TFM

Análisis preliminar para el TFM de Helena Banus.

Objetivo:

En una submuestra de 280 personas del estudio PREDIMED-Plus con datos de isoformas de APOCIII, se busca determinar la asociación entre la concentración de APOCIII y sus isoformas con la incidencia de diabetes.

Objetivos secundarios:

- Asociar la concentración de APOCIII y sus isoformas con el perfil lipídico.
- Asociar la concentración de APOCIII y sus isoformas con la hemoglobina glicosilada, la insulina y la glucosa.
- Asociar la concentración de APOCIII y sus isoformas con la adherencia a la dieta mediterránea medida con el p17 y el perfil de ácidos grasos de los alimentos.

Bases de datos utilizadas:

- Para los datos generales del PREDIMED-Plus: PREDIMEDplus 2024 01 18.dta
- Para la incidencia de diabetes: ev_diab_2023-11-14.sav
- Para la insulina: PPLUS_PRIME_HOMA_1a_01092021.xlsx
- Para la concentración de APOCIII y las isoformas: Copia Resultats glicoformes Tanda1 3.xlsx

Librerías utilizadas:

QC e intergración de las bases de datos:

Apertura de la BBDD:

```
PPlus <- read_dta("BBDD/PREDIMEDplus_2024_01_18.dta")
diab <- read_sav("BBDD/ev_diab_2023-11-14.sav")
insulina <- read_excel("BBDD/PPLUS_PRIME_HOMA_1a_01092021.xlsx")
isoformas <- read_excel("BBDD/Copia_Resultats_glicoformes_Tanda1_3.xlsx")
```

Integración de las bases de datos:

Efecto Batch de isoformas:

Compruebo efecto batch en las isoformas:

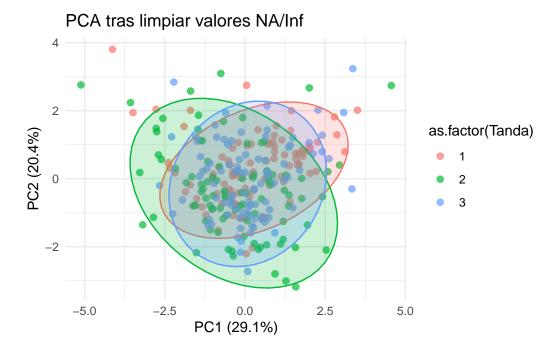
```
pca_iso_pre = isoformas[3:10]
```

Para este análisis no me complico la vida e imputo a los participantes con NAs, pero habría que revisar variable por variable cuántos NAs y dependiendo del %, plantearse si usarla o no, y cómo usarla:

```
registerDoParallel(cores=8)
set.seed(1)
IMP = missForest(as.matrix(pca iso pre), verbose = T, parallelize = "forest")
  parallelizing computation of the random forest model objects
 missForest iteration 1 in progress...done!
    estimated error(s): 0.2952273
    difference(s): 1.889283e-05
    time: 0.25 seconds
  missForest iteration 2 in progress...done!
    estimated error(s): 0.3027388
    difference(s): 9.607022e-05
    time: 0.44 seconds
IMP$00Berror
    NRMSE
0.2952273
IMP = data.frame(IMP$ximp)
Genero z-scores y hago PCA:
IMP[2:8] = scale(IMP[2:8], center = T, scale = T)
res_pca <- prcomp(IMP[2:8], center = FALSE, scale. = FALSE)</pre>
scores <- data.frame(cbind(res pca$x, Tanda = IMP$Tanda))</pre>
var_exp <- res_pca$sdev^2 / sum(res_pca$sdev^2) * 100</pre>
ggplot(scores, aes(PC1, PC2, color = as.factor(Tanda))) +
  geom_point(alpha = 0.7, size = 2) +
  stat_ellipse(aes(fill = as.factor(Tanda)), alpha = 0.2, geom = "polygon", show.legend = FALSE) +
  labs(x = paste0("PC1 (", round(var_exp[1], 1), "%)"),
```

y = paste0("PC2 (", round(var_exp[2], 1), "%)"),
title = "PCA tras limpiar valores NA/Inf") +

theme_minimal()



No parece haber efecto batch visual (good job)

```
dist_IMP = dist(IMP[2:8])
adonis2(dist_IMP ~ Tanda, data = IMP, permutations = 999)
Permutation test for adonis under reduced model
Permutation: free
Number of permutations: 999
adonis2(formula = dist_IMP ~ Tanda, data = IMP, permutations = 999)
          Df SumOfSqs
                         R2
                                  F Pr(>F)
Model
                11.15 0.00567 1.5958 0.141
Residual 280 1955.85 0.99433
Total
         281 1967.00 1.00000
dist APOC3 = dist(IMP[2])
adonis2(dist_APOC3 ~ Tanda, data = IMP, permutations = 999)
```

Confirmo que estadísticamente no hay efecto batch. Creo la base de datos de trabajo:

```
isoformas1 = data.frame(c(isoformas[2], IMP))
```

Permutation test for adonis under reduced model

```
BBDD = merge(PPlus1, isoformas1, by = "paciente")
BBDD = merge(BBDD, insulina1, by = "paciente", all.x = T)
BBDD = merge(BBDD, diab1, by = "paciente", all.x = T)
```

QC:

