Sex and Age but not Body Mass Index (BMI) are Significant Predictors of Serum Retinol Binding Protein 4 (RBP4) and Transthyretin (TTR) Concentrations

Statistical Analysis Code and Output
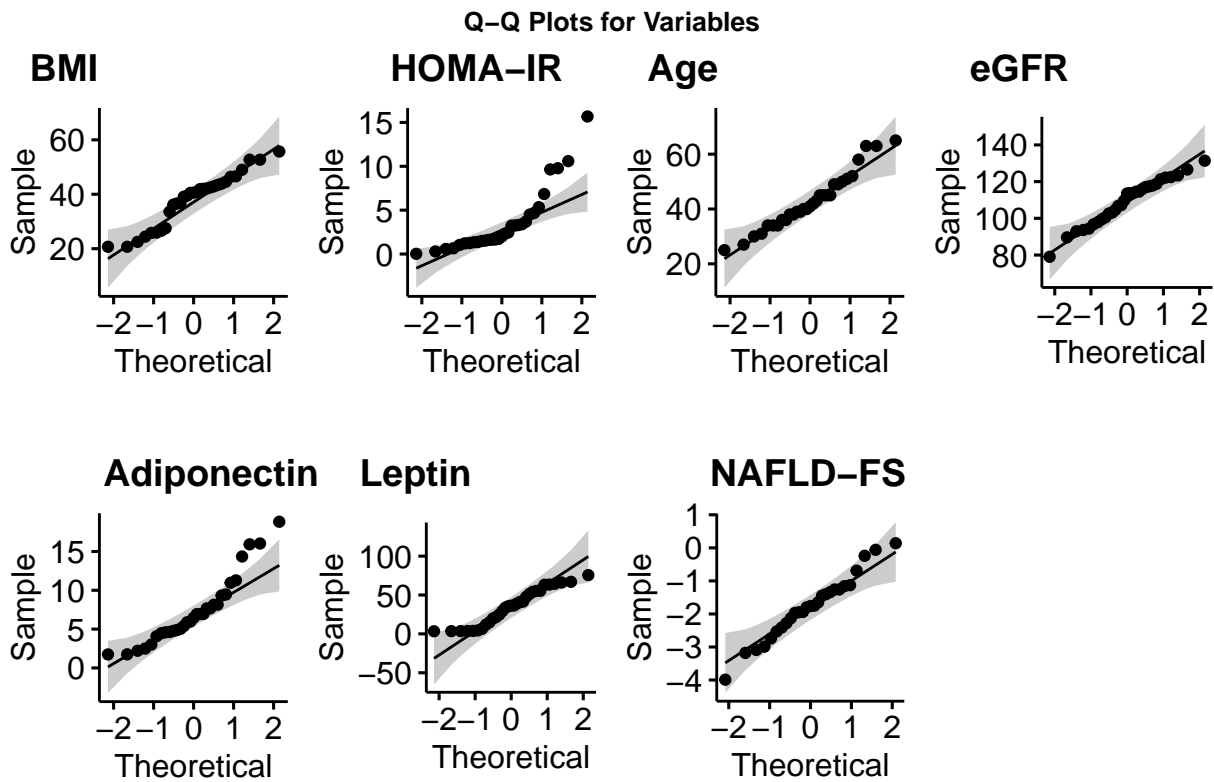
Aprajita S. Yadav

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Contents

Load Data

Determine Normality

for Shapiro-Wilk test p-value<0.05 indicates variables does not have normal distribution

Q–Q Plots for Variables

Shapiro-Wilk Normality Test	
Variable	p-value
BMI	0.078
HOMA-IR	1.56e-05
Age	0.274
eGFR	0.606
Adiponectin	0.008
Leptin	0.036
NAFLD-FS	0.927

Note: data with p-value<0.05 will be log-transformed

Determine Variable Correlation

ANOVA Results with Sex	
Variable	p-value
BMI	8.04e-03
HOMA-IR	0.54
Age	0.59
eGFR	0.63
Adiponectin	0.92
Leptin	4.36e-05
NAFLD-FS	0.67

Spearman Correlation		
Variable Pair	rho	p-value
BMI and Adiponectin	-0.35	0.06
BMI and Leptin	0.52	2.94e-03
HOMA-IR and Adiponectin	-0.59	6.19e-04
HOMA-IR and Leptin	0.25	0.17

ANOVA Results	
Variable Pair	p-value
BMI and Sex	0.008
HOMA-IR and Sex	0.540
Age and Sex	0.587

Sex will be used for model building along with BMI, HOMA-IR, and Age

Spearman Correlation		
Variable Pair	rho	p-value
BMI and Age	-0.37	0.042
BMI and HOMA-IR	0.52	0.003
Age and HOMA-IR	-0.41	0.022

These variables will be used for model building along with the variable Sex

Scatterplot Matrix of Variables
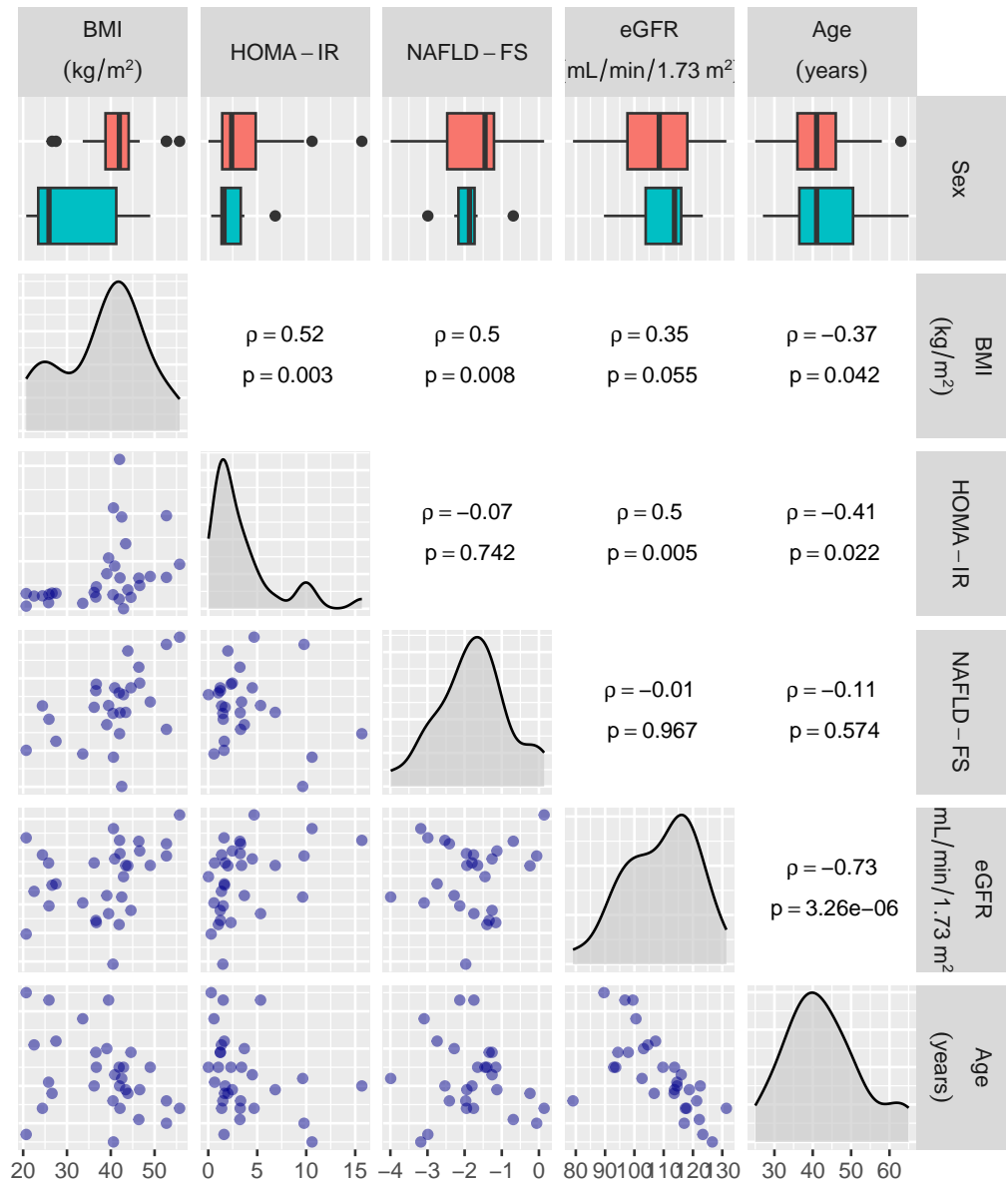
RBP4 Model

```r
#log transform RBP4 concentrations
vao$LRBP4<-log10(vao$RBP4)

#linear regression with BMI, Sex, Age and HOMAIR
model1=lm(LRBP4~BMI+Sex+Age+LHOMAIR,vao)
vif(model1)
```

```
##      BMI      Sex      Age  LHOMAIR
## 1.597502 1.292650 1.233974 1.259206
```

```r
#remove one variable at a time
model2=lm(LRBP4~BMI+Sex+Age,vao) #remove HOMAIR
model3=lm(LRBP4~BMI+Sex+LHOMAIR, vao) #remove Age
model4=lm(LRBP4~BMI+Age+LHOMAIR, vao) #remove Sex
model5=lm(LRBP4~Sex+Age+LHOMAIR, vao) #remove BMI

AIC<-AIC(model1,model2,model3,model4,model5) #summary of AIC
AIC_df<-data.frame(
  Model=c("Model 1: Full Model", "Model 2: No HOMA-IR", "Model 3: No Age",
          "Model 4: No Sex", "Model 5: No BMI"),
  AIC = round(AIC$AIC, 3),
  DF = AIC$df)

aic_table <- AIC_df %>%
  flextable() %>%
  set_header_labels(Model = "Model Description", AIC = "AIC Value",
                    DF="Degrees of Freedom") %>%
  add_header_lines(values = "AIC Comparison of Models") %>%
  align(part="header", align="center" ) %>%
  add_footer_lines(values = "Note: Lower AIC values indicate a better model.") %>%
  fontsize(part = "footer", size = 8) %>%
  set_table_properties(layout = "autofit")
aic_table
```

