Analyses

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knitr::opts\_chunk$set(echo = TRUE, warning = F, message = F)

# Prepare Workspace

Load packages

require( robumeta )  
require( Hmisc )  
require( ggplot2 )

Load the data frame

load( 'dfsub.RData' )

# Descriptives

Look at the descriptive statistics for the key modeling variables

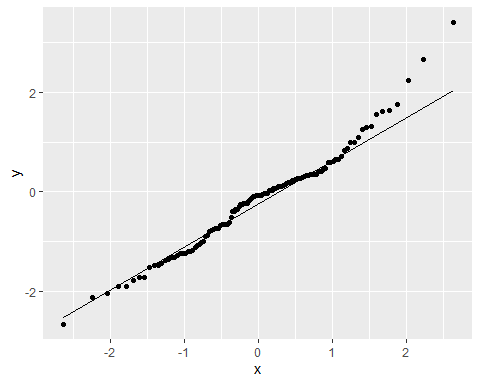
dfsub1 <- dfsub[, c('es','es.se','exp.012','mingen','hosp' ) ]  
dfsub1$loges <- log( dfsub1$es )  
label( dfsub1$loges ) <- 'Effect estimate on log scale'  
label( dfsub1$es ) <- 'Effect estimate on linear scale'  
label( dfsub1$es.se ) <- 'Standard error of log effect estimate'  
html( describe( dfsub1 ) )

require( table1 )   
  
  
table1( ~exp.012 + mingen + hosp, data = dfsub1, rowlabelhead = 'Effect Estimate Characteristics' )

## Effect Estimate Characteristics Overall  
## 1 (N=342)  
## 2 LRTI Exposure Ascertainment Window   
## 3   Not limited to first year of life 222 (64.9%)  
## 4   Limited to first year of life 120 (35.1%)  
## 5 Estimate Adjusted for Potential Genetic Confounding?   
## 6   No adjustment 285 (83.3%)  
## 7   Adjustment 57 (16.7%)  
## 8 LRTI Required Emergency Care of Hospitalization   
## 9   Emergency/Hospitalization Not Required 63 (18.4%)  
## 10   Emergency/Hospitalization Required 279 (81.6%)

Plot the effect estimates on the log scale

dfsub$w <- 1/dfsub$es.se  
qqplot <- ggplot( dfsub, aes( sample = log( es ) ) ) +  
 stat\_qq( ) +  
 stat\_qq\_line( )  
qqplot



# Analyses

## Marginal model

Run an intercept-only model, providing just a marginal weighted mean effect size.

m1 <- robu( log( es ) ~ 1,   
 studynum = record\_id,   
 var.eff.size = es.se^2,  
 data = dfsub,  
 modelweights = 'CORR',  
 small = T,  
 rho=.8  
 )  
print( m1 )

## RVE: Correlated Effects Model with Small-Sample Corrections   
##   
## Model: log(es) ~ 1   
##   
## Number of studies = 58   
## Number of outcomes = 118 (min = 1 , mean = 2.03 , median = 2 , max = 11 )  
## Rho = 0.8   
## I.sq = 76.87278   
## Tau.sq = 0.3519515   
##   
## Estimate StdErr t-value dfs P(|t|>) 95% CI.L 95% CI.U Sig  
## 1 X.Intercept. -0.326 0.108 -3.01 49.4 0.00416 -0.544 -0.108 \*\*\*  
## ---  
## Signif. codes: < .01 \*\*\* < .05 \*\* < .10 \*  
## ---  
## Note: If df < 4, do not trust the results

Anti-log the estimate and confidence intervals to get odds ratios

( model1.eff <- data.frame( OddsRatioEstimate=round( exp( m1$reg\_table$b.r ), digits = 2 ),   
 LCI=round( exp( m1$reg\_table$CI.L ), digits = 2 ),  
 UCI=round( exp( m1$reg\_table$CI.U ), digits = 2 )   
 )   
 )

## OddsRatioEstimate LCI UCI  
## 1 0.72 0.58 0.9

#save(model1.eff, file='model1.eff.RData')

Marginal weighted mean effect estimates () compatible with our data range from 0.58 (lower bound 95% CI) to 0.90 (upper bound 95% CI) with a point estimate of . Having an RSV LRTI relative to non-RSV LRTI is associated with a 10-42% reduction in odds for subsequent wheezing illness. An increase in the odds of subsequent wheezing illness with RSV LRTI vs. non-RSV LRTI is not compatible with our data with .

