

PVS analysis

Nkosi Sampson

2024-08-19

```
library(readxl)
library(ggplot2)
library(reshape2)
library(ggpubr)
library(dplyr)
library(corrplot)
library(Hmisc)
```

```
t_lm <- readxl::read_excel("LASI_DAD_neuroimaging_withIDs.xlsx")
wmpv<- readr::read_csv("wmPVSnew.csv")
bgpv<- readr::read_csv("bgPVSnew.csv")
```

```
pvsNew <- left_join(wmpv, bgpv, "Subject")
pvsNew$wm_vol = pvsNew$wm_volume
pvsNew$bg_vol = pvsNew$bg_volume
pvsNew$pvs_wm_vol = pvsNew$wm_pvs_volume
pvsNew$pvs_bg_vol = pvsNew$bg_pvs_volume
```

```
# Calculate the mean for each variable for each BaseID
vars_to_average <- c('pvs_wm_vol', 'wm_vol', 'pvs_bg_vol', 'bg_vol')

# Extract the base ID (removing the '_1' or '_2' suffix)
pvsNew <- pvsNew %>%
  mutate(BaseID = sub("_[12]$", "", Subject)) %>%
  group_by(BaseID) %>%
  summarise(across(all_of(vars_to_average), mean, na.rm = TRUE))
```

Data Cleaning

```
## Warning: There was 1 warning in 'summarise()'.
## i In argument: 'across(all_of(vars_to_average), mean, na.rm = TRUE)'.
## i In group 1: 'BaseID = "2YZJ5G"'.
## Caused by warning:
## ! The '...' argument of 'across()' is deprecated as of dplyr 1.1.0.
## Supply arguments directly to '.fns' through an anonymous function instead.
##
## # Previously
## across(a:b, mean, na.rm = TRUE)
```

```
##
## # Now
## across(a:b, \(x) mean(x, na.rm = TRUE))
```

#There are 126 observations in the t_lm dataste and 118 in the WMPav dataset. Which ones are in the one and not the other?

```
# Identify which BaseIDs in t_lm are not in WMPVav
missing_ids1 <- setdiff(t_lm$SubjectID, pvsNew$BaseID)
print(missing_ids1)
```

```
## [1] "5JP3BN" "82GNEE" "B5GZ5Z" "BMR3PH" "DOFXYN" "ECX6X7"
## [7] "KA8PQN" "PZDMS8" "RJP7L" "Scan_003" "T2DQ2J" "YGZBGR"
## [13] "ZAJXLD" "ZJSF2H"
```

