Task1 Seminar1

Group A3

2025-10-06

Task Introduction

Task 1: DiGeHormone - Investigating Factors Influencing Gastric Emptying in Type II Diabetes Mellitus A large cross-sectional study, named DiGeHormone, has been carried out in a population of individuals suffering from Type II Diabetes Mellitus (T2DM). The aim of the study is to investigate the association between a set of endogenous gastrointestinal (GI) hormones, T2DM disease factors and gastric emptying (GE).

The dataset (Data_T1.csv Download Data_T1.csv) includes basic demographic information, T2DM related factors, and GI biomarkers in 450 individuals with a T2DM diagnosis. A full description of the variables follow in Table 1 below.

Data Exploration

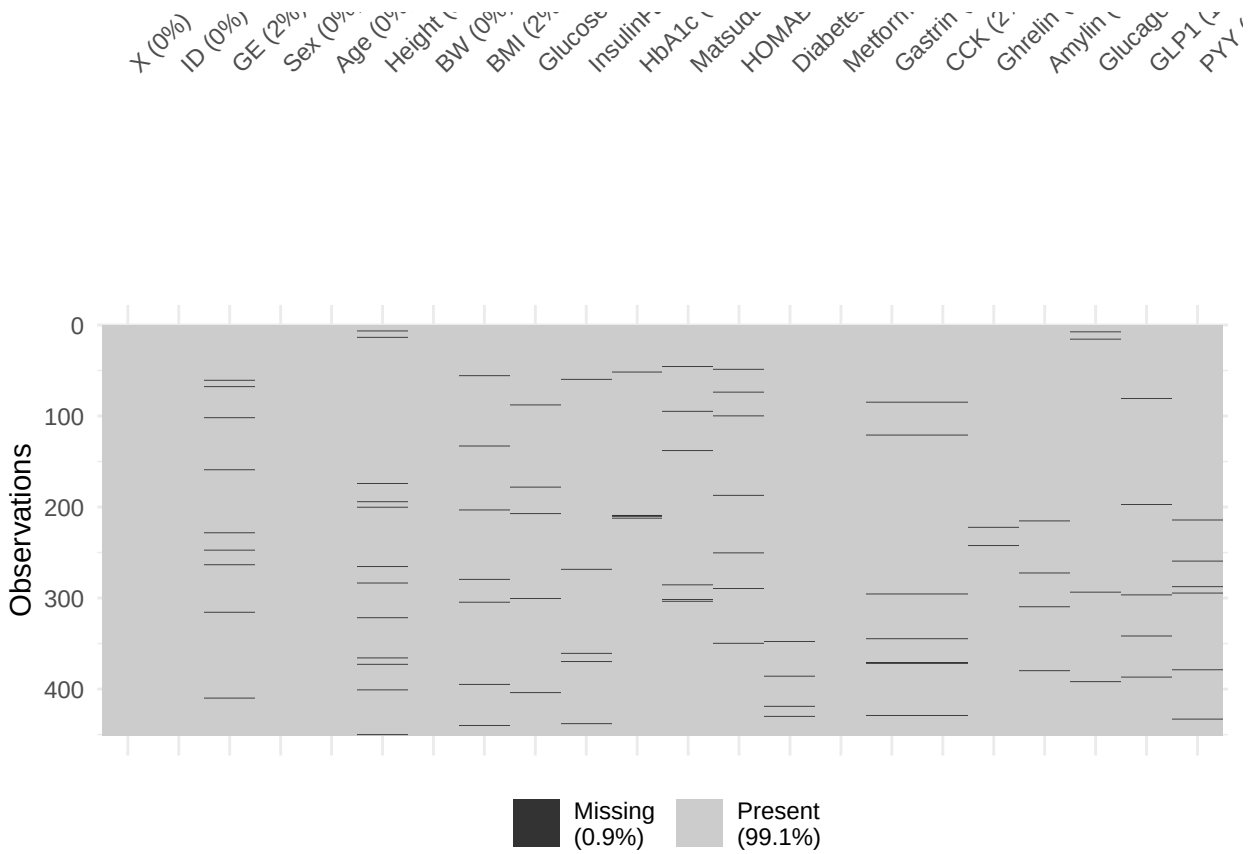
Step 1: data loading We load the data and visualized GE data.

```
### load data
dat <- read.csv("Data_T1.csv")
## showing data
head(dat)
```

```
##   X ID   GE Sex Age Height BW   BMI GlucoseFasting InsulinFasting HbA1c
## 1 1  1 29.8   1  40    164 90 33.46          9.620          9.645  8.08
## 2 2  2 53.2   1  35    159 59 23.34          9.833          6.760  8.26
## 3 3  3 44.4   0  48    174 81 26.75          8.717          9.307  8.74
## 4 4  4 58.8   0  37    154 65 27.41         11.179          6.948  8.89
## 5 5  5 54.9   0  47    179 65 20.29          8.613          5.198  7.89
## 6 6  6 37.6   0  55    179 82 25.59          9.461         10.941  8.47
##   MatsudaIdx   HOMAB DiabetesComplications Metformin Gastrin   CCK Ghrelin
## 1       4.12 12.8500                     0         0   93.87 93.87   319.8
## 2       5.28  8.9750                     0         1   86.37 86.37   189.3
## 3       4.17 11.4050                     0         0   73.19 73.19   227.1
## 4       5.41  9.8900                     0         0   81.32 81.32   326.1
## 5       6.47  7.4175                     1         0   59.48 59.48   388.3
## 6       3.62 12.3500                     0         0   60.82 60.82   327.5
##   Amylin Glucagon GLP1   PYY
## 1  16.76    9.002 2.35 99.75
## 2  13.23   13.711 5.41 84.85
## 3  15.79   16.701 3.97 86.47
## 4  16.17    9.890 4.69 57.50
```

```
## 5  11.98   11.074 2.81 55.99
## 6  12.32   12.669 3.62 83.64
```

```
library(naniar)
vis_miss(dat)
```



As shown in the figure, approximately 1% of the data is missing in the dataset. Missing data is relatively few, so we can delete the missing lines in data analysis.

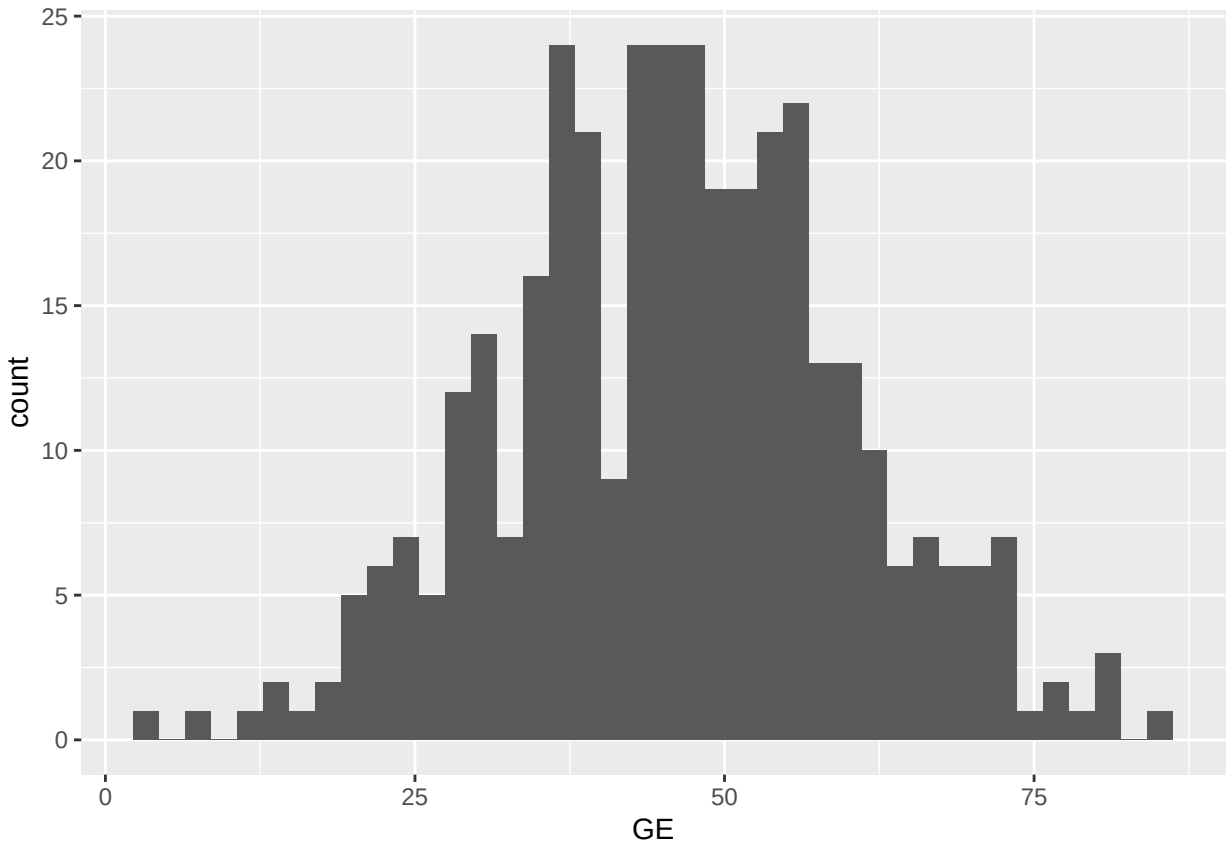
Step 2: Data exploring

We use visualizations and statistic tests to have an understanding of the data, in order to build suitable models. GE is shown below.

