

In this case, the expected joint risk ratio (6.34) is greater than the observed joint risk ratio (4.89), which is consistent with a negative effect modification on a multiplicative scale.

Please make sure you understand why this is the correct answer. You may use the "Previous" button below to update your answer if your original answer was incorrect.

Click the "Next" button below to move on to the next question.

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# Q5. Calculate expected joint AR

[Numerical Answer]

Calculate the expected joint risk difference in the exposed (additive model). The table from the previous question is provided below. Please round your answers to two decimal places.

| Alcohol drinking | HCV | No. of persons | Incidence rates/100,000 | RR | RD |
| --- | --- | --- | --- | --- | --- |
| Absent | Negative | 8968 | 78.7 | Reference | Reference |
| Positive | 2352 | 127.1 | 1.61 | 48.40 |
| Present | Negative | 461 | 309.7 | 3.94 | 231.00 |
| Positive | 90 | 384.9 | 4.89 | 306.20 |

# Q5. Feedback

| Alcohol drinking | HCV | No. of persons | Incidence rates/100,000 | RR | RD |
| --- | --- | --- | --- | --- | --- |
| Absent | Negative | 8968 | 78.7 | Reference | Reference |
| Positive | 2352 | 127.1 | 1.61 | 48.40 |
| Present | Negative | 461 | 309.7 | 3.94 | 231.00 |
| Positive | 90 | 384.9 | 4.89 | 306.20 |

Expected joint risk difference = (RD in HCV alone) + (RD in alcohol alone)

Expected joint risk difference = 48.40 + 231.00

Expected joint risk difference = 279.40

Please make sure you understand why this is the correct answer. You may use the "Previous" button below to update your answer if your original answer was incorrect.

Click the "Next" button below to move on to the next question.

# Q6. Additive effect modification?

[Multiple Choice]

Based on your previous knowledge of alcohol consumption, HCV, and hepatocellular carcinoma, a difference in the incidence rate of 20 or more per 100,000 people would constitute a meaningful difference in the rate of hepatocellular carcinoma on the risk difference scale. Assuming there is no random variability, is there evidence in this sample that alcohol consumption modifies the relationship between hepatitis C virus and newly developed hepatocellular carcinoma on the *additive scale*? The table from the previous question is provided below.

| Alcohol drinking | HCV | No. of persons | Incidence rates/100,000 | RR | RD |
| --- | --- | --- | --- | --- | --- |
| Absent | Negative | 8968 | 78.7 | Reference | Reference |
| Positive | 2352 | 127.1 | 1.61 | 48.40 |
| Present | Negative | 461 | 309.7 | 3.94 | 231.00 |
| Positive | 90 | 384.9 | 4.89 | 306.20 |

| ✅ | Yes | |
| --- | --- | --- |
|  | No | |

# Q6. Feedback

| Alcohol drinking | HCV | No. of persons | Incidence rates/100,000 | RR | RD |
| --- | --- | --- | --- | --- | --- |
| Absent | Negative | 8968 | 78.7 | Reference | Reference |
| Positive | 2352 | 127.1 | 1.61 | 48.40 |
| Present | Negative | 461 | 309.7 | 3.94 | 231.00 |
| Positive | 90 | 384.9 | 4.89 | 306.20 |

Yes, there is evidence of effect modification on the additive scale because the expected joint risk difference (279.40) is different from the observed joint risk difference (306.20) by 26.8 per 100,000. Based on your previous knowledge of alcohol consumption, HCV, and hepatocellular carcinoma, a difference in the incidence rate of 20 or more per 100,000 people constitutes a meaningful difference in the rate of hepatocellular carcinoma on the risk difference scale.

Please make sure you understand why this is the correct answer. You may use the "Previous" button below to update your answer if your original answer was incorrect.

Click the "Next" button below to move on to the next question.

# Q7. Positive or negative?

[Multiple Choice]

We previously determined that the expected joint risk difference was 279.40 and the observed joint risk difference was 306.20, and therefore, there was evidence of effect modification on an additive scale. Is that effect modification positive or negative?

| ✅ | Positive | |
| --- | --- | --- |
|  | Negative | |

# Q7. Feedback

“If interaction exists and the presence of the effect modifier strengthens (accentuates) the effect of the exposure of interest, the variable and exposure are said to be synergistic (positive interaction); if the presence of the effect modifier diminishes or eliminates the effect of the exposure of interest, it can be said that the effect modifier and the exposure are antagonistic (negative interaction).”

Szklo, Moyses, Nieto, F. Javier. Epidemiology (pg. 209).

In this case, the expected joint risk difference (279.40/100,00) is lower than the observed joint risk difference (306.20/100,000), which is consistent with a positive effect modification on an additive scale.

Please make sure you understand why this is the correct answer. You may use the "Previous" button below to update your answer if your original answer was incorrect.

Click the "Next" button below to move on to the next question.

# Q8. Calculate using homogeneity strategy

[Fill in Multiple Blanks]

Using the homogeneity strategy and alcohol as the effect modifier, confirm your answers to the previous questions. Please round your answers to two decimal places.

| Alcohol drinking | HCV | No. of persons | Incidence rates/100,000 | RR | RD |
| --- | --- | --- | --- | --- | --- |
| Absent | Negative | 8968 | 78.7 | [rr1] | [rd1] |
| Positive | 2352 | 127.1 | [rr2] | [rd2] |
| Present | Negative | 461 | 309.7 | [rr3] | [rd3] |
| Positive | 90 | 384.9 | [rr4] | [rd4] |

# Q8. Feedback

| Alcohol drinking | HCV | No. of persons | Incidence rates/100,000 | RR (within alcohol) | RD (within alcohol) |
| --- | --- | --- | --- | --- | --- |
| Absent | Negative | 8968 | 78.7 | Reference | Reference |
| Positive | 2352 | 127.1 | 1.61 | 48.40 |
| Present | Negative | 461 | 309.7 | Reference | Reference |
| Positive | 90 | 384.9 | 1.24 | 75.20 |

Using alcohol as the effect modifier, the risk ratios and risk differences for those exposed to HCV follow:

The risk ratio of hepatocellular carcinoma among those with HCV vs. those without:

* Alcohol drinking absent: 1.61
* Alcohol drinking present: 1.24

The risk difference of hepatocellular carcinoma among those with HCV vs. those without:

* Alcohol drinking absent: 48.40
* Alcohol drinking present: 75.20

Thus, the homogeneity strategy confirmed the findings obtained from the comparison between expected and observed joint effects.

The risk ratio of hepatocellular carcinoma among those with HCV exposure compared to those without HCV is lower in the alcohol present stratum than it is in the alcohol absent stratum (negative multiplicative effect modification).

The risk difference for hepatocellular carcinoma among those with HCV exposure compared to those without HCV is higher for the alcohol present stratum than for the alcohol absent stratum (positive additive effect modification).

Please make sure you understand why the example answer is correct. You may use the "Previous" button to update your answer if you feel like you can now give a more correct/complete answer.

Click the "Submit" button below if you are ready to submit this lab.

**Feedback**

**Optional**: Please feel free to leave any comments below about the usefulness of this lab. Which parts were helpful? What could I do to improve it? What is still unclear?