#Looks like there are also some observations in the WMPVav dataset that aren't in the t_lm dataset. These are:

```
# Identify which BaseIDs in t_lm are not in WMPVav
missing_ids2 <- setdiff(pvsNew$BaseID, t_lm$SubjectID)
print(missing_ids2)
```

```
## [1] "DKZ36X" "HJHMMN" "HWABB4" "JBYGHJ" "XZ95WG"
```

```
# Filter out the scans from t_lm that are not in WMPVav
filtered_t_lm <- t_lm %>%
  filter(!SubjectID %in% missing_ids1)

# Display the resulting filtered dataset
print(filtered_t_lm)
```

```
## # A tibble: 112 x 43
##   SubjectID ImageID prim_key Age Sex EducationYears hmse_score at_risk
##   <chr>      <dbl> <dbl> <dbl> <dbl> <dbl> <dbl> <dbl>
## 1 2YZJ5G 1130396 1.27e14 63 0 11 27 1
## 2 42NSBC 1017575 1.29e14 69 1 0 15 1
## 3 4C5G6B 1257305 1.19e14 70 1 0 18 0
## 4 5CQ5AE 1026211 1.29e14 72 0 5 26 1
## 5 6SFEH8 1287417 1.19e14 61 0 3 29 1
## 6 7BECRF 1007458 1.29e14 62 0 12 28 0
## 7 7XH95C 1283511 1.19e14 76 1 7 26 1
## 8 89PEPN 1168591 1.27e14 68 1 11 28 0
## 9 8YFJ5J 1030788 1.29e14 80 1 4 26 1
## 10 98LMPT 1010523 1.29e14 70 0 9 29 1
## # i 102 more rows
## # i 35 more variables: lasi_score <dbl>, Literate <dbl>, Urban <dbl>,
## # Rural <dbl>, BMI <dbl>, WMH <dbl>, eTIV <dbl>, vol_hippocampus <dbl>,
## # vol_cortex <dbl>, AirPollution_2016 <dbl>, UsesUncleanCookingFuel <dbl>,
## # UsesUncleanHouseholdFuel <dbl>, Hypertension <dbl>,
## # Depressed_TimesPerWeek <dbl>, Lonely_TimesPerWeek <dbl>,
## # WalkingFrequency <dbl>, ExerciseFrequency <dbl>, WorkFrequency <dbl>, ...
```

```
# Filter out the scans from t_lm that are not in WMPVav
filtered_pvsNew <- pvsNew %>%
  filter(!BaseID %in% missing_ids2)
```

```
# Display the resulting filtered dataset
print(filtered_pvsNew)
```

```
## # A tibble: 112 x 5
##   BaseID pvs_wm_vol  wm_vol pvs_bg_vol bg_vol
##   <chr>      <dbl>    <dbl>    <dbl>  <dbl>
## 1 2YZJ5G      3035  395905      219  38871
## 2 42NSBC       576.  331627       81  28472.
## 3 4C5G6B     2370.  318324      273  33478.
## 4 5CQ5AE     2148  438082.     250  39932.
## 5 6SFEH8     2239  340448.     108.  33078.
## 6 7BECRF      352  430546.     141  40498
## 7 7XH95C     4466.  316908.     258.  34268
## 8 89PEPN     2305  402424     474  33957
## 9 8YFJ5J     1707  289364.     214.  31158.
## 10 98LMPT     1493  375424     175  33484
## # i 102 more rows
```

```
df <- left_join(filtered_t_lm, filtered_pvsNew, by = join_by(SubjectID == BaseID))
print(df)
```

```
## # A tibble: 112 x 47
##   SubjectID ImageID prim_key  Age  Sex EducationYears hmse_score at_risk
##   <chr>      <dbl>    <dbl> <dbl> <dbl>      <dbl>    <dbl>  <dbl>
## 1 2YZJ5G    1130396  1.27e14  63   0         11         27     1
## 2 42NSBC    1017575  1.29e14  69   1          0         15     1
## 3 4C5G6B    1257305  1.19e14  70   1          0         18     0
## 4 5CQ5AE    1026211  1.29e14  72   0          5         26     1
## 5 6SFEH8    1287417  1.19e14  61   0          3         29     1
## 6 7BECRF    1007458  1.29e14  62   0         12         28     0
## 7 7XH95C    1283511  1.19e14  76   1          7         26     1
## 8 89PEPN    1168591  1.27e14  68   1         11         28     0
## 9 8YFJ5J    1030788  1.29e14  80   1          4         26     1
## 10 98LMPT    1010523  1.29e14  70   0          9         29     1
## # i 102 more rows
## # i 39 more variables: lasi_score <dbl>, Literate <dbl>, Urban <dbl>,
## #   Rural <dbl>, BMI <dbl>, WMH <dbl>, eTIV <dbl>, vol_hippocampus <dbl>,
## #   vol_cortex <dbl>, AirPollution_2016 <dbl>, UsesUncleanCookingFuel <dbl>,
## #   UsesUncleanHouseholdFuel <dbl>, Hypertension <dbl>,
## #   Depressed_TimesPerWeek <dbl>, Lonely_TimesPerWeek <dbl>,
## #   WalkingFrequency <dbl>, ExerciseFrequency <dbl>, WorkFrequency <dbl>, ...
```

```
cdr <- readxl::read_excel("H_DAD_mri_cdr_v2.xlsx")
```

```
df <- left_join(df, cdr, by = join_by(prim_key == prim_key))
print(df)
```

```
## # A tibble: 112 x 83
##   SubjectID ImageID prim_key   Age   Sex EducationYears hmse_score at_risk
##   <chr>      <dbl>   <dbl> <dbl> <dbl>      <dbl>      <dbl> <dbl>
## 1 2YZJ5G    1130396 1.27e14 63    0         11         27     1
## 2 42NSBC    1017575 1.29e14 69    1         0         15     1
## 3 4C5G6B    1257305 1.19e14 70    1         0         18     0
## 4 5CQ5AE    1026211 1.29e14 72    0         5         26     1
## 5 6SFEH8    1287417 1.19e14 61    0         3         29     1
## 6 7BECRF    1007458 1.29e14 62    0        12         28     0
## 7 7XH95C    1283511 1.19e14 76    1         7         26     1
## 8 89PEPN    1168591 1.27e14 68    1        11         28     0
## 9 8YFJ5J    1030788 1.29e14 80    1         4         26     1
## 10 98LMPT   1010523 1.29e14 70    0         9         29     1
## # i 102 more rows
## # i 75 more variables: lasi_score <dbl>, Literate <dbl>, Urban <dbl>,
## #   Rural <dbl>, BMI <dbl>, WMH <dbl>, eTIV <dbl>, vol_hippocampus <dbl>,
## #   vol_cortex <dbl>, AirPollution_2016 <dbl>, UsesUncleanCookingFuel <dbl>,
## #   UsesUncleanHouseholdFuel <dbl>, Hypertension <dbl>,
## #   Depressed_TimesPerWeek <dbl>, Lonely_TimesPerWeek <dbl>,
## #   WalkingFrequency <dbl>, ExerciseFrequency <dbl>, WorkFrequency <dbl>, ...
```

```
df$cdnew = ifelse(df$cdr == "0", 0, 1)
df$LOGpvs_bg_vol = log(df$pvs_bg_vol)
df$LOGpvs_wm_vol = log(df$pvs_wm_vol)
df$LOGAirPollution_2016 = log(df$AirPollution_2016)
df$vol_cortex = log(df$vol_cortex)
```

```
#df <- filter(df, cdrnew == "0")
```

```
# List of all fields including the response variable
all_fields <- c('Age', 'Sex', 'EducationYears', 'wm_vol', 'eTIV', 'LOGpvs_bg_vol', 'bg_vol', 'AirPollution_2016', 'vol_hippocampus', 'vol_cortex', 'Rural', 'BMI', 'WMH', 'UsesUncleanCookingFuel', 'UsesUncleanHouseholdFuel', 'Hypertension', 'Depressed_TimesPerWeek', 'Lonely_TimesPerWeek', 'WalkingFrequency', 'ExerciseFrequency', 'WorkFrequency')

dont_standardize <- c('Urban', 'Literate', 'PreparesHotMeal', 'UsesPublicTransport', 'UsesUncleanCookingFuel', 'Hypertension', 'Depressed_TimesPerWeek', 'Lonely_TimesPerWeek', 'WalkingFrequency', 'ExerciseFrequency', 'WorkFrequency')

# Custom standardization functionz
nanzscore <- function(x) {
  return((x - mean(x, na.rm = TRUE)) / sd(x, na.rm = TRUE))
}

# Standardize the data
df <- df %>%
  mutate(across(all_fields[!all_fields %in% dont_standardize], nanzscore))
```

```
#Check Assumptions of linear regression
```

```
library(ggplot2)

# List of all fields excluding the response variable
all_fields <- c('EducationYears', 'BMI', 'DiastolicBP', 'Nap_HoursPerDay', 'Chores_HoursPerDay', 'EducationYears', 'HearingTest_l', 'HearingTest_r', 'Urban', 'SystolicBP', 'Chores_HoursPerDay', 'StoreFrequency')
```

```

    'Lonely_TimesPerWeek', 'TV_HoursPerDay', 'Reading_HoursPerDay',
    'WalkingFrequency', 'Computer_HoursPerDay', 'smoking_per_day', 'AlcoholFrequency')

# Function to create partial residual plots for a given variable
create_partial_residual_plot <- function(variable, full_model_formula, df) {

  # Skip the "Sex" variable
  if (variable == "Sex" ) {
    print("Skipping variable 'Sex'")
    return(NULL)
  }

  # Define the reduced model formula by removing the current variable
  reduced_model_formula <- as.formula(paste("LOGpvs_bg_vol ~", paste(setdiff(all.vars(full_model_formula),
    variable), collapse = " "), sep = ""))

  # Use complete cases to ensure no missing values
  complete_cases <- complete.cases(df[all.vars(full_model_formula)])
  df_complete <- df[complete_cases, ]

  # Fit the models and handle errors
  full_model <- tryCatch(lm(full_model_formula, data = df_complete), error = function(e) NULL)
  reduced_model <- tryCatch(lm(reduced_model_formula, data = df_complete), error = function(e) NULL)

  # If the models cannot be fitted, skip this variable
  if (is.null(full_model) || is.null(reduced_model)) {
    print(paste("Skipping variable due to singularity or other issues:", variable))
    return(NULL)
  }

  # Calculate residuals from the reduced model
  residuals_reduced <- resid(reduced_model)

  # Extract the coefficient for the predictor of interest from the full model
  beta_X <- tryCatch(coef(full_model)[variable], error = function(e) NULL)

  # Check if the coefficient could be extracted
  if (is.null(beta_X)) {
    print(paste("Skipping variable due to coefficient extraction issue:", variable))
    return(NULL)
  }

  # Extract the values of the predictor of interest
  X_values <- df_complete[[variable]]

  # Calculate partial residuals
  partial_residuals <- residuals_reduced + beta_X * X_values

  # Create the plot using ggplot2
  p <- ggplot(data.frame(X_values, partial_residuals), aes(x = X_values, y = partial_residuals)) +
    geom_point() +
    geom_smooth(method = "lm", col = "red") +
    labs(x = variable, y = "Partial Residuals", title = paste("Partial Residual Plot for", variable))
}

```

```

    return(p)
  }

  # Store all plots in a list
  plot_list <- list()

  # Outer loop through each variable in the list to build the full model
  for (full_model_variable in all_fields) {
    full_model_formula <- as.formula(paste("LOGpvs_bg_vol ~ Age + Sex + eTIV + bg_vol +", full_model_vari

    # Inner loop to create partial residual plots for each variable in the full model
    for (variable in c('Age', 'Sex', 'eTIV', 'bg_vol', full_model_variable)) {
      plot <- create_partial_residual_plot(variable, full_model_formula, df)
      if (!is.null(plot)) {
        plot_list <- c(plot_list, list(plot))
      }
    }
  }

  # Save all plots to a multi-page PDF file
  pdf("partial_residual_plots.pdf", width = 8.5, height = 11) # Standard page size, adjust if needed
  for (p in plot_list) {
    print(p)
  }
  dev.off()