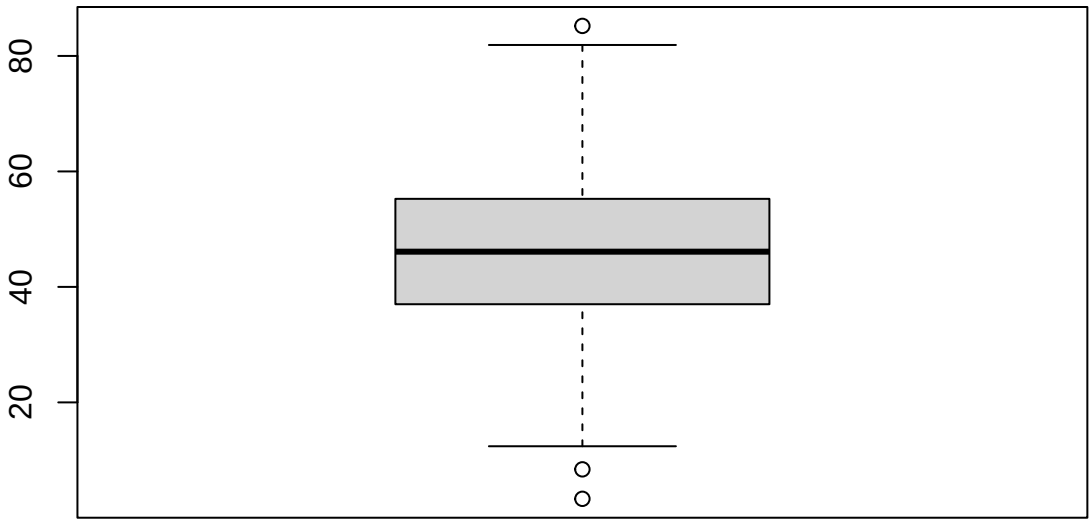
```
dat <- dat[complete.cases(dat), ]

library(ggplot2)
library(dplyr)
```

```
##
## Attaching package: 'dplyr'

## The following objects are masked from 'package:stats':
##
##     filter, lag

## The following objects are masked from 'package:base':
##
##     intersect, setdiff, setequal, union
```

```
library(tidyr)

ggplot(dat, aes(GE)) + geom_histogram(bins=40)
```




```
boxplot(dat$GE)
```



We devided the variables into 3 types as follow:

Biomarkers: Gastrin, CCK, Ghrelin, Amylin, Glucagon, GLP1, PYY. All values are continuous.

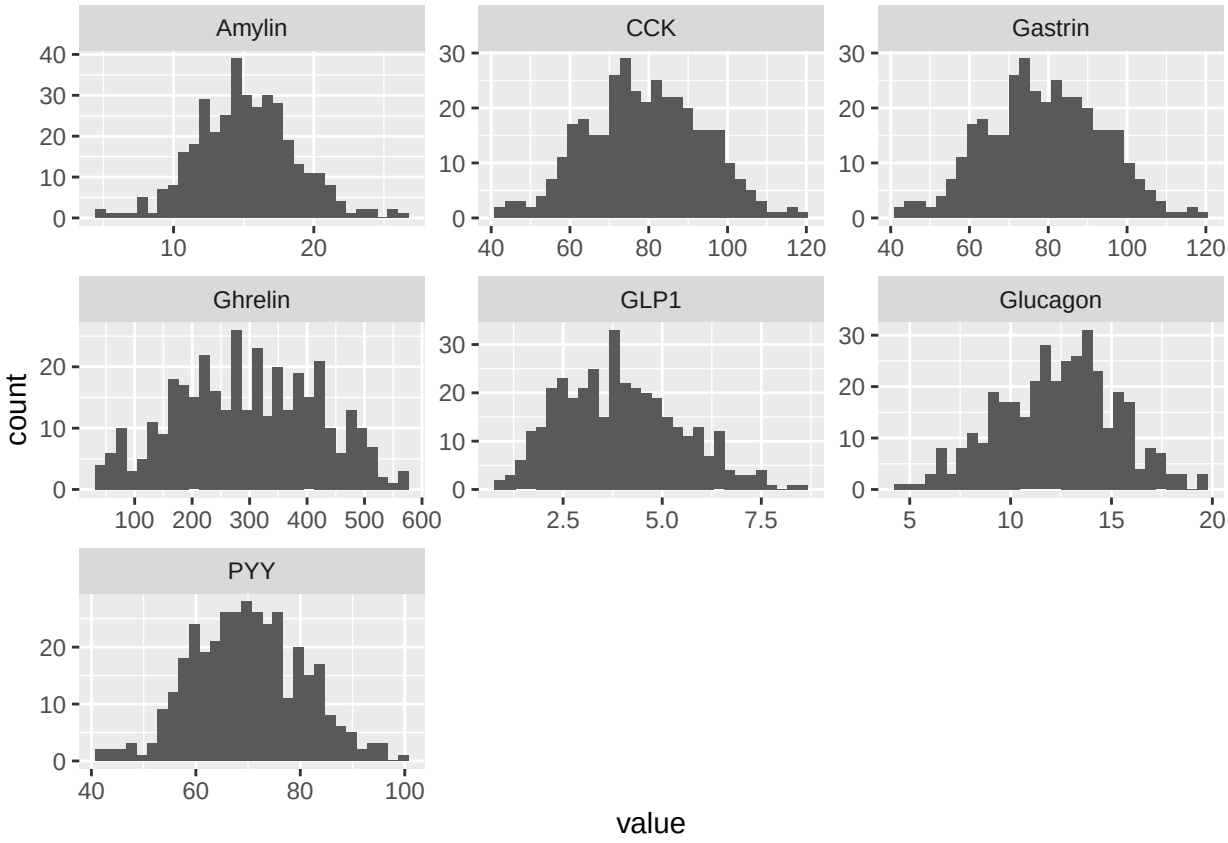
Continuous Variables: Age, BW, BMI, GlucoseFasting, InsulinFasting, HbA1c, MatsudaIdx, HOMAB. All values are continuous.

Categorical Variables: Sex, Metformin usage, DiabetesComplications. All values are 0-1.

First, we visualize variables with continuous values, which is Biomarkers and Continuous Variables.