colnames(BBDD)

```
[1] "paciente"
                       "idcluster"
                                         grupo_int_v00"
                                                           "nodo"
 [5] "sexo s1"
                       "escola v00"
                                         "geaf tot v00"
                                                           "fuma s1"
[9] "imc_v00"
                       "glucosa_v00"
                                         "coltot_v00"
                                                           "hdl_v00"
[13] "ldl_calc_v00"
                       "trigli_v00"
                                         "hba1c_v00"
                                                           "tto_col_v00"
[17] "hc_v00"
                       "prot_v00"
                                         "gratot_v00"
                                                           "mo_v00"
                       "sa_v00"
                                         "alcoholg_v00"
[21] "po_v00"
                                                           "energiat_v00"
[25] "porc_hc_v00"
                       "porc_pr_v00"
                                         "porc_gr_v00"
                                                           "porc_mo_v00"
[29] "porc_po_v00"
                       "porc_sa_v00"
                                         "fibra v00"
                                                           "col v00"
                       "edad_s1"
                                         "Tanda"
[33] "p17_total_v00"
                                                           "ApoC3"
[37] "apoC30a_apoC31"
                       "apoC30b_apoC31" "apoC31d_apoC31"
                                                           "apoC32d_apoC31"
[41] "apoC32_apoC31"
                       "apoC30f_apoC31" "insulin_v00"
                                                           "HOMA.IR"
[45] "diabetes"
BBDD$diabetes[is.na(BBDD$diabetes)] <- 0
factores = c(3, 4, 5, 6, 8, 16, 35, 45)
BBDD[, factores] = lapply(BBDD[, factores], factor)
summary(BBDD)
```

```
paciente
                  idcluster
                                grupo_int_v00
                                                   nodo
                                                           sexo_s1 escola_v00
     : 1024
                     : 1024
                                              4
                                                           0:146
                                                                   1: 39
Min.
                Min.
                                0:157
                                                     :67
1st Qu.: 3071
                1st Qu.: 3138
                                1:125
                                              5
                                                           1:136
                                                     :48
                                                                   2: 17
Median: 4226
                Median: 4265
                                              3
                                                     :47
                                                                   3: 94
                      : 6957
Mean : 4726
                Mean
                                              1
                                                     :35
                                                                   4:130
3rd Qu.: 5294
                3rd Qu.: 6074
                                              6
                                                     :31
                                                                   5: 2
Max. :19020
                       :42303
                                              2
                                                     :29
                Max.
                                              (Other):25
 geaf_tot_v00
                  fuma_s1
                             imc_v00
                                           glucosa_v00
                                                            coltot_v00
                                          Min. : 76.0
Min. :
           0.0
                  1: 35
                          Min.
                                 :26.82
                                                          Min.
                                                                 :108.0
1st Qu.: 839.2
                  2: 10
                          1st Qu.:30.71
                                          1st Qu.:104.0
                                                          1st Qu.:177.0
Median : 2107.2
                  3: 17
                          Median :32.71
                                          Median :112.0
                                                          Median:200.0
Mean
     : 2763.3
                  4:103
                          Mean
                                :33.19
                                          Mean
                                                :113.5
                                                          Mean
                                                                 :202.6
3rd Qu.: 4010.5
                  5:115
                          3rd Qu.:35.53
                                          3rd Qu.:121.8
                                                          3rd Qu.:224.0
Max.
       :14895.1
                  9: 2
                                 :41.88
                                                 :149.0
                                                          Max.
                                                                 :311.0
                          Max.
                                          Max.
                                                          NA's
                                                                 : 1
   hdl v00
                 ldl calc v00
                                  trigli v00
                                                  hba1c v00
                                                                tto col v00
       :28.00
                Min. : 39.0
                                     : 54.0
                                                       :4.000
                                                                0:145
Min.
                                Min.
                                                Min.
1st Qu.:39.00
                1st Qu.:105.5
                                1st Qu.:101.0
                                                1st Qu.:5.660
                                                                1:136
                                                Median :5.900
Median :47.00
                Median :123.0
                                Median :132.5
                                                                9: 1
       :48.45
                       :125.2
                                       :146.4
Mean
                Mean
                                Mean
                                                Mean
                                                       :5.917
3rd Qu.:55.00
                3rd Qu.:144.0
                                3rd Qu.:173.0
                                                3rd Qu.:6.200
Max.
       :91.00
                Max.
                       :232.0
                                Max. :502.0
                                                Max.
                                                       :7.600
NA's
                NA's
                       :11
                                                NA's
                                                       :22
       : 1
                    prot_v00
    hc_v00
                                    gratot_v00
                                                       mo_v00
                 Min. : 29.50
Min.
      : 95.25
                                  Min. : 36.64
                                                   Min. : 16.66
1st Qu.:182.55
                 1st Qu.: 81.16
                                  1st Qu.: 85.75
                                                   1st Qu.: 42.44
Median :231.17
                 Median : 94.86
                                  Median :106.56
                                                   Median: 55.60
```

```
Mean
       :242.89
                 Mean : 96.37
                                 Mean
                                        :107.96
                                                  Mean : 55.33
3rd Qu.:285.75
                 3rd Qu.:111.86
                                 3rd Qu.:128.15
                                                  3rd Qu.: 66.86
       :600.92
                        :197.42
Max.
                                 Max.
                                        :210.80
                                                  Max.
                                                         :109.87
                 Max.
NA's
       :1
                 NA's
                        :1
                                        : 1
                                                  NA's
                                                         :1
    po_v00
                                                    energiat_v00
                     sa_v00
                                  alcoholg_v00
Min. : 5.291
                                 Min. : 0.000
                                                   Min.
                                                        :1051
                 Min. : 9.936
1st Qu.:13.334
                 1st Qu.:20.275
                                 1st Qu.: 1.292
                                                   1st Qu.:1926
                                 Median : 5.769
                                                   Median:2395
Median :17.193
                 Median :26.032
                                 Mean : 12.507
Mean
      :18.317
                 Mean :27.854
                                                   Mean :2416
                 3rd Qu.:34.189
                                 3rd Qu.: 18.565
                                                   3rd Qu.:2817
3rd Qu.:22.252
Max.
       :48.543
                 Max.
                       :82.991
                                 Max. :103.150
                                                   Max.
                                                        :5021
NA's
      :1
                 NA's :1
                                 NA's :1
                                                   NA's
                                                        :1
                 porc pr v00
                                 porc gr v00
                                                 porc mo v00
 porc hc v00
Min. :21.27
                Min. : 9.266
                                Min. :22.82
                                                Min. : 8.456
                                                1st Qu.:18.043
1st Qu.:35.61
                1st Qu.:14.260
                                 1st Qu.:35.69
Median :40.25
                Median :16.068
                                Median :40.72
                                                Median :20.438
Mean :40.04
                Mean :16.305
                                 Mean :40.17
                                                Mean :20.651
3rd Qu.:44.47
                3rd Qu.:18.305
                                 3rd Qu.:44.21
                                                3rd Qu.:23.040
Max.
       :55.93
                Max. :27.018
                                 Max.
                                      :56.32
                                                Max. :32.873
NA's
                                                NA's
                NA's
                       :1
                                 NA's
                                                     :1
       :1
                                       : 1
 porc_po_v00
                  porc_sa_v00
                                   fibra v00
                                                     col v00
                 Min. : 4.990
Min. : 3.732
                                 Min. : 7.154
                                                  Min. :106.4
1st Qu.: 5.513
                 1st Qu.: 8.756
                                 1st Qu.:18.772
                                                  1st Qu.:316.6
Median : 6.465
                 Median :10.190
                                                  Median :371.0
                                 Median :23.991
Mean : 6.805
                 Mean :10.273
                                 Mean
                                        :25.992
                                                  Mean :387.1
3rd Qu.: 7.740
                 3rd Qu.:11.675
                                 3rd Qu.:32.024
                                                  3rd Qu.:464.8
Max.
       :16.776
                 Max.
                       :16.116
                                 Max.
                                        :79.543
                                                  Max.
                                                        :782.1
NA's
      :1
                 NA's
                       :1
                                 NA's
                                        :1
                                                  NA's
                                                         :1
p17_total_v00
                   edad s1
                                Tanda
                                          ApoC3
                                                        apoC30a_apoC31
Min. : 1.00
                                1:94
                Min.
                       :55.00
                                      Min. :-2.1243
                                                        Min. :-1.2861
1st Qu.: 6.00
                1st Qu.:60.00
                                2:94
                                      1st Qu.:-0.6446
                                                        1st Qu.:-0.5877
Median: 8.00
                                3:94
                Median :65.00
                                      Median :-0.1518
                                                        Median :-0.1516
Mean : 7.94
                Mean
                       :64.62
                                      Mean : 0.0000
                                                        Mean : 0.0000
3rd Qu.:10.00
                3rd Qu.:68.75
                                      3rd Qu.: 0.5597
                                                        3rd Qu.: 0.2729
Max. :16.00
                Max.
                      :75.00
                                      Max. : 4.1273
                                                        Max. : 9.5285
                  apoC31d_apoC31
apoC30b_apoC31
                                                     apoC32_apoC31
                                   apoC32d_apoC31
Min. :-2.3348
                  Min. :-2.0690
                                   Min. :-2.0104
                                                     Min. :-1.7414
1st Qu.:-0.6727
                  1st Qu.:-0.4713
                                    1st Qu.:-0.7940
                                                     1st Qu.:-0.7197
Median :-0.1045
                  Median :-0.1227
                                   Median :-0.1800
                                                     Median :-0.2229
Mean : 0.0000
                  Mean : 0.0000
                                   Mean : 0.0000
                                                     Mean : 0.0000
3rd Qu.: 0.5635
                  3rd Qu.: 0.3468
                                    3rd Qu.: 0.6735
                                                     3rd Qu.: 0.5709
Max. : 3.9551
                  Max. : 6.8186
                                   Max. : 5.0159
                                                     Max. : 4.0699
apoC30f_apoC31
                   insulin v00
                                    HOMA.IR
                                                   diabetes
Min.
      :-1.6246
                  Min. : 2.80
                                 Min. : 0.6983
                                                   0:143
1st Qu.:-0.7984
                  1st Qu.:14.10
                                 1st Qu.: 3.7956
                                                   1:139
Median :-0.2389
                  Median :19.30
                                 Median: 5.2385
Mean : 0.0000
                  Mean :21.97
                                 Mean : 6.2566
3rd Qu.: 0.6490
                  3rd Qu.:26.40
                                 3rd Qu.: 7.6042
Max. : 3.7184
                  Max. :93.60
                                 Max. :32.9985
                  NA's
                                 NA's
                         :5
                                        :5
vars_numéricas <- BBDD %>%
```