```

```
library(car)
```

```
## Loading required package: carData
```

```
##
```

```
## Attaching package: 'car'
```

```
## The following object is masked from 'package:dplyr':
```

```
##
```

```
## recode
```

```
# List of all fields
```

```
all_fields <- c( 'EducationYears', 'Age', 'Sex', 'eTIV', 'bg_vol', 'logWMHvol', 'SystolicBP', 'BMI', 'C
  'UsesPublicTransport', 'WorkFrequency', 'Depressed_TimesPerWeek', 'Literate',
  'PreparesHotMeal', 'AirPollution_2016', 'Nap_HoursPerDay', 'ExerciseFrequency',
  'Lonely_TimesPerWeek', 'UsesUncleanHouseholdFuel', 'TV_HoursPerDay', 'Reading_HoursPer
  'WalkingFrequency', 'EducationYears', 'UsesUncleanCookingFuel',
  'smoking_per_day', 'HearingTest', 'AlcoholFrequency', 'Urban', 'Literate', 'PreparesHot
```

```
# Loop through each variable in the list
```

```
for (variable in all_fields) {
  # Define the formula for the linear model
  formula <- as.formula(paste("LOGpvs_wm_vol ~ Age + Sex + eTIV + wm_vol +", variable))

```

```
# Fit the linear model
```

```
lm_model <- lm(formula, data = df)
```

```

#plot(resid(lm_model))

# Perform the Kolmogorov-Smirnov test
ks_test <- ks.test(resid(lm_model), "pnorm", mean = mean(resid(lm_model)), sd = sd(resid(lm_model)))

# Calculate the VIF values
vif_values <- vif(lm_model)

# Check for p-value < 0.05
if (ks_test$p.value < 0.05) {
  print(paste("Warning: p-value < 0.05 for variable:", variable))
}

# Check for VIF > 5
if (any(vif_values > 5)) {
  print(paste("Warning: VIF > 5 for variable:", variable))
}
}

```

```
## [1] "Warning: p-value < 0.05 for variable: DiastolicBP"
```

This process was repeated for the model with LOGpvs_bg_vol as the response variable

#Additional R squared analysis

```

# List of all fields including the response variable
all_fields <- c('EducationYears', 'AirPollution_2016', 'Age', 'Sex', 'wm_vol', 'SystolicBP', 'BMI', 'Cholesterol',
               'UsesPublicTransport', 'WorkFrequency', 'Depressed_TimesPerWeek', 'Literate',
               'PreparesHotMeal', 'Nap_HoursPerDay', 'ExerciseFrequency',
               'Lonely_TimesPerWeek', 'UsesUncleanHouseholdFuel', 'TV_HoursPerDay', 'Reading_HoursPerDay',
               'WalkingFrequency', 'EducationYears', 'Computer_HoursPerDay', 'UsesUncleanCookingFuel',
               'smoking_per_day', 'HearingTest', 'AlcoholFrequency')

dont_standardize <- c('Urban', 'Literate', 'PreparesHotMeal', 'UsesPublicTransport', 'UsesUncleanCookingFuel')

# Custom standardization function
nanzscore <- function(x) {
  return((x - mean(x, na.rm = TRUE)) / sd(x, na.rm = TRUE))
}

# Standardize the data
df_std <- df %>%
  mutate(across(all_fields[!all_fields %in% dont_standardize], nanzscore))

# Baseline model
mdl_baseline <- lm(LOGpvs_wm_vol ~ Age + Sex + eTIV + wm_vol + logWMHvol, data = df_std)
summary(mdl_baseline)

```

```
##
## Call:
```

```
## lm(formula = LOGpvs_wm_vol ~ Age + Sex + eTIV + wm_vol + logWMHvol,
##     data = df_std)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -1.7898 -0.3955  0.1233  0.4260  1.3984
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)  4.57770    0.65359   7.004 2.37e-10 ***
## Age          0.03700    0.07099   0.521  0.6033
## Sex          0.15898    0.07876   2.019  0.0461 *
## eTIV         0.01743    0.10862   0.160  0.8728
## wm_vol       0.21022    0.10517   1.999  0.0482 *
## logWMHvol    0.79269    0.16544   4.791 5.42e-06 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.6504 on 106 degrees of freedom
## Multiple R-squared:  0.2657, Adjusted R-squared:  0.2311
## F-statistic: 7.672 on 5 and 106 DF,  p-value: 3.449e-06
```

```
# Calculate baseline R-squared
```

```
explain_variance_baseline <- summary mdl_baseline)$r.squared
```

```
all_fields_predictors <- all_fields
```

```
# Initialize output dataframe
```

```
pvsWM_out_all <- data.frame(field_name = all_fields_predictors,
                             add_Rsquared = numeric(length(all_fields_predictors)),
                             t = numeric(length(all_fields_predictors)),
                             p = numeric(length(all_fields_predictors)))
```

```
# Analyze each field
```

```
for (i in seq_along(all_fields_predictors)) {
  formula_str <- paste('LOGpvs_wm_vol ~ Age + Sex + eTIV + wm_vol + logWMHvol +', all_fields_predictors[i])
  mdl_i <- lm(as.formula(formula_str), data = df_std)
  summary_i <- summary(mdl_i)
```

```
# Extract coefficient index correctly (depends on how many predictors you have)
```

```
coeff_index <- which(names(coef(mdl_i)) == all_fields_predictors[i])
```

```
pvsWM_out_all$t[i] <- coef(summary_i)[coeff_index, "t value"]
```

```
pvsWM_out_all$p[i] <- coef(summary_i)[coeff_index, "Pr(>|t|)"]
```

```
pvsWM_out_all$add_Rsquared[i] <- round((summary_i$r.squared - explain_variance_baseline) * 100, 1)
```

```
}
```

```
# Adjust p-values using Benjamini-Hochberg method
```

```
pvsWM_out_all$p_wo_rural_FDR <- p.adjust(pvsWM_out_all$p, method = "BH")
```

```
# Sort by additional R-squared
```

```
pvsWM_out_all <- pvsWM_out_all[order(-pvsWM_out_all$add_Rsquared), ]
```

```
# Display the additional R-squared table
```



```
print(pvsWM_out_all)
```