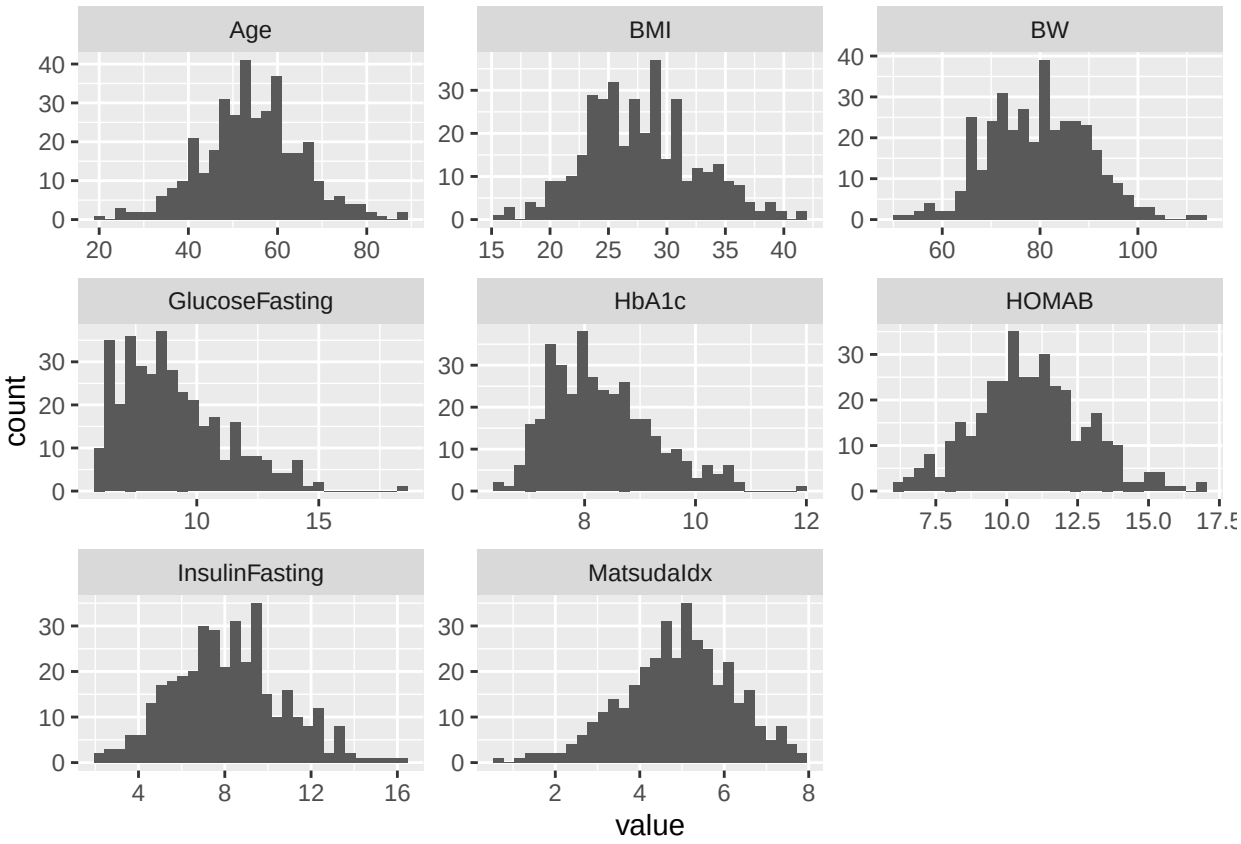
```
# histogram of biomarkers & contimuous_vars
library(tidyr)
biomarkers <- c("Gastrin","CCK","Ghrelin","Amylin","Glucagon","GLP1","PYY")
continuous_vars <- c("Age","BW","BMI","GlucoseFasting","InsulinFasting","HbA1c","MatsudaIdx","HOMAB")
categorical_vars <- c("Sex","Metformin","DiabetesComplications")

dat %>% select(all_of(biomarkers)) %>%
  pivot_longer(everything(), names_to="marker", values_to="value") %>%
  ggplot(aes(x=value)) + facet_wrap(~marker, scales="free") + geom_histogram()
```

```
## `stat_bin()` using `bins = 30`. Pick better value `binwidth`.
```




```
dat %>% select(all_of(continuous_vars)) %>%
  pivot_longer(everything(), names_to="marker", values_to="value") %>%
  ggplot(aes(x=value)) + facet_wrap(~marker, scales="free") + geom_histogram()
```

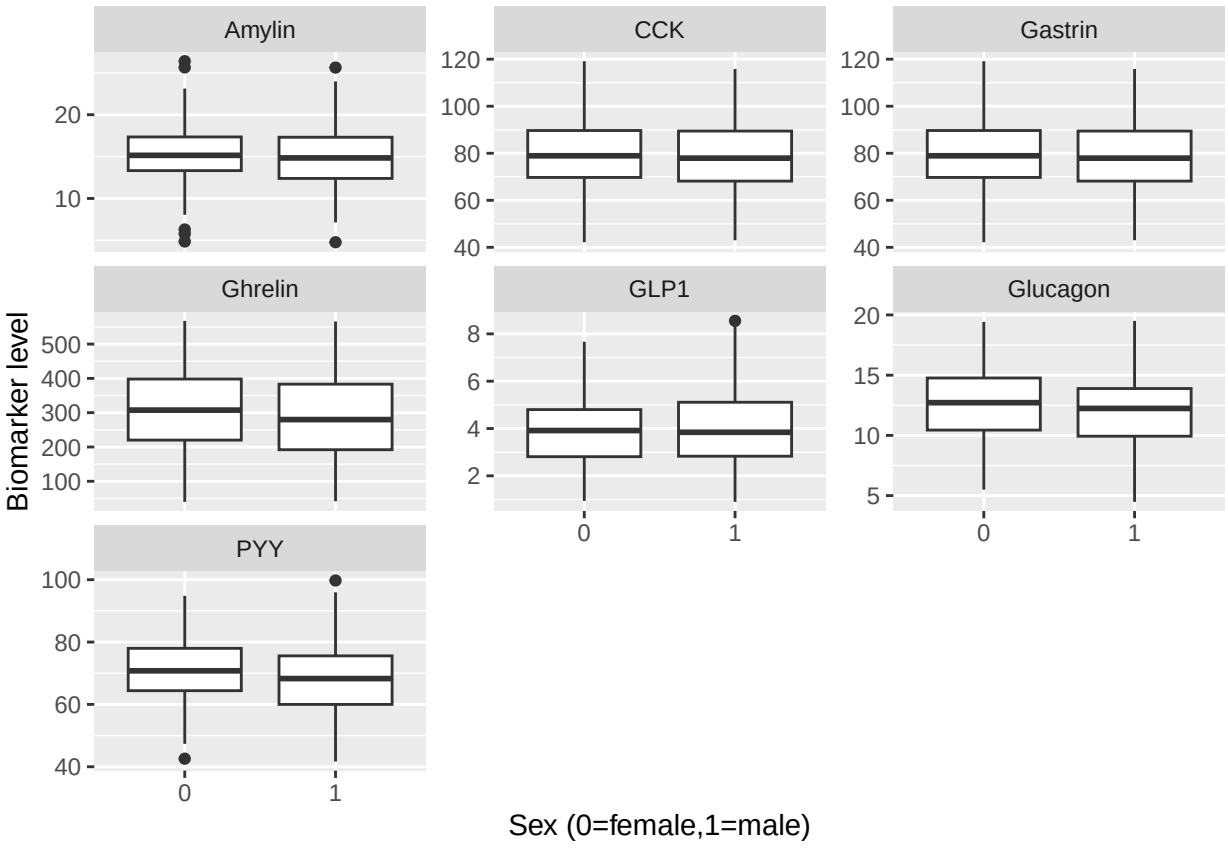
```
## `stat_bin()` using `bins = 30`. Pick better value `binwidth`.
```



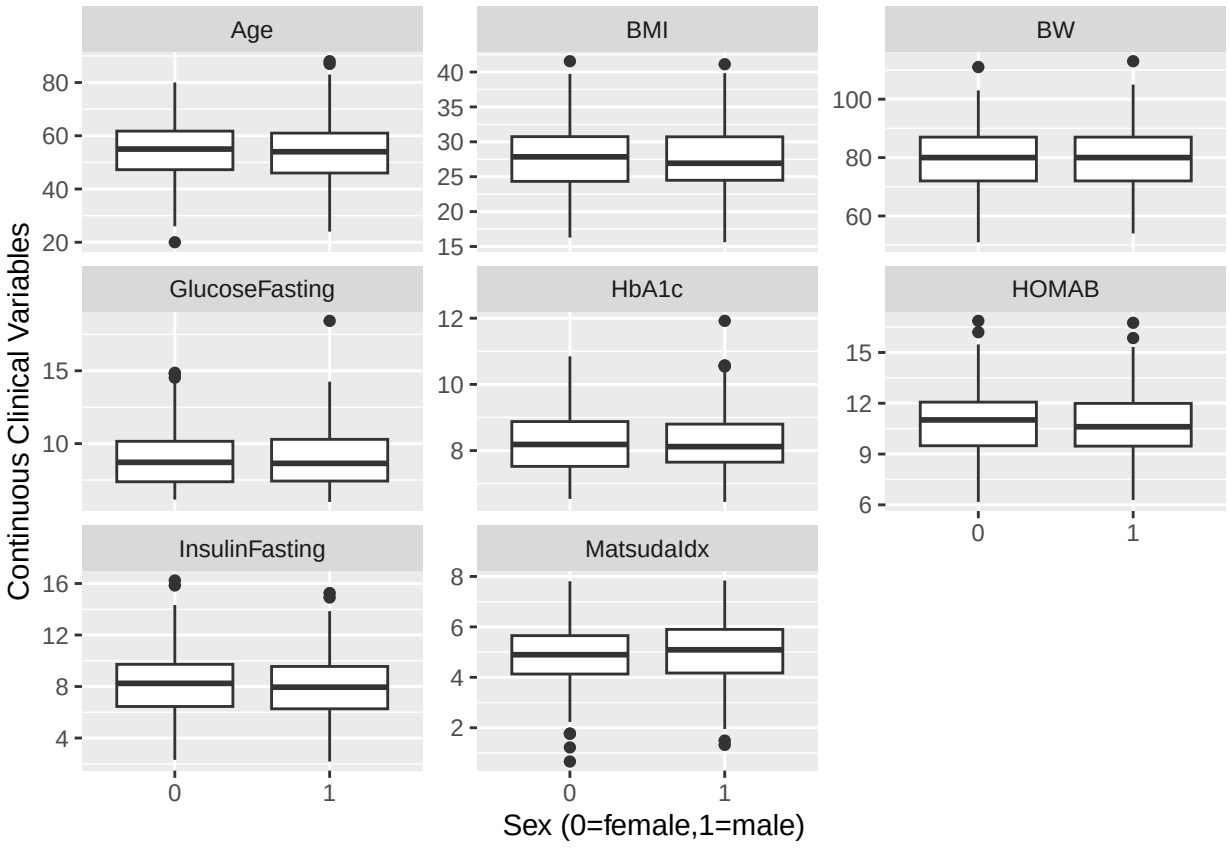
As shown if the figure, most biomarkers looks approximately normally distributed while some of the continuous variables looks scewed.

