

Web Appendix for **Depression and incident HIV in adolescent girls and young women in HPTN 068: Targets for prevention and mediating factors**

Dana E. Goin, Rebecca M. Pearson, Michelle G. Craske, Alan Stein, Audrey Pettifor, Sheri A. Lippman, Kathleen Kahn, Torsten B. Neilands, Erica L. Hamilton, Amanda Selin, Catherine MacPhail, Ryan G. Wagner, F. Xavier Gomez-Olive, Rhian Twine, James P. Hughes, Yaw Agyei, Oliver Laeyendecker, Stephen Tollman, and Jennifer Ahern

Web Appendix 1—page 2.

Web Appendix 2—page 2.

Web Appendix 3—pages 3-4.

Web Tables 1-4—pages 5-12.

Web Appendix 4—pages 13-23.

Web Appendix 1.

Measurement of parental monitoring and involvement

Parental monitoring and involvement were assessed from 7 questions the young women answered about the adult most involved in her life outside of school. The questions asked the young women to recount whether the adult never, sometimes, or always tried to find out about who her friends were, how she spends her free time, where she goes after school, and how she spends her money. Additional questions asked the young women to report whether she feels very much, somewhat, or not at all as though the adult cares about her, whether she is close to the adult, how free/open she feels to discuss issues of sex and sexuality with the adult, and how free/open she feels to discuss issues of HIV prevention with the adult. We created a continuous score by assigning 1, 2 or 3 to each response, where responses aligning with lower parental monitoring or involvement were coded as lower on the scale. We then summed across the 7 questions to create the final score.

Web Appendix 2.

Covariates

We controlled for baseline covariates that may affect depression, HIV incidence, and each of the mediators. These were assessed based on self-report by the young women and/or their heads of household. Covariates included any negative life events that occurred within the household (this included death of a family member, death of a friend or someone relied upon for financial assistance, serious illness or injury of a family member, widespread crop failure or death or livestock, job loss of a breadwinner, decline in remittances or government grants, destruction of household property, or inheriting household debt from a deceased family member), and any positive life events that occurred within the household (this included a new regular job for a family member, increased remittances or government grants, inheritance or payment from a company, or scholarship or bursary). Additional covariates were the percent of household members receiving a government grant (this is represented as a continuous variable in the main analysis but is reported as above or below 25% for simplicity in Table 1), single (one parent deceased) or double (two parents deceased) orphan status, mother's education attainment, father's educational attainment, pregnancy prior to baseline visit, young woman's age at baseline, and arm of the conditional cash transfer trial. We also controlled for household food insecurity and deciles of per capita consumption.

Household food insecurity was measured as a binary indicator using the following three questions. The respondents were told to assess over the past 30 days how often was there no food in the household because there was not enough money, how often any member of the household felt hungry when they went to sleep at night, and how often any member of the household went a whole day without eating anything because there was not enough food. Respondents could choose never, rarely, sometimes, or often for each question. For any response other than never, the food insecure variable was coded as 1.

Deciles of per capita household consumption were constructed by summing total per capita food and total non-food expenditures and taking the natural log. If either total per-capita food expenditure or total per capita non-food expenditure were equal to zero or missing, the log per-capita expenditure was set to missing. We then divided log per capita expenditures into deciles to create a categorical variable. Total per capita food expenditure was calculated by summing the market value of all food items grown, purchased, or borrowed over the last 30 days and dividing this amount by the total number of household members. Respondents reported on the total market value of food items that were purchased or grown but not those that were

borrowed. When the total market value of a food item consumed was missing (all borrowed food items and some food items that were purchased or grown), we imputed an estimated market value that was equal to the median per unit market price of that food item multiplied by the quantity consumed by that household. Median per unit market prices for each food item were calculated using cost data from purchased items; specifically, we divided the amount spent on each food item by the quantity consumed and identified the median value using data across all households. Median per unit prices derived from fewer than 20 households were considered not robust and were therefore not used to impute missing cost data. In cases where we lacked the sufficient data to compute a robust median per unit price for a particular food item, we excluded that food item from the calculation of total per capita food expenditure. Total per capita non-food expenditure was calculated by summing the amount spent on non-food items over the past 30 days, specifically personal items, transportation, utilities, insurance, household items, clothing and shoes, health care, education, and miscellaneous purchases.

Web Appendix 3.

Quantitative bias analysis

We conducted a quantitative bias analysis to assess how strong mediator-outcome confounding would need to be to change our results (1). The approach assumes that there is no unmeasured exposure-mediator or exposure-outcome confounding, and involves specifying a range of values for two sensitivity parameters that rely on an unmeasured confounder of the mediator-outcome relationship (2).

These two parameters correspond to the conditional risk ratios for the confounder-outcome relationship (γ) and the collider bias of the exposure-confounder relationship due to conditioning on the mediator (λ) (1). This sensitivity analysis is designed for conditional mediation parameters on the relative scale, so we replicated the analysis using a modified Poisson regression to calculate the mediation analysis results on the risk ratio scale and performed the sensitivity analysis using the relative scale results. The risk ratio estimates used for the quantitative bias analysis showed similar patterns to the risk difference estimates in the main text (Web Table 2).

For example, to reduce the observed direct effect to a null association, a hypothetical unmeasured confounder would need to increase the likelihood of HIV incidence among participants with depression through pathways other than the mediators (γ) with a risk ratio (RR) of 2.0. Because it is possible that the mediators and the unmeasured confounder interact to affect the outcome, and therefore this RR may vary across levels of the mediators, the risk ratio of 2.0 should correspond to the maximum RR across strata of the mediators. Simultaneously, the risk ratio relating the unmeasured confounder to the exposure, conditional on the mediators (λ) (i.e., the collider bias), must be 1.3. Because the strength of this collider bias could also differ based on the level of the mediators, the required collider bias RR of 1.3 refers to the maximum potential bias across the strata of the mediators. Therefore, the RRs of $\gamma=2.0$ and $\lambda=1.3$ correspond to the largest associations that might be observed across strata of the mediators for the hypothetical relationships between this unmeasured confounder, the mediators, and the outcome. These RRs, however, are the *smallest* required for the direct effect to be reduced to a null association, and larger RRs would result in an observed association with a sign in the opposite direction from the true association.

Therefore, to reduce the observed direct effect to a null association, the unmeasured confounder would need to have a strong relationship with the outcome (RR=2.0) among exposed subjects within strata of the mediators while at the same time, be moderately associated with exposure via collider bias from conditioning

on the mediators (RR=1.3). We expect such a combination is unlikely, given that these associations would need to persist despite adjusting for the set of baseline covariates already included in the model, although it is not impossible. This is just one example of parameters that would reduce the observed association to the null. All combinations of bias parameters that would result in a null or reverse direction of association for the direct effect are highlighted in grey in Web Table 3. To reduce the estimated indirect effect to a null association, the unmeasured confounder would need to have $\gamma=0.4$ and $\lambda=1.2$. Therefore, a strong negative relationship would need to exist between the unmeasured confounder and the outcome (RR=0.4), while simultaneously inducing a moderate positive relationship between the exposure and confounder via conditioning on the mediators (RR=1.2). Again, we expect such a combination is unlikely. The other combinations that would reduce the association to the null or change the direction of the association are also highlighted in grey in Web Table 4.

References

1. Ding P, Vanderweele TJ. Sharp sensitivity bounds for mediation under unmeasured mediator-outcome confounding. *Biometrika*. 2016 Jun 1;103(2):483–90.
2. VanderWeele TJ. Mediation Analysis: A Practitioner's Guide. *Annu Rev Public Health*. 2016;37:17–32.