AIC Comparison of Models		
Model Description	AIC Value	Degrees of Freedom
Model 1: Full Model	-34.866	6
Model 2: No HOMA-IR	-36.135	5
Model 3: No Age	-35.123	5
Model 4: No Sex	-33.703	5
Model 5: No BMI	-36.196	5

Note: Lower AIC values indicate a better model.

```
##remove BMI (lowest AIC), add interaction terms
model6=lm(LRBP4~Sex+Age+LHOMAIR+Age*Sex+LHOMAIR*Sex,vao)
summary(model6)
```

```
##
## Call:
## lm(formula = LRBP4 ~ Sex + Age + LHOMAIR + Age * Sex + LHOMAIR *
##     Sex, data = vao)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -0.21429 -0.07825  0.02313  0.06886  0.20592
##
## Coefficients:
##                 Estimate Std. Error t value Pr(>|t|)
## (Intercept)    -0.071668   0.135146  -0.530  0.60058
## SexMale         0.507136   0.207240   2.447  0.02177 *
## Age             0.008636   0.002998   2.880  0.00803 **
## LHOMAIR        -0.048056   0.045468  -1.057  0.30065
## SexMale:Age    -0.009698   0.004385  -2.212  0.03636 *
## SexMale:LHOMAIR 0.072444   0.113449   0.639  0.52892
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.1123 on 25 degrees of freedom
## Multiple R-squared:  0.4636, Adjusted R-squared:  0.3563
## F-statistic: 4.322 on 5 and 25 DF,  p-value: 0.005699
```

```
AIC(model6,model5)
```

	df	AIC
model6	7	-40.24879
model5	5	-36.19628

```
#remove interaction terms one at a time
model7=lm(LRBP4~Sex+Age+LHOMAIR+LHOMAIR*Age,vao)
model8=lm(LRBP4~Sex+Age+LHOMAIR+Age*Sex,vao)
summary(model7)
```

```
##
## Call:
## lm(formula = LRBP4 ~ Sex + Age + LHOMAIR + LHOMAIR * Age, data = vao)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -0.24923 -0.06776  0.01125  0.07561  0.20708
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept) 0.183427   0.135373   1.355   0.1871
```

6

```
## SexMale      0.106354    0.047271    2.250    0.0331 *
## Age          0.002726    0.002839    0.960    0.3458
## LHOMAIR     -0.156739    0.218925   -0.716    0.4804
## Age:LHOMAIR  0.002452    0.004827    0.508    0.6157
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.1248 on 26 degrees of freedom
## Multiple R-squared:  0.3113, Adjusted R-squared:  0.2054
## F-statistic: 2.939 on 4 and 26 DF,  p-value: 0.03955
```

```
summary(model8)
```

```
##
## Call:
## lm(formula = LRBP4 ~ Sex + Age + LHOMAIR + Age * Sex, data = vao)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -0.21447 -0.05720  0.02090  0.07151  0.20229
##
## Coefficients:
##               Estimate Std. Error t value Pr(>|t|)
## (Intercept) -0.087232   0.131407   -0.664  0.51264
## SexMale      0.571891   0.178663    3.201  0.00359 **
## Age          0.008906   0.002934    3.035  0.00541 **
## LHOMAIR     -0.036421   0.041179   -0.884  0.38456
## SexMale:Age -0.010753   0.004015   -2.678  0.01267 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.111 on 26 degrees of freedom
## Multiple R-squared:  0.4549, Adjusted R-squared:  0.371
## F-statistic: 5.424 on 4 and 26 DF,  p-value: 0.002596
```

```
AIC(model6,model7,model8) #remove HOMAIR x Age
```

	df	AIC
model6	7	-40.24879
model7	6	-34.50246
model8	6	-41.74725

```
AIC_RBP4_iterm<-AIC(model6,model7,model8) #summary of AIC
AIC_df_RBP4_iterm<-data.frame(
  Model=c("Model 6: Includes interaction terms", "Model 7: Remove Age x Sex",
          "Model 8: Remove HOMA-IR x Sex"),
  AIC = round(AIC_RBP4_iterm$AIC,3),
  DF = AIC_RBP4_iterm$df)

aic_RBP4_iterm_table <- AIC_df_RBP4_iterm %>%
  flextable() %>%
```

```
  set_header_labels(Model = "Model Description", AIC = "AIC Value",
                    DF="Degrees of Freedom") %>%
  add_header_lines(values = "AIC Comparison of Models") %>%
  align(part="header", align="center" ) %>%
  add_footer_lines(values = "Note: Lower AIC values indicate a better model.") %>%
  fontsize(part = "footer", size = 8) %>%
  set_table_properties(layout = "autofit")
aic_RBP4_iterm_table
```

AIC Comparison of Models		
Model Description	AIC Value	Degrees of Freedom
Model 6: Includes interaction terms	-40.249	7
Model 7: Remove Age x Sex	-34.502	6
Model 8: Remove HOMA-IR x Sex	-41.747	6