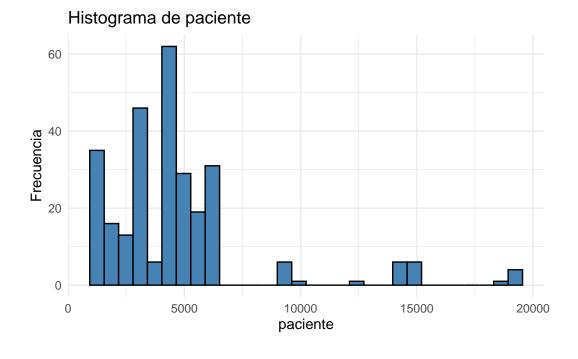
```
dplyr::select(where(is.numeric)) %>%
  names()

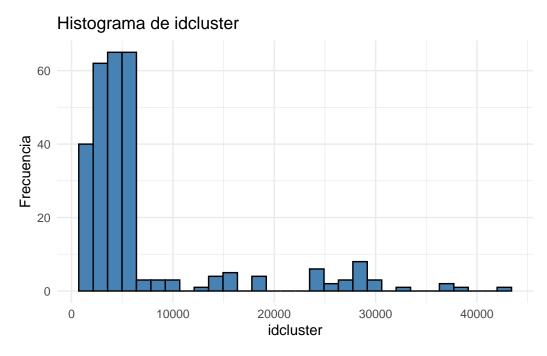
crear_histograma <- function(var) {
  ggplot(BBDD, aes_string(x = var)) +
    geom_histogram(bins = 30, color = "black", fill = "steelblue") +
    labs(title = paste("Histograma de", var), x = var, y = "Frecuencia") +
    theme_minimal()
}

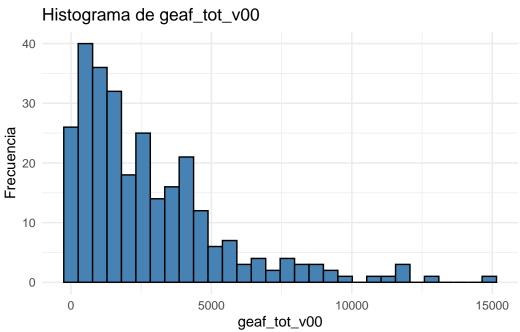
lista_plots <- map(vars_numéricas, crear_histograma)</pre>
```

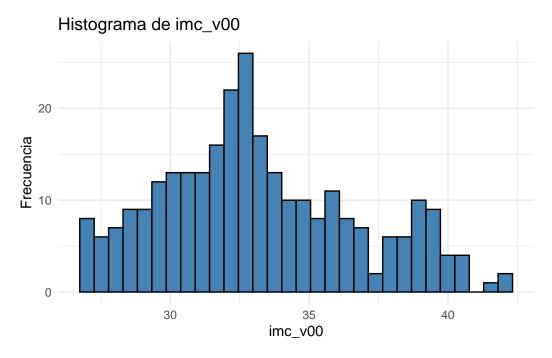
Warning: `aes_string()` was deprecated in ggplot2 3.0.0.
i Please use tidy evaluation idioms with `aes()`.
i See also `vignette("ggplot2-in-packages")` for more information.

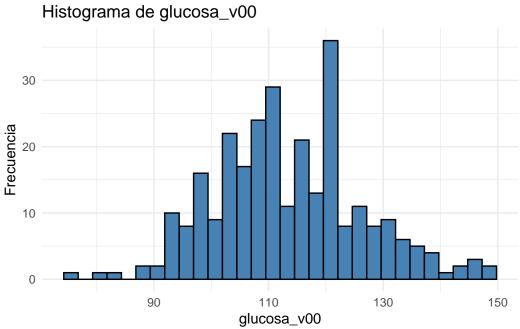
walk(lista_plots, print)