Web Table 1. Total effects of depressive symptoms on HIV incidence and natural direct and indirect effects using inverse probability of censoring weights with several mediators in the HPTN 068 cohort, Mpumalanga, South Africa

	Risk Difference	
Total effect (95% CI)	3.8% (0.3%, 7.3%)	
Mediators	Natural direct effect (95% CI)	Natural indirect effect (95% CI)
Health and school behaviors		
Alcohol use in the past month	2.6% (-0.8%, 6.0%)	1.2% (-0.4%, 2.8%)
More than 5 days of missed school on average per month in the past year	2.3% (-1.0%, 5.6%)	1.5% (-0.2%, 3.1%)
High school attendance between rounds (>80%)	2.5% (-0.9%, 5.9%)	1.2% (-0.4%, 2.9%)
Parental monitoring and involvement	2.1% (-1.2%, 5.3%)	1.7% (0.0%, 3.4%)
Community engagement (number of community organizations involved in)	2.8% (-0.6%, 6.3%)	1.0% (-0.6%, 2.6%)
Sexual behaviors and self-efficacy		
Had a recent sexual partner 5 years or more older than oneself	2.7% (-0.8%, 6.2%)	1.1% (-0.5%, 2.7%)
Number of partners in the past 12 months (0, 1, 2 or more)	2.5% (-0.9%, 5.9%)	1.3% (-0.4%, 2.9%)
Had unprotected sex in the past 3 months	2.4% (-1.0%, 5.7%)	1.4% (-0.2%, 3.0%)
Engaged in transactional sex in the past 12 months	2.7% (-0.8%, 6.3%)	1.0% (-0.6%, 2.7%)
Sexual relationship power: partner would hit me if I requested he use a condom	2.2% (-1.2%, 5.6%)	1.6% (-0.2%, 3.3%)
Sexual relationship power: partner would be angry if I requested he use a condom	2.5% (-0.9%, 5.9%)	1.3% (-0.4%, 3.0%)
Sexual relationship power: partner would assume I'm cheating if I ask him to use a condom	2.4% (-1.0%, 5.8%)	1.4% (-0.2%, 3.0%)
Low power according to sexual relationship power scale	2.6% (-0.8%, 6.0%)	1.2% (-0.5%, 2.9%)
Experienced intimate partner violence in the past 12 months	2.5% (-0.9%, 5.9%)	1.3% (-0.3%, 2.9%)
Purchased birth control or condoms	2.6% (-0.9%, 6.0%)	1.2% (-0.4%, 2.8%)
All mediators	1.3% (-1.9%, 4.6%)	2.5% (0.3%, 4.6%)

Web Table 2. Total effects of depressive symptoms on HIV incidence and natural direct and indirect effects with several mediators in the HPTN 068 cohort, Mpumalanga, South Africa

	Risk Ratio	
Total effect (95% CI)	1.42 (1.02, 1.98)	
Mediators	Natural direct effect (95% CI)	Natural indirect effect (95% CI)
Health and school behaviors		
Alcohol use in the past month	1.31 (0.89, 1.92)	1.09 (0.92, 1.28)
More than 5 days of missed school on average per month in the past year	1.26 (0.86, 1.86)	1.12 (0.95, 1.33)
High school attendance between rounds (>80%)	1.30 (0.88, 1.91)	1.10 (0.93, 1.30)
Parental monitoring and involvement	1.23 (0.85, 1.79)	1.15 (0.97, 1.37)
Community engagement (number of community organizations involved in)	1.33 (0.91, 1.96)	1.06 (0.90, 1.25)
Sexual behaviors and self-efficacy		
Had a recent sexual partner 5 years or more older than oneself	1.32 (0.90, 1.93)	1.08 (0.91, 1.27)
Number of partners in the past 12 months (0, 1, 2 or more)	1.29 (0.88, 1.90)	1.10 (0.92, 1.30)
Had unprotected sex in the past 3 months	1.27 (0.87, 1.86)	1.11 (0.94, 1.33)
Engaged in transactional sex in the past 12 months	1.32 (0.90, 1.94)	1.07 (0.91, 1.27)
Sexual relationship power: partner would hit me if I requested he use a condom	1.25 (0.86, 1.82)	1.13 (0.94, 1.36)
Sexual relationship power: partner would be angry if I requested he use a condom	1.28 (0.87, 1.89)	1.10 (0.93, 1.32)
Sexual relationship power: partner would assume I'm cheating if I ask him to use a condom	1.27 (0.87, 1.87)	1.11 (0.94, 1.32)
High power according to sexual relationship power scale	1.29 (0.89, 1.88)	1.10 (0.93, 1.30)
Experienced intimate partner violence in the past 12 months	1.29 (0.88, 1.88)	1.10 (0.94, 1.30)
Purchased birth control or condoms	1.30 (0.89, 1.91)	1.09 (0.92, 1.29)
All mediators	1.13 (0.75, 1.70)	1.25 (0.99, 1.59)

Web Table 3. Sensitivity Analysis Using Sharp Bounds for the Direct Effect on the Risk Ratio Scale

	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0	1.1	1.2	1.3	1.4	1.5	1.6	1.7	1.8	1.9	2.0	2.1	2.2	2.3	2.4	2.5	2.6	2.7	2.8	2.9	3.0
0.0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
0.1	90.65	39.66	22.66	14.16	9.06	5.67	-3.24	1.42	0.00	1.13	2.06	2.83	3.49	4.05	4.53	4.96	5.33	5.67	5.93	6.23	6.47	6.70	6.90	7.08	7.25	7.41	7.55	7.69	7.81	7.93
0.2	39.66	17.00	9.44	5.67	3.40	1.89	-0.81	0.00	0.63	1.13	1.55	1.89	2.12	2.43	2.68	2.83	3.00	3.11	3.22	3.43	3.51	3.66	3.66	3.77	3.88	3.99	3.99	4.00	4.11	4.11
0.3	22.66	9.44	5.04	2.83	1.51	0.63	0.00	0.47	0.84	1.13	1.37	1.51	1.74	1.88	2.00	2.11	2.22	2.33	2.33	2.44	2.55	2.55	2.66	2.66	2.77	2.77	2.88	2.88	2.88	2.99
0.4	14.16	5.67	2.83	1.42	0.50	0.00	0.40	0.71	0.90	1.13	1.22	1.42	1.51	1.66	1.77	1.77	1.88	1.88	1.99	1.99	2.00	2.00	2.00	2.11	2.11	2.11	2.22	2.22	2.22	2.22
0.5	9.06	3.40	1.51	0.50	0.00	0.30	0.65	0.84	1.00	1.13	1.22	1.33	1.33	1.44	1.55	1.55	1.66	1.66	1.66	1.77	1.77	1.77	1.77	1.77	1.88	1.88	1.88	1.88	1.88	1.88
0.6	5.67	1.89	0.63	0.00	0.30	0.60	0.81	0.90	1.00	1.13	1.22	1.22	1.33	1.33	1.33	1.44	1.44	1.44	1.44	1.55	1.55	1.55	1.55	1.55	1.55	1.66	1.66	1.66	1.66	1.66
0.7	3.24	0.84	0.00	0.40	0.60	0.80	0.92	1.00	1.00	1.13	1.13	1.22	1.22	1.22	1.22	1.33	1.33	1.33	1.33	1.33	1.33	1.44	1.44	1.44	1.44	1.44	1.44	1.44	1.44	1.44
0.8	1.42	0.00	0.40	0.70	0.80	0.90	1.01	1.00	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11
0.9	0.00	0.63	0.84	0.90	1.00	1.00	1.08	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11
1.0	1.13	1.13	1.13	1.13	1.13	1.13	1.13	1.13	1.13	1.13	1.13	1.13	1.13	1.13	1.13	1.13	1.13	1.13	1.13	1.13	1.13	1.13	1.13	1.13	1.13	1.13	1.13	1.13	1.13	1.13
1.1	2.06	1.55	1.33	1.22	1.22	1.22	1.18	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
1.2	2.83	1.88	1.51	1.42	1.33	1.22	1.21	1.11	1.11	1.11	1.11	1.11	1.11	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
1.3	3.49	2.12	1.74	1.51	1.33	1.33	1.25	1.20	1.11	1.11	1.11	1.11	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
1.4	4.05	2.43	1.88	1.66	1.42	1.33	1.27	1.20	1.11	1.11	1.11	1.11	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
1.5	4.53	2.68	2.00	1.74	1.51	1.33	1.29	1.20	1.11	1.11	1.11	1.11	1.00	1.00	1.00	1.00	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99