Note: Lower AIC values indicate a better model.

```
#remove HOMA-IR
model9=lm(LRBP4~Sex+Age+Age*Sex,vao)
summary(model9)
```

```
##
## Call:
## lm(formula = LRBP4 ~ Sex + Age + Age * Sex, data = vao)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -0.21781 -0.06921  0.01956  0.07634  0.19094
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept) -0.135948   0.118824  -1.144  0.26262
## SexMale      0.591144   0.176615   3.347  0.00241 **
## Age          0.009749   0.002764   3.527  0.00152 **
## SexMale:Age -0.011126   0.003977  -2.798  0.00938 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.1106 on 27 degrees of freedom
## Multiple R-squared:  0.4385, Adjusted R-squared:  0.3761
## F-statistic: 7.027 on 3 and 27 DF,  p-value: 0.001216
```

```
AIC(model8,model9) # removing HOMA-IR leads to lower AIC
```

	df	AIC
model8	6	-41.74725
model9	5	-42.82834

```
#does adding BMI back into the model improve the model?
model10=lm(LRBP4~Sex+Age+Age*Sex+BMI,vao)
summary(model10)
```

```
##
## Call:
## lm(formula = LRBP4 ~ Sex + Age + Age * Sex + BMI, data = vao)
##
## Residuals:
##       Min       1Q    Median       3Q       Max
## -0.195947 -0.053725  0.009708  0.071413  0.190375
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept) -0.007224   0.187983  -0.038  0.96964
## SexMale      0.557203   0.181412   3.071  0.00494 **
## Age          0.008911   0.002932   3.040  0.00534 **
## BMI         -0.002252   0.002542  -0.886  0.38370
## SexMale:Age -0.010792   0.004011  -2.691  0.01229 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.111 on 26 degrees of freedom
## Multiple R-squared:  0.4549, Adjusted R-squared:  0.3711
## F-statistic: 5.425 on 4 and 26 DF,  p-value: 0.002593
```

```
AIC(model9,model10)
```

	df	AIC
model9	5	-42.82834
model10	6	-41.75058

```
anova(model9,model10) #no, both from ANOVA and AIC, BMI does not improve the model
```

Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
27	0.3302089	NA	NA	NA	NA
26	0.3205299	1	0.009679	0.7851149	0.3837037

```
#does the interaction term improve the model?
model11=lm(LRBP4~Sex+Age,vao)
AIC(model9,model11)
```

	df	AIC
model9	5	-42.82834
model11	4	-36.93776

```
anova(model9,model11) #yes
```

Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
27	0.3302089	NA	NA	NA	NA
28	0.4259237	-1	-0.0957148	7.82626	0.0093797

```
#is this the simplest model?
model12=lm(LRBP4~Sex,vao) #Sex alone
model13=lm(LRBP4~Age,vao) #Age alone

#summary of AIC
 AICR_3 <- AIC(model9,model12,model13)
 AICR_3df <- data.frame(
   Model = c("Age + Sex + Age x Sex", "Age", "Sex"),
   AIC = round(AICR_3$AIC, 3),
   DF = AICR_3$df)
 AICR_3df %>% flextable() %>%
   set_header_labels(Model = "Model Description", AIC = "AIC Value",
                     DF = "Degrees of Freedom") %>%
   add_header_lines(values = "AIC Comparison of Models for RBP4") %>%
   align(part = "header", align = "center") %>%
   add_footer_lines(values = "Note: Lower AIC values indicate a better model.") %>%
fontsize(part = "footer", size = 8) %>%
set_table_properties(layout = "autofit")
```

AIC Comparison of Models for RBP4		
Model Description	AIC Value	Degrees of Freedom
Age + Sex + Age x Sex	-42.828	5
Age	-34.898	3
Sex	-33.200	3

Note: Lower AIC values indicate a better model.

```
#summary of anova results
 p_values<-data.frame(
   Comparison=c("Age+Sex+AgexSex v Age", "Age+Sex+AgexSex v Sex"),
   P_value=c(round(anova(model9,model12)$"Pr(>F)"[2],3),
            round(anova(model9,model13)$"Pr(>F)"[2],3)))

 p_values %>% flextable() %>%
    set_header_labels(Comparison="Models", P_value="P-value: Probability >F") %>%
    add_header_lines(values="Is this the simplest model that fits the data best?") %>%
    align(part="header", align="center" ) %>%
    set_table_properties(layout = "autofit") %>%
    add_footer_lines(values = "Note: p<0.05 cut-off for retaining more complex model") %>%
    fontsize(part = "footer", size = 8)
```

Is this the simplest model that fits the data best?	
Models	P-value: Probability >F
Age+Sex+AgexSex v Age	0.006
Age+Sex+AgexSex v Sex	0.003

Note: p<0.05 cut-off for retaining more complex model

```
#lower AIC, and anova p<0.05 for the more complex model of Age + Sex + Age x Sex
##final model##
summary(model9)
```

```
##
## Call:
## lm(formula = LRBP4 ~ Sex + Age + Age * Sex, data = vao)
##
## Residuals:
##      Min      1Q   Median      3Q      Max
## -0.21781 -0.06921  0.01956  0.07634  0.19094
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept) -0.135948   0.118824  -1.144  0.26262
## SexMale      0.591144   0.176615   3.347  0.00241 **
## Age          0.009749   0.002764   3.527  0.00152 **
## SexMale:Age -0.011126   0.003977  -2.798  0.00938 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.1106 on 27 degrees of freedom
## Multiple R-squared:  0.4385, Adjusted R-squared:  0.3761
## F-statistic: 7.027 on 3 and 27 DF,  p-value: 0.001216
```

```
#variance inflation factors
vif(model9,type=c("predictor")) #because this model has interaction terms we need to use the GVIF
```

	GVIF	Df	GVIF^(1/(2*Df))	Interacts With	Other Predictors
Sex	1	3	1	Age	–
Age	1	3	1	Sex	–

RBP4 Final Model

RBP4 Final Model: RBP4 ~ Age + Sex + Age x Sex (p=0.009)