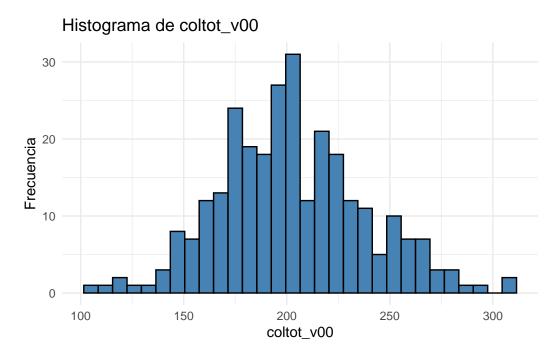


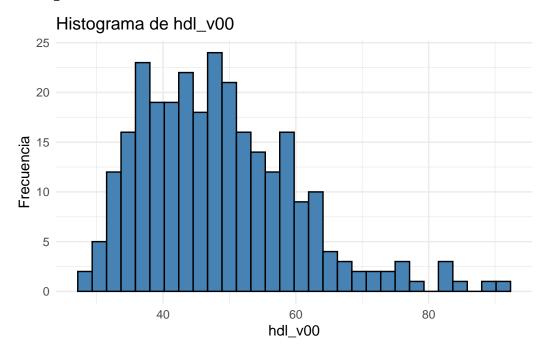


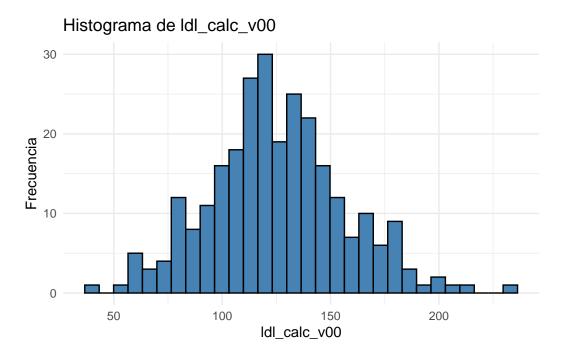


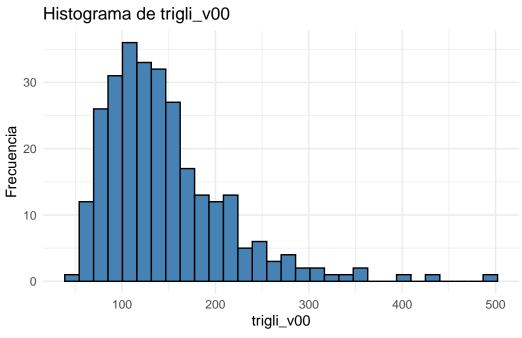


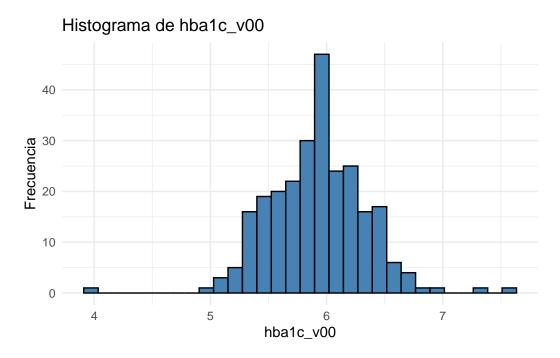


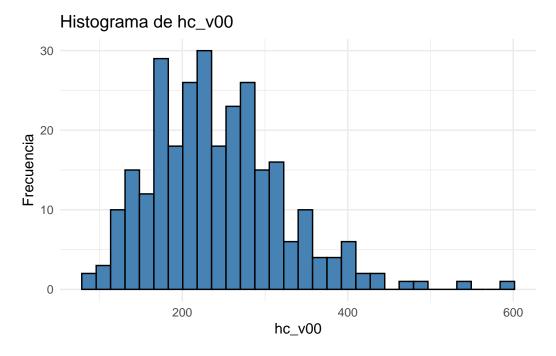


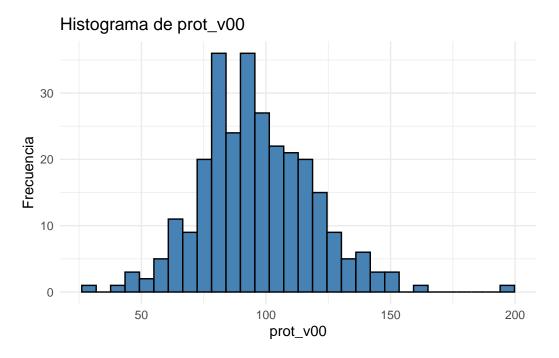


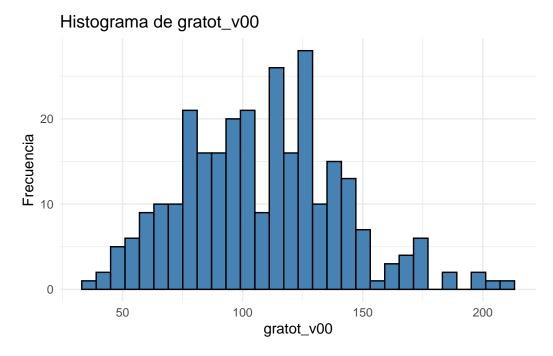


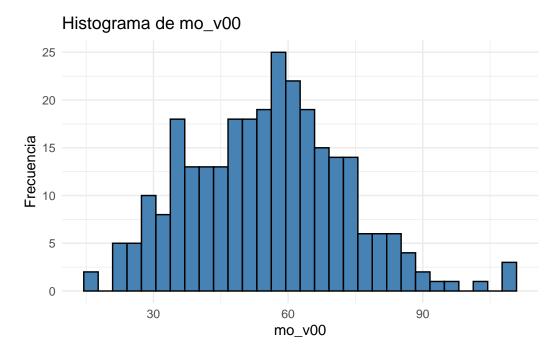


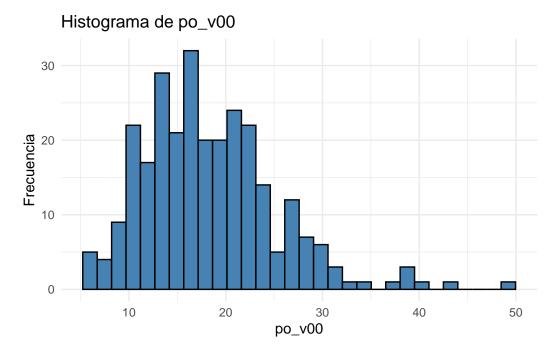


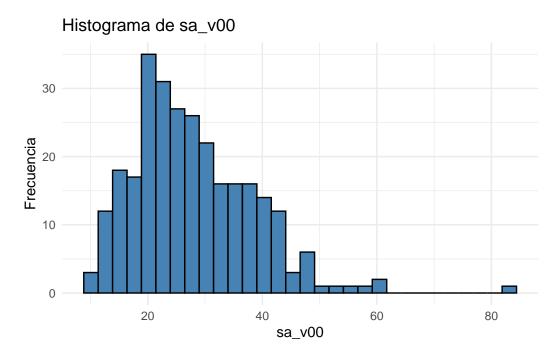


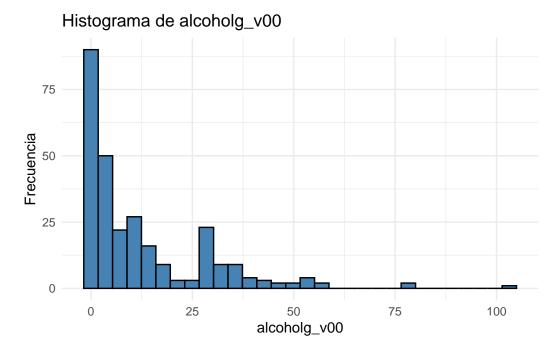


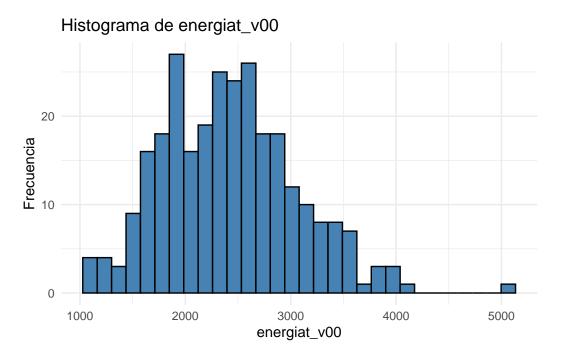


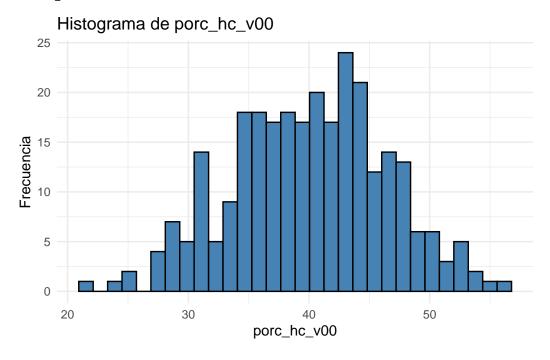


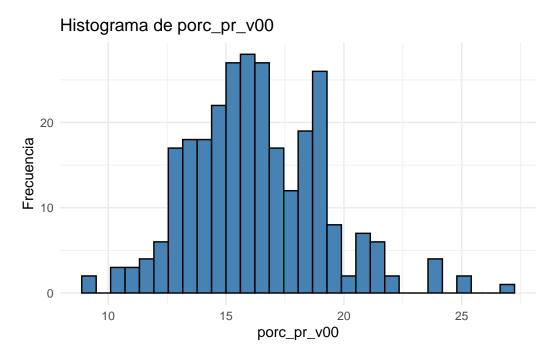


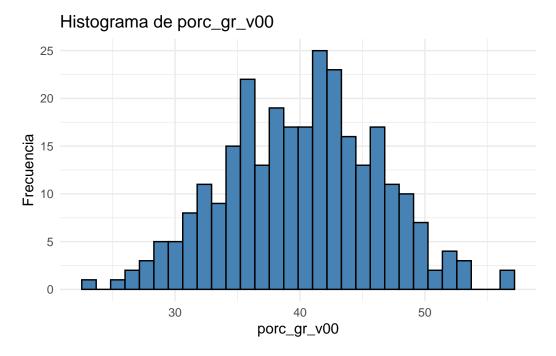


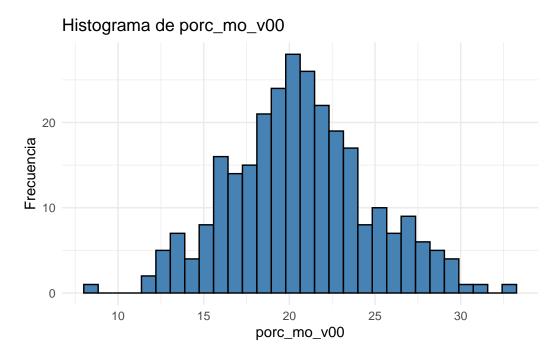


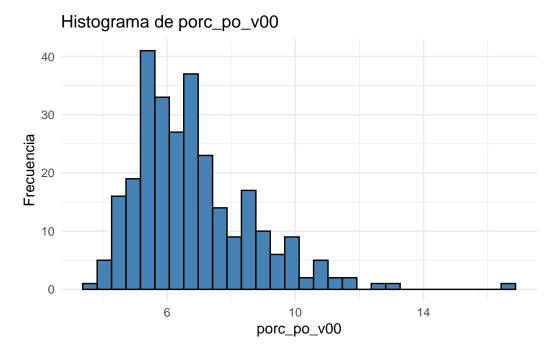


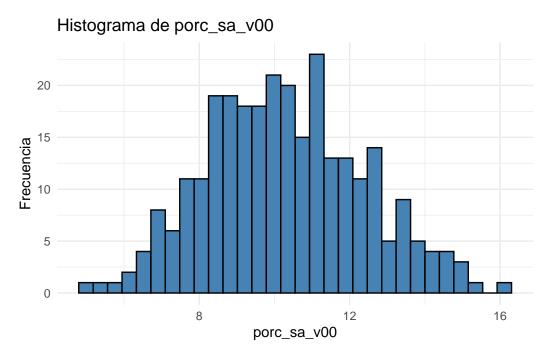


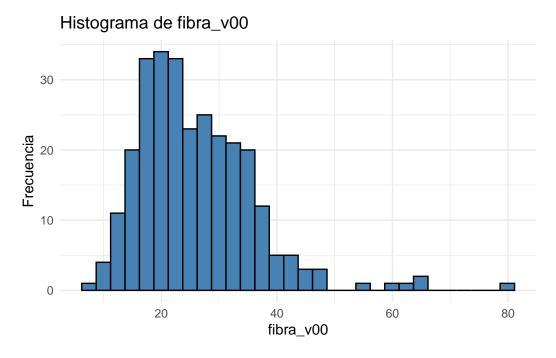


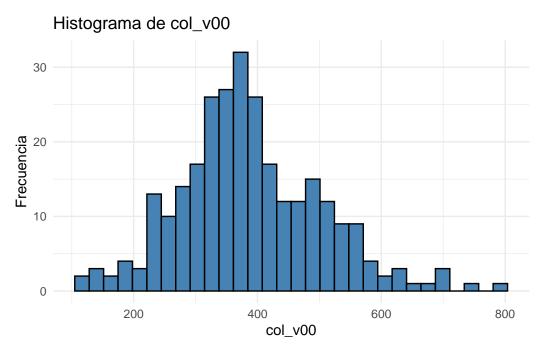


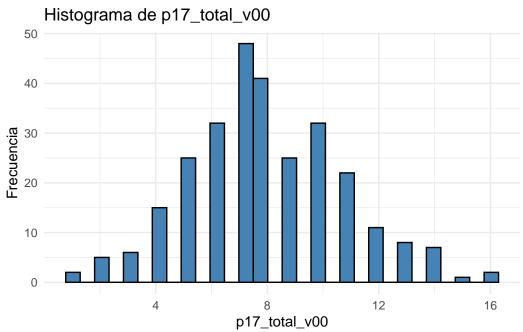


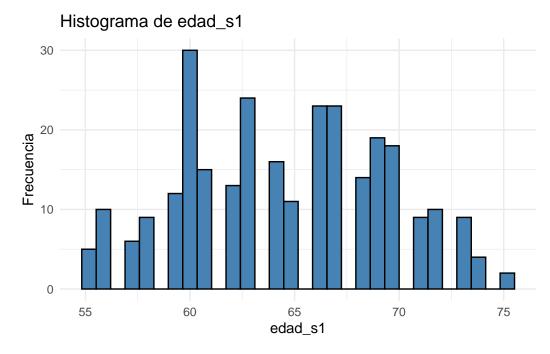


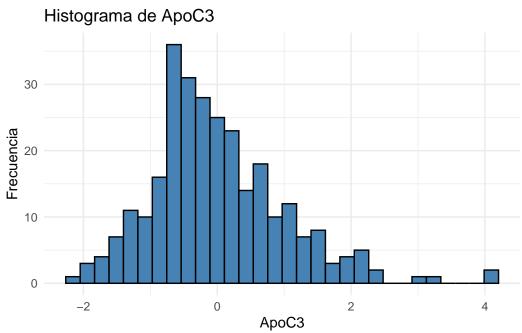


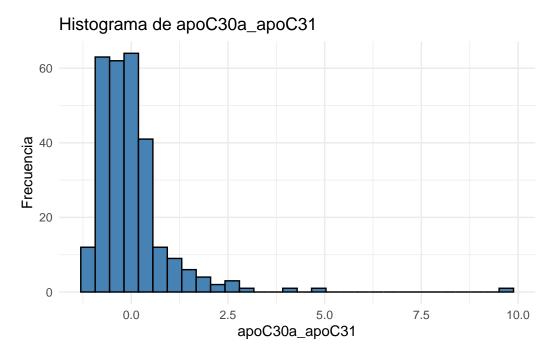


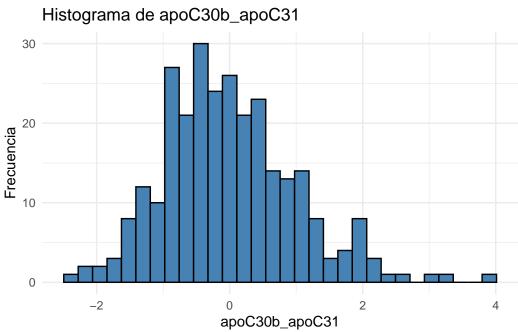


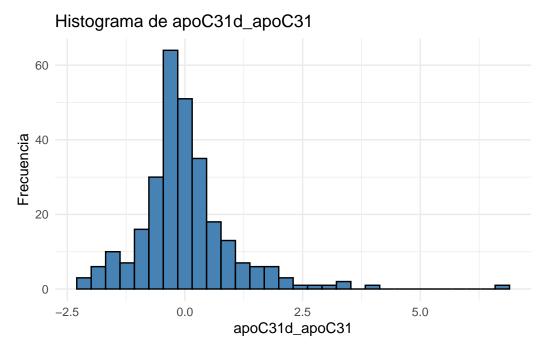


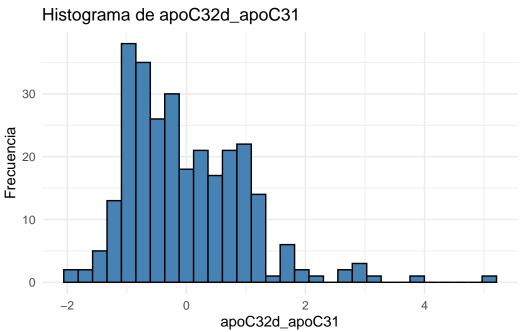


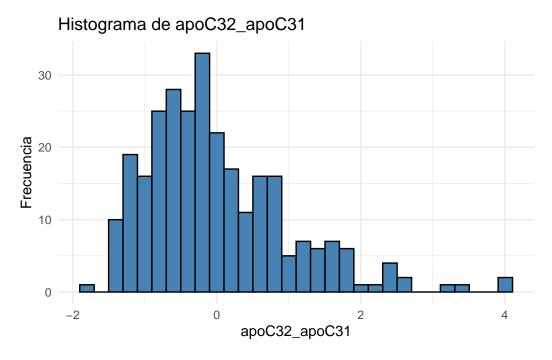




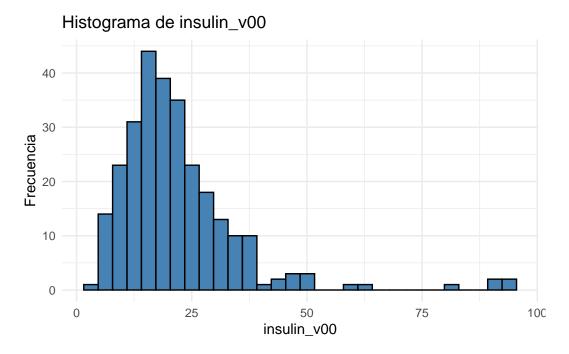




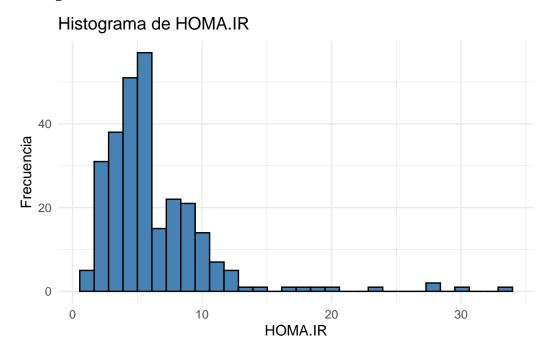




Histograma de apoC30f_apoC31



Warning: Removed 5 rows containing non-finite outside the scale range (int_{0}).



 $\label{lem:condition} Variables \ a \ revisar: geaf_tot_v00, \ imc_v00, \ hdl_v00, \ trigli_v00, \ hc_v00, \ alcoholg_v00, \ energiat_v00, \ porc_po_v00, \ fibra_v00, \ apoC3, \ "apoC30a_apoC31", \ "apoC30b_apoC31", \ "apoC31d_apoC31", \ "apoC32d_apoC31", \ apoC32_apoC31, \ apoC30f_apoC31, \ insulin_v00, \ HOMA.IR.$

Análisis:

Empiezo los modelos, las variables con distribución muy lejos de la normalidad, las transformo con log

Objetivo 1:

Regresiones lineales: modelos ajustados por: idcluster, centro, sexo, educación, actividad física, tabaco, MEDAS, IMC y tratamiendo dislipidémico.

glucosa v00

```
r_glm = c()
SE = c()
p_valor = c()
for (i in 36:42){
   mod_glm <- lm(log(glucosa_v00) ~ BBDD[[i]] + idcluster + edad_s1 +</pre>
                    nodo + sexo_s1 + escola_v00 + geaf_tot_v00 + fuma_s1 +
                    imc_v00 + p17_total_v00 + tto_col_v00,
                     data = BBDD)
   r_glm[[i]] = round(summary(mod_glm)$coef[2,1],3)
   SE[[i]] = round(summary(mod_glm)$coef[2,2],3)
   p_valor[[i]] = round(summary(mod_glm)$coef[2,4],3)
}
df_coef <- map_dfr(r_glm, ~ as_tibble(.x))</pre>
df_SE <- map_dfr(SE, ~ as_tibble(.x))</pre>
df_p_valor <- map_dfr(p_valor, ~ as_tibble(.x))</pre>
df_rlog = data.frame(cbind(df_coef, df_SE, df_p_valor))
df_rlog <- cbind(variable = colnames(BBDD)[36:42], df_rlog)</pre>
colnames(df_rlog) = c("Variable", "Coeficiente", "Error_Estandar", "P_valor")
export(df_rlog, "Resultados/regresiones_lineales_glucosa.xlsx")
```

$insulin_v00$

```
r_glm = c()
SE = c()
p_valor = c()
for (i in 36:42){
   mod_glm <- lm(log(insulin_v00) ~ BBDD[[i]] + idcluster + edad_s1 +</pre>
                    nodo + sexo_s1 + escola_v00 + geaf_tot_v00 + fuma_s1 +
                    imc_v00 + p17_total_v00 + tto_col_v00,
                     data = BBDD)
   r_glm[[i]] = round(summary(mod_glm)$coef[2,1],3)
   SE[[i]] = round(summary(mod_glm)$coef[2,2],3)
   p_valor[[i]] = round(summary(mod_glm)$coef[2,4],3)
}
df_coef <- map_dfr(r_glm, ~ as_tibble(.x))</pre>
df_SE <- map_dfr(SE, ~ as_tibble(.x))</pre>
df_p_valor <- map_dfr(p_valor, ~ as_tibble(.x))</pre>
df_rlog = data.frame(cbind(df_coef, df_SE, df_p_valor))
df_rlog <- cbind(variable = colnames(BBDD)[36:42], df_rlog)</pre>
colnames(df_rlog) = c("Variable", "Coeficiente", "Error_Estandar", "P_valor")
export(df_rlog, "Resultados/regresiones_lineales_insulin.xlsx")
```