1.	4.9	2.8	2.1	1.7	1.5	1.4		1.2	1.1	1.1	1.0	1.0	1.0	1.0	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8			
6	6	3	2	7	6	2	1.32	4	8	3	9	6	4	1	9	7	6	4	3	2	1	0	9	9	8	7	7	6	5	5							
1.	5.3	3.0	2.2	1.8	1.6	1.4		1.2	1.1	1.1	1.0	1.0	1.0	1.0	1.0	0.9	0.9	0.9	0.9	0.9	0.9	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	
7	3	0	2	3	0	4	1.33	5	8	3	9	6	3	0	8	6	4	3	1	0	9	8	7	6	5	5	4	3	3	2							
1.	5.6	3.1	2.3	1.8	1.6	1.4		1.2	1.1	1.1	1.0	1.0	1.0	0.9	0.9	0.9	0.9	0.9	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	
8	7	5	1	9	4	7	1.35	6	9	3	9	5	2	9	7	4	3	1	9	8	7	6	5	4	3	2	2	1	0	0							
1.	5.9	3.2	2.3	1.9	1.6	1.4		1.2	1.1	1.1	1.0	1.0	1.0	0.9	0.9	0.9	0.9	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.7	0.7	0.7	0.7	0.7	0.7	0.7	
9	6	8	9	4	7	9	1.36	7	9	3	8	4	1	8	5	3	1	9	8	6	5	4	3	2	1	0	0	9	8	8							
2.	6.2	3.4	2.4	1.9	1.7	1.5		1.2	1.2	1.1	1.0	1.0	1.0	1.0	0.9	0.9	0.9	0.9	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	
0	3	0	6	8	0	1	1.38	7	0	3	8	4	0	7	4	2	0	8	6	5	4	2	1	0	9	8	8	7	6	6							
2.	6.4	3.5	2.5	2.0	1.7	1.5		1.2	1.2	1.1	1.0	1.0	1.0	1.0	0.9	0.9	0.9	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	
1	7	1	2	2	3	3	1.39	8	0	3	8	3	0	6	4	1	9	7	5	4	2	1	0	9	8	7	6	5	4	4							
2.	6.7	3.6	2.5	2.0	1.7	1.5		1.2	1.2	1.1	1.0	1.0	0.9	0.9	0.9	0.9	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	
2	0	1	8	6	5	5	1.40	9	0	3	8	3	9	6	3	0	8	6	4	2	1	0	8	7	6	5	4	4	3	2							
2.	6.9	3.6	2.6	2.0	1.7	1.5		1.2	1.2	1.1	1.0	1.0	0.9	0.9	0.9	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	
3	0	9	3	9	7	6	1.41	9	0	3	7	3	9	5	2	9	7	5	3	1	0	8	7	6	5	4	3	2	1	1							
2.	7.0	3.7	2.6	2.1	1.7	1.5		1.3	1.2	1.1	1.0	1.0	0.9	0.9	0.9	0.8	0.8	0.8	0.8	0.8	0.8	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.6	0.6
4	8	8	8	2	9	7	1.42	0	1	3	7	2	8	4	1	9	6	4	2	0	9	7	6	5	4	3	2	1	0	9							
2.	7.2	3.8	2.7	2.1	1.8	1.5		1.3	1.2	1.1	1.0	1.0	0.9	0.9	0.9	0.8	0.8	0.8	0.8	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.6	0.6	0.6	
5	5	5	2	5	1	9	1.42	0	1	3	7	2	8	4	1	8	5	3	1	9	8	6	5	4	3	1	1	0	9	8							
2.	7.4	3.9	2.7	2.1	1.8	1.6		1.3	1.2	1.1	1.0	1.0	0.9	0.9	0.9	0.8	0.8	0.8	0.8	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.6	0.6	0.6	0.6	0.6	0.6	0.6	
6	1	2	6	8	3	0	1.43	1	1	3	7	2	7	3	0	7	5	2	0	8	7	5	4	3	1	0	9	8	8	7							
2.	7.5	3.9	2.8	2.2	1.8	1.6		1.3	1.2	1.1	1.0	1.0	0.9	0.9	0.9	0.8	0.8	0.8	0.8	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	
7	5	9	0	0	5	1	1.44	1	1	3	7	1	7	3	0	7	4	2	0	8	6	4	3	2	1	9	8	7	7	6							
2.	7.6	4.0	2.8	2.2	1.8	1.6		1.3	1.2	1.1	1.0	1.0	0.9	0.9	0.8	0.8	0.8	0.8	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	
8	9	5	3	3	6	2	1.45	2	1	3	7	1	6	2	9	6	3	1	9	7	5	4	2	1	0	8	7	6	6	5							
2.	7.8	4.1	2.8	2.2	1.8	1.6		1.3	1.2	1.1	1.0	1.0	0.9	0.9	0.8	0.8	0.8	0.8	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	
9	1	0	7	5	8	3	1.45	2	2	3	7	1	6	2	9	5	3	0	8	6	4	3	1	0	9	8	7	6	5	4							
3.	7.9	4.1	2.9	2.2	1.8	1.6		1.3	1.2	1.1	1.0	1.0	0.9	0.9	0.8	0.8	0.8	0.8	0.7	0.7	0.7	0.7	0.7	0.7	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	
0	3	5	0	7	9	4	1.46	2	2	3	6	1	6	2	8	5	2	0	8	6	4	2	1	9	8	7	6	5	4	3							

Note: These are the results of a sensitivity analysis for the direct effect of depressive symptoms on HIV incidence. This sensitivity analysis assumes that exposure-outcome confounding is controlled and exposure-mediator confounding is controlled but that there may be uncontrolled mediator-outcome confounding. This uncontrolled confounder cannot be affected by the exposure. The gamma parameter is the maximum risk ratio relating the unmeasured confounder U and the outcome Y and the exposed subjects across the strata of the mediator, conditional on covariates. This is the maximum of the ratios for which U is associated with increased likelihood of Y via pathways other than through the mediator. The lambda parameter is the maximum risk ratio relating the exposure A to U across levels of the mediator, conditional on covariates. These parameters are used to create a bias factor, B, which equals $(\gamma * \lambda) / (\lambda + \gamma - 1)$. The direct effect estimate is divided by B to obtain the "bias-corrected" estimates displayed in this table. For more information and more in depth discussion of these parameters and their derivations, see VanderWeele TJ. Mediation Analysis: A Practitioner's Guide. Annu Rev Public Health. 2016;37:17–32 and Sharp sensitivity bounds for mediation under unmeasured mediator-outcome confounding. Biometrika. 2016 Jun 1;103(2):483–90.

Web Table 4. Sensitivity Analysis Using Sharp Bounds for the Indirect Effect on the Risk Ratio Scale

	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0	1.1	1.2	1.3	1.4	1.5	1.6	1.7	1.8	1.9	2.0	2.1	2.2	2.3	2.4	2.5	2.6	2.7	2.8	2.9	3.0		
0.1	-	-	-	-	-	-	-	-		1.2	0.6	0.5	0.4	0.3	0.3	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.1	0.1	0.1	0.1	0.1	
1.1	2	4	6	0	6	5	4	0	Inf	5	9	0	1	5	1	9	7	5	4	3	2	1	1	0	0	9	9	8	8	8	8	
0.2	-	-	-	-	-	-	-																									
0.2	0.0	0.0	0.1	0.2	0.4	0.7	1.7		2.2	1.2	0.9	0.7	0.6	0.5	0.5	0.5	0.4	0.4	0.4	0.4	0.4	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	
2.2	4	8	5	5	2	5	5	Inf	6	5	2	5	5	8	4	0	7	5	3	2	0	9	8	8	8	7	6	6	5	5	4	4
0.3	-	-	-	-	-	-																										
0.3	0.0	0.1	0.2	0.5	0.9	2.2		3.0	1.6	1.2	1.0	0.9	0.8	0.7	0.7	0.6	0.6	0.6	0.6	0.6	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.4
3.3	6	5	8	0	4	6	Inf	1	9	5	3	0	1	5	0	7	4	2	0	8	6	5	4	3	2	1	1	0	0	0	0	9
0.4	-	-	-	-	-																											
0.4	0.1	0.2	0.5	1.0	2.5		3.5	2.0	1.5	1.2	1.1	1.0	0.9	0.8	0.8	0.8	0.7	0.7	0.7	0.7	0.7	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
4.4	0	5	0	0	1	Inf	1	0	0	5	0	0	3	8	4	0	7	5	3	2	0	9	8	7	6	5	4	4	3	3	3	3
0.5	-	-	-	-																												
0.5	0.1	0.4	0.9	2.5		3.7	2.1	1.6	1.4	1.2	1.1	1.0	1.0	0.9	0.9	0.9	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7
5.5	6	2	4	1	Inf	6	9	7	1	5	5	7	2	7	4	1	9	7	5	4	2	1	0	9	8	8	7	6	6	6	5	5
0.6	-	-	-																													
0.6	0.2	0.7	2.2		3.7	2.2	1.7	1.5	1.3	1.2	1.1	1.1	1.0	1.0	1.0	1.0	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.8	0.8	0.8	0.8	0.8
6.6	5	5	6	Inf	6	6	5	0	5	5	8	3	9	5	3	0	8	7	5	4	3	2	1	0	0	9	8	8	7	7	7	7
0.7	-	-																														
0.7	0.4	1.7		3.5	2.1	1.7	1.5	1.4	1.3	1.2	1.2	1.1	1.1	1.1	1.1	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	0.9
7.7	4	5	Inf	1	9	5	3	0	2	5	1	7	4	2	0	8	7	5	4	3	2	2	1	0	0	9	9	9	8	8	8	7
0.8	-																															
0.8	1.0		3.0	2.0	1.6	1.5	1.4	1.3	1.2	1.2	1.2	1.2	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
8.8	0	Inf	1	0	7	0	0	4	9	5	3	0	8	7	6	5	4	3	2	1	1	0	0	9	9	9	9	8	8	8	8	7
0.9		2.2	1.6	1.5	1.4	1.3	1.3	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1
9.9	Inf	6	9	0	1	5	2	9	7	5	4	3	2	1	1	0	0	9	9	9	8	8	8	8	8	7	7	7	7	7	7	7
1.0	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2
10.0	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
1.1	0.6	0.9	1.0	1.1	1.1	1.1	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3
11.1	9	2	3	0	5	8	1	3	4	5	6	7	8	9	9	0	0	1	1	1	1	2	2	2	2	3	3	3	3	3	3	3
1.2	0.5	0.7	0.9	1.0	1.0	1.1	1.1	1.2	1.2	1.2	1.2	1.2	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.4	1.4	1.4	1.4	1.4	1.4
12.2	0	5	0	0	7	3	7	0	3	5	7	9	0	2	3	4	5	5	6	7	7	8	8	9	9	0	0	0	0	1	1	1
1.3	0.4	0.6	0.8	0.9	1.0	1.0	1.1	1.1	1.2	1.2	1.2	1.3	1.3	1.3	1.3	1.3	1.3	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4
13.3	1	5	1	3	2	9	4	8	2	5	8	0	2	4	6	7	8	0	1	2	3	3	4	5	5	6	7	7	8	8	8	
1.4	0.3	0.5	0.7	0.8	0.9	1.0	1.1	1.1	1.2	1.2	1.2	1.3	1.3	1.3	1.3	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
14.4	5	8	5	8	7	5	2	7	1	5	9	2	4	6	8	0	2	4	5	6	7	8	9	0	1	2	3	3	4	5	5	
1.5	0.3	0.5	0.7	0.8	0.9	1.0	1.1	1.1	1.2	1.2	1.2	1.3	1.3	1.3	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.6	1.6	1.6
15.5	1	4	0	4	4	3	0	6	1	5	9	3	6	8	1	3	5	7	9	0	2	3	4	6	7	8	9	9	0	1	1	
1.6	0.2	0.5	0.6	0.8	0.9	1.0	1.0	1.1	1.2	1.2	1.3	1.3	1.3	1.4	1.4	1.4	1.4	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6
16.6	9	0	7	0	1	0	8	5	0	5	0	4	7	0	3	6	8	0	2	4	6	8	9	0	2	3	4	5	6	7	7	