RBP4 Model Plots

RBP4 Age and Sex

RBP4 Age and Sex
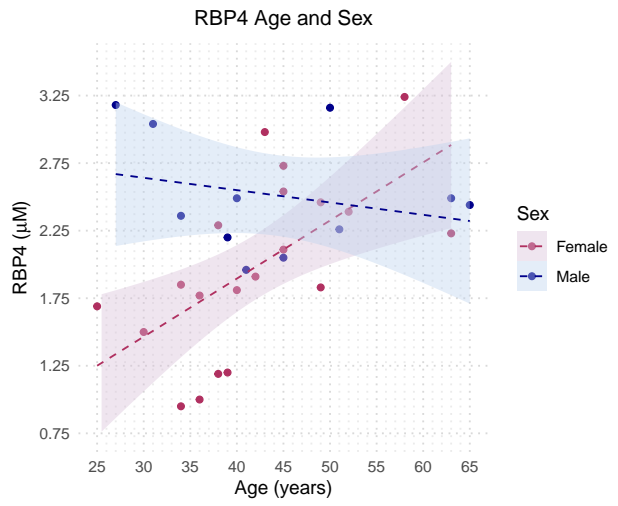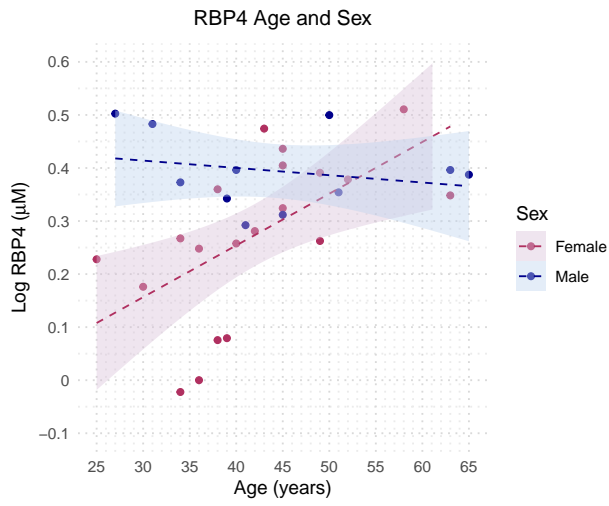
Post-hoc analysis of RBP4 and eGFR

```r
summary(lm(LRBP4~eGFR,vao))
```

```
##
## Call:
## lm(formula = LRBP4 ~ eGFR, data = vao)
##
## Residuals:
##       Min        1Q    Median        3Q       Max
## -0.277030 -0.051103  0.009991  0.070393  0.232258
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)  0.673248   0.222715   3.023  0.00519 **
## eGFR        -0.003267   0.002029  -1.611  0.11810
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.1364 on 29 degrees of freedom
## Multiple R-squared:  0.0821, Adjusted R-squared:  0.05045
## F-statistic: 2.594 on 1 and 29 DF,  p-value: 0.1181
```

```r
summary(lm(LRBP4~eGFR*Sex,vao))
```

```
##
## Call:
## lm(formula = LRBP4 ~ eGFR * Sex, data = vao)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -0.20730 -0.06922  0.01266  0.07022  0.23966
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)  0.832255   0.224461   3.708 0.000954 ***
## eGFR        -0.005153   0.002057  -2.505 0.018573 *
## SexMale     -0.546204   0.470518  -1.161 0.255861
## eGFR:SexMale 0.006133   0.004256   1.441 0.161035
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.1206 on 27 degrees of freedom
## Multiple R-squared:  0.3319, Adjusted R-squared:  0.2576
## F-statistic: 4.471 on 3 and 27 DF,  p-value: 0.0113
```

eGFR is not a significant correlate for RBP4 (p=0.12) eGFR as an interaction term with sex is also not significant (p=0.16)

TTR Model

```
vao$LTTR<-log10(vao$TTR)

#linear regression with BMI, Sex, Age and HOMA-IR
Tmodel1=lm(LTTR~BMI+Sex+Age+LHOMAIR,vao)
summary(Tmodel1)
```

```
##
## Call:
## lm(formula = LTTR ~ BMI + Sex + Age + LHOMAIR, data = vao)
##
## Residuals:
##       Min       1Q    Median       3Q       Max
## -0.221583 -0.037441  0.002198  0.057781  0.207524
##
## Coefficients:
##               Estimate Std. Error t value Pr(>|t|)
## (Intercept)  1.3295758  0.1437198    9.251 1.04e-09 ***
## BMI         -0.0021577  0.0023340   -0.924   0.3637
## SexMale      0.0955022  0.0418519    2.282   0.0309 *
## Age          0.0007957  0.0019475    0.409   0.6862
## LHOMAIR     -0.0137659  0.0377648   -0.365   0.7184
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.09806 on 26 degrees of freedom
## Multiple R-squared:  0.3276, Adjusted R-squared:  0.2242
## F-statistic: 3.167 on 4 and 26 DF,  p-value: 0.0302
```

```
vif(Tmodel1)
```

```
##      BMI      Sex      Age  LHOMAIR
## 1.597502 1.292650 1.233974 1.259206
```

```
#remove one variable at a time
Tmodel2=lm(LTTR~BMI+Sex+Age,vao) #remove HOMA-IR
Tmodel3=lm(LTTR~BMI+Sex+LHOMAIR, vao) #remove Age
Tmodel4=lm(LTTR~BMI+Age+LHOMAIR, vao) #remove Sex
Tmodel5=lm(LTTR~Sex+Age+LHOMAIR, vao) #remove BMI

AIC(Tmodel1,Tmodel2,Tmodel3,Tmodel4,Tmodel5) #summary of AIC
```

	df	AIC
Tmodel1	6	-49.45143
Tmodel2	5	-51.29340
Tmodel3	5	-51.25302
Tmodel4	5	-45.79239
Tmodel5	5	-50.44884

```
AICT<-AIC(Tmodel1,Tmodel2,Tmodel3,Tmodel4,Tmodel5) #summary of AIC
AICT_df<-data.frame(
  Model=c("Model 1: Full Model", "Model 2: No HOMA-IR", "Model 3: No Age",
          "Model 4: No Sex", "Model 5: No BMI"),
  AIC = round(AICT$AIC,3), DF = AICT$df)

aicT_table <- AICT_df %>%
  flextable() %>%
  set_header_labels(Model = "Model Description", AIC = "AIC Value",
                    DF="Degrees of Freedom") %>%
  add_header_lines(values = "AIC Comparison of Models for TTR") %>%
  align(part="header", align="center" ) %>%
  add_footer_lines(values = "Note: Lower AIC values indicate a better model.") %>%
  fontsize(part = "footer", size = 8) %>%
  set_table_properties(layout = "autofit")
aicT_table
```

AIC Comparison of Models for TTR		
Model Description	AIC Value	Degrees of Freedom
Model 1: Full Model	-49.451	6
Model 2: No HOMA-IR	-51.293	5
Model 3: No Age	-51.253	5
Model 4: No Sex	-45.792	5
Model 5: No BMI	-50.449	5

Note: Lower AIC values indicate a better model.

```
##remove HOMA-IR (lowest AIC)
#add interaction terms for Age and Sex which are not correlated
Tmodel6=lm(LTTR~Sex+Age+BMI+Age*Sex,vao)
summary(Tmodel6)
```

```
##
## Call:
## lm(formula = LTTR ~ Sex + Age + BMI + Age * Sex, data = vao)
##
## Residuals:
##       Min        1Q    Median        3Q       Max
## -0.202202 -0.031876 -0.006347  0.048701  0.199926
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)  1.150995   0.151538   7.595 4.61e-08 ***
## SexMale      0.421700   0.146241   2.884  0.00779 **
## Age          0.004725   0.002363   1.999  0.05613 .
## BMI         -0.001957   0.002049  -0.955  0.34846
## SexMale:Age -0.007491   0.003233  -2.317  0.02864 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
##
## Residual standard error: 0.08951 on 26 degrees of freedom
## Multiple R-squared:  0.4398, Adjusted R-squared:  0.3537
## F-statistic: 5.104 on 4 and 26 DF,  p-value: 0.003592
```

```
AIC(Tmodel6,Tmodel2)
```

	df	AIC
Tmodel6	6	-55.11268
Tmodel2	5	-51.29340

```
anova(Tmodel6,Tmodel2)
```

Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
26	0.2082919	NA	NA	NA	NA
27	0.2513029	-1	-0.043011	5.368841	0.0286386

```
##inclusion of interaction term improves model
###Model now TTR~Sex+BMI+Age+Age*Sex

#remove terms
Tmodel7=lm(LTTR~Sex+Age+Age*Sex,vao) # remove BMI
Tmodel8=lm(LTTR~Sex+BMI,vao) # remove Age
Tmodel9=lm(LTTR~Age+BMI,vao) #remove Sex

AICT_iterm<-AIC(Tmodel6,Tmodel7,Tmodel8,Tmodel9) #summary of AIC
AICT_iterm_df<-data.frame(
  Model=c("Full Model: Sex+Age+BMI+AgexSex",
          "Remove BMI: Sex+Age+AgexSex",
          "Remove Age: Sex+BMI",
          "Remove Sex: Age+BMI"),
  AIC = round(AICT_iterm$AIC,3), DF = AICT_iterm$df)

aicT_iterm_table <- AICT_iterm_df %>%
  flextable() %>%
  set_header_labels(Model = "Model Description", AIC = "AIC Value",
                    DF="Degrees of Freedom") %>%
  add_header_lines(values = "AIC Comparison of Models for TTR") %>%
  align(part="header", align="center" ) %>%
  add_footer_lines(values = "Note: Lower AIC values indicate a better model.") %>%
  fontsize(part = "footer", size = 8) %>%
  set_table_properties(layout = "autofit")
aicT_iterm_table
```