Conduct a sensitivity analysis to see if selection of values of (an estimate of the within study correlation among effect sizes) alters the results in any meaningful way. (Specification of a value for is needed to calculate efficient weights.)

sensitivity( m1 )

## RVE: Correlated Effects Model with Small-Sample Corrections   
## Model: log(es) ~ 1   
##   
## Sensitivity Analysis   
##   
## Rho = 0 Rho = 0.2 Rho = 0.4 Rho = 0.6 Rho = 0.8  
## X.Intercept. Coefficient -0.326 -0.326 -0.326 -0.326 -0.326   
## Std. Error 0.108 0.108 0.108 0.108 0.108   
## Tau.sq Estimate 0.351 0.351 0.352 0.352 0.352   
## Rho = 1  
## -0.326   
## 0.108   
## 0.352

We see that the value of , whether it is 0 or 1, makes no meaningful difference in estimates of coefficients, standard errors, or .

# Adjusted model

Add predictors coding whether studies limited exposure ascertainment to the first year of life (**exp.012**), adjusted for genetic confounding (**mingen**), and whether hospitalization/emergency care was required for LRTI exposure (**hosp**). The intercept of this model is the weighed mean effect size when all covariates are held at their reference values representing the modal (most common) level.

m2 <- robu( log( es ) ~ exp.012 + mingen + relevel( hosp, ref = 'Emergency/Hospitalization Required'),   
 studynum = record\_id,   
 var.eff.size = es.se^2,  
 data = dfsub,  
 modelweights = 'CORR',  
 small = T  
 )  
options( digits = 2 )  
print( m2 )

## RVE: Correlated Effects Model with Small-Sample Corrections   
##   
## Model: log(es) ~ exp.012 + mingen + relevel(hosp, ref = "Emergency/Hospitalization Required")   
##   
## Number of studies = 58   
## Number of outcomes = 118 (min = 1 , mean = 2.03 , median = 2 , max = 11 )  
## Rho = 0.8   
## I.sq = 70   
## Tau.sq = 0.44   
##   
##   
## 1 X.Intercept.  
## 2 exp.012Limited.to.first.year.of.life  
## 3 mingenAdjustment  
## 4 relevel.hosp..ref....Emergency.Hospitalization.Required..Emergency.Hospitalization.Not.Required  
## Estimate StdErr t-value dfs P(|t|>) 95% CI.L 95% CI.U Sig  
## 1 -0.50528 0.147 -3.4449 32.11 0.00161 -0.804 -0.207 \*\*\*  
## 2 0.33613 0.229 1.4675 35.21 0.15111 -0.129 0.801   
## 3 -0.00822 0.295 -0.0279 14.80 0.97813 -0.637 0.621   
## 4 0.32518 0.338 0.9607 6.86 0.36932 -0.479 1.129   
## ---  
## Signif. codes: < .01 \*\*\* < .05 \*\* < .10 \*  
## ---  
## Note: If df < 4, do not trust the results

( model2.eff <- data.frame( Predictor=c('Intercept','Exposure Ascertainment Period','Genetic Adjustment','Emergency Care or Hospitalization Required'),  
 df= m2$reg\_table$dfs,   
 OR=round( exp( m2$reg\_table$b.r ), digits = 2 ),   
 LCI=round( exp( m2$reg\_table$CI.L ), digits = 2 ),  
 UCI=round( exp( m2$reg\_table$CI.U ), digits = 2 )  
 )  
 )

## Predictor df OR LCI UCI  
## 1 Intercept 32.1 0.60 0.45 0.81  
## 2 Exposure Ascertainment Period 35.2 1.40 0.88 2.23  
## 3 Genetic Adjustment 14.8 0.99 0.53 1.86  
## 4 Emergency Care or Hospitalization Required 6.9 1.38 0.62 3.09

save( model2.eff, file='model2.eff.RData')

The adjusted weighted mean odds ratio, holding all covariates at their modal levels, was with values from 0.45 to 0.81 compatible with our data. There is insufficient evidence that any of the covariates modify the effects of RSV LRTI vs non-RSV LRTI on subsequent wheezing illness. `