After that, we want to see if these biomarkers and other continuous variables are related to categorical variables of sex, metformin and diabetes complications. We did boxplots of variables with continuous values in different sex, metformin and diabetes complications, and ran statistic tests according to normality.

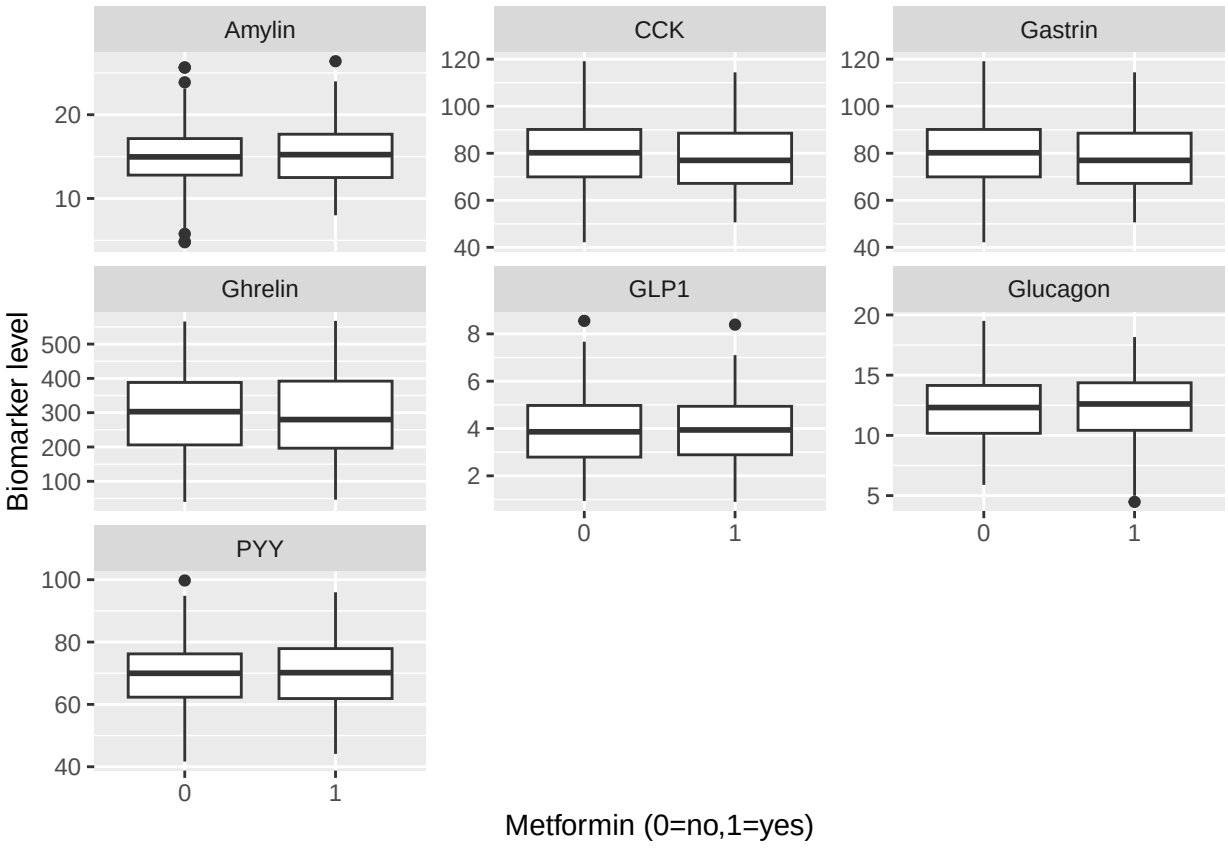
```
# biomarkers, continuous_vars grouped by sex, Metformin, DBComplications
dat %>%
  pivot_longer(cols = all_of(biomarkers), names_to = "marker", values_to = "value") %>%
  ggplot(aes(x = factor(Sex), y = value)) +
  geom_boxplot() +
  facet_wrap(~marker, scales = "free_y") +
  labs(x = "Sex (0=female,1=male)", y = "Biomarker level")
```



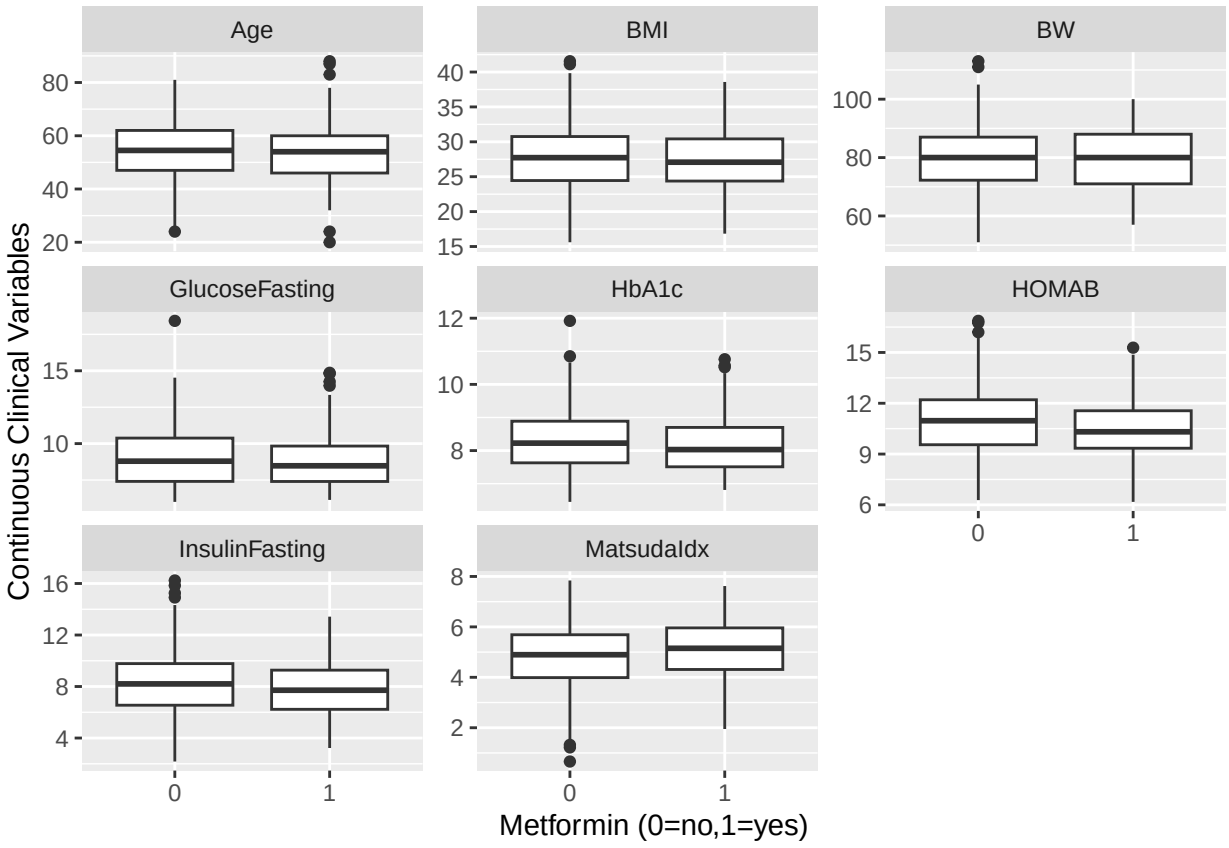

```
dat %>%
  pivot_longer(cols = all_of(continuous_vars), names_to = "marker", values_to = "value") %>%
  ggplot(aes(x = factor(Sex), y = value)) +
  geom_boxplot() +
  facet_wrap(~marker, scales = "free_y") +
  labs(x = "Sex (0=female,1=male)", y = "Continuous Clinical Variables")
```