AIC Comparison of Models for TTR		
Model Description	AIC Value	Degrees of Freedom
Full Model: Sex+Age+BMI+AgexSex	-55.113	6

AIC Comparison of Models for TTR		
Model Description	AIC Value	Degrees of Freedom
Remove BMI: Sex+Age+AgexSex	-56.044	5
Remove Age: Sex+BMI	-52.979	4
Remove Sex: Age+BMI	-47.742	4

Note: Lower AIC values indicate a better model.

```
#lowest AIC removing BMI
#confirm with anova
anova(Tmodel7,Tmodel8)
```

Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
27	0.2155956	NA	NA	NA	NA
28	0.2538616	-1	-0.038266	4.792217	0.0374116

```
anova(Tmodel6,Tmodel7) # removing BMI leads to lower AIC, stat. sig.
```

Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
26	0.2082919	NA	NA	NA	NA
27	0.2155956	-1	-0.0073038	0.911693	0.3484596

```
###Model now TTR ~ Sex + Age + Age * Sex

#does adding HOMA-IR back into the model improve the model?
Tmodel10=lm(LTTR~Sex+Age+Age*Sex+LHOMAIR,vao)
summary(Tmodel10)
```

```
##
## Call:
## lm(formula = LTTR ~ Sex + Age + Age * Sex + LHOMAIR, data = vao)
##
## Residuals:
##       Min       1Q    Median        3Q       Max
## -0.219463 -0.034099 -0.000104  0.048686  0.205280
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept)  1.060046   0.107323   9.877 2.74e-10 ***
## SexMale      0.442935   0.145917   3.036   0.0054 **
## Age          0.005092   0.002397   2.124   0.0433 *
## LHOMAIR     -0.015603   0.033632  -0.464   0.6465
## SexMale:Age -0.007621   0.003279  -2.324   0.0282 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.09069 on 26 degrees of freedom
```

```
## Multiple R-squared:  0.425,   Adjusted R-squared:  0.3365
## F-statistic: 4.803 on 4 and 26 DF,  p-value: 0.004906
```

```
AIC(Tmodel7, Tmodel10)
```

	df	AIC
Tmodel7	5	-56.04428
Tmodel10	6	-54.29986

```
anova(Tmodel7, Tmodel10) #no, both from ANOVA and AIC, HOMA does not improve the model
```

Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
27	0.2155956	NA	NA	NA	NA
26	0.2138255	1	0.0017702	0.2152428	0.6465498

```
#does the interaction term improve the model?
Tmodel11=lm(LTTR~Sex+Age,vao)
AIC(Tmodel7,Tmodel11)
```

	df	AIC
Tmodel7	5	-56.04428
Tmodel11	4	-51.95223

```
anova(Tmodel7,Tmodel11) #yes
```

Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
27	0.2155956	NA	NA	NA	NA
28	0.2624138	-1	-0.0468181	5.863243	0.022454

```
#is this the simplest model?
Tmodel12=lm(LTTR~Sex,vao) #Sex alone
Tmodel13=lm(LTTR~Age,vao) #Age alone


AICT2<-AIC(Tmodel7,Tmodel11,Tmodel12,Tmodel13) #summary of AIC
AICT2_df<-data.frame(
  Model=c("Sex + Age + Sex x Age",
          "Sex + Age","Sex", "Age"),
  AIC = round(AICT2$AIC,3), DF = AICT2$df)

aicT2_table <- AICT2_df %>%
  flextable() %>%
  set_header_labels(Model = "Model Description", AIC = "AIC Value",
                  DF="Degrees of Freedom") %>%
  add_header_lines(values = "AIC Comparison of Models for TTR") %>%
```

```
  align(part="header", align="center" ) %>%
  add_footer_lines(values="Note: Lower AIC values indicate a better model.") %>%
  fontsize(part = "footer", size = 8) %>%
  set_table_properties(layout = "autofit")
aicT2_table
```

AIC Comparison of Models for TTR		
Model Description	AIC Value	Degrees of Freedom
Sex + Age + Sex x Age	-56.044	5
Sex + Age	-51.952	4
Sex	-52.919	3
Age	-44.500	3

Note: Lower AIC values indicate a better model.

```
#summary of anova results
 p_values<-data.frame(
   Comparison=c("Age+Sex+AgexSex v Age+Sex", "Age+Sex+AgexSex v Age",
                "Age+Sex+AgexSex v Sex"),
   P_value=c(round(anova(Tmodel7,Tmodel11)$"Pr(>F)"[2],3),
             round(anova(Tmodel7,Tmodel12)$"Pr(>F)"[2],3),
             round(anova(Tmodel7,Tmodel13)$"Pr(>F)"[2],3)))

 p_values %>% flextable() %>%
    set_header_labels(Comparison="Models", P_value="P-value: Probability >F") %>%
    add_header_lines(values="Is this the simplest model that fits the data best?") %>%
    align(part="header", align="center" ) %>%
    set_table_properties(layout = "autofit") %>%
    add_footer_lines(values = "Note: p<0.05 cut-off for retaining more complex model") %>%
    fontsize(part = "footer", size = 8)
```

Is this the simplest model that fits the data best?	
Models	P-value: Probability >F
Age+Sex+AgexSex v Age+Sex	0.022
Age+Sex+AgexSex v Age	0.045
Age+Sex+AgexSex v Sex	0.001

Note: p<0.05 cut-off for retaining more complex model

```
  ##final model for TTR
summary(Tmodel7)
```

```
## 
## Call:
## lm(formula = LTTR ~ Sex + Age + Age * Sex, data = vao)
## 
```

```
## Residuals:
##       Min        1Q    Median        3Q       Max
## -0.219703 -0.039820  0.003317  0.047080  0.200418
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)  1.039175   0.096013  10.823 2.53e-11 ***
## SexMale      0.451183   0.142710   3.162  0.00385 **
## Age          0.005453   0.002233   2.442  0.02145 *
## SexMale:Age -0.007781   0.003213  -2.421  0.02245 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.08936 on 27 degrees of freedom
## Multiple R-squared:  0.4202, Adjusted R-squared:  0.3558
## F-statistic: 6.522 on 3 and 27 DF,  p-value: 0.00184
```
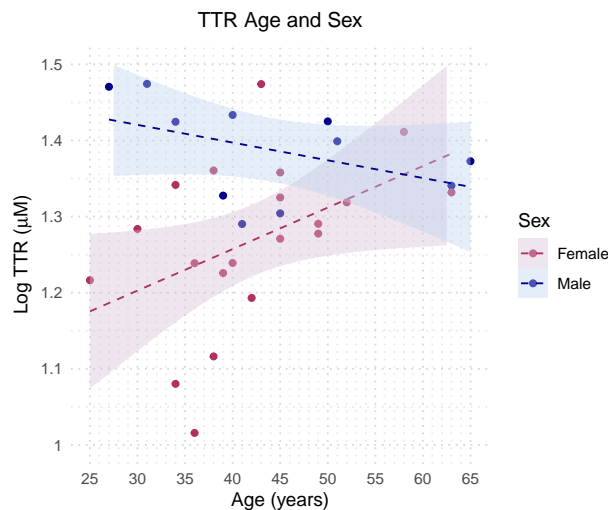
```
#variance inflation factors
vif(Tmodel7,type=c("predictor")) #because this model has interaction terms we need to use the GVIF
```