HOMA.IR

```
r_glm = c()
SE = c()
p_valor = c()
for (i in 36:42){
   mod_glm <- lm(log(HOMA.IR) ~ BBDD[[i]] + idcluster + edad_s1 +</pre>
                    nodo + sexo s1 + escola v00 + geaf tot v00 + fuma s1 +
                    imc_v00 + p17_total_v00 + tto_col_v00,
                     data = BBDD)
   r_glm[[i]] = round(summary(mod_glm)$coef[2,1],3)
   SE[[i]] = round(summary(mod_glm)$coef[2,2],3)
   p_valor[[i]] = round(summary(mod_glm)$coef[2,4],3)
}
df_coef <- map_dfr(r_glm, ~ as_tibble(.x))</pre>
df_SE <- map_dfr(SE, ~ as_tibble(.x))</pre>
df_p_valor <- map_dfr(p_valor, ~ as_tibble(.x))</pre>
df_rlog = data.frame(cbind(df_coef, df_SE, df_p_valor))
df_rlog <- cbind(variable = colnames(BBDD)[36:42], df_rlog)</pre>
colnames(df_rlog) = c("Variable", "Coeficiente", "Error_Estandar", "P_valor")
export(df_rlog, "Resultados/regresiones_lineales_HOMA.IR.xlsx")
```

hba1c_v00 (es más o menos normal, no log)

```
r_glm = c()
SE = c()
p_valor = c()
for (i in 36:42){
   mod_glm <- lm(hba1c_v00 ~ BBDD[[i]] + idcluster + edad_s1 +</pre>
                    nodo + sexo_s1 + escola_v00 + geaf_tot_v00 + fuma_s1 +
                    imc_v00 + p17_total_v00 + tto_col_v00,
                    data = BBDD)
   r_glm[[i]] = round(summary(mod_glm)$coef[2,1],3)
   SE[[i]] = round(summary(mod_glm)$coef[2,2],3)
   p_valor[[i]] = round(summary(mod_glm)$coef[2,4],3)
}
df_coef <- map_dfr(r_glm, ~ as_tibble(.x))</pre>
df_SE <- map_dfr(SE, ~ as_tibble(.x))</pre>
df_p_valor <- map_dfr(p_valor, ~ as_tibble(.x))</pre>
df_rlog = data.frame(cbind(df_coef, df_SE, df_p_valor))
df_rlog <- cbind(variable = colnames(BBDD)[36:42], df_rlog)</pre>
colnames(df_rlog) = c("Variable", "Coeficiente", "Error_Estandar", "P_valor")
export(df_rlog, "Resultados/regresiones_lineales_hba1c_v00.xlsx")
```

hba1c_v00 (versión log)

```
r_glm = c()
SE = c()
p_valor = c()
```

```
for (i in 36:42){
   mod_glm <- lm(log(hba1c_v00) ~ BBDD[[i]] + idcluster + edad_s1 +</pre>
                    nodo + sexo_s1 + escola_v00 + geaf_tot_v00 + fuma_s1 +
                    imc_v00 + p17_total_v00 + tto_col_v00,
                     data = BBDD)
   r_glm[[i]] = round(summary(mod_glm)$coef[2,1],3)
   SE[[i]] = round(summary(mod_glm)$coef[2,2],3)
   p_valor[[i]] = round(summary(mod_glm)$coef[2,4],3)
}
df_coef <- map_dfr(r_glm, ~ as_tibble(.x))</pre>
df_SE <- map_dfr(SE, ~ as_tibble(.x))</pre>
df_p_valor <- map_dfr(p_valor, ~ as_tibble(.x))</pre>
df_rlog = data.frame(cbind(df_coef, df_SE, df_p_valor))
df_rlog <- cbind(variable = colnames(BBDD)[36:42], df_rlog)</pre>
colnames(df rlog) = c("Variable", "Coeficiente", "Error Estandar", "P valor")
export(df_rlog, "Resultados/regresiones_lineales_hba1c_log.xlsx")
```

$coltot_v00$

```
r glm = c()
SE = c()
p_valor = c()
for (i in 36:42){
   mod_glm <- lm(coltot_v00 ~ BBDD[[i]] + idcluster + edad_s1 +</pre>
                    nodo + sexo_s1 + escola_v00 + geaf_tot_v00 + fuma_s1 +
                    imc_v00 + p17_total_v00 + tto_col_v00,
                     data = BBDD)
   r_glm[[i]] = round(summary(mod_glm)$coef[2,1],3)
   SE[[i]] = round(summary(mod_glm)$coef[2,2],3)
   p_valor[[i]] = round(summary(mod_glm)$coef[2,4],3)
}
df_coef <- map_dfr(r_glm, ~ as_tibble(.x))</pre>
df_SE <- map_dfr(SE, ~ as_tibble(.x))</pre>
df_p_valor <- map_dfr(p_valor, ~ as_tibble(.x))</pre>
df_rlog = data.frame(cbind(df_coef, df_SE, df_p_valor))
df rlog <- cbind(variable = colnames(BBDD)[36:42], df rlog)</pre>
colnames(df_rlog) = c("Variable", "Coeficiente", "Error_Estandar", "P_valor")
export(df_rlog, "Resultados/regresiones_lineales_coltot.xlsx")
```

hdl v00

```
data = BBDD)
r_glm[[i]] = round(summary(mod_glm)$coef[2,1],3)
SE[[i]] = round(summary(mod_glm)$coef[2,2],3)
p_valor[[i]] = round(summary(mod_glm)$coef[2,4],3)
}

df_coef <- map_dfr(r_glm, ~ as_tibble(.x))
df_SE <- map_dfr(SE, ~ as_tibble(.x))
df_p_valor <- map_dfr(p_valor, ~ as_tibble(.x))
df_rlog = data.frame(cbind(df_coef, df_SE, df_p_valor))
df_rlog <- cbind(variable = colnames(BBDD)[36:42], df_rlog)
colnames(df_rlog) = c("Variable", "Coeficiente", "Error_Estandar", "P_valor")
export(df_rlog, "Resultados/regresiones_lineales_hdl.xlsx")</pre>
```

ldl calc v00

```
r_glm = c()
SE = c()
p_valor = c()
for (i in 36:42){
   mod_glm <- lm(ldl_calc_v00 ~ BBDD[[i]] + idcluster + edad_s1 +</pre>
                    nodo + sexo_s1 + escola_v00 + geaf_tot_v00 + fuma_s1 +
                    imc_v00 + p17_total_v00 + tto_col_v00,
                     data = BBDD)
   r_glm[[i]] = round(summary(mod_glm)$coef[2,1],3)
   SE[[i]] = round(summary(mod_glm)$coef[2,2],3)
   p_valor[[i]] = round(summary(mod_glm)$coef[2,4],3)
}
df_coef <- map_dfr(r_glm, ~ as_tibble(.x))</pre>
df_SE <- map_dfr(SE, ~ as_tibble(.x))</pre>
df_p_valor <- map_dfr(p_valor, ~ as_tibble(.x))</pre>
df_rlog = data.frame(cbind(df_coef, df_SE, df_p_valor))
df rlog <- cbind(variable = colnames(BBDD)[36:42], df rlog)</pre>
colnames(df_rlog) = c("Variable", "Coeficiente", "Error_Estandar", "P_valor")
export(df_rlog, "Resultados/regresiones_lineales_ldl.xlsx")
```

trigli_v00

```
df_coef <- map_dfr(r_glm, ~ as_tibble(.x))
df_SE <- map_dfr(SE, ~ as_tibble(.x))
df_p_valor <- map_dfr(p_valor, ~ as_tibble(.x))
df_rlog = data.frame(cbind(df_coef, df_SE, df_p_valor))
df_rlog <- cbind(variable = colnames(BBDD)[36:42], df_rlog)
colnames(df_rlog) = c("Variable", "Coeficiente", "Error_Estandar", "P_valor")
export(df_rlog, "Resultados/regresiones_lineales_TG.xlsx")</pre>
```

Objetivo 2:

Diferencias entre grupos:

```
medias = c()
SD = c()
P_v_a = c()
for (i in 36:42) {
  medias[[i]] = round(tapply(BBDD[[i]], BBDD[[45]], mean, na.rm = T),3)
  SD[[i]] = round(tapply(BBDD[[i]], BBDD[[45]], sd, na.rm = T),3)
 modelo = wilcox.test(BBDD[[i]] ~ BBDD[[45]])
  P v a[[i]] = round(modelo$p.value,3)
df_medias <- bind_rows(map(medias, ~ as.list(.x)))</pre>
df_SD <- bind_rows(map(SD, ~ as.list(.x)))</pre>
df_p_v_a <- map_dfr(P_v_a, ~ as_tibble(.x))</pre>
df_medias = data.frame(cbind(df_medias, df_SD, df_p_v_a))
df_medias <- cbind(variable = colnames(BBDD)[36:42], df_medias)</pre>
colnames(df_medias) = c("variables", "Media No diab", "Media Diab",
                         "SD No diab", "SD Diab", "P_valor")
export(df_medias, "Resultados/wilcox_diabetes.xlsx")
```

Modelos de regresión logistica: idcluster, centro, sexo, educación, actividad física, tabaco, MEDAS, IMC y tratamiendo dislipidémico. Aquí también añado grupo intervención porque si que puede haber una influencia sobre la incidencia de diabetes. Ojo: añado edad como categórica dicotómica porque parace tener una relación con apoC30aapoC31. Este modelo, sin edad, sale similar al resultado actual, con edad como continúa, su p es igual a 1 -> punto influyente pero sin interacción.

```
df_rlog = data.frame(cbind(df_coef, df_SE, df_p_valor))
df_rlog <- cbind(variable = colnames(BBDD)[36:42], df_rlog)
colnames(df_rlog) = c("Variable", "Coeficiente", "Error_Estandar", "P_valor")
export(df_rlog, "Resultados/regresiones_logisticas_diabetes.xlsx")</pre>
```

No hay suficientes participantes para utilizar nodos de forma normal y produce un sesgo. Para evitar la tendencia a infinito de algunos nodos, convierto la variable en numérica y hago terciles que se distribuirán en función a la cantidad de participantes por centro, reequilibrando la distribución.

Objetivo 3:

ANOVAS:

Pruebo primero con terciles de adherencia de MedDiet:

```
BBDD$ter_medas = cut2(BBDD$p17_total_v00, g = 3)
medias = c()
SD = c()
P_v_a = c()
for (i in 36:42) {
  medias[[i]] = round(tapply(BBDD[[i]], BBDD[[46]], mean, na.rm = T),2)
  SD[[i]] = round(tapply(BBDD[[i]], BBDD[[46]], sd, na.rm = T),2)
  modelo = lm(BBDD[[i]] \sim BBDD[[46]])
  P_v_a[[i]] = round(anova(modelo)[1,5],3)
df_medias <- bind_rows(map(medias, ~ as.list(.x)))</pre>
df_SD <- bind_rows(map(SD, ~ as.list(.x)))</pre>
df_p_v_a <- map_dfr(P_v_a, ~ as_tibble(.x))</pre>
df_medias = data.frame(cbind(df_medias, df_SD, df_p_v_a))
df_medias <- cbind(variable = colnames(BBDD)[36:42], df_medias)</pre>
colnames(df_medias) = c("Variables", "Media Ter 1 (1,8)", "Media Ter 2 (8, 10)", "Media Ter 3 (10, 17)"
                         "SD Ter 1 (1,8)", "SD Ter 2 (8, 10)", "SD Ter 3 (10, 17)",
                         "P valor")
export(df_medias, "Resultados/medias_ter_MEDAS_aov.xlsx")
```

Ancovas: ajustadas por: idcluster, centro, sexo, educación, actividad física, tabaco, IMC y tratamiendo dislipidémico.

Regresiones lineales:

Terciles de MEDAS:

Regresión lineal asociaciones de terciles: modelos ajustados idcluster, centro, sexo, educación, actividad física, tabaco, IMC y tratamiendo dislipidémico.

```
r glm1 = c()
r_glm2 = c()
SE1 = c()
SE2 = c()
p_valor1 = c()
p_valor2 = c()
for (i in 36:42){
   mod_glm <- lm(BBDD[[i]] ~ ter_medas + idcluster + edad_s1 +</pre>
                    nodo + sexo_s1 + escola_v00 + geaf_tot_v00 + fuma_s1 +
                    imc_v00 + tto_col_v00,
                    data = BBDD)
   r_glm1[[i]] = round(summary(mod_glm)$coef[2,1],3)
   r_glm2[[i]] = round(summary(mod_glm)$coef[3,1],3)
   SE1[[i]] = round(summary(mod_glm)$coef[2,2],3)
   SE2[[i]] = round(summary(mod glm)$coef[3,2],3)
   p_valor1[[i]] = round(summary(mod_glm)$coef[2,4],3)
   p_valor2[[i]] = round(summary(mod_glm)$coef[3,4],3)
}
df_coef1 <- map_dfr(r_glm1, ~ as_tibble(.x))</pre>
df_coef2 <- map_dfr(r_glm2, ~ as_tibble(.x))</pre>
df_SE1 <- map_dfr(SE1, ~ as_tibble(.x))</pre>
df_SE2 <- map_dfr(SE2, ~ as_tibble(.x))</pre>
df_p_valor1 <- map_dfr(p_valor1, ~ as_tibble(.x))</pre>
df_p_valor2 <- map_dfr(p_valor2, ~ as_tibble(.x))</pre>
df_rlog = data.frame(cbind(df_coef1, df_SE1, df_p_valor1, df_coef2, df_SE2,
                            df_p_valor2))
df_rlog <- cbind(variable = colnames(BBDD)[36:42], df_rlog)</pre>
colnames(df_rlog) = c("Variables" ,"Coef Ter 2 (1,8)", "SE Ter 2 (8,10)", "P_valor Ter2",
                       "Coef Ter 3 (8, 10)", "SE Ter 3 (10, 17)", "P_valor Ter3")
export(df rlog, "Resultados/regresiones lineales ter Medas.xlsx")
```

Regresiones lineales para MEDAS y macronutrientes ajustadas por: idcluster, centro, sexo, educación, actividad física, tabaco, IMC y tratamiendo dislipidémico.

MEDAS:

```
r_glm = c()
SE = c()
p_valor = c()
```

```
for (i in 36:42){
   mod_glm \leftarrow lm(BBDD[[i]] \sim p17_total_v00 + idcluster + edad_s1 +
                    nodo + sexo_s1 + escola_v00 + geaf_tot_v00 + fuma_s1 +
                    imc_v00 + tto_col_v00,
                     data = BBDD)
   r_glm[[i]] = round(summary(mod_glm)$coef[2,1],3)
   SE[[i]] = round(summary(mod_glm)$coef[2,2],3)
   p_valor[[i]] = round(summary(mod_glm)$coef[2,4],3)
}
df_coef <- map_dfr(r_glm, ~ as_tibble(.x))</pre>
df_SE <- map_dfr(SE, ~ as_tibble(.x))</pre>
df_p_valor <- map_dfr(p_valor, ~ as_tibble(.x))</pre>
df_rlog = data.frame(cbind(df_coef, df_SE, df_p_valor))
df_rlog <- cbind(variable = colnames(BBDD)[36:42], df_rlog)</pre>
colnames(df_rlog) = c("Variable", "Coeficiente", "Error_Estandar", "P_valor")
export(df_rlog, "Resultados/regresiones_lineales_MEDAS.xlsx")
```

HC:

Porcentaje:

```
r glm = c()
SE = c()
p \ valor = c()
for (i in 36:42){
   mod_glm <- lm(BBDD[[i]] ~ porc_hc_v00 + idcluster + edad_s1 +</pre>
                    nodo + sexo_s1 + escola_v00 + geaf_tot_v00 + fuma_s1 +
                    imc_v00 + tto_col_v00 + porc_pr_v00 + porc_gr_v00 +
                    alcoholg_v00 + fibra_v00,
                     data = BBDD)
   r_glm[[i]] = round(summary(mod_glm)$coef[2,1],3)
   SE[[i]] = round(summary(mod_glm)$coef[2,2],3)
   p_valor[[i]] = round(summary(mod_glm)$coef[2,4],3)
}
df_coef <- map_dfr(r_glm, ~ as_tibble(.x))</pre>
df_SE <- map_dfr(SE, ~ as_tibble(.x))</pre>
df_p_valor <- map_dfr(p_valor, ~ as_tibble(.x))</pre>
df_rlog = data.frame(cbind(df_coef, df_SE, df_p_valor))
df rlog <- cbind(variable = colnames(BBDD)[36:42], df rlog)
colnames(df_rlog) = c("Variable", "Coeficiente", "Error_Estandar", "P_valor")
export(df_rlog, "Resultados/regresiones_lineales_HC_pct.xlsx")
```