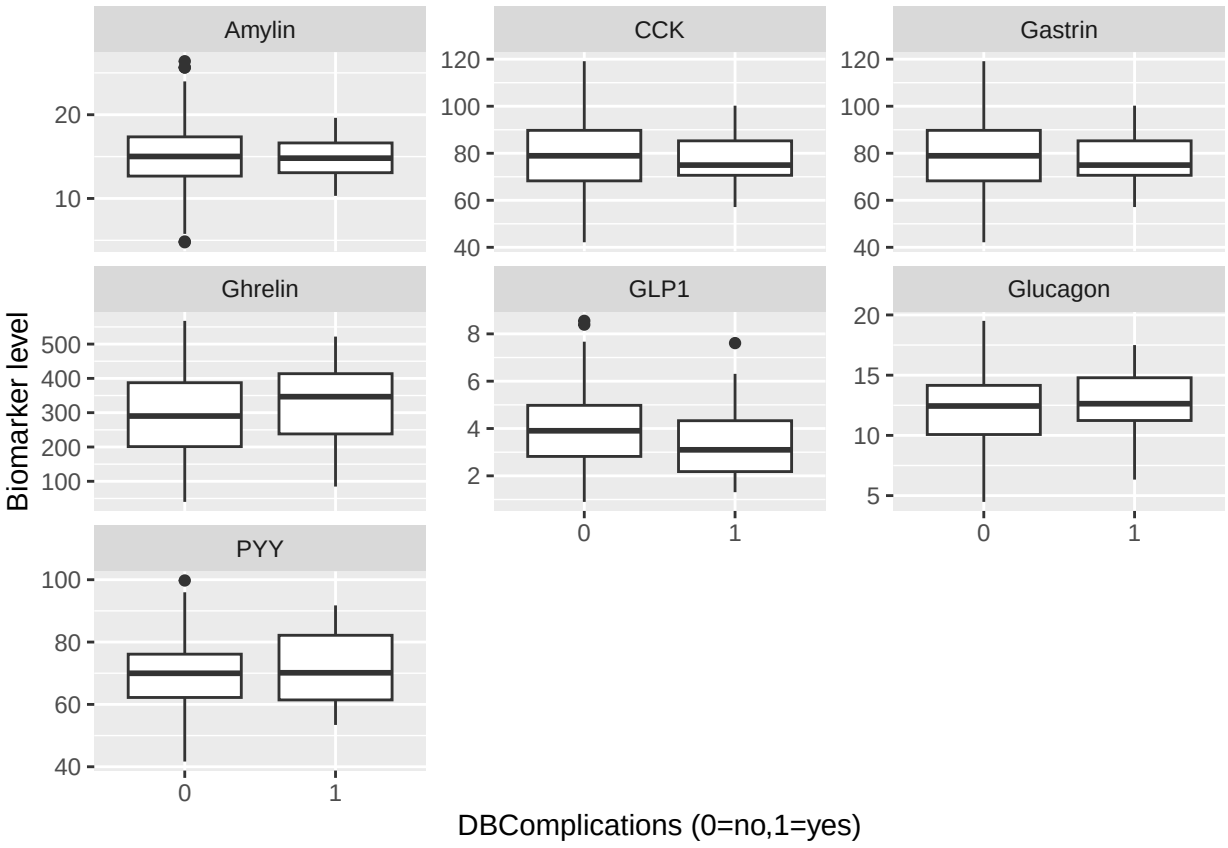

```
dat %>%
  pivot_longer(cols = all_of(biomarkers), names_to = "marker", values_to = "value") %>%
  ggplot(aes(x = factor(Metformin), y = value)) +
  geom_boxplot() +
  facet_wrap(~marker, scales = "free_y") +
  labs(x = "Metformin (0=no,1=yes)", y = "Biomarker level")
```



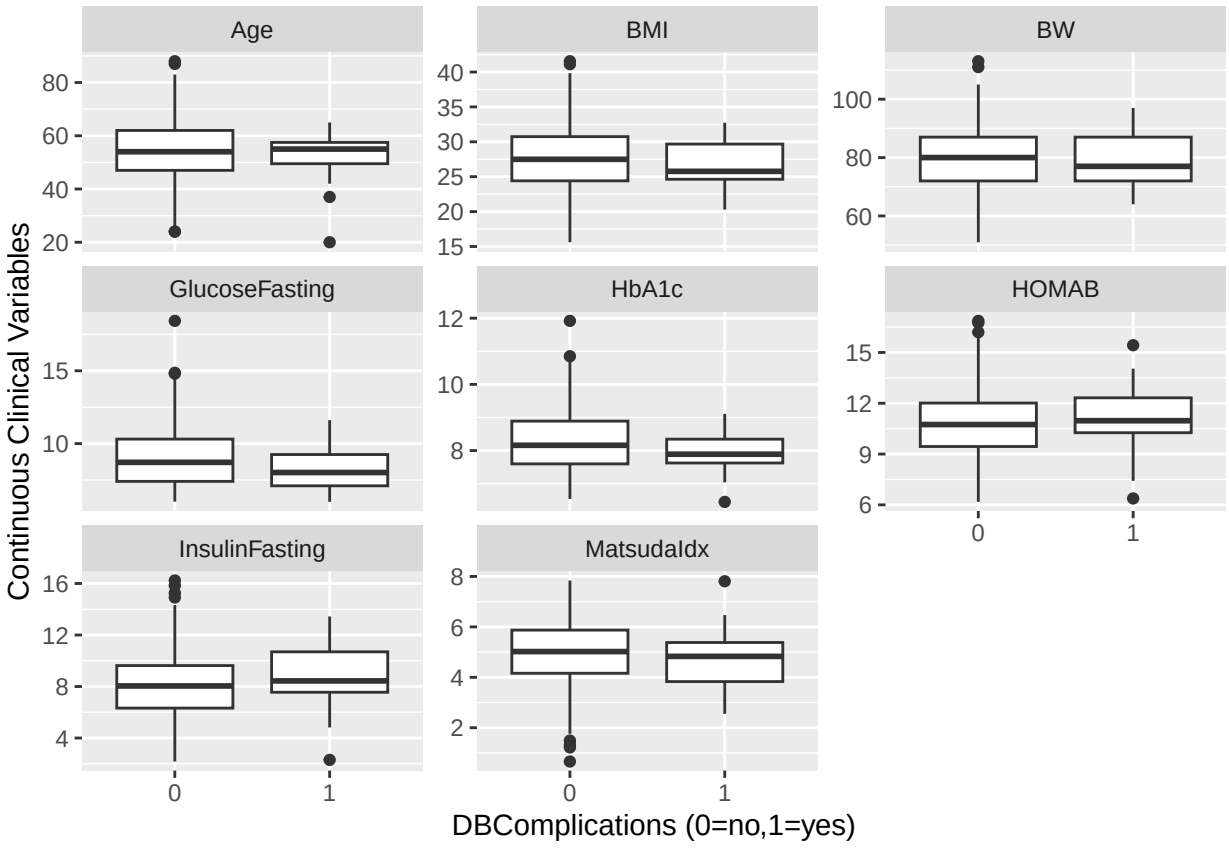

```
dat %>%
  pivot_longer(cols = all_of(continuous_vars), names_to = "marker", values_to = "value") %>%
  ggplot(aes(x = factor(Metformin), y = value)) +
  geom_boxplot() +
  facet_wrap(~marker, scales = "free_y") +
  labs(x = "Metformin (0=no,1=yes)", y = "Continuous Clinical Variables")
```




```
dat %>%
  pivot_longer(cols = all_of(biomarkers), names_to = "marker", values_to = "value") %>%
  ggplot(aes(x = factor(DiabetesComplications), y = value)) +
  geom_boxplot() +
  facet_wrap(~marker, scales = "free_y") +
  labs(x = "DBComplications (0=no,1=yes)", y = "Biomarker level")
```




```
dat %>%
  pivot_longer(cols = all_of(continuous_vars), names_to = "marker", values_to = "value") %>%
  ggplot(aes(x = factor(DiabetesComplications), y = value)) +
  geom_boxplot() +
  facet_wrap(~marker, scales = "free_y") +
  labs(x = "DBComplications (0=no,1=yes)", y = "Continuous Clinical Variables")
```




```r
# normalization check
all_vars <- c(biomarkers, continuous_vars)
results <- data.frame(Group = character(),
                      Variable = character(),
                      Test = character(),
                      P_value = numeric())

for (g in categorical_vars) {
  for (v in all_vars) {
    x <- dat[[v]]
    group <- dat[[g]]
    df <- data.frame(x, group)
    df <- df[complete.cases(df), ]
    x <- df$x
    group <- df$group
    sw1 <- shapiro.test(x[group == unique(group)[1]])$p.value
    sw2 <- shapiro.test(x[group == unique(group)[2]])$p.value
    if (sw1 > 0.05 & sw2 > 0.05) {
      p <- t.test(x ~ group)$p.value
      test_used <- "t-test"
    } else {
      p <- wilcox.test(x ~ group)$p.value
      test_used <- "Wilcoxon"
    }
    results <- rbind(results, data.frame(Group = g,
                                         Variable = v,
                                         Test = test_used,
```

```
                                        P_value = round(p, 4)))
  }
}
print(results)
```