	GVIF	Df	GVIF^(1/(2*Df))	Interacts With	Other Predictors
Sex	1	3	1	Age	–
Age	1	3	1	Sex	–

TTR Final Model

TTR Final Model: TTR ~ Age + Sex + Age x Sex (p=0.02)

TTR Model Plots

Retinol Model

```
vao$LROL<-log10(vao$Sretinol)

#linear regression with BMI, Sex, Age and HOMAIR
Rmodel1=lm(LROL~BMI+Sex+Age+LHOMAIR,vao)
vif(Rmodel1)
```

```
##      BMI      Sex      Age  LHOMAIR
## 1.597502 1.292650 1.233974 1.259206
```

```
#remove one variable at a time
Rmodel2=lm(LROL~BMI+Sex+Age,vao) #remove HOMA-IR
Rmodel3=lm(LROL~BMI+Sex+LHOMAIR, vao) #remove Age
Rmodel4=lm(LROL~BMI+Age+LHOMAIR, vao) #remove Sex
Rmodel5=lm(LROL~Sex+Age+LHOMAIR, vao) #remove BMI

AIC(Rmodel1,Rmodel2,Rmodel3,Rmodel4,Rmodel5) #summary of AIC
```

	df	AIC
Rmodel1	6	-37.11641
Rmodel2	5	-38.95172
Rmodel3	5	-37.12858
Rmodel4	5	-37.23750
Rmodel5	5	-38.03374

```
AICR<-AIC(Rmodel1,Rmodel2,Rmodel3,Rmodel4,Rmodel5) #summary of AIC
AICR_df<-data.frame(
  Model=c("Model 1: Full Model", "Model 2: No HOMA-IR", "Model 3: No Age",
          "Model 4: No Sex", "Model 5: No BMI"),
  AIC = AICR$AIC,
  DF = AICR$df)
aicR_table <- AICR_df %>%
  flextable() %>%
  set_header_labels(Model = "Model Description", AIC = "AIC Value",
                    DF="Degrees of Freedom") %>%
  add_header_lines(values = "AIC Comparison of Models for Retinol") %>%
  align(part="header", align="center" ) %>%
  add_footer_lines(values = "Note: Lower AIC values indicate a better model.") %>%
  fontsize(part = "footer", size = 8) %>%
  set_table_properties(layout = "autofit")
aicR_table
```

AIC Comparison of Models for Retinol		
Model Description	AIC Value	Degrees of Freedom
Model 1: Full Model	-37.11641	6
Model 2: No HOMA-IR	-38.95172	5

AIC Comparison of Models for Retinol		
Model Description	AIC Value	Degrees of Freedom
Model 3: No Age	-37.12858	5
Model 4: No Sex	-37.23750	5
Model 5: No BMI	-38.03374	5

Note: Lower AIC values indicate a better model.

```
##remove HOMA-IR (lowest AIC), add interaction term
Rmodel6=lm(LROL~Age+BMI+Sex+Age*Sex,vao)
summary(Rmodel6)
```

```
##
## Call:
## lm(formula = LROL ~ Age + BMI + Sex + Age * Sex, data = vao)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -0.23533 -0.07032  0.00921  0.05459  0.24907
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept) -0.005764   0.197897  -0.029   0.9770
## Age          0.005830   0.003086   1.889   0.0701 .
## BMI         -0.002747   0.002676  -1.026   0.3142
## SexMale      0.281136   0.190980   1.472   0.1530
## Age:SexMale -0.004974   0.004222  -1.178   0.2494
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.1169 on 26 degrees of freedom
## Multiple R-squared:  0.3144, Adjusted R-squared:  0.2089
## F-statistic:  2.98 on 4 and 26 DF,  p-value: 0.03764
```

```
#can we justify inclusion of interaction terms?
AIC(Rmodel6,Rmodel2)
```

	df	AIC
Rmodel6	6	-38.56389
Rmodel2	5	-38.95172

```
anova(Rmodel6,Rmodel2)
```

Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
26	0.3552323	NA	NA	NA	NA
27	0.3741953	-1	-0.0189629	1.387927	0.2494263

```
#cannot justify interaction terms

#remove each term
Rmodel7=lm(LROL~Age+BMI,vao) #remove Sex
Rmodel8=lm(LROL~Age+Sex,vao) # remove BMI
Rmodel9=lm(LROL~BMI+Sex,vao) # remove Age

p_values<-data.frame(
  Comparison=c("Age+Sex+BMI v Age+BMI", "Age+Sex+BMI v Age+Sex",
               "Age+Sex+BMI v BMI+Sex"),
  P_value=c(round(anova(Rmodel2,Rmodel7)$"Pr(>F)"[2],3),
            round(anova(Rmodel2,Rmodel8)$"Pr(>F)"[2],3),
            round(anova(Rmodel2,Rmodel9)$"Pr(>F)"[2],3)))

  p_values %>% flextable() %>%
    set_header_labels(Comparison="Comparison", P_value="P-value: Probability >F") %>%
    add_header_lines(values="ANOVA Comparison") %>%
    align(part="header", align="center" ) %>%
    set_table_properties(layout = "autofit") %>%
    add_footer_lines(values = "Note: p<0.05 cut-off for retaining more complex model") %>%
    fontsize(part = "footer", size = 8)
```

ANOVA Comparison	
Comparison	P-value: Probability >F
Age+Sex+BMI v Age+BMI	0.213
Age+Sex+BMI v Age+Sex	0.267
Age+Sex+BMI v BMI+Sex	0.152

Note: p<0.05 cut-off for retaining more complex model

```
{AICR_2<-AIC(Rmodel2,Rmodel7,Rmodel8,Rmodel9) #summary of AIC
AICR_2df<-data.frame(
  Model=c("Age + BMI + Sex","Age + BMI","Age + Sex",
          "BMI + Sex"),
  AIC = AICR_2$AIC, DF = AICR_2$df)

aicR_2_table <- AICR_2df %>%
  flextable() %>%
  set_header_labels(Model = "Model Description", AIC = "AIC Value",
                    DF="Degrees of Freedom") %>%
  add_header_lines(values = "AIC Comparison of Models for Retinol") %>%
  align(part="header", align="center" ) %>%
  add_footer_lines(values = "Note: Lower AIC values indicate a better model.") %>%
  fontsize(part = "footer", size = 8) %>%
  set_table_properties(layout = "autofit")}
aicR_2_table
```

AIC Comparison of Models for Retinol		
Model Description	AIC Value	Degrees of Freedom
Age + BMI + Sex	-38.95172	5
Age + BMI	-39.14023	4
Age + Sex	-39.50958	4
BMI + Sex	-38.55048	4

Note: Lower AIC values indicate a better model.

```
#Age and Sex has the lowest AIC
#single regressions
Rmodel10=lm(LROL~Age,vao)
Rmodel11=lm(LROL~Sex,vao)
AIC(Rmodel11, Rmodel10,Rmodel8)
```

	df	AIC
Rmodel11	3	-37.36999
Rmodel10	3	-37.28122
Rmodel8	4	-39.50958

```
anova(Rmodel10,Rmodel8) #not better than Age alone
```

Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
29	0.4493028	NA	NA	NA	NA
28	0.3920143	1	0.0572885	4.09189	0.0527329

```
anova(Rmodel11,Rmodel8) #not better than Sex alone
```

Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
29	0.4480181	NA	NA	NA	NA
28	0.3920143	1	0.0560038	4.000128	0.0552816

```
summary(Rmodel10)
```

```
##
## Call:
## lm(formula = LROL ~ Age, data = vao)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -0.31522 -0.04495  0.01325  0.06391  0.26545
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
```

```
## (Intercept) -0.040082    0.097843   -0.410    0.6851
## Age           0.004689    0.002225    2.107    0.0438 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.1245 on 29 degrees of freedom
## Multiple R-squared:  0.1328, Adjusted R-squared:  0.1029
## F-statistic: 4.441 on 1 and 29 DF,  p-value: 0.04385
```

```r
summary(Rmodel11)
```

```
##
## Call:
## lm(formula = LROL ~ Sex, data = vao)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -0.32125 -0.04191  0.00414  0.05189  0.23507
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept)  0.12539    0.02779    4.512 9.83e-05 ***
## SexMale      0.09938    0.04666    2.130   0.0418 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.1243 on 29 degrees of freedom
## Multiple R-squared:  0.1353, Adjusted R-squared:  0.1055
## F-statistic: 4.537 on 1 and 29 DF,  p-value: 0.04178
```

```r
#what about BMI alone
Rmodel12=lm(LROL~BMI,vao)
summary(Rmodel12)
```

```
##
## Call:
## lm(formula = LROL ~ BMI, data = vao)
##
## Residuals:
##       Min        1Q    Median        3Q       Max
## -0.254853 -0.039187  0.007799  0.053518  0.304417
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept)  0.382573   0.089540    4.273  0.00019 ***
## BMI         -0.005809   0.002274   -2.555  0.01615 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.1208 on 29 degrees of freedom
## Multiple R-squared:  0.1837, Adjusted R-squared:  0.1555
## F-statistic: 6.526 on 1 and 29 DF,  p-value: 0.01615
```

25

```
#best p-value for BMI alone

{AICR_3<-AIC(Rmodel7,Rmodel8,Rmodel9,Rmodel10,Rmodel11,Rmodel12) #summary of AIC
AICR_3df<-data.frame(
  Model=c("Age + BMI","Age + Sex",
          "BMI + Sex", "Age", "Sex", "BMI"),
  AIC = AICR_3$AIC, DF = AICR_3$df)

aicR_3_table <- AICR_3df %>%
  flextable() %>%
  set_header_labels(Model = "Model Description", AIC = "AIC Value",
                    DF="Degrees of Freedom") %>%
  add_header_lines(values = "AIC Comparison of Models for Retinol") %>%
  align(part="header", align="center" ) %>%
  add_footer_lines(values = "Note: Lower AIC values indicate a better model.") %>%
  fontsize(part = "footer", size = 8) %>%
  set_table_properties(layout = "autofit")}
aicR_3_table
```

AIC Comparison of Models for Retinol		
Model Description	AIC Value	Degrees of Freedom
Age + BMI	-39.14023	4
Age + Sex	-39.50958	4
BMI + Sex	-38.55048	4
Age	-37.28122	3
Sex	-37.36999	3
BMI	-39.15575	3

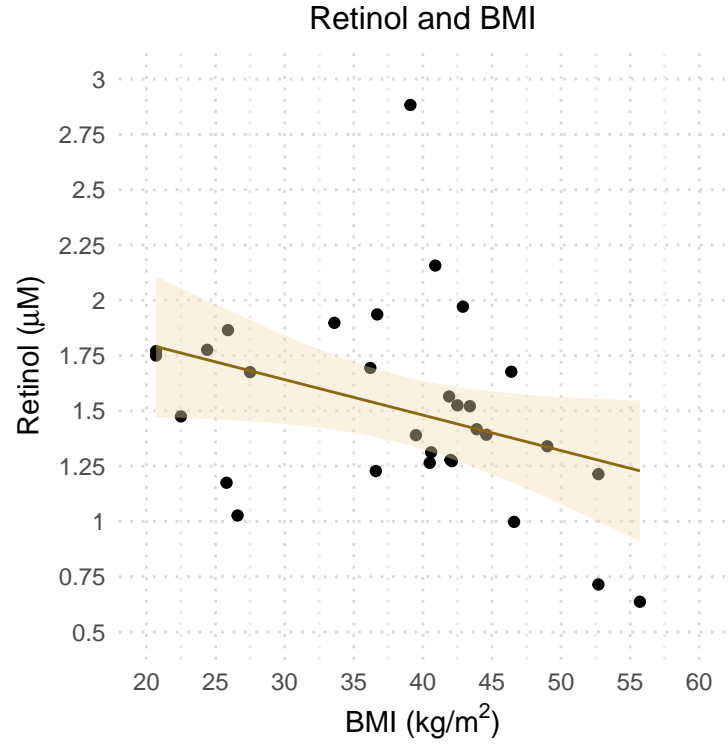Note: Lower AIC values indicate a better model.

```
#BMI alone also has lowest AIC
##final model is ROL ~ BMI
```

Retinol Final Model

Retinol Final Model: Retinol ~ BMI (p=0.016)

Retinol Model Plots

Retinol and BMI

Sensitivity Analysis of Retinol and BMI

```
vaono23 <-vao %>% filter(ID!= "51-3523") #omit 23 from data set
Rmodel12no23<-lm(LROL~BMI,vaono23)
summary(Rmodel12no23)
```

```
##
## Call:
## lm(formula = LROL ~ BMI, data = vaono23)
##
## Residuals:
##       Min       1Q    Median        3Q       Max
## -0.258376 -0.049593  0.003565  0.047807  0.293192
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)  0.321821   0.086169   3.735 0.000852 ***
## BMI         -0.003968   0.002226  -1.783 0.085468 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.1114 on 28 degrees of freedom
## Multiple R-squared:  0.1019, Adjusted R-squared:  0.06987
## F-statistic: 3.178 on 1 and 28 DF,  p-value: 0.08547
```

Omission of participant with liver fibrosis and overt retinol deficiency from the regression model increased the p-value of correlation between BMI and retinol to p=0.09

Retinol Regressions Omitting Participant with Retinol Deficiency and Apparent Liver Fibrosis

```
Rno23model1=lm(LROL~BMI+Sex+Age+LHOMAIR,vaono23)
summary(Rno23model1)
```

```
##
## Call:
## lm(formula = LROL ~ BMI + Sex + Age + LHOMAIR, data = vaono23)
##
## Residuals:
##       Min       1Q    Median        3Q       Max
## -0.255391 -0.062874 -0.002688  0.052888  0.230952
##
## Coefficients:
##               Estimate Std. Error t value Pr(>|t|)
## (Intercept)  0.0639189  0.1612890   0.396    0.695
## BMI         -0.0008989  0.0027014  -0.333    0.742
## SexMale      0.0677670  0.0466130   1.454    0.158
## Age          0.0028660  0.0021708   1.320    0.199
## LHOMAIR     -0.0193169  0.0420587  -0.459    0.650
##
```

```
## Residual standard error: 0.1092 on 25 degrees of freedom
## Multiple R-squared:  0.2294, Adjusted R-squared:  0.1061
## F-statistic:  1.86 on 4 and 25 DF,  p-value: 0.1489
```

```r
#remove one variable at a time
Rno23model2=lm(LROL~BMI+Sex+Age,vaono23) #remove HOMAIR
Rno23model3=lm(LROL~BMI+Sex+LHOMAIR, vaono23) #remove Age
Rno23model4=lm(LROL~BMI+Age+LHOMAIR, vaono23) #remove Sex
Rno23model5=lm(LROL~Sex+Age+LHOMAIR, vaono23) #remove BMI

AICR<-AIC(Rno23model1, Rno23model2, Rno23model3, Rno23model4,Rno23model5) #summary of AIC
AICR_df<-data.frame(
  Model=c("Model 1: Full Model", "Model 2: No HOMA-IR", "Model 3: No Age",
          "Model 4: No Sex", "Model 5: No BMI"),
  AIC = AICR$AIC,
  DF = AICR$df)
aicR_table <- AICR_df %>%
  flextable() %>%
  set_header_labels(Model = "Model Description", AIC = "AIC Value",
                    DF="Degrees of Freedom") %>%
  add_header_lines(values = "AIC Comparison of Models for Retinol (Omitting 23)") %>%
  align(part="header", align="center" ) %>%
  add_footer_lines(values = "Note: Lower AIC values indicate a better model.") %>%
  fontsize(part = "footer", size = 8) %>%
  set_table_properties(layout = "autofit")
aicR_table
```

