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##### Rscript to perform the analyses from Do et al., Nature Genetics 2013 #####
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# the object "sumStat_lipids" corresponds to supplementary table 1 from Do et al., Nature Genetics 2013 which contains the summary statistics of 185 SNPs on LDL-C, HDL-C, Triglycerides and CAD. The column names "LDL_beta", "HDL_beta", "TG_beta" and "CAD_beta" containing the effect sizes associated with the three lipid traits and CAD must be present in the datatable "sumStat_lipids".
```

```
Predictors <- paste(c("LDL", "HDL", "TG"), "beta", sep = "_") # the three possible predictors on CAD are LDL-C, HDL-C and TG
```

```
resultsTable3 <- do.call("rbind", lapply(Predictors, function(predictor) {
```

```
  # 1 - Run the basis model from which the residuals will be used to run the MR on CAD
  modBasis_NULL <- lm(as.formula(paste0("CAD_beta ~ 1")), data = sumStat_lipids) # no covariate
```

```
  modBasis_1 <- lm(as.formula(paste0("CAD_beta ~ 1 + ", setdiff(Predictors, predictor)[2])), data = sumStat_lipids) # covariate 1
```

```
  modBasis_2 <- lm(as.formula(paste0("CAD_beta ~ 1 + ", setdiff(Predictors, predictor)[1])), data = sumStat_lipids) # covariate 2
```

```
  modBasis_all <- lm(as.formula(paste0("CAD_beta ~ 1 + ", paste(setdiff(Predictors, predictor), collapse = " + "))), data = sumStat_lipids) # covariate 1 and 2
```

```
  # 2- For each one of the four basis model, run the MR model on the residuals
  resAllMR <- do.call("rbind", lapply(list(modBasis_NULL, modBasis_1, modBasis_2, modBasis_all), function(modBasis){
    resMR <- summary(lm(as.formula(paste0("Residuals ~ 1 + ", predictor)), data = cbind(sumStat_lipids, Residuals = modBasis$residuals)))$coefficients[predictor, c(1, 2, 4)]
    names(resMR) <- c("Beta", "SE", "Pvalue")
    resMR <- cbind.data.frame(Covariate = paste(setdiff(names(modBasis$coefficients), "(Intercept)"), collapse = ", "), t(resMR))
    return(resMR)
  }))
```

```
  # 3- Format the results
  resAllMR <- cbind.data.frame(Outcome = "CAD_beta", Predictor = predictor, resAllMR)
  return(resAllMR)
})
```

```
# print the result table
resultsTable3
```

```
# All Predictor in the same model
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```
resultsAllLipids <- cbind.data.frame(Outcome = "CAD_beta", Predictor = Predictors,  
summary(lm(as.formula(paste0("CAD_beta ~ 1 + ", paste(Predictors, collapse = " + "))), data =  
sumStat_lipids))$coefficients[-1, c(1, 2, 4)])  
resultsAllLipids
```