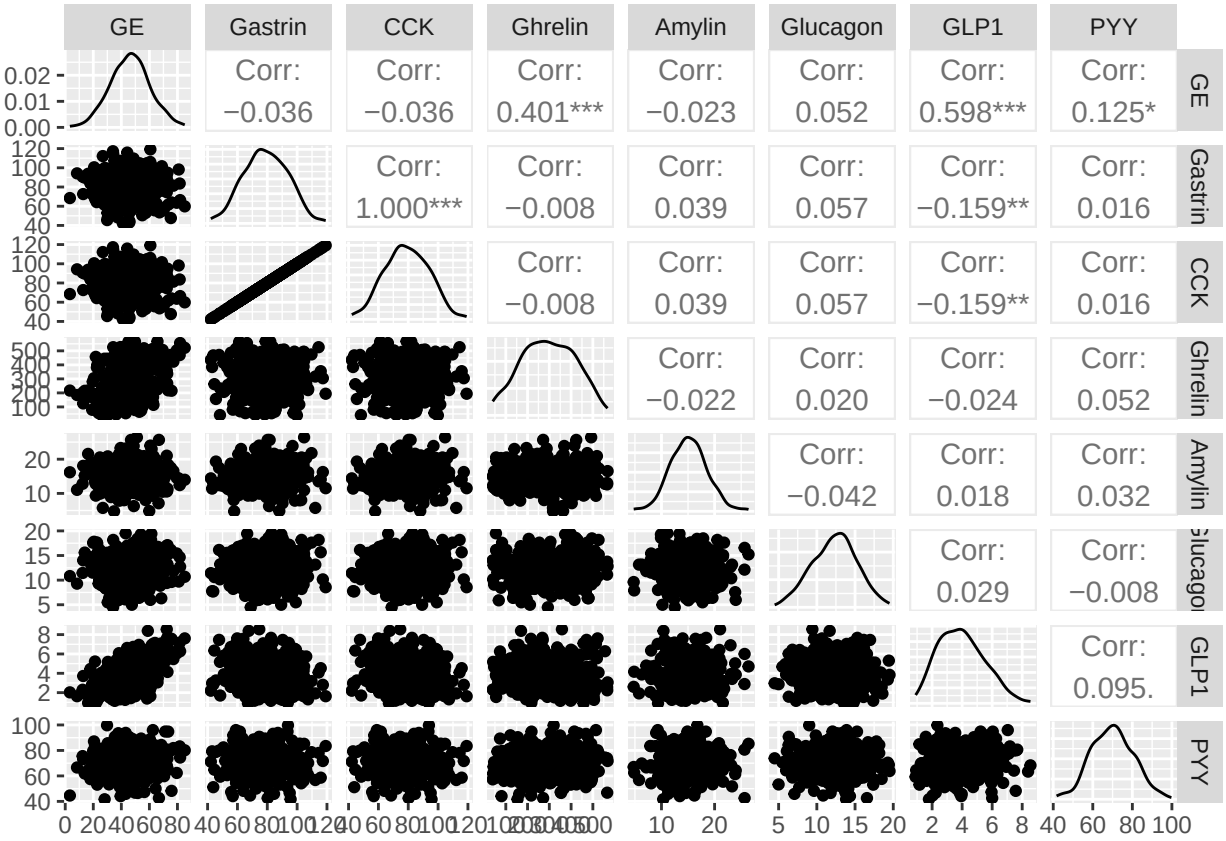
```
##                    Group       Variable     Test P_value
## 1                    Sex        Gastrin   t-test  0.5444
## 2                    Sex            CCK   t-test  0.5444
## 3                    Sex        Ghrelin Wilcoxon  0.1134
## 4                    Sex         Amylin   t-test  0.3241
## 5                    Sex       Glucagon   t-test  0.0456
## 6                    Sex           GLP1 Wilcoxon  0.8351
## 7                    Sex            PYY   t-test  0.0268
## 8                    Sex            Age   t-test  0.5273
## 9                    Sex             BW   t-test  0.7198
## 10                   Sex            BMI   t-test  0.6742
## 11                   Sex GlucoseFasting Wilcoxon  0.8281
## 12                   Sex InsulinFasting   t-test  0.4974
## 13                   Sex          HbA1c Wilcoxon  0.9721
## 14                   Sex     MatsudaIdx   t-test  0.3282
## 15                   Sex          HOMAB   t-test  0.4467
## 16             Metformin        Gastrin   t-test  0.4116
## 17             Metformin            CCK   t-test  0.4116
## 18             Metformin        Ghrelin Wilcoxon  0.4346
## 19             Metformin         Amylin   t-test  0.5009
## 20             Metformin       Glucagon Wilcoxon  0.7983
## 21             Metformin           GLP1 Wilcoxon  0.6293
## 22             Metformin            PYY   t-test  0.8813
## 23             Metformin            Age   t-test  0.7596
## 24             Metformin             BW   t-test  0.5189
## 25             Metformin            BMI   t-test  0.2562
## 26             Metformin GlucoseFasting Wilcoxon  0.2591
## 27             Metformin InsulinFasting   t-test  0.1080
## 28             Metformin          HbA1c Wilcoxon  0.3589
## 29             Metformin     MatsudaIdx   t-test  0.0920
## 30             Metformin          HOMAB   t-test  0.0640
## 31 DiabetesComplications        Gastrin   t-test  0.7495
## 32 DiabetesComplications            CCK   t-test  0.7495
## 33 DiabetesComplications        Ghrelin Wilcoxon  0.1605
## 34 DiabetesComplications         Amylin   t-test  0.6412
## 35 DiabetesComplications       Glucagon   t-test  0.5375
## 36 DiabetesComplications           GLP1 Wilcoxon  0.0761
## 37 DiabetesComplications            PYY   t-test  0.4216
## 38 DiabetesComplications            Age Wilcoxon  0.4659
## 39 DiabetesComplications             BW   t-test  0.8189
## 40 DiabetesComplications            BMI   t-test  0.1937
## 41 DiabetesComplications GlucoseFasting Wilcoxon  0.0986
## 42 DiabetesComplications InsulinFasting Wilcoxon  0.1969
## 43 DiabetesComplications          HbA1c Wilcoxon  0.1807
## 44 DiabetesComplications     MatsudaIdx   t-test  0.4673
## 45 DiabetesComplications          HOMAB   t-test  0.5828
```

As we can see in the result, Sex has significant impact on Glucagon and PYY, because p-value of statistic tests