1.7	0.2	0.4	0.6	0.7	0.8	0.9	1.0	1.1	1.2	1.2	1.3	1.3	1.3	1.4	1.4	1.4	1.5	1.5	1.5	1.5	1.6	1.6	1.6	1.6	1.6	1.6	1.7	1.7	1.7		
7	7	7	4	7	9	8	7	4	0	5	0	5	8	2	5	8	1	3	6	8	0	2	3	5	6	8	9	0	2	3	
1.8	0.2	0.4	0.6	0.7	0.8	0.9	1.0	1.1	1.1	1.2	1.3	1.3	1.4	1.4	1.4	1.5	1.5	1.5	1.5	1.6	1.6	1.6	1.6	1.6	1.7	1.7	1.7	1.7	1.7	1.7	
8	5	5	2	5	7	7	5	3	9	5	1	5	0	4	7	0	3	6	9	1	3	5	7	9	1	2	4	5	7	8	
1.9	0.2	0.4	0.6	0.7	0.8	0.9	1.0	1.1	1.1	1.2	1.3	1.3	1.4	1.4	1.4	1.5	1.5	1.5	1.6	1.6	1.6	1.6	1.7	1.7	1.7	1.7	1.7	1.8	1.8	1.8	
9	4	3	0	3	5	5	4	2	9	5	1	6	1	5	9	2	6	9	2	4	7	9	1	3	5	7	9	0	2	3	
2.0	0.2	0.4	0.5	0.7	0.8	0.9	1.0	1.1	1.1	1.2	1.3	1.3	1.4	1.4	1.5	1.5	1.5	1.6	1.6	1.6	1.7	1.7	1.7	1.7	1.7	1.8	1.8	1.8	1.8	1.8	
0	3	2	8	2	4	4	3	1	9	5	1	7	2	6	0	4	8	1	4	7	0	2	5	7	9	1	3	5	6	8	
2.1	0.2	0.4	0.5	0.7	0.8	0.9	1.0	1.1	1.1	1.2	1.3	1.3	1.4	1.4	1.5	1.5	1.6	1.6	1.6	1.7	1.7	1.7	1.7	1.8	1.8	1.8	1.8	1.8	1.8	1.9	1.9
1	2	0	6	0	2	3	2	1	8	5	2	7	3	7	2	6	0	3	7	0	3	5	8	0	3	5	7	9	1	3	
2.2	0.2	0.3	0.5	0.6	0.8	0.9	1.0	1.1	1.1	1.2	1.3	1.3	1.4	1.4	1.5	1.5	1.6	1.6	1.6	1.7	1.7	1.7	1.8	1.8	1.8	1.8	1.9	1.9	1.9	1.9	
2	1	9	5	9	1	2	2	0	8	5	2	8	3	8	3	8	2	5	9	2	5	8	1	4	6	9	1	3	5	7	
2.3	0.2	0.3	0.5	0.6	0.8	0.9	1.0	1.1	1.1	1.2	1.3	1.3	1.4	1.4	1.5	1.5	1.6	1.6	1.7	1.7	1.7	1.8	1.8	1.8	1.9	1.9	1.9	1.9	1.9	2.0	
3	1	8	4	8	0	1	1	0	8	5	2	8	4	9	4	9	3	7	1	5	8	1	4	7	0	2	5	7	9	1	
2.4	0.2	0.3	0.5	0.6	0.7	0.9	1.0	1.0	1.1	1.2	1.3	1.3	1.4	1.5	1.5	1.6	1.6	1.6	1.7	1.7	1.8	1.8	1.8	1.9	1.9	1.9	1.9	2.0	2.0	2.0	
4	0	8	3	7	9	0	0	9	8	5	2	9	5	0	6	0	5	9	3	7	0	4	7	0	3	5	8	0	3	5	
2.5	0.2	0.3	0.5	0.6	0.7	0.9	1.0	1.0	1.1	1.2	1.3	1.3	1.4	1.5	1.5	1.6	1.6	1.7	1.7	1.7	1.8	1.8	1.9	1.9	1.9	1.9	2.0	2.0	2.0	2.0	
5	0	7	2	6	8	0	0	9	7	5	3	9	5	1	7	2	6	1	5	9	3	6	0	3	6	9	1	4	6	9	
2.6	0.1	0.3	0.5	0.6	0.7	0.8	0.9	1.0	1.1	1.2	1.3	1.4	1.4	1.5	1.5	1.6	1.6	1.7	1.7	1.8	1.8	1.8	1.9	1.9	1.9	2.0	2.0	2.0	2.1	2.1	
6	9	6	1	5	8	9	9	9	7	5	3	0	6	2	8	3	8	2	7	1	5	9	2	5	9	2	5	7	0	2	
2.7	0.1	0.3	0.5	0.6	0.7	0.8	0.9	1.0	1.1	1.2	1.3	1.4	1.4	1.5	1.5	1.6	1.6	1.7	1.7	1.8	1.8	1.9	1.9	1.9	2.0	2.0	2.0	2.1	2.1	2.1	
7	9	6	1	4	7	8	9	8	7	5	3	0	7	3	9	4	9	4	9	3	7	1	5	8	1	5	8	1	3	6	
2.8	0.1	0.3	0.5	0.6	0.7	0.8	0.9	1.0	1.1	1.2	1.3	1.4	1.4	1.5	1.5	1.6	1.7	1.7	1.8	1.8	1.8	1.9	1.9	2.0	2.0	2.0	2.1	2.1	2.1	2.1	
8	8	5	0	4	6	8	8	8	7	5	3	0	7	3	9	5	0	5	0	5	9	3	7	0	4	7	1	4	6	9	
2.9	0.1	0.3	0.5	0.6	0.7	0.8	0.9	1.0	1.1	1.2	1.3	1.4	1.4	1.5	1.6	1.6	1.7	1.7	1.8	1.8	1.9	1.9	1.9	2.0	2.0	2.1	2.1	2.1	2.2	2.2	
9	8	5	0	3	6	7	8	8	7	5	3	1	8	4	0	6	2	7	2	6	1	5	9	3	6	0	3	6	0	2	
3.0	0.1	0.3	0.4	0.6	0.7	0.8	0.9	1.0	1.1	1.2	1.3	1.4	1.4	1.5	1.6	1.6	1.7	1.7	1.8	1.8	1.9	1.9	2.0	2.0	2.0	2.1	2.1	2.1	2.2	2.2	
0	8	4	9	3	5	7	7	7	7	5	3	1	8	5	1	7	3	8	3	8	3	7	1	5	9	2	6	9	2	6	

Note: These are the results of a sensitivity analysis for the indirect effect of depressive symptoms on HIV incidence. This sensitivity analysis assumes that exposure-outcome confounding is controlled and exposure-mediator confounding is controlled but that there may be uncontrolled mediator-outcome confounding. This uncontrolled confounder cannot be affected by the exposure. The gamma parameter is the maximum risk ratio relating the unmeasured confounder U and the outcome Y and the exposed subjects across the strata of the mediator, conditional on covariates. This is the maximum of the ratios for which U is associated with increased likelihood of Y via pathways other than through the mediator. The lambda parameter is the maximum risk ratio relating the exposure A to U across levels of the mediator, conditional on covariates. These parameters are used to create a bias factor, B, which equals $(\gamma * \lambda) / (\lambda + \gamma - 1)$. The indirect effect estimate is multiplied by B to obtain the "bias-corrected" estimates displayed in this table. For more information and more in depth discussion of these parameters and their derivations, see VanderWeele TJ. Mediation Analysis: A Practitioner's Guide. *Annu Rev Public Health*. 2016;37:17–32. and Sharp sensitivity bounds for mediation under unmeasured mediator-outcome confounding. *Biometrika*. 2016 Jun 1;103(2):483–90.