##	field_name	add_Rsquared	t	p
## 2	AirPollution_2016	28.4	8.13707074	8.755791e-13
## 9	Urban	11.7	4.46337746	2.035329e-05
## 17	Nap_HoursPerDay	4.0	2.46480638	1.533047e-02
## 8	Chores_HoursPerDay	3.6	-2.32412675	2.204413e-02
## 20	UsesUncleanHouseholdFuel	2.9	-2.07536674	4.039622e-02
## 11	StoreFrequency	2.4	1.90083287	6.006599e-02
## 28	HearingTest	1.9	-0.67668994	5.001196e-01
## 14	Depressed_TimesPerWeek	1.8	1.61257841	1.098379e-01
## 7	BMI	1.3	-1.13386164	2.594847e-01
## 15	Literate	1.3	1.35736473	1.775757e-01
## 18	ExerciseFrequency	1.1	1.23855103	2.182736e-01
## 26	UsesUncleanCookingFuel	1.1	-1.23638956	2.190723e-01
## 13	WorkFrequency	0.9	1.15694220	2.499213e-01
## 22	Reading_HoursPerDay	0.8	-1.05856427	2.922274e-01
## 1	EducationYears	0.7	0.99227790	3.233432e-01
## 24	EducationYears	0.7	0.99227790	3.233432e-01
## 12	UsesPublicTransport	0.5	-0.81189233	4.186902e-01
## 25	Computer_HoursPerDay	0.5	0.83020178	4.083084e-01
## 21	TV_HoursPerDay	0.4	0.72389892	4.707376e-01
## 29	AlcoholFrequency	0.3	1.45513168	1.486446e-01
## 23	WalkingFrequency	0.2	0.56578838	5.727448e-01
## 10	DiastolicBP	0.1	0.32115297	7.487328e-01
## 3	Age	0.0	0.52123871	6.032878e-01
## 4	Sex	0.0	2.01860033	4.605386e-02
## 5	wm_vol	0.0	1.99874618	4.819577e-02
## 6	SystolicBP	0.0	-0.20859737	8.351667e-01
## 16	PreparesHotMeal	0.0	-0.02064381	9.835690e-01
## 19	Lonely_TimesPerWeek	0.0	0.24366681	8.079643e-01
## 27	smoking_per_day	-0.1	1.25785056	2.112627e-01
##	p_wo_rural_FDR			
## 2		2.539179e-11		
## 9		2.951227e-04		
## 17		1.481945e-01		
## 8		1.598199e-01		
## 20		1.996682e-01		
## 11		2.177392e-01		
## 28		6.305855e-01		
## 14		3.539220e-01		
## 7		4.703161e-01		
## 15		4.537927e-01		
## 18		4.537927e-01		
## 26		4.537927e-01		
## 13		4.703161e-01		
## 22		4.935238e-01		
## 1		4.935238e-01		
## 24		4.935238e-01		
## 12		5.781912e-01		
## 25		5.781912e-01		
## 21		6.205177e-01		
## 29		4.310694e-01		

```
## 23 6.920666e-01
## 10 8.351251e-01
## 3 6.998138e-01
## 4 1.996682e-01
## 5 1.996682e-01
## 6 8.649941e-01
## 16 9.835690e-01
## 19 8.649941e-01
## 27 4.537927e-01
```

```
summary(lm(LOGpvs_wm_vol ~ Age + Sex + eTIV + wm_vol + logWMHvol, df_std))
```

```
##
## Call:
## lm(formula = LOGpvs_wm_vol ~ Age + Sex + eTIV + wm_vol + logWMHvol,
##     data = df_std)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -1.7898 -0.3955  0.1233  0.4260  1.3984
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)  4.57770    0.65359   7.004 2.37e-10 ***
## Age          0.03700    0.07099   0.521  0.6033
## Sex          0.15898    0.07876   2.019  0.0461 *
## eTIV         0.01743    0.10862   0.160  0.8728
## wm_vol       0.21022    0.10517   1.999  0.0482 *
## logWMHvol    0.79269    0.16544   4.791 5.42e-06 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.6504 on 106 degrees of freedom
## Multiple R-squared:  0.2657, Adjusted R-squared:  0.2311
## F-statistic: 7.672 on 5 and 106 DF, p-value: 3.449e-06
```

```
# List of all fields including the response variable
```

```
all_fields <- c('EducationYears', 'AirPollution_2016', 'Age', 'Sex', 'wm_vol', 'SystolicBP', 'BMI', 'Cholesterol',
               'UsesPublicTransport', 'WorkFrequency', 'Depressed_TimesPerWeek', 'Literate',
               'PreparesHotMeal', 'Nap_HoursPerDay', 'ExerciseFrequency',
               'Lonely_TimesPerWeek', 'UsesUncleanHouseholdFuel', 'TV_HoursPerDay', 'Reading_HoursPerDay',
               'WalkingFrequency', 'EducationYears', 'Computer_HoursPerDay', 'UsesUncleanCookingFuel',
               'smoking_per_day', 'HearingTest', 'AlcoholFrequency')
```

```
dont_standardize <- c('Urban', 'Literate', 'PreparesHotMeal', 'UsesPublicTransport', 'UsesUncleanCookingFuel')
```

```
# Custom standardization function
```

```
nanzscore <- function(x) {
  return((x - mean(x, na.rm = TRUE)) / sd(x, na.rm = TRUE))
}
```

```
# Standardize the data
```

```
df_std <- df %>%
  mutate(across(all_fields[!all_fields %in% dont_standardize], nanzscore))

# Baseline model
mdl_baseline <- lm(LOGpvs_bg_vol ~ Age + Sex + eTIV + bg_vol, data = df_std)
summary(mdl_baseline)
```

```
##
## Call:
## lm(formula = LOGpvs_bg_vol ~ Age + Sex + eTIV + bg_vol, data = df_std)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -2.29204 -0.59989 -0.06056  0.46771  2.61631
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept) -2.327e-16  8.419e-02   0.000 1.000000
## Age          3.389e-01  9.120e-02   3.716 0.000324 ***
## Sex          1.423e-01  1.109e-01   1.283 0.202273
## eTIV         1.863e-02  1.104e-01   0.169 0.866358
## bg_vol       5.214e-01  1.078e-01   4.838 4.43e-06 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.891 on 107 degrees of freedom
## Multiple R-squared:  0.2348, Adjusted R-squared:  0.2062
## F-statistic: 8.207 on 4 and 107 DF, p-value: 8.228e-06
```

```
# Calculate baseline R-squared
explain_variance_baseline <- summary(mdl_baseline)$r.squared
```

```
all_fields_predictors <- all_fields
```

```
# Initialize output dataframe
```

```
pvsWM_out_all <- data.frame(field_name = all_fields_predictors,
                             add_Rsquared = numeric(length(all_fields_predictors)),
                             t = numeric(length(all_fields_predictors)),
                             p = numeric(length(all_fields_predictors)))
```

```
# Analyze each field
```

```
for (i in seq_along(all_fields_predictors)) {
  formula_str <- paste('LOGpvs_bg_vol ~ Age + Sex + eTIV + bg_vol +', all_fields_predictors[i])
  mdl_i <- lm(as.formula(formula_str), data = df_std)
  summary_i <- summary(mdl_i)
```

```
# Extract coefficient index correctly (depends on how many predictors you have)
coeff_index <- which(names(coef(mdl_i)) == all_fields_predictors[i])
```

```
pvsWM_out_all$t[i] <- coef(summary_i)[coeff_index, "t value"]
pvsWM_out_all$p[i] <- coef(summary_i)[coeff_index, "Pr(>|t|)"]
pvsWM_out_all$add_Rsquared[i] <- round((summary_i$r.squared - explain_variance_baseline) * 100, 1)
```

```

}

# Adjust p-values using Benjamini-Hochberg method
pvsWM_out_all$p_wo_rural_FDR <- p.adjust(pvsWM_out_all$p, method = "BH")

# Sort by additional R-squared
pvsWM_out_all <- pvsWM_out_all[order(-pvsWM_out_all$add_Rsquared), ]

# Display the additional R-squared table
print(pvsWM_out_all)