Prot:

Porcentaje:

```
r_glm = c()
SE = c()
p_valor = c()

for (i in 36:42){
    mod_glm <- lm(BBDD[[i]] ~ porc_pr_v00 + idcluster + edad_s1 +</pre>
```

Grasas totales:

Porcentaje:

```
r_glm = c()
SE = c()
p_valor = c()
for (i in 36:42){
   mod_glm <- lm(BBDD[[i]] ~ porc_gr_v00 + idcluster + edad_s1 +</pre>
                    nodo + sexo_s1 + escola_v00 + geaf_tot_v00 + fuma_s1 +
                    imc v00 + tto col v00 + porc hc v00 + porc pr v00 +
                    alcoholg_v00 + fibra_v00,
                     data = BBDD)
   r_glm[[i]] = round(summary(mod_glm)$coef[2,1],3)
   SE[[i]] = round(summary(mod_glm)$coef[2,2],3)
   p_valor[[i]] = round(summary(mod_glm)$coef[2,4],3)
}
df_coef <- map_dfr(r_glm, ~ as_tibble(.x))</pre>
df_SE <- map_dfr(SE, ~ as_tibble(.x))</pre>
df_p_valor <- map_dfr(p_valor, ~ as_tibble(.x))</pre>
df_rlog = data.frame(cbind(df_coef, df_SE, df_p_valor))
df_rlog <- cbind(variable = colnames(BBDD)[36:42], df_rlog)</pre>
colnames(df_rlog) = c("Variable", "Coeficiente", "Error_Estandar", "P_valor")
export(df_rlog, "Resultados/regresiones_lineales_Grasas_totales_pct.xlsx")
```

AGrasas Monoinsaturados:

Porcentaje:

AGrasas Polinsaturados:

Porcentaje:

```
r_glm = c()
SE = c()
p_valor = c()
for (i in 36:42){
   mod_glm <- lm(BBDD[[i]] ~ porc_po_v00 + idcluster + edad_s1 +</pre>
                    nodo + sexo_s1 + escola_v00 + geaf_tot_v00 + fuma_s1 +
                    imc_v00 + tto_col_v00 + porc_hc_v00 + porc_pr_v00 +
                    alcoholg_v00 + fibra_v00,
                    data = BBDD)
   r_glm[[i]] = round(summary(mod_glm)$coef[2,1],3)
   SE[[i]] = round(summary(mod_glm)$coef[2,2],3)
   p_valor[[i]] = round(summary(mod_glm)$coef[2,4],3)
}
df_coef <- map_dfr(r_glm, ~ as_tibble(.x))</pre>
df_SE <- map_dfr(SE, ~ as_tibble(.x))</pre>
df_p_valor <- map_dfr(p_valor, ~ as_tibble(.x))</pre>
df_rlog = data.frame(cbind(df_coef, df_SE, df_p_valor))
df_rlog <- cbind(variable = colnames(BBDD)[36:42], df_rlog)</pre>
colnames(df_rlog) = c("Variable", "Coeficiente", "Error_Estandar", "P_valor")
export(df_rlog, "Resultados/regresiones_lineales_AGP_pct.xlsx")
```

AGrasas Saturados:

Porcentaje:

Alcoholg:

Gramos:

```
r_glm = c()
SE = c()
p_valor = c()
for (i in 36:42){
   mod_glm <- lm(BBDD[[i]] ~ alcoholg_v00 + idcluster + edad_s1 +</pre>
                    nodo + sexo_s1 + escola_v00 + geaf_tot_v00 + fuma_s1 +
                    imc_v00 + tto_col_v00 + porc_hc_v00 + porc_pr_v00 + energiat_v00 +
                    porc_sa_v00 + fibra_v00,
                    data = BBDD)
   r_glm[[i]] = round(summary(mod_glm)$coef[2,1],3)
   SE[[i]] = round(summary(mod_glm)$coef[2,2],3)
   p_valor[[i]] = round(summary(mod_glm)$coef[2,4],3)
}
df_coef <- map_dfr(r_glm, ~ as_tibble(.x))</pre>
df_SE <- map_dfr(SE, ~ as_tibble(.x))</pre>
df_p_valor <- map_dfr(p_valor, ~ as_tibble(.x))</pre>
df_rlog = data.frame(cbind(df_coef, df_SE, df_p_valor))
df_rlog <- cbind(variable = colnames(BBDD)[36:42], df_rlog)</pre>
colnames(df_rlog) = c("Variable", "Coeficiente", "Error_Estandar", "P_valor")
export(df_rlog, "Resultados/regresiones_lineales_alcohol_g.xlsx")
```

Fibra:

Gramos:

```
data = BBDD)
  r_glm[[i]] = round(summary(mod_glm)$coef[2,1],3)
  SE[[i]] = round(summary(mod_glm)$coef[2,2],3)
  p_valor[[i]] = round(summary(mod_glm)$coef[2,4],3)
}

df_coef <- map_dfr(r_glm, ~ as_tibble(.x))
  df_SE <- map_dfr(SE, ~ as_tibble(.x))
  df_p_valor <- map_dfr(p_valor, ~ as_tibble(.x))
  df_rlog = data.frame(cbind(df_coef, df_SE, df_p_valor))
  df_rlog <- cbind(variable = colnames(BBDD)[36:42], df_rlog)
  colnames(df_rlog) = c("Variable", "Coeficiente", "Error_Estandar", "P_valor")
  export(df_rlog, "Resultados/regresiones_lineales_fibra_g.xlsx")</pre>
```

Energiat:

Kcal: la energía tiene un poco de cola a la derecha, utilizo transformación logarítmica para una mejor comprensión de las unidades y neutralizar el efecto de la cola:

```
r_glm = c()
SE = c()
p_valor = c()
for (i in 36:42){
   mod_glm <- lm(BBDD[[i]] ~ log(energiat_v00) + idcluster + edad s1 +</pre>
                    nodo + sexo_s1 + escola_v00 + geaf_tot_v00 + fuma_s1 +
                    imc_v00 + tto_col_v00 + fibra_v00 + alcoholg_v00,
                    data = BBDD)
   r_glm[[i]] = round(summary(mod_glm)$coef[2,1],3)
   SE[[i]] = round(summary(mod_glm)$coef[2,2],3)
   p_valor[[i]] = round(summary(mod_glm)$coef[2,4],3)
}
df coef <- map dfr(r glm, ~ as tibble(.x))</pre>
df_SE <- map_dfr(SE, ~ as_tibble(.x))</pre>
df_p_valor <- map_dfr(p_valor, ~ as_tibble(.x))</pre>
df_rlog = data.frame(cbind(df_coef, df_SE, df_p_valor))
df_rlog <- cbind(variable = colnames(BBDD)[36:42], df_rlog)</pre>
colnames(df rlog) = c("Variable", "Coeficiente", "Error Estandar", "P valor")
export(df_rlog, "Resultados/regresiones_lineales_energia_kcal.xlsx")
```

Características basales:

```
table1_df = print(table1, quote = FALSE, noSpaces = TRUE, printToggle = FALSE)
table1_df = data.frame(Variable = rownames(table1_df), table1_df, row.names = NULL)
wb = createWorkbook()
addWorksheet(wb, "TableOne")
writeData(wb, "TableOne", table1_df)
saveWorkbook(wb, file = "Resultados/tabla_caract_basals.xlsx", overwrite = TRUE)
```

Conclusiones:

Por objetivos, se puede llegar a las siguientes conclusiones generales: - Objetivo 1: Hay relación entre los ratios de varias isoformas con Colesterol total, HDL, LDL y TG, siendo más fuerte esas asociaciones con Colesterol total y TG. En cuanto al metabolismo de la glucosa, también salen algunas asociaciones interesantes. - Objetivo 2: Un ratio y casi otro parecen asociarse con la diabetes, pero no hay diferencias de medias. - Objetivo 3: La dieta mediterránea no parece relacionarse en exceso con las isoformas salvo un ratio y en diferencia de medias. En modelos continuos no parece hacer relación y, en cuanto a los macronutrientes, en general no parece haber asociaciones salvo alguna asociación puntual.

Otras cuestiones a tener en cuenta: No he aplicado FDR porque probablemente nos quedemos en nada, al menos en los objetivos 2 y 3, por lo que recomiendo presentarlo como un estudio piloto.