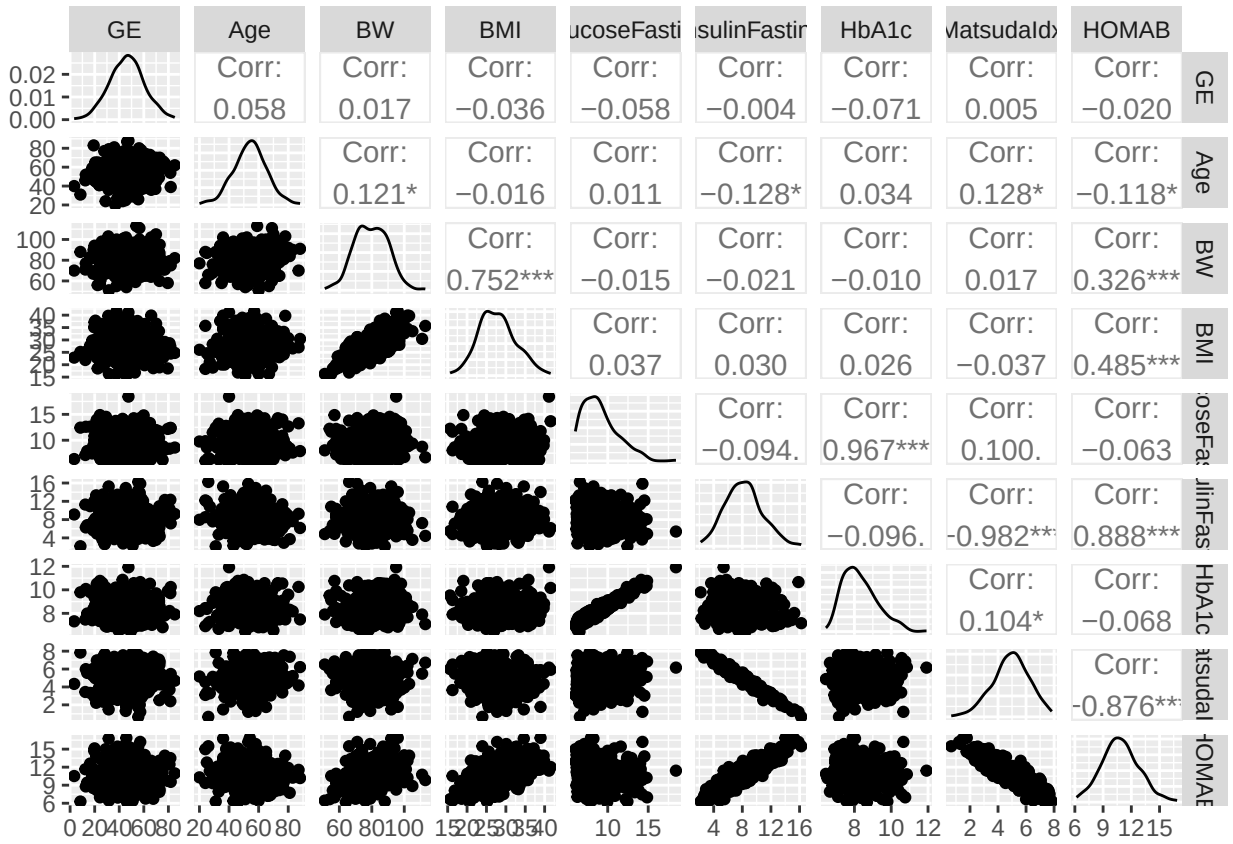
are lower than 0.05. Moreover, p values are between 0.05-1 of Metformin-MatsudaIdx, Metformin-HOMAB, DiabetesComplications-GLP1, and DiabetesComplications-GlucoseFasting.

Next, we examine whether variables with continuous value are correlated with each other.

```
# pair plot biomarkers & continuous_vars & GE
library(GGally)
selected <- dat %>% select(GE, all_of(biomarkers))
ggpairs(selected, columns=1:ncol(selected))
```



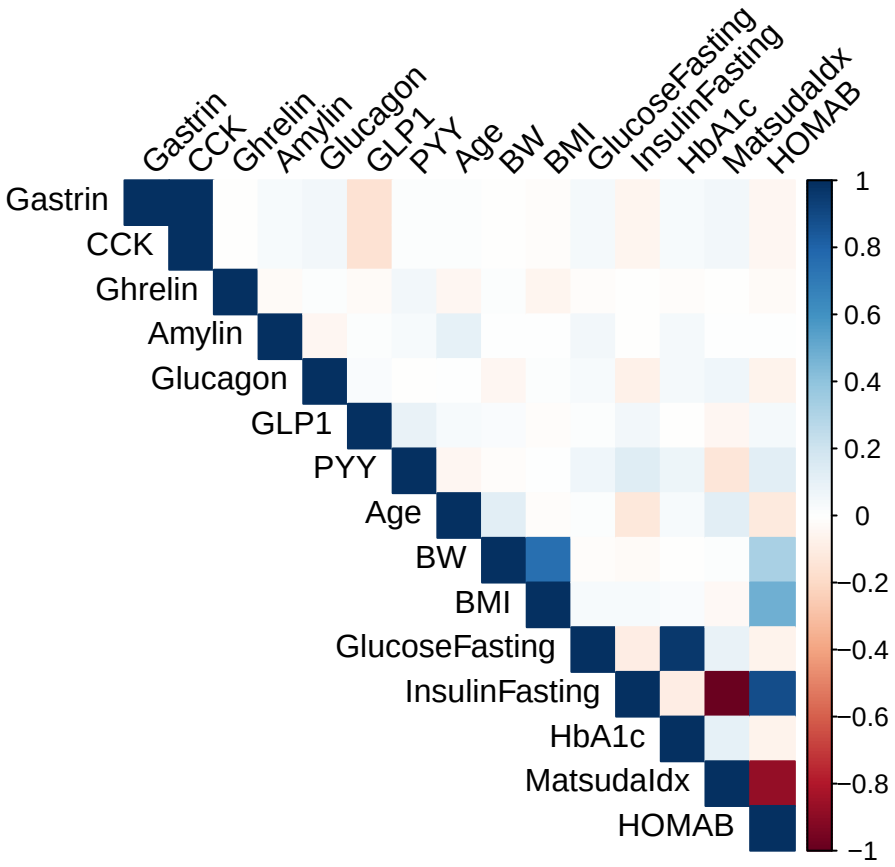

```
selected <- dat %>% select(GE, all_of(continuous_vars))
ggpairs(selected, columns=1:ncol(selected))
```




```
# heatbplot
library(corrplot)
```

```
## corrplot 0.95 loaded
```

```
mat <- cor(dat %>% select(all_of(biomarkers), all_of(continuous_vars)), use="pairwise.complete.obs")
corrplot(mat, method="color", type="upper", tl.col="black", tl.srt=45)
```




```
round(mat, 2)
```

```
##                Gastrin   CCK Ghrelin Amylin Glucagon  GLP1   PYY   Age    BW
## Gastrin           1.00  1.00   -0.01   0.04     0.06 -0.16  0.02  0.02 -0.01
## CCK               1.00  1.00   -0.01   0.04     0.06 -0.16  0.02  0.02 -0.01
## Ghrelin          -0.01 -0.01    1.00  -0.02     0.02 -0.02  0.05 -0.04  0.02
## Amylin            0.04  0.04   -0.02   1.00    -0.04  0.02  0.03  0.11  0.01
## Glucagon          0.06  0.06    0.02  -0.04     1.00  0.03 -0.01  0.00 -0.04
## GLP1             -0.16 -0.16   -0.02   0.02     0.03  1.00  0.09  0.03  0.02
## PYY               0.02  0.02    0.05   0.03    -0.01  0.09  1.00 -0.05 -0.01
## Age               0.02  0.02   -0.04   0.11     0.00  0.03 -0.05  1.00  0.12
## BW               -0.01 -0.01    0.02   0.01    -0.04  0.02 -0.01  0.12  1.00
## BMI              -0.01 -0.01   -0.05   0.00     0.01 -0.01  0.01 -0.02  0.75
## GlucoseFasting    0.04  0.04   -0.01   0.05     0.04  0.02  0.06  0.01 -0.01
## InsulinFasting   -0.05 -0.05    0.00   0.00    -0.08  0.06  0.13 -0.13 -0.02
## HbA1c             0.03  0.03   -0.02   0.04     0.04 -0.01  0.08  0.03 -0.01
## MatsudaIdx        0.05  0.05   -0.01   0.01     0.06 -0.05 -0.14  0.13  0.02
## HOMAB            -0.05 -0.05   -0.02   0.00    -0.06  0.04  0.12 -0.12  0.33
##                  BMI GlucoseFasting InsulinFasting HbA1c MatsudaIdx HOMAB
## Gastrin        -0.01           0.04          -0.05  0.03       0.05 -0.05
## CCK            -0.01           0.04          -0.05  0.03       0.05 -0.05
## Ghrelin        -0.05          -0.01           0.00 -0.02      -0.01 -0.02
## Amylin          0.00           0.05           0.00  0.04       0.01  0.00
## Glucagon        0.01           0.04          -0.08  0.04       0.06 -0.06
## GLP1           -0.01           0.02           0.06 -0.01      -0.05  0.04
## PYY             0.01           0.06           0.13  0.08      -0.14  0.12
```

```
## Age              -0.02          0.01          -0.13  0.03        0.13 -0.12
## BW                0.75         -0.01          -0.02 -0.01        0.02  0.33
## BMI               1.00          0.04           0.03  0.03       -0.04  0.48
## GlucoseFasting    0.04          1.00          -0.09  0.97        0.10 -0.06
## InsulinFasting    0.03         -0.09           1.00 -0.10       -0.98  0.89
## HbA1c             0.03          0.97          -0.10  1.00        0.10 -0.07
## MatsudaIdx       -0.04          0.10          -0.98  0.10        1.00 -0.88
## HOMAB             0.48         -0.06           0.89 -0.07       -0.88  1.00
```

From the figures, we can get the following conclusion:

There is a positive correlation between Body Weight-BMI, Glucose Faster-HbA1c, Insulin Fasting-HOMAB.

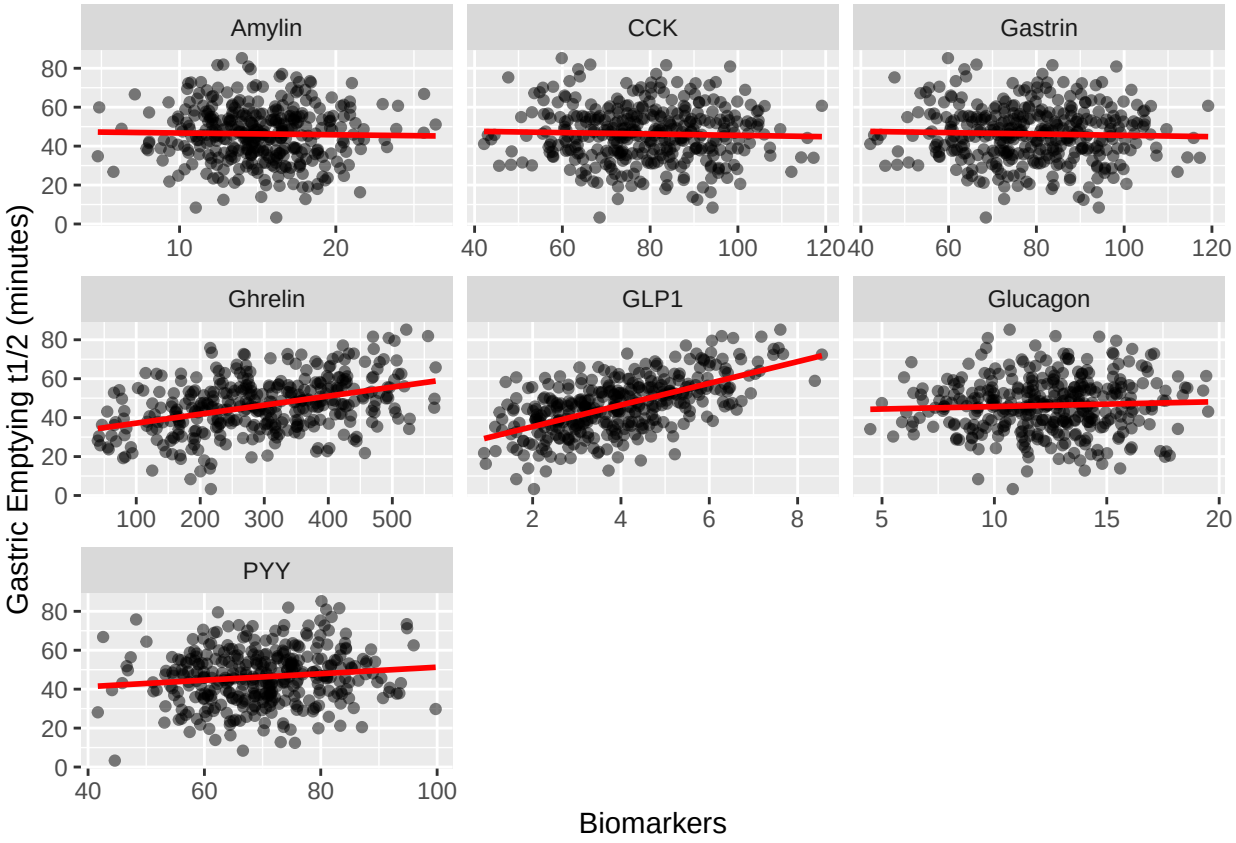
There is a negetive corraltion between Insulin Fasting-MatsudaIdx, MatsudaIdx-HOMAB.

It seems like CCK shares the exact same value with Gastrin.

We also looked at variables separately to see their correlation with GE.

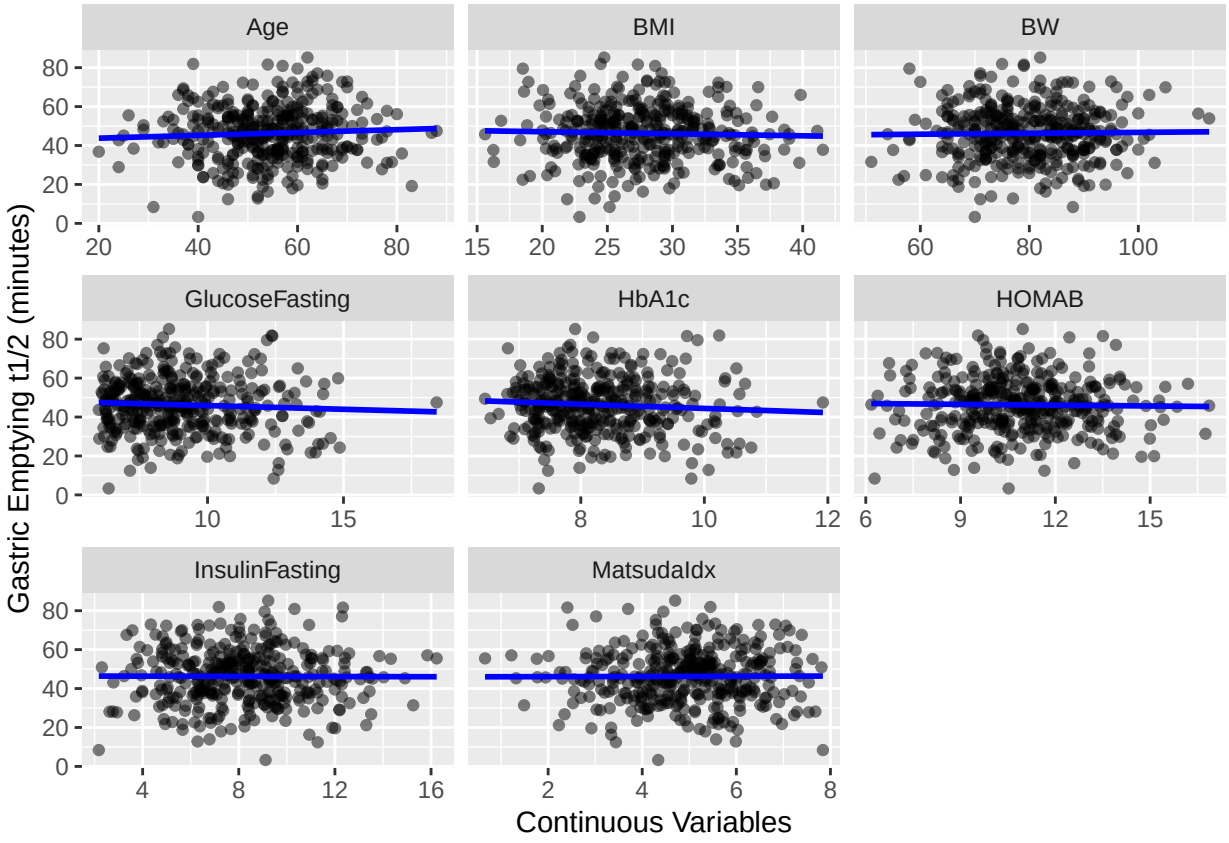
```
# scatter GE-biomarkers/continuous_vars
dat %>%
  pivot_longer(cols = all_of(biomarkers), names_to = "variable", values_to = "value") %>%
  ggplot(aes(x = value, y = GE)) +
  geom_point(alpha = 0.5) +
  geom_smooth(method = "lm", se = FALSE, color = "red") +
  facet_wrap(~variable, scales = "free_x") +
  labs(x = "Biomarkers", y = "Gastric Emptying t1/2 (minutes)")
```

```
## `geom_smooth()` using formula = 'y ~ x'
```