```

```

##           field_name add_Rsquared      t      p
## 2      AirPollution_2016      12.1  4.46689485 1.991793e-05
## 6           SystolicBP      10.5  4.10869904 7.858881e-05
## 9              Urban      10.2  4.04040908 1.012630e-04
## 5              wm_vol       4.1 -2.45640394 1.565740e-02
## 10         DiastolicBP       3.1  2.12663589 3.577093e-02
## 12    UsesPublicTransport       2.9 -2.03265828 4.458689e-02
## 8      Chores_HoursPerDay       2.2 -1.76785032 7.996324e-02
## 18     ExerciseFrequency       1.8  1.57696759 1.177828e-01
## 15           Literate       1.3  1.33895332 1.834502e-01
## 17      Nap_HoursPerDay       1.3  1.34869774 1.803085e-01
## 14  Depressed_TimesPerWeek       1.2  1.31776476 1.904233e-01
## 20  UsesUncleanHouseholdFuel       0.9 -1.09526328 2.758837e-01
## 7              BMI       0.6  0.76927678 4.434726e-01
## 11      StoreFrequency       0.5 -0.81714169 4.156803e-01
## 26  UsesUncleanCookingFuel       0.5 -0.80717077 4.213756e-01
## 23      WalkingFrequency       0.4  0.72954875 4.672751e-01
## 21      TV_HoursPerDay       0.3 -0.60990419 5.432305e-01
## 1      EducationYears       0.2  0.58191593 5.618589e-01
## 13      WorkFrequency       0.2  0.57493430 5.665540e-01
## 19    Lonely_TimesPerWeek       0.2  0.49957238 6.184116e-01
## 22    Reading_HoursPerDay       0.2 -0.52460881 6.009506e-01
## 24      EducationYears       0.2  0.58191593 5.618589e-01
## 16    PreparesHotMeal       0.1 -0.37659918 7.072243e-01
## 25    Computer_HoursPerDay       0.1  0.45374264 6.509417e-01
## 3              Age       0.0  3.71578640 3.240095e-04
## 4              Sex       0.0  1.28297441 2.022731e-01
## 29    AlcoholFrequency       0.0  0.48853065 6.261928e-01
## 27      smoking_per_day      -0.2 -0.08007193 9.363325e-01
## 28      HearingTest      -0.5 -1.53578387 1.276282e-01
##      p_wo_rural_FDR
## 2      0.0005776200
## 6      0.0009788757
## 9      0.0009788757
## 5      0.0908129221
## 10     0.1728928461
## 12     0.1847171356
## 8      0.2898667590
## 18     0.3701217455
## 15     0.4189942559
## 17     0.4189942559
## 14     0.4189942559

```

```
## 20 0.5333751064
## 7 0.6984457927
## 11 0.6984457927
## 26 0.6984457927
## 23 0.6984457927
## 21 0.6984457927
## 1 0.6984457927
## 13 0.6984457927
## 19 0.6984457927
## 22 0.6984457927
## 24 0.6984457927
## 16 0.7324823039
## 25 0.6991595941
## 3 0.0023490686
## 4 0.4189942559
## 29 0.6984457927
## 27 0.9363324667
## 28 0.3701217455
```

```
summary(lm(LOGpvs_bg_vol ~ Age + Sex + eTIV + bg_vol, df_std))
```

```
##
## Call:
## lm(formula = LOGpvs_bg_vol ~ Age + Sex + eTIV + bg_vol, data = df_std)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -2.29204 -0.59989 -0.06056  0.46771  2.61631
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept) -2.327e-16  8.419e-02   0.000 1.000000
## Age          3.389e-01  9.120e-02   3.716 0.000324 ***
## Sex          1.423e-01  1.109e-01   1.283 0.202273
## eTIV         1.863e-02  1.104e-01   0.169 0.866358
## bg_vol       5.214e-01  1.078e-01   4.838 4.43e-06 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.891 on 107 degrees of freedom
## Multiple R-squared:  0.2348, Adjusted R-squared:  0.2062
## F-statistic: 8.207 on 4 and 107 DF,  p-value: 8.228e-06
```

Mediation Analysis

Assumptions of linear regression were checked with the same methods as before, for each path of the mediation analysis.

```
# List of all fields including the response variable
all_fields <- c('Age', 'Sex', 'EducationYears', 'wm_vol', 'eTIV', 'LOGpvs_wm_vol', 'bg_vol', 'AirPollut
```

```

dont_standardize <- c('Urban', 'Literate', 'PreparesHotMeal', 'UsesPublicTransport', 'UsesUncleanCooking')

# Custom standardization functionz
nanzscore <- function(x) {
  return((x - mean(x, na.rm = TRUE)) / sd(x, na.rm = TRUE))
}

# Standardize the data
df_std <- df %>%
  mutate(across(all_fields[!all_fields %in% dont_standardize], nanzscore))

```

```
library(lavaan)
```

```

## This is lavaan 0.6-18
## lavaan is FREE software! Please report any bugs.

```

```

set.seed(01)

model1 <- "
# Path c' (direct effect)
LOGpvs_wm_vol ~ c*Urban + Age + Sex + EducationYears + eTIV + wm_vol + logWMHvol

#Path a
AirPollution_2016 ~ a*Urban + Age + Sex + EducationYears + eTIV + wm_vol + logWMHvol

#Path b
LOGpvs_wm_vol ~ b*AirPollution_2016 + Age + Sex + EducationYears + eTIV + wm_vol + logWMHvol

#Indirect Effect (a*b)
ab := a*b
"

# Fit the model with bootstrap resampling
fitmod1 <- sem(model1, data = df_std)

# Summarize the results with BCA confidence intervals
summary(fitmod1, fit.measures = TRUE, rsquare = TRUE, ci = TRUE)

```

```

## lavaan 0.6-18 ended normally after 1 iteration
##
##      Estimator              ML
##      Optimization method    NLMINB
##      Number of model parameters    17
##
##      Number of observations    112
##
## Model Test User Model:
##
##      Test statistic    0.000
##      Degrees of freedom    0
##

```

```

## Model Test Baseline Model:
##
##   Test statistic           149.269
##   Degrees of freedom       15
##   P-value                   0.000
##
## User Model versus Baseline Model:
##
##   Comparative Fit Index (CFI)           1.000
##   Tucker-Lewis Index (TLI)             1.000
##
## Loglikelihood and Information Criteria:
##
##   Loglikelihood user model (H0)         -242.203
##   Loglikelihood unrestricted model (H1)  -242.203
##
##   Akaike (AIC)                         518.407
##   Bayesian (BIC)                       564.621
##   Sample-size adjusted Bayesian (SABIC) 510.895
##
## Root Mean Square Error of Approximation:
##
##   RMSEA                               0.000
##   90 Percent confidence interval - lower 0.000
##   90 Percent confidence interval - upper 0.000
##   P-value H_0: RMSEA <= 0.050          NA
##   P-value H_0: RMSEA >= 0.080          NA
##
## Standardized Root Mean Square Residual:
##
##   SRMR                               0.000
##
## Parameter Estimates:
##
##   Standard errors           Standard
##   Information               Expected
##   Information saturated (h1) model Structured
##
## Regressions:
##
##           Estimate Std.Err  z-value  P(>|z|)  ci.lower ci.upper
## LOGpvs_wm_vol ~
##   Urban      (c)      0.124   0.187   0.665   0.506   -0.242   0.490
##   Age         0.190   0.075   2.528   0.011    0.043   0.338
##   Sex         0.143   0.080   1.787   0.074   -0.014   0.299
##   EducatnYrs  0.162   0.069   2.343   0.019    0.026   0.297
##   eTIV        -0.067   0.109  -0.612   0.541   -0.280   0.147
##   wm_vol      0.261   0.107   2.428   0.015    0.050   0.472
##   logWMHvol   0.762   0.172   4.442   0.000    0.426   1.098
## AirPollution_2016 ~
##   Urban      (a)      1.322   0.188   7.041   0.000    0.954   1.689
##   Age         0.002   0.091   0.023   0.982   -0.176   0.180
##   Sex         0.057   0.096   0.591   0.554   -0.132   0.246
##   EducatnYrs  -0.170   0.082  -2.085   0.037   -0.330  -0.010
##   eTIV        0.076   0.131   0.582   0.560   -0.181   0.334