AIC Comparison of Models for Retinol (Omitting 23)		
Model Description	AIC Value	Degrees of Freedom
Model 1: Full Model	-41.21348	6
Model 2: No HOMA-IR	-42.96142	5
Model 3: No Age	-41.19143	5
Model 4: No Sex	-40.77869	5
Model 5: No BMI	-43.08092	5

Note: Lower AIC values indicate a better model.

```r
#remove BMI, add interaction terms
Rno23model6=lm(LROL~Sex+Age+LHOMAIR+Sex*Age,vaono23)
Rno23model7=lm(LROL~Sex+Age+Sex*Age,vaono23) #remove HOMA
Rno23model8=lm(LROL~Sex+Age,vaono23) #remove HOMA and Sex * Age
Rno23model9=lm(LROL~Sex+LHOMAIR,vaono23) #remove Age
Rno23model10=lm(LROL~Age+LHOMAIR,vaono23) #remove Sex

AIC(Rno23model5, Rno23model6,Rno23model7,Rno23model8,Rno23model9,Rno23model10)
```

	df	AIC
Rno23model5	5	-43.08092

	df	AIC
Rno23model6	6	-42.14048
Rno23model7	5	-43.85300
Rno23model8	4	-44.68606
Rno23model9	4	-42.70304
Rno23model10	4	-41.45723

```
#model 8 has the lowest AIC
#Sex + Age
summary(Rno23model8)
```

```
##
## Call:
## lm(formula = LROL ~ Sex + Age, data = vaono23)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -0.26566 -0.06596 -0.01165  0.04795  0.21500
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept) -0.004218   0.085347  -0.049   0.9609
## SexMale      0.076579   0.040293   1.901   0.0681 .
## Age          0.003450   0.001926   1.791   0.0845 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.106 on 27 degrees of freedom
## Multiple R-squared:  0.2157, Adjusted R-squared:  0.1576
## F-statistic: 3.713 on 2 and 27 DF,  p-value: 0.03763
```

```
#how does this compare to the predictors alone
Rno23model11=lm(LROL~Sex,vaono23) #Sex alone
Rno23model12=lm(LROL~Age,vaono23) #Age alone
AIC(Rno23model8, Rno23model11, Rno23model12)
```

	df	AIC
Rno23model8	4	-44.68606
Rno23model11	3	-43.31838
Rno23model12	3	-42.91924

```
anova(Rno23model8,Rno23model11) #not better than Sex alone
```

Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
27	0.3033459	NA	NA	NA	NA
28	0.3393832	-1	-0.0360373	3.207581	0.0845163

```
anova(Rno23model8,Rno23model12) #not better than Age alone
```

Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
27	0.3033459	NA	NA	NA	NA
28	0.3439287	-1	-0.0405828	3.612165	0.0680846

```
summary(Rno23model11) #p>0.05
```

```
## 
## Call:
## lm(formula = LROL ~ Sex, data = vaono23)
## 
## Residuals:
##       Min        1Q    Median        3Q       Max
## -0.287994 -0.050487  0.001027  0.044673  0.235073
## 
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept)  0.14230    0.02526   5.634 4.92e-06 ***
## SexMale      0.08247    0.04171   1.977   0.0579 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## 
## Residual standard error: 0.1101 on 28 degrees of freedom
## Multiple R-squared:  0.1225, Adjusted R-squared:  0.09117
## F-statistic: 3.909 on 1 and 28 DF,  p-value: 0.05794
```

```
summary(Rno23model12) #p>0.05
```

```
## 
## Call:
## lm(formula = LROL ~ Age, data = vaono23)
## 
## Residuals:
##       Min        1Q    Median        3Q       Max
## -0.291619 -0.052172  0.005761  0.063472  0.261440
## 
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept) 0.010978   0.088847   0.124   0.9025
## Age         0.003749   0.002007   1.868   0.0723 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## 
## Residual standard error: 0.1108 on 28 degrees of freedom
## Multiple R-squared:  0.1108, Adjusted R-squared:  0.079
## F-statistic: 3.488 on 1 and 28 DF,  p-value: 0.07233
```

```r
summary(lm(LROL~BMI,vaono23))
```

```
## 
## Call:
## lm(formula = LROL ~ BMI, data = vaono23)
## 
## Residuals:
##       Min       1Q   Median       3Q      Max 
## -0.258376 -0.049593  0.003565  0.047807  0.293192 
## 
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)    
## (Intercept)  0.321821   0.086169   3.735 0.000852 ***
## BMI         -0.003968   0.002226  -1.783 0.085468 .  
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## 
## Residual standard error: 0.1114 on 28 degrees of freedom
## Multiple R-squared:  0.1019, Adjusted R-squared:  0.06987 
## F-statistic: 3.178 on 1 and 28 DF,  p-value: 0.08547
```

No significant correlates for retinol after omission participant with gross morphology of liver fibrosis and overt retinol deficiency

Genotype effect on Retinol, RBP4, and TTR

ANOVA Results Table		
Analyte	SNP	p-value
Retinol	TTRsnp	0.63
Retinol	RBP4snp	0.86
RBP4	TTRsnp	0.48
RBP4	RBP4snp	0.70
TTR	TTRsnp	0.64
TTR	RBP4snp	0.36

Table S2, S3

Analyte Conc. Stratified by *RBP4* Genotype (rs10882272)			
Genotype	RBP4 (µM)	TTR (µM)	Retinol (µM)
1/1	1.91 (1.00, 3.16)	19.20 (10.37, 26.61)	1.35 (0.71, 2.88)
1/2	2.15 (1.19, 3.24)	21.27 (13.07, 29.81)	1.52 (1.00, 2.16)
2/2	2.10 (0.95, 3.18)	20.24 (12.03, 29.55)	1.42 (0.64, 1.97)

Concentrations shown as geometric mean and range

For the *RBP4* genotype, 1/1 refers to T/T, 1/2 to T/C and 2/2 to C/C for single nucleotide polymorphism in the 3' untranslated region

Analyte Conc. Stratified by *TTR* Genotype (rs1667255)			
Genotype	RBP4 (µM)	TTR (µM)	Retinol (µM)
1/1	1.88 (0.95, 3.16)	18.84 (12.03, 26.61)	1.42 (0.64, 2.88)
1/2	2.10 (1.00, 3.04)	20.39 (10.37, 29.81)	1.38 (0.71, 1.69)
2/2	2.27 (1.50, 3.24)	22.27 (16.46, 29.79)	1.56 (1.21, 2.16)

Concentrations shown as geometric mean and range

For the *TTR* genotype, 1/1 refers to A/A, 1/2 to A/C and 2/2 to C/C for intronic single nucleotide polymorphism

Figure 2