Web Appendix 4.

Analysis R code

```
rm(list=ls())

library(haven)
library(dplyr)
library(mice)

# -----
#
#           mediation analysis
#
# -----

mediators <- c("alcohol_c", "lowattend", "high_att", "parental_involve",
              "cm_engage", "older_prt_n", "number_partners", "any_unp", "exchange_sex",
              "ps_hit", "ps_angry", "ps_cheat", "high_power", "ipv", "purchase_bc")

for (z in 1:length(mediators)) {

  # probability of being censored
  c_fit <- with(imp, glm(censored ~ depress_c + high_att + cm_engage + food_insecure + ps_hit +
                        ps_angry + ps_cheat + number_partners + purchase_bc + parental_involve +
                        lowattend + prt12m_c + any_unp + older_prt_n + alcohol_c + high_power +
                        ipv + exchange_sex + factor(total_capita_decile) +
                        any_neg_event + any_pos_event +
                        pct_govt_grant + orphan2 +
                        orphan1 + factor(mat_educ) +
                        factor(pat_educ) + pregnant + yw_age + arm, family="binomial"))

  mi_df <- list()

  for (i in 1:M) {
    mi_df[[i]] <- mice::complete(imp,i)
  }

  cp <- list()
  for (m in 1:M) {
    cp[[m]] <- predict(c_fit$analyses[[m]], newdata=mi_df[[m]], type="response")
  }
  cp_df <- do.call(cbind, cp)
  cp <- rowMeans(cp_df)

  ipcw <- 1/(1-cp)

  # estimate mediator - exposure relationship

  em_fit <- with(imp, glm(depress_c ~ get(mediators[z]) + food_insecure + factor(total_capita_decile) +
                          any_neg_event + any_pos_event +
                          pct_govt_grant + orphan2 +
                          orphan1 + factor(mat_educ) +
                          factor(pat_educ) + pregnant + yw_age + arm, family="binomial"))
```

```

# predict probability of depression for each imputed data set and average
mi_df <- list()

for (i in 1:M) {
  mi_df[[i]] <- mice::complete(imp,i)
}

p <- list()
for (m in 1:M) {
  p[[m]] <- predict(em_fit$analyses[[m]], newdata=mi_df[[m]], type="response")
}
p_df <- do.call(cbind, p)

p <- rowMeans(p_df)

iow <- (1 - p)/p
iow[imp$data$depress_c==0] <- 1

# direct effect of exposure using weighted glm
de_fitOR <- with(imp, glm(hiv_pbstat ~ depress_c +
  food_insecure + factor(total_capita_decile) +
  any_neg_event + any_pos_event +
  pct_govt_grant + orphan2 +
  orphan1 + factor(mat_educ) +
  factor(pat_educ) + pregnant + yw_age + arm, family="binomial", weights=iow))

de_fitRR <- with(imp, glm(formula = hiv_pbstat ~ depress_c +
  food_insecure + factor(total_capita_decile) +
  any_neg_event + any_pos_event +
  pct_govt_grant + orphan2 +
  orphan1 + factor(mat_educ) +
  factor(pat_educ) + pregnant + yw_age + arm, family=poisson(link="log"), weights=iow))

de_fitRD <- with(imp, glm(formula = hiv_pbstat ~ depress_c +
  food_insecure + factor(total_capita_decile) +
  any_neg_event + any_pos_event +
  pct_govt_grant + orphan2 +
  orphan1 + factor(mat_educ) +
  factor(pat_educ) + pregnant + yw_age + arm, family="gaussian", weights=iow))

# total effect of exposure using glm

te_fitOR <- with(imp, glm(hiv_pbstat ~ depress_c + food_insecure + factor(total_capita_decile) +
  any_neg_event + any_pos_event +
  pct_govt_grant + orphan2 +
  orphan1 + factor(mat_educ) +
  factor(pat_educ) + pregnant + yw_age + arm, family="binomial"))

```

```

te_fitRR <- with(imp, glm(hiv_pbstat ~ depress_c + food_insecure + factor(total_capita_decile) +
  any_neg_event + any_pos_event +
  pct_govt_grant + orphan2 +
  orphan1 + factor(mat_educ) +
  factor(pat_educ) + pregnant + yw_age + arm, family=poisson(link="log")))

te_fitRD <- with(imp, glm(hiv_pbstat ~ depress_c + food_insecure + factor(total_capita_decile) +
  any_neg_event + any_pos_event +
  pct_govt_grant + orphan2 +
  orphan1 + factor(mat_educ) +
  factor(pat_educ) + pregnant + yw_age + arm, family="gaussian"))

main_resultsOR <- data.frame(summary(pool(te_fitOR))[2], summary(pool(de_fitOR))[2], summary(pool(te_fitOR))[2] -
summary(pool(de_fitOR))[2])
  names(main_resultsOR) <- c("Total effect OR", "Direct effect OR", "Indirect effect OR")

main_resultsRR <- data.frame(summary(pool(te_fitRR))[2], summary(pool(de_fitRR))[2], summary(pool(te_fitRR))[2] -
summary(pool(de_fitRR))[2])
  names(main_resultsRR) <- c("Total effect RR", "Direct effect RR", "Indirect effect RR")

main_resultsRD <- data.frame(summary(pool(te_fitRD))[2], summary(pool(de_fitRD))[2], summary(pool(te_fitRD))[2] -
summary(pool(de_fitRD))[2])
  names(main_resultsRD) <- c("Total effect RD", "Direct effect RD", "Indirect effect RD")

# -----

#   define bootstrap function

# -----

boot_fit <- function(iteration, m_iter) {
  print(m_iter)
  print(iteration)

  b_df <- mice::complete(imp,m_iter)

  boot_df <- b_df[sample(nrow(b_df), replace=T),]

  # probability of being censored
  boot_c_fit <- glm(censored ~ depress_c + high_att + cm_engage + food_insecure + ps_hit +
    ps_angry + ps_cheat + number_partners + purchase_bc + parental_involve +
    lowattend + prt12m_c + any_unp + older_prt_n + alcohol_c + high_power +
    ipv + exchange_sex + factor(total_capita_decile) +
    any_neg_event + any_pos_event +
    pct_govt_grant + orphan2 +
    orphan1 + factor(mat_educ) +
    factor(pat_educ) + pregnant + yw_age + arm, family="binomial", data=boot_df)

  cp <- predict(boot_c_fit, type="response")
  ipcw <- 1/(1-cp)

```

```

# estimate mediator - exposure relationship
boot_em_fit <- glm(depress_c ~ get(mediators[z]) + food_insecure + factor(total_capita_decile) +
  any_neg_event + any_pos_event +
  pct_govt_grant + orphan2 +
  orphan1 + factor(mat_educ) +
  factor(pat_educ) + pregnant + yw_age + arm, data=boot_df, family="binomial")

# predict probability of depression
p <- predict(boot_em_fit, type="response")

iow <- (1 - p)/p
iow[boot_df$depress_c==0] <- 1

# direct and total effects of exposure
boot_de_fitOR <- glm(hiv_pbstat ~ depress_c + factor(total_capita_decile) +
  food_insecure +
  any_neg_event + any_pos_event +
  pct_govt_grant + orphan2 +
  orphan1 + factor(mat_educ) +
  factor(pat_educ) + pregnant + yw_age + arm, family="binomial", data=boot_df, weights=iow)

boot_te_fitOR <- glm(hiv_pbstat ~ depress_c + factor(total_capita_decile)+ food_insecure +
  any_neg_event + any_pos_event +
  pct_govt_grant + orphan2 +
  orphan1 + factor(mat_educ) +
  factor(pat_educ) + pregnant + yw_age + arm, family="binomial", data=boot_df)

boot_de_fitRR <- glm(hiv_pbstat ~ depress_c + factor(total_capita_decile) +
  food_insecure +
  any_neg_event + any_pos_event +
  pct_govt_grant + orphan2 +
  orphan1 + factor(mat_educ) +
  factor(pat_educ) + pregnant + yw_age + arm, family=poisson(link="log"), data=boot_df, weights=iow)

boot_te_fitRR <- glm(hiv_pbstat ~ depress_c + factor(total_capita_decile)+ food_insecure +
  any_neg_event + any_pos_event +
  pct_govt_grant + orphan2 +
  orphan1 + factor(mat_educ) +
  factor(pat_educ) + pregnant + yw_age + arm, family=poisson(link="log"), data=boot_df)

boot_de_fitRD <- glm(hiv_pbstat ~ depress_c + factor(total_capita_decile) +
  food_insecure +
  any_neg_event + any_pos_event +
  pct_govt_grant + orphan2 +
  orphan1 + factor(mat_educ) +
  factor(pat_educ) + pregnant + yw_age + arm, family="gaussian", data=boot_df, weights=iow)

boot_te_fitRD <- glm(hiv_pbstat ~ depress_c + factor(total_capita_decile)+ food_insecure +

```

```

any_neg_event + any_pos_event +
pct_govt_grant + orphan2 +
orphan1 + factor(mat_educ) +
factor(pat_educ) + pregnant + yw_age + arm, family="gaussian", data=boot_df)

```

```
# organize results
```

```

b_resultsOR <- data.frame(coef(boot_te_fitOR)[2], coef(boot_de_fitOR)[2], coef(boot_te_fitOR)[2] - coef(boot_de_fitOR)[2])
b_resultsRR <- data.frame(coef(boot_te_fitRR)[2], coef(boot_de_fitRR)[2], coef(boot_te_fitRR)[2] - coef(boot_de_fitRR)[2])
b_resultsRD <- data.frame(coef(boot_te_fitRD)[2], coef(boot_de_fitRD)[2], coef(boot_te_fitRD)[2] - coef(boot_de_fitRD)[2])

```

```

names(b_resultsOR) <- c(paste0(c("Total effect", "Direct effect", "Indirect effect"), "OR"))
names(b_resultsRR) <- c(paste0(c("Total effect", "Direct effect", "Indirect effect"), "RR"))
names(b_resultsRD) <- c(paste0(c("Total effect", "Direct effect", "Indirect effect"), "RD"))

```

```

return(cbind(b_resultsOR, b_resultsRR, b_resultsRD))
}

```

```
# calculate bootstrap results and combine into a data frame
```

```

b_frame <- list()
var_frame <- list()

```

```

for (m in 1:M) {
  boot_results <- lapply(1:250, function(x) boot_fit(x, m))

```

```

  b_frame[[m]] <- do.call(rbind, boot_results)

```

```

  var_frame[[m]] <- apply(b_frame[[m]], 2, var)

```

```

  #NOTE: (100-1)^(-1)*sum((b_frame[,1] - mean(b_frame[,1]))^2) is equivalent to var(b_frame[,1])

```

```

}

```

```
# variance within imputed data set estimated using bootstrap sample
```

```

var <- data.frame(do.call(rbind, var_frame))
names(var) <- c("te_OR", "de_OR", "ie_OR", "te_RR", "de_RR", "ie_RR", "te_RD", "de_RD", "ie_RD")

```

```

# now need to estimate variance across imputed data set getting results from each imputed data set from main analysis results
above

```

```

theta_te_ORm <- data.frame(te_OR = matrix(ncol=1, nrow=M))
theta_de_ORm <- data.frame(de_OR = matrix(ncol=1, nrow=M))
theta_ie_ORm <- data.frame(ie_OR = matrix(ncol=1, nrow=M))

```

```

theta_te_RRm <- data.frame(te_RR = matrix(ncol=1, nrow=M))
theta_de_RRm <- data.frame(de_RR = matrix(ncol=1, nrow=M))
theta_ie_RRm <- data.frame(ie_RR = matrix(ncol=1, nrow=M))

```

```

theta_te_RDm <- data.frame(te_RD = matrix(ncol=1, nrow=M))
theta_de_RDm <- data.frame(de_RD = matrix(ncol=1, nrow=M))
theta_ie_RDm <- data.frame(ie_RD = matrix(ncol=1, nrow=M))

```

```

for (i in 1:M) {

```



```

theta_te_ORm[i,1] <- coef(te_fitOR$analyses[[i]])[2]
theta_de_ORm[i,1] <- coef(de_fitOR$analyses[[i]])[2]
theta_ie_ORm[i,1] <- coef(te_fitOR$analyses[[i]])[2] - coef(de_fitOR$analyses[[i]])[2]

theta_te_RRm[i,1] <- coef(te_fitRR$analyses[[i]])[2]
theta_de_RRm[i,1] <- coef(de_fitRR$analyses[[i]])[2]
theta_ie_RRm[i,1] <- coef(te_fitRR$analyses[[i]])[2] - coef(de_fitRR$analyses[[i]])[2]

theta_te_RDm[i,1] <- coef(te_fitRD$analyses[[i]])[2]
theta_de_RDm[i,1] <- coef(de_fitRD$analyses[[i]])[2]
theta_ie_RDm[i,1] <- coef(te_fitRD$analyses[[i]])[2] - coef(de_fitRD$analyses[[i]])[2]
}

# pool within and between variance using combining rules
var_te_OR <- mean(var$te_OR) + ((M+1)/M)*var(theta_te_ORm$te_OR)
var_de_OR <- mean(var$de_OR) + ((M+1)/M)*var(theta_de_ORm$de_OR)
var_ie_OR <- mean(var$ie_OR) + ((M+1)/M)*var(theta_ie_ORm$ie_OR)

var_te_RR <- mean(var$te_RR) + ((M+1)/M)*var(theta_te_RRm$te_RR)
var_de_RR <- mean(var$de_RR) + ((M+1)/M)*var(theta_de_RRm$de_RR)
var_ie_RR <- mean(var$ie_RR) + ((M+1)/M)*var(theta_ie_RRm$ie_RR)

var_te_RD <- mean(var$te_RD) + ((M+1)/M)*var(theta_te_RDm$te_RD)
var_de_RD <- mean(var$de_RD) + ((M+1)/M)*var(theta_de_RDm$de_RD)
var_ie_RD <- mean(var$ie_RD) + ((M+1)/M)*var(theta_ie_RDm$ie_RD)

# NOTE: (M+1)/(M*(M-1))*sum((theta_te_ORm$te_OR - mean(theta_te_ORm$te_OR))^2) is equivalent to (M+1)/M *
var(theta_te_ORm$te_OR)

# calculate confidence intervals and output results

qlb_OR <- data.frame(cbind(main_resultsOR$`Total effect OR` - 1.96*sqrt(var_te_OR), main_resultsOR$`Direct effect OR` -
1.96*sqrt(var_de_OR), main_resultsOR$`Indirect effect OR` - 1.96*sqrt(var_ie_OR)))
qub_OR <- data.frame(cbind(main_resultsOR$`Total effect OR` + 1.96*sqrt(var_te_OR), main_resultsOR$`Direct effect OR` +
1.96*sqrt(var_de_OR), main_resultsOR$`Indirect effect OR` + 1.96*sqrt(var_ie_OR)))
names(qlb_OR) <- names(main_resultsOR)
names(qub_OR) <- names(main_resultsOR)

# here is where you exponentiate the results to get back to the OR scale
resultsOR <- data.frame(rbind(exp(main_resultsOR), exp(qlb_OR), exp(qub_OR)))
rownames(resultsOR) <- c("point estimate", "95% CI lb", "95% CI ub")

qlb_RR <- data.frame(cbind(main_resultsRR$`Total effect RR` - 1.96*sqrt(var_te_RR), main_resultsRR$`Direct effect RR` -
1.96*sqrt(var_de_RR), main_resultsRR$`Indirect effect RR` - 1.96*sqrt(var_ie_RR)))
qub_RR <- data.frame(cbind(main_resultsRR$`Total effect RR` + 1.96*sqrt(var_te_RR), main_resultsRR$`Direct effect RR` +
1.96*sqrt(var_de_RR), main_resultsRR$`Indirect effect RR` + 1.96*sqrt(var_ie_RR)))
names(qlb_RR) <- names(main_resultsRR)
names(qub_RR) <- names(main_resultsRR)

# here is where you exponentiate the results to get back to the RR scale
resultsRR <- data.frame(rbind(exp(main_resultsRR), exp(qlb_RR), exp(qub_RR)))
rownames(resultsRR) <- c("point estimate", "95% CI lb", "95% CI ub")

```

```

# risk difference using LPM
qlb_RD <- data.frame(cbind(main_resultsRD$`Total effect RD` - 1.96*sqrt(var_te_RD), main_resultsRD$`Direct effect RD` -
1.96*sqrt(var_de_RD), main_resultsRD$`Indirect effect RD` - 1.96*sqrt(var_ie_RD)))
qub_RD <- data.frame(cbind(main_resultsRD$`Total effect RD` + 1.96*sqrt(var_te_RD), main_resultsRD$`Direct effect RD` +
1.96*sqrt(var_de_RD), main_resultsRD$`Indirect effect RD` + 1.96*sqrt(var_ie_RD)))
names(qlb_RD) <- names(main_resultsRD)
names(qub_RD) <- names(main_resultsRD)

resultsRD <- data.frame(rbind(main_resultsRD, qlb_RD, qub_RD))
rownames(resultsRD) <- c("point estimate", "95% CI lb", "95% CI ub")

}

# -----
#
#           all mediators joint analysis no interaction
#
# -----
M <- 30

# probability of being censored
c_fit <- with(imp, glm(censored ~ depress_c + high_att + cm_engage + food_insecure + ps_hit +
ps_angry + ps_cheat + number_partners + purchase_bc + parental_involve +
lowattend + prt12m_c + any_unp + older_prt_n + alcohol_c + high_power +
ipv + exchange_sex + factor(total_capita_decile) +
any_neg_event + any_pos_event +
pct_govt_grant + orphan2 +
orphan1 + factor(mat_educ) +
factor(pat_educ) + pregnant + yw_age + arm, family="binomial"))

mi_df <- list()

for (i in 1:M) {
  mi_df[[i]] <- mice::complete(imp,i)
}

cp <- list()
for (m in 1:M) {
  cp[[m]] <- predict(c_fit$analyses[[m]], newdata=mi_df[[m]], type="response")
}
cp_df <- do.call(cbind, cp)
cp <- rowMeans(cp_df)

ipcw <- 1/(1-cp)

# estimate mediator - exposure relationship

em_fit <- with(imp, glm(depress_c ~ alcohol_c + lowattend + prt12m_c + any_unp + older_prt_n +
high_power + ps_hit + ps_angry + ps_cheat + number_partners + purchase_bc +
parental_involve + high_att + cm_engage + ipv + exchange_sex +
food_insecure + factor(total_capita_decile) +
any_neg_event + any_pos_event +
pct_govt_grant + orphan2 +
orphan1 + factor(mat_educ) +

```

```

factor(pat_educ) + pregnant + yw_age + arm, family="binomial"))

# predict probability of depression for each imputed data set and average
mi_df <- list()

for (i in 1:M) {
  mi_df[[i]] <- mice::complete(imp,i)
}

p <- list()
for (m in 1:M) {
  p[[m]] <- predict(em_fit$analyses[[m]], newdata=mi_df[[m]], type="response")
}
p_df <- do.call(cbind, p)

p <- rowMeans(p_df)

iow <- (1 - p)/p
iow[imp$data$depress_c==0] <- 1

# direct effect of exposure using weighted glm
de_fitOR <- with(imp, glm(hiv_pbstat ~ depress_c +
  food_insecure + factor(total_capita_decile) +
  any_neg_event + any_pos_event +
  pct_govt_grant + orphan2 +
  orphan1 + factor(mat_educ) +
  factor(pat_educ) + pregnant + yw_age + arm, family="binomial", weights=iow))

de_fitRR <- with(imp, glm(formula = hiv_pbstat ~ depress_c +
  food_insecure + factor(total_capita_decile) +
  any_neg_event + any_pos_event +
  pct_govt_grant + orphan2 +
  orphan1 + factor(mat_educ) +
  factor(pat_educ) + pregnant + yw_age + arm, family=poisson(link="log"), weights=iow))

de_fitRD <- with(imp, glm(formula = hiv_pbstat ~ depress_c +
  food_insecure + factor(total_capita_decile) +
  any_neg_event + any_pos_event +
  pct_govt_grant + orphan2 +
  orphan1 + factor(mat_educ) +
  factor(pat_educ) + pregnant + yw_age + arm, family="gaussian", weights=iow))

te_fitOR <- with(imp, glm(hiv_pbstat ~ depress_c + food_insecure + factor(total_capita_decile) +
  any_neg_event + any_pos_event +
  pct_govt_grant + orphan2 +
  orphan1 + factor(mat_educ) +
  factor(pat_educ) + pregnant + yw_age + arm, family="binomial"))

te_fitRR <- with(imp, glm(hiv_pbstat ~ depress_c + food_insecure + factor(total_capita_decile) +
  any_neg_event + any_pos_event +

```

```

pct_govt_grant + orphan2 +
orphan1 + factor(mat_educ) +
factor(pat_educ) + pregnant + yw_age + arm, family=poisson(link="log"))

te_fitRD <- with(imp, glm(hiv_pbstat ~ depress_c + food_insecure + factor(total_capita_decile) +
any_neg_event + any_pos_event +
pct_govt_grant + orphan2 +
orphan1 + factor(mat_educ) +
factor(pat_educ) + pregnant + yw_age + arm, family="gaussian"))

main_resultsOR <- data.frame(summary(pool(te_fitOR))[2], summary(pool(de_fitOR))[2], summary(pool(te_fitOR))[2] -
summary(pool(de_fitOR))[2])
names(main_resultsOR) <- c("Total effect OR", "Direct effect OR", "Indirect effect OR")

main_resultsRR <- data.frame(summary(pool(te_fitRR))[2], summary(pool(de_fitRR))[2], summary(pool(te_fitRR))[2] -
summary(pool(de_fitRR))[2])
names(main_resultsRR) <- c("Total effect RR", "Direct effect RR", "Indirect effect RR")

main_resultsRD <- data.frame(summary(pool(te_fitRD))[2], summary(pool(de_fitRD))[2], summary(pool(te_fitRD))[2] -
summary(pool(de_fitRD))[2])
names(main_resultsRD) <- c("Total effect RD", "Direct effect RD", "Indirect effect RD")

# define bootstrap function

boot_fit <- function(iteration, m_iter) {
print(m_iter)
print(iteration)

b_df <- mice::complete(imp,m_iter)

boot_df <- b_df[sample(nrow(b_df), replace=T),]

# estimate mediator - exposure relationship
boot_em_fit <- glm(depress_c ~ alcohol_c + lowattend + prt12m_c + any_unp + older_prt_n +
high_power + ps_hit + ps_angry + ps_cheat + number_partners + purchase_bc +
parental_involve + high_att + cm_engage +
food_insecure + factor(total_capita_decile) +
any_neg_event + any_pos_event +
pct_govt_grant + orphan2 +
orphan1 + factor(mat_educ) +
factor(pat_educ) + pregnant + yw_age + arm, data=boot_df, family="binomial")

# predict probability of depression
p <- predict(boot_em_fit, type="response")

iow <- (1 - p)/p
iow[boot_df$depress_c==0] <- 1

```

```

# direct effect of exposure using weighted glm
boot_de_fitOR <- glm(hiv_pbstat ~ depress_c + factor(total_capita_decile) +
  food_insecure +
  any_neg_event + any_pos_event +
  pct_govt_grant + orphan2 +
  orphan1 + factor(mat_educ) +
  factor(pat_educ) + pregnant + yw_age + arm, family="binomial", data=boot_df, weights=iow)

boot_te_fitOR <- glm(hiv_pbstat ~ depress_c + factor(total_capita_decile)+ food_insecure +
  any_neg_event + any_pos_event +
  pct_govt_grant + orphan2 +
  orphan1 + factor(mat_educ) +
  factor(pat_educ) + pregnant + yw_age + arm, family="binomial", data=boot_df)

boot_de_fitRR <- glm(hiv_pbstat ~ depress_c + factor(total_capita_decile) +
  food_insecure +
  any_neg_event + any_pos_event +
  pct_govt_grant + orphan2 +
  orphan1 + factor(mat_educ) +
  factor(pat_educ) + pregnant + yw_age + arm, family=poisson(link="log"), data=boot_df, weights=iow)

boot_te_fitRR <- glm(hiv_pbstat ~ depress_c + factor(total_capita_decile)+ food_insecure +
  any_neg_event + any_pos_event +
  pct_govt_grant + orphan2 +
  orphan1 + factor(mat_educ) +
  factor(pat_educ) + pregnant + yw_age + arm, family=poisson(link="log"), data=boot_df)

boot_de_fitRD <- glm(hiv_pbstat ~ depress_c + factor(total_capita_decile) +
  food_insecure +
  any_neg_event + any_pos_event +
  pct_govt_grant + orphan2 +
  orphan1 + factor(mat_educ) +
  factor(pat_educ) + pregnant + yw_age + arm, family="gaussian", data=boot_df, weights=iow)

boot_te_fitRD <- glm(hiv_pbstat ~ depress_c + factor(total_capita_decile)+ food_insecure +
  any_neg_event + any_pos_event +
  pct_govt_grant + orphan2 +
  orphan1 + factor(mat_educ) +
  factor(pat_educ) + pregnant + yw_age + arm, family="gaussian", data=boot_df)

# organize results

b_resultsOR <- data.frame(coef(boot_te_fitOR)[2], coef(boot_de_fitOR)[2], coef(boot_te_fitOR)[2] - coef(boot_de_fitOR)[2])
b_resultsRR <- data.frame(coef(boot_te_fitRR)[2], coef(boot_de_fitRR)[2], coef(boot_te_fitRR)[2] - coef(boot_de_fitRR)[2])
b_resultsRD <- data.frame(coef(boot_te_fitRD)[2], coef(boot_de_fitRD)[2], coef(boot_te_fitRD)[2] - coef(boot_de_fitRD)[2])

```

```

names(b_resultsOR) <- c(paste0(c("Total effect", "Direct effect", "Indirect effect"), "OR"))
names(b_resultsRR) <- c(paste0(c("Total effect", "Direct effect", "Indirect effect"), "RR"))
names(b_resultsRD) <- c(paste0(c("Total effect", "Direct effect", "Indirect effect"), "RD"))

return(cbind(b_resultsOR, b_resultsRR, b_resultsRD))

}

# calculate bootstrap results and combine into a data frame
b_frame <- list()
var_frame <- list()

for (m in 1:M) {
  boot_results <- lapply(1:250, function(x) boot_fit(x, m))

  b_frame[[m]] <- do.call(rbind, boot_results)

  var_frame[[m]] <- apply(b_frame[[m]], 2, var)

  #NOTE: (100-1)^(-1)*sum((b_frame[,1] - mean(b_frame[,1]))^2) is equivalent to var(b_frame[,1])

}

# variance within imputed data set estimated using bootstrap sample
var <- data.frame(do.call(rbind, var_frame))
names(var) <- c("te_OR", "de_OR", "ie_OR", "te_RR", "de_RR", "ie_RR", "te_RD", "de_RD", "ie_RD")

# now need to estimate variance across imputed data set getting results from each imputed data set from main analysis results
above
theta_te_ORm <- data.frame(te_OR = matrix(ncol=1, nrow=M))
theta_de_ORm <- data.frame(de_OR = matrix(ncol=1, nrow=M))
theta_ie_ORm <- data.frame(ie_OR = matrix(ncol=1, nrow=M))

theta_te_RRm <- data.frame(te_RR = matrix(ncol=1, nrow=M))
theta_de_RRm <- data.frame(de_RR = matrix(ncol=1, nrow=M))
theta_ie_RRm <- data.frame(ie_RR = matrix(ncol=1, nrow=M))

theta_te_RDm <- data.frame(te_RD = matrix(ncol=1, nrow=M))
theta_de_RDm <- data.frame(de_RD = matrix(ncol=1, nrow=M))
theta_ie_RDm <- data.frame(ie_RD = matrix(ncol=1, nrow=M))

for (i in 1:M) {
  theta_te_ORm[i,1] <- coef(te_fitOR$analyses[[i]])[2]
  theta_de_ORm[i,1] <- coef(de_fitOR$analyses[[i]])[2]
  theta_ie_ORm[i,1] <- coef(te_fitOR$analyses[[i]])[2] - coef(de_fitOR$analyses[[i]])[2]

  theta_te_RRm[i,1] <- coef(te_fitRR$analyses[[i]])[2]
  theta_de_RRm[i,1] <- coef(de_fitRR$analyses[[i]])[2]
  theta_ie_RRm[i,1] <- coef(te_fitRR$analyses[[i]])[2] - coef(de_fitRR$analyses[[i]])[2]

  theta_te_RDm[i,1] <- coef(te_fitRD$analyses[[i]])[2]
  theta_de_RDm[i,1] <- coef(de_fitRD$analyses[[i]])[2]
  theta_ie_RDm[i,1] <- coef(te_fitRD$analyses[[i]])[2] - coef(de_fitRD$analyses[[i]])[2]
}

```

```

}

# pool within and between variance using combining rules
var_te_OR <- mean(var$te_OR) + ((M+1)/M)*var(theta_te_ORm$te_OR)
var_de_OR <- mean(var$de_OR) + ((M+1)/M)*var(theta_de_ORm$de_OR)
var_ie_OR <- mean(var$ie_OR) + ((M+1)/M)*var(theta_ie_ORm$ie_OR)

var_te_RR <- mean(var$te_RR) + ((M+1)/M)*var(theta_te_RRm$te_RR)
var_de_RR <- mean(var$de_RR) + ((M+1)/M)*var(theta_de_RRm$de_RR)
var_ie_RR <- mean(var$ie_RR) + ((M+1)/M)*var(theta_ie_RRm$ie_RR)

var_te_RD <- mean(var$te_RD) + ((M+1)/M)*var(theta_te_RDm$te_RD)
var_de_RD <- mean(var$de_RD) + ((M+1)/M)*var(theta_de_RDm$de_RD)
var_ie_RD <- mean(var$ie_RD) + ((M+1)/M)*var(theta_ie_RDm$ie_RD)

# NOTE: (M+1)/(M*(M-1))*sum((theta_te_ORm$te_OR - mean(theta_te_ORm$te_OR))^2) is equivalent to (M+1)/M *
var(theta_te_ORm$te_OR)

# calculate confidence intervals and output results

qlb_OR <- data.frame(cbind(main_resultsOR$`Total effect OR` - 1.96*sqrt(var_te_OR), main_resultsOR$`Direct effect OR` -
1.96*sqrt(var_de_OR), main_resultsOR$`Indirect effect OR` - 1.96*sqrt(var_ie_OR)))
qub_OR <- data.frame(cbind(main_resultsOR$`Total effect OR` + 1.96*sqrt(var_te_OR), main_resultsOR$`Direct effect OR` +
1.96*sqrt(var_de_OR), main_resultsOR$`Indirect effect OR` + 1.96*sqrt(var_ie_OR)))
names(qlb_OR) <- names(main_resultsOR)
names(qub_OR) <- names(main_resultsOR)

# here is where you finally exponentiate the results to get back to the OR scale
resultsOR <- data.frame(rbind(exp(main_resultsOR), exp(qlb_OR), exp(qub_OR)))
rownames(resultsOR) <- c("point estimate", "95% CI lb", "95% CI ub")

qlb_RR <- data.frame(cbind(main_resultsRR$`Total effect RR` - 1.96*sqrt(var_te_RR), main_resultsRR$`Direct effect RR` -
1.96*sqrt(var_de_RR), main_resultsRR$`Indirect effect RR` - 1.96*sqrt(var_ie_RR)))
qub_RR <- data.frame(cbind(main_resultsRR$`Total effect RR` + 1.96*sqrt(var_te_RR), main_resultsRR$`Direct effect RR` +
1.96*sqrt(var_de_RR), main_resultsRR$`Indirect effect RR` + 1.96*sqrt(var_ie_RR)))
names(qlb_RR) <- names(main_resultsRR)
names(qub_RR) <- names(main_resultsRR)

# here is where you finally exponentiate the results to get back to the RR scale
resultsRR <- data.frame(rbind(exp(main_resultsRR), exp(qlb_RR), exp(qub_RR)))
rownames(resultsRR) <- c("point estimate", "95% CI lb", "95% CI ub")

qlb_RD <- data.frame(cbind(main_resultsRD$`Total effect RD` - 1.96*sqrt(var_te_RD), main_resultsRD$`Direct effect RD` -
1.96*sqrt(var_de_RD), main_resultsRD$`Indirect effect RD` - 1.96*sqrt(var_ie_RD)))
qub_RD <- data.frame(cbind(main_resultsRD$`Total effect RD` + 1.96*sqrt(var_te_RD), main_resultsRD$`Direct effect RD` +
1.96*sqrt(var_de_RD), main_resultsRD$`Indirect effect RD` + 1.96*sqrt(var_ie_RD)))
names(qlb_RD) <- names(main_resultsRD)
names(qub_RD) <- names(main_resultsRD)

resultsRD <- data.frame(rbind(main_resultsRD, qlb_RD, qub_RD))
rownames(resultsRD) <- c("point estimate", "95% CI lb", "95% CI ub")

```