```

```
##      wm_vol      0.073    0.130    0.561    0.575   -0.181    0.327
##      logWMHvol    0.095    0.207    0.459    0.646   -0.311    0.500
##      LOGpvs_wm_vol ~
##      ArPl1_2016 (b)    0.551    0.078    7.037    0.000    0.397    0.704
##
## Variances:
##              Estimate Std.Err  z-value  P(>|z|) ci.lower ci.upper
##      .LOGpvs_wm_vol    0.422    0.056    7.483    0.000    0.311    0.532
##      .AirPolltn_2016    0.615    0.082    7.483    0.000    0.454    0.776
##
## R-Square:
##              Estimate
##      LOGpvs_wm_vol    0.575
##      AirPolltn_2016    0.380
##
## Defined Parameters:
##              Estimate Std.Err  z-value  P(>|z|) ci.lower ci.upper
##      ab              0.728    0.146    4.977    0.000    0.441    1.014
```

```
# Fit separate models for paths a and b
fit_a <- lm(AirPollution_2016 ~ Urban + Age + Sex + EducationYears + eTIV + wm_vol + logWMHvol, data = d)
fit_b <- lm(LOGpvs_wm_vol ~ AirPollution_2016 + Age + Sex + EducationYears + eTIV + wm_vol + logWMHvol, data = d)

# Extract residuals
residuals_a <- residuals(fit_a)
residuals_b <- residuals(fit_b)

# Calculate correlation between residuals
correlation <- cor(residuals_a, residuals_b)

# Print the correlation
print(correlation)
```

```
## [1] -0.03475169
```

```
library(RMediation)
```

```
## Loading required package: e1071
```

```
##
```

```
## Attaching package: 'e1071'
```

```
## The following object is masked from 'package:Hmisc':
```

```
##
```

```
##      impute
```

```
## Loading required package: OpenMx
```

```
## OpenMx may run faster if it is compiled to take advantage of multiple cores.
```

```
## Loading required package: MASS
```



```
##
## Attaching package: 'MASS'

## The following object is masked from 'package:dplyr':
##
##      select

medci(mu.x = 18.76, mu.y = .03028, se.x = 2.765, se.y = 0.003539, rho = -0.03475169, alpha = 0.05, type = "ci")

## $'95% CI'
## [1] 0.3742413 0.7870480
##
## $Estimate
## [1] 0.5677127
##
## $SE
## [1] 0.1054852

# Assuming your dataframe is named df

# Fit the linear model
model <- lm(LOGpvs_wm_vol ~ Urban + Age + Sex + EducationYears + eTIV + wm_vol + logWMHvol, data = df)

# Calculate the confidence intervals for the coefficients
conf_intervals <- confint(model)

# Extract the confidence interval for Urban
conf_intervals["Urban", ]

##      2.5 %      97.5 %
## 0.3469715 0.9167652

# Load necessary package
library(boot)

##
## Attaching package: 'boot'

## The following object is masked from 'package:car':
##
##      logit

# Fit the models
model_c <- lm(LOGpvs_wm_vol ~ Urban + Age + Sex + eTIV + wm_vol + logWMHvol, data = df)
model_a <- lm(AirPollution_2016 ~ Urban + Age + Sex + eTIV + wm_vol + logWMHvol, data = df)
model_b <- lm(LOGpvs_wm_vol ~ AirPollution_2016 + Urban + Age + Sex + eTIV + wm_vol + logWMHvol, data = df)

# Extract coefficients
a <- coef(model_a)["Urban"]
b <- coef(model_b)["AirPollution_2016"]
c <- coef(model_c)["Urban"]
```

```

c_prime <- coef(model_b)["Urban"]

# Compute effects
indirect_effect <- a * b
direct_effect <- c_prime
total_effect <- abs(direct_effect) + abs(indirect_effect)
proportion_mediated <- (abs(total_effect) - abs(direct_effect)) / abs(total_effect)

# Define a function to compute the effects for bootstrapping
boot_function <- function(data, indices) {
  d <- data[indices, ] # Resample with replacement
  model_a <- lm(AirPollution_2016 ~ Urban + Age + Sex + eTIV + wm_vol + logWMHvol, data = d)
  model_b <- lm(LOGpvs_wm_vol ~ AirPollution_2016 + Urban + Age + Sex + eTIV + wm_vol + logWMHvol, data = d)
  model_c <- lm(LOGpvs_wm_vol ~ Urban + Age + Sex + eTIV + wm_vol + logWMHvol, data = d)

  a <- coef(model_a)["Urban"]
  b <- coef(model_b)["AirPollution_2016"]
  c <- coef(model_c)["Urban"]
  c_prime <- coef(model_b)["Urban"]

  indirect_effect <- a * b
  direct_effect <- c_prime
  total_effect <- abs(direct_effect) + abs(indirect_effect)
  proportion_mediated <- (abs(total_effect) - abs(direct_effect)) / abs(total_effect)

  return(c(indirect_effect, direct_effect, total_effect, proportion_mediated))
}

# Perform bootstrapping
set.seed(123)
boot_results <- boot(data = df, statistic = boot_function, R = 10000)

# Extract bootstrap estimates
bootstrap_estimates <- boot_results$t

# Calculate 95% confidence intervals
a_ci <- quantile(bootstrap_estimates[,1], c(0.025, 0.975))
b_ci <- quantile(bootstrap_estimates[,2], c(0.025, 0.975))
indirect_effect_ci <- quantile(bootstrap_estimates[,1], c(0.025, 0.975))
direct_effect_ci <- quantile(bootstrap_estimates[,2], c(0.025, 0.975))
total_effect_ci <- quantile(bootstrap_estimates[,3], c(0.025, 0.975))
proportion_mediated_ci <- quantile(bootstrap_estimates[,4], c(0.025, 0.975))

# Display results
print("Path a (Urban -> AirPollution_2016):")

## [1] "Path a (Urban -> AirPollution_2016):"

print(a)

##      Urban
## 1.297513

```

```

print("95% CI for Path a:")

## [1] "95% CI for Path a:"

print(a_ci)

##      2.5%      97.5%
## 0.3179303 0.6961586

print("Path b (AirPollution_2016 -> LOGpvs_bg_vol):")

## [1] "Path b (AirPollution_2016 -> LOGpvs_bg_vol):"

print(b)

## AirPollution_2016
##      0.3821507

print("95% CI for Path b:")

## [1] "95% CI for Path b:"

print(b_ci)

##      2.5%      97.5%
## -0.1472653 0.4899954

# Display results
print("Indirect Effect (a*b):")

## [1] "Indirect Effect (a*b):"

print(indirect_effect)

##      Urban
## 0.4958457

print("95% CI for Indirect Effect:")

## [1] "95% CI for Indirect Effect:"

print(indirect_effect_ci)

##      2.5%      97.5%
## 0.3179303 0.6961586

```

```
print("Direct Effect (c):")
```

```
## [1] "Direct Effect (c):"
```

```
print(direct_effect)
```

```
##      Urban  
## 0.1431056
```

```
print("95% CI for Direct Effect:")
```

```
## [1] "95% CI for Direct Effect:"
```

```
print(direct_effect_ci)
```

```
##      2.5%      97.5%  
## -0.1472653  0.4899954
```

```
print("Total Effect (c):")
```

```
## [1] "Total Effect (c):"
```

```
print(total_effect)
```

```
##      Urban  
## 0.6389513
```

```
print("95% CI for Total Effect:")
```

```
## [1] "95% CI for Total Effect:"
```

```
print(total_effect_ci)
```

```
##      2.5%      97.5%  
## 0.4137942 0.9777387
```

```
print("Proportion Mediated (c-c'/c):")
```

```
## [1] "Proportion Mediated (c-c'/c):"
```

```
print(proportion_mediated)
```

```
##      Urban  
## 0.7760304
```

```
print("95% CI for Proportion Mediated:")
```

```
## [1] "95% CI for Proportion Mediated:"
```

```
print(proportion_mediated_ci)
```

```
##      2.5%      97.5%  
## 0.4493164 0.9862231
```

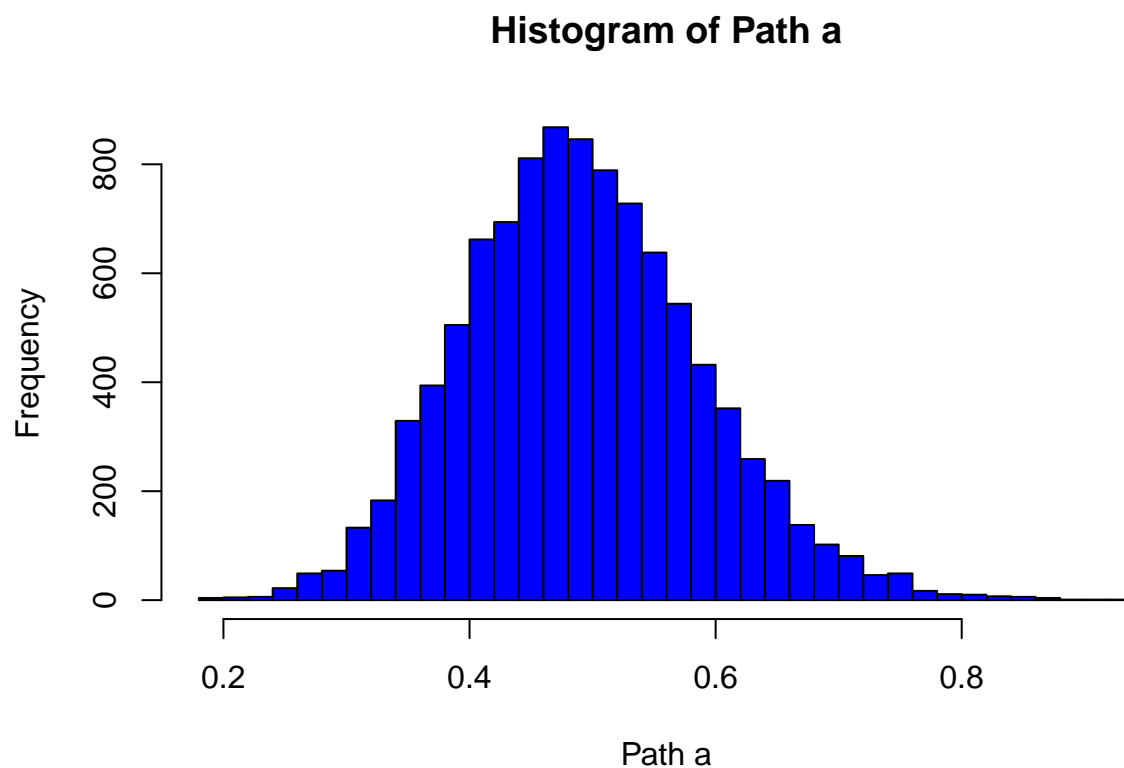
```
# Extract paths a and b from the bootstrap results
```

```
a_path <- bootstrap_estimates[, 1]
```

```
b_path <- bootstrap_estimates[, 2]
```

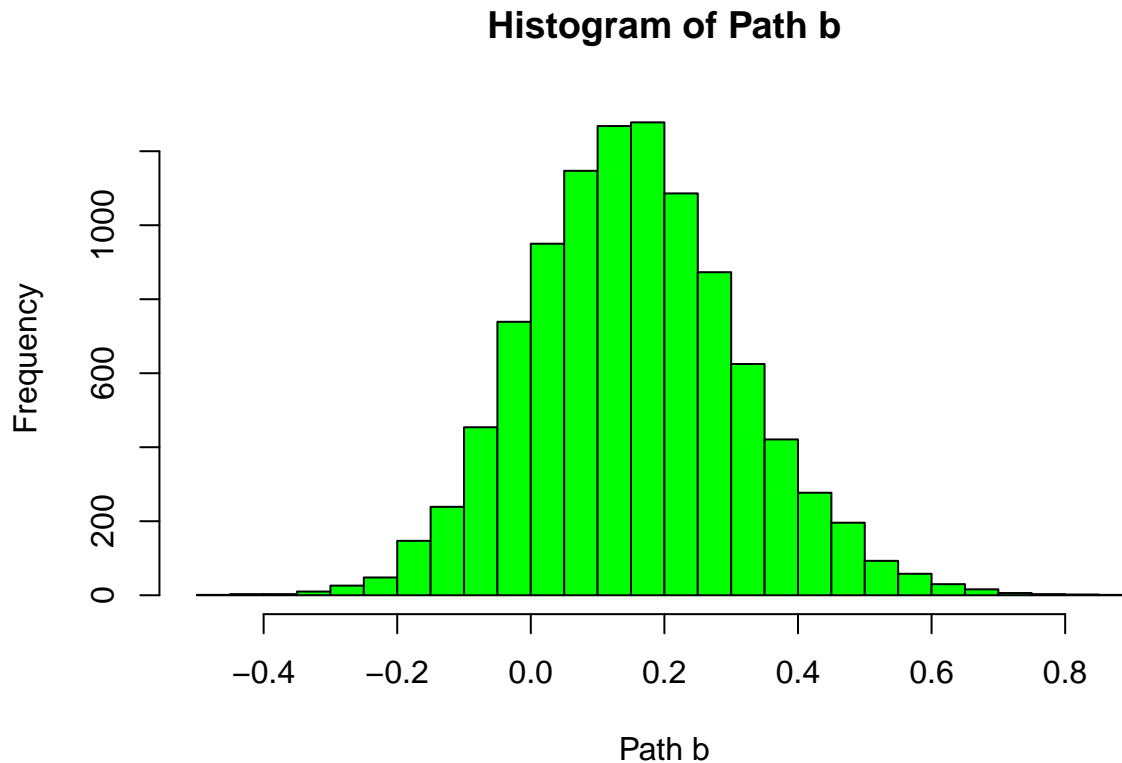
```
# Plot histogram for path a
```

```
hist(a_path, main="Histogram of Path a", xlab="Path a", col="blue", breaks=30)
```



```
# Plot histogram for path b
```

```
hist(b_path, main="Histogram of Path b", xlab="Path b", col="green", breaks=30)
```



```
# Load necessary package
library(boot)

# Fit the models
model_c <- lm(LOGpvs_bg_vol ~ Urban + Age + Sex + eTIV + bg_vol, data = df)
model_a <- lm(AirPollution_2016 ~ Urban + Age + Sex + eTIV + bg_vol, data = df)
model_b <- lm(LOGpvs_bg_vol ~ AirPollution_2016 + Urban + Age + Sex + eTIV + bg_vol, data = df)

# Extract coefficients
a <- coef(model_a)["Urban"]
b <- coef(model_b)["AirPollution_2016"]
c <- coef(model_c)["Urban"]
c_prime <- coef(model_b)["Urban"]

# Compute effects
indirect_effect <- a * b
direct_effect <- c_prime
total_effect <- abs(direct_effect) + abs(indirect_effect)
proportion_mediated <- (abs(total_effect) - abs(direct_effect)) / abs(total_effect)

# Define a function to compute the effects for bootstrapping
boot_function <- function(data, indices) {
  d <- data[indices, ] # Resample with replacement
  model_a <- lm(AirPollution_2016 ~ Urban + Age + Sex + EducationYears + eTIV + bg_vol, data = d)
  model_b <- lm(LOGpvs_bg_vol ~ AirPollution_2016 + Urban + Age + Sex + EducationYears + eTIV + bg_vol, data = d)
  model_c <- lm(LOGpvs_bg_vol ~ Urban + Age + Sex + EducationYears + eTIV + bg_vol, data = d)
```

```

a <- coef(model_a)["Urban"]
b <- coef(model_b)["AirPollution_2016"]
c <- coef(model_c)["Urban"]
c_prime <- coef(model_b)["Urban"]

indirect_effect <- a * b
direct_effect <- c_prime
total_effect <- abs(direct_effect) + abs(indirect_effect)
proportion_mediated <- (abs(total_effect) - abs(direct_effect)) / abs(total_effect)

return(c(indirect_effect, direct_effect, total_effect, proportion_mediated))
}

# Perform bootstrapping
set.seed(123)
boot_results <- boot(data = df, statistic = boot_function, R = 10000)

# Extract bootstrap estimates
bootstrap_estimates <- boot_results$t

# Calculate 95% confidence intervals
a_ci <- quantile(bootstrap_estimates[,1], c(0.025, 0.975))
b_ci <- quantile(bootstrap_estimates[,2], c(0.025, 0.975))
indirect_effect_ci <- quantile(bootstrap_estimates[,1], c(0.025, 0.975))
direct_effect_ci <- quantile(bootstrap_estimates[,2], c(0.025, 0.975))
total_effect_ci <- quantile(bootstrap_estimates[,3], c(0.025, 0.975))
proportion_mediated_ci <- quantile(bootstrap_estimates[,4], c(0.025, 0.975))

# Display results
print("Path a (Urban -> AirPollution_2016):")

## [1] "Path a (Urban -> AirPollution_2016):"

print(a)

##      Urban
## 1.325672

print("95% CI for Path a:")

## [1] "95% CI for Path a:"

print(a_ci)

##      2.5%      97.5%
## 0.09030773 0.70395092

print("Path b (AirPollution_2016 -> LOGpvs_bg_vol):")

## [1] "Path b (AirPollution_2016 -> LOGpvs_bg_vol):"

```

```

print(b)

## AirPollution_2016
##      0.2557909

print("95% CI for Path b:")

## [1] "95% CI for Path b:"

print(b_ci)

##      2.5%      97.5%
## -0.1080695  0.8970221

# Display results
print("Indirect Effect (c-c'):")

## [1] "Indirect Effect (c-c'):"

print(indirect_effect)

##      Urban
## 0.3390948

print("95% CI for Indirect Effect:")

## [1] "95% CI for Indirect Effect:"

print(indirect_effect_ci)

##      2.5%      97.5%
## 0.09030773 0.70395092

print("Direct Effect (c'):")

## [1] "Direct Effect (c'):"

print(direct_effect)

##      Urban
## 0.4229796

print("95% CI for Direct Effect:")

## [1] "95% CI for Direct Effect:"

```



```
print(direct_effect_ci)
```

```
##      2.5%      97.5%  
## -0.1080695  0.8970221
```

```
print("Total Effect (c):")
```

```
## [1] "Total Effect (c):"
```

```
print(total_effect)
```

```
##      Urban  
## 0.7620744
```

```
print("95% CI for Total Effect:")
```

```
## [1] "95% CI for Total Effect:"
```

```
print(total_effect_ci)
```

```
##      2.5%      97.5%  
## 0.4000679 1.1663594
```

```
print("Proportion Mediated (a*b/c):")
```

```
## [1] "Proportion Mediated (a*b/c):"
```

```
print(proportion_mediated)
```

```
##      Urban  
## 0.4449628
```

```
print("95% CI for Proportion Mediated:")
```

```
## [1] "95% CI for Proportion Mediated:"
```

```
print(proportion_mediated_ci)
```

```
##      2.5%      97.5%  
## 0.1098081 0.9549832
```

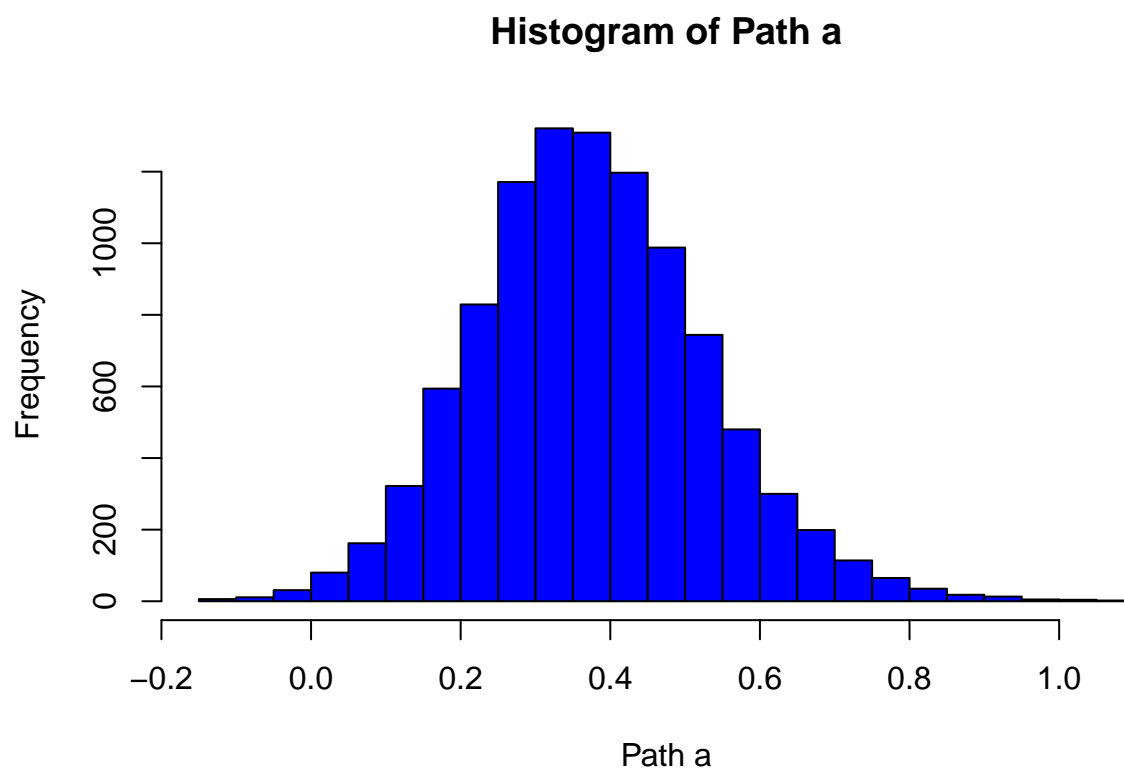
```
# Extract paths a and b from the bootstrap results
```

```
a_path <- bootstrap_estimates[, 1]
```

```
b_path <- bootstrap_estimates[, 2]
```

```
# Plot histogram for path a
```

```
hist(a_path, main="Histogram of Path a", xlab="Path a", col="blue", breaks=30)
```



```
# Plot histogram for path b  
hist(b_path, main="Histogram of Path b", xlab="Path b", col="green", breaks=30)
```