Again, we see from the sensitivity analysis below that the value of provided in the analysis makes no practical difference.

sensitivity( m2 )

## RVE: Correlated Effects Model with Small-Sample Corrections   
## Model: log(es) ~ exp.012 + mingen + relevel(hosp, ref = "Emergency/Hospitalization Required")   
##   
## Sensitivity Analysis   
##   
##   
## X.Intercept.   
##   
## exp.012Limited.to.first.year.of.life   
##   
## mingenAdjustment   
##   
## relevel.hosp..ref....Emergency.Hospitalization.Required..Emergency.Hospitalization.Not.Required  
##   
## Tau.sq   
## Rho = 0 Rho = 0.2 Rho = 0.4 Rho = 0.6 Rho = 0.8 Rho = 1   
## Coefficient -0.50490 -0.50500 -0.50509 -0.50519 -0.50528 -0.50538  
## Std. Error 0.14671 0.14670 0.14669 0.14668 0.14668 0.14667  
## Coefficient 0.33561 0.33574 0.33587 0.33600 0.33613 0.33627  
## Std. Error 0.22898 0.22900 0.22902 0.22903 0.22905 0.22907  
## Coefficient -0.00794 -0.00801 -0.00808 -0.00815 -0.00822 -0.00829  
## Std. Error 0.29470 0.29471 0.29472 0.29473 0.29474 0.29474  
## Coefficient 0.32519 0.32519 0.32518 0.32518 0.32518 0.32517  
## Std. Error 0.33810 0.33819 0.33828 0.33837 0.33846 0.33856  
## Estimate 0.44035 0.44131 0.44227 0.44323 0.44420 0.44516

```r  
m2a <- robu( log( es ) ~ relevel( exp.012, ref = 'Limited to first year of life') + mingen + relevel( hosp, ref = 'Emergency/Hospitalization Required'),   
 studynum = record\_id,   
 var.eff.size = es.se^2,  
 data = dfsub,  
 modelweights = 'CORR',  
 small = T  
 )  
print( m2a )

## RVE: Correlated Effects Model with Small-Sample Corrections   
##   
## Model: log(es) ~ relevel(exp.012, ref = "Limited to first year of life") + mingen + relevel(hosp, ref = "Emergency/Hospitalization Required")   
##   
## Number of studies = 58   
## Number of outcomes = 118 (min = 1 , mean = 2.03 , median = 2 , max = 11 )  
## Rho = 0.8   
## I.sq = 70   
## Tau.sq = 0.44   
##   
##   
## 1 X.Intercept.  
## 2 relevel.exp.012..ref....Limited.to.first.year.of.life..Not.limited.to.first.year.of.life  
## 3 mingenAdjustment  
## 4 relevel.hosp..ref....Emergency.Hospitalization.Required..Emergency.Hospitalization.Not.Required  
## Estimate StdErr t-value dfs P(|t|>) 95% CI.L 95% CI.U Sig  
## 1 -0.16915 0.204 -0.8288 16.75 0.419 -0.600 0.262   
## 2 -0.33613 0.229 -1.4675 35.21 0.151 -0.801 0.129   
## 3 -0.00822 0.295 -0.0279 14.80 0.978 -0.637 0.621   
## 4 0.32518 0.338 0.9607 6.86 0.369 -0.479 1.129   
## ---  
## Signif. codes: < .01 \*\*\* < .05 \*\* < .10 \*  
## ---  
## Note: If df < 4, do not trust the results

( model2a.eff <- data.frame( OddsRatioEstimate=round( exp( m2a$reg\_table$b.r ), digits = 2 ),   
 LCI=round( exp( m2a$reg\_table$CI.L ), digits = 2 ),  
 UCI=round( exp( m2a$reg\_table$CI.U ), digits = 2 ),  
 Predictor=c('Intercept','Exposure Period','Genetic Adjustment','Emergency/Hospitalization')  
 )   
 )

## OddsRatioEstimate LCI UCI Predictor  
## 1 0.84 0.55 1.3 Intercept  
## 2 0.71 0.45 1.1 Exposure Period  
## 3 0.99 0.53 1.9 Genetic Adjustment  
## 4 1.38 0.62 3.1 Emergency/Hospitalization

save( model2a.eff, file='model2a.eff.RData')