For this version of the analysis, we define mediation effects using the so-called ``product method''. That is, we fit regression models to predict M using X, C and to predict Y using M, X, C. Write the linear predictors for these models as a\_0 + a\_x \* X + A\_C^T C and b\_0 + b\_m \* M + b\_x \* X + B\_C^T C respectively. We define the direct effect of X on Y as exp(b\_x), the indirect effect as exp(a\_x \* b\_m), and the total effect as their product. Note that these mediation effects are defined on the odds-ratio scale.

Our analysis proceeds by first fitting the two regression models. In our setting, these are GLMMs, with random effects for a\_0, a\_x, b\_0, b\_m and b\_x, all varying by country. We assume that the random effects are iid normal across countries, and independent across models (e.g. the REs for a\_0 and b\_0 are independent). We tested for the presence of an interaction effect between X and M in our model for Y and found no significant evidence for it.

**Point Estimation**

Our simplest results are point estimates for the global mediation effects. That is, the non-country-specific mediation effects. These come from reading the coefficients from the models, then multiplying and exponentiating as appropriate.

Getting point estimates for the country-specific effects is a bit trickier. For this, we “predict” the random effects’ values within each country. The terminology here is “predict” rather than “estimate” because the random effects are random variables (albeit unobserved ones), not parameters. This prediction is done within a single country by computing the conditional mode of the random effects given the observed data from that country.[[1]](#footnote-1) Once we have predicted random effects for each country, we combine these with the fixed effects to get our actual predicted/estimated coefficients for each country (i.e. the mixed effects). Finally, we use these mixed effects to compute the mediation effect for each country.

**Uncertainty Quantification**

Uncertainty quantification here is a bit tricky. Standard output for the *lme4* package contains (asymptotic) standard errors for the fixed effects. In principle, we could plug these into the delta method to get asymptotic standard errors for the global mediation effects. However, this approach doesn’t help us with the country-specific mediation effects[[2]](#footnote-2). To overcome this challenge, we use the bootstrap. Specifically, the non-parametric bootstrap, with confidence intervals computed using the basic and percentile methods. Empirical studies throughout the literature have found that the bias-corrected and accelerated bootstrap performs poorly, at least for linear mixed-effects models, so we omit this method from our analysis.

The non-parametric bootstrap proceeds by repeatedly re-sampling the observed data with replacement, performing our analysis on each of the “bootstrap samples”, and using the resulting “bootstrap distribution” of our estimator to quantify uncertainty about that estimator computed on the original data. Since our data are grouped by country, we re-sample independently across countries. This ensures that the size of a bootstrap sample matches the size of our original sample, not just globally but also within countries. From there, we just repeat our above analysis to get point estimates for the global and country-specific mediation effects from each bootstrap sample.

All that remains is to turn our bootstrap estimates into a confidence interval for the true global and country-specific mediation effects. We use two methods to do so: the percentile and basic intervals. The percentile interval is very simple, just take the 2.5th and 97.5th percentiles of the bootstrap samples for each mediation effect. The basic interval is slightly more complicated. Here, we subtract those same percentiles from twice the estimators computed from our original dataset. That is, if theta\_hat is our estimator on the original dataset, and theta\_2.5 and theta\_97.5 are the bootstrap percentiles, the percentile interval is just (theta\_2.5, theta\_97.5), and the basic interval is (2 \* theta\_hat – theta\_97.5, 2 \* theta\_hat - theta\_2.5). Note that the percentiles are swapped for the basic interval because subtracting the larger percentile gives a smaller number, the lower endpoint of the interval.

**Results**

I give plots of the various intervals in an attached .pdf file. Let me know if there’s anything else you want and I’ll get it to you as quickly as I can.

1. The joint distribution of the response and the random effects is fairly straightforward to write-down. Given the random effects, the outcome just follows a GLM, while the marginal distribution of the random effects is just normal. We then get the conditional by treating the joint distribution as a function of only the random effects and scaling so that the resulting function is a density. [↑](#footnote-ref-1)
2. I recently learned that *lme4* can produce conditional covariance matrices for the random effects given the observed data within each country. This would make it easier to do everything by the delta method. Maybe we can look into this later. [↑](#footnote-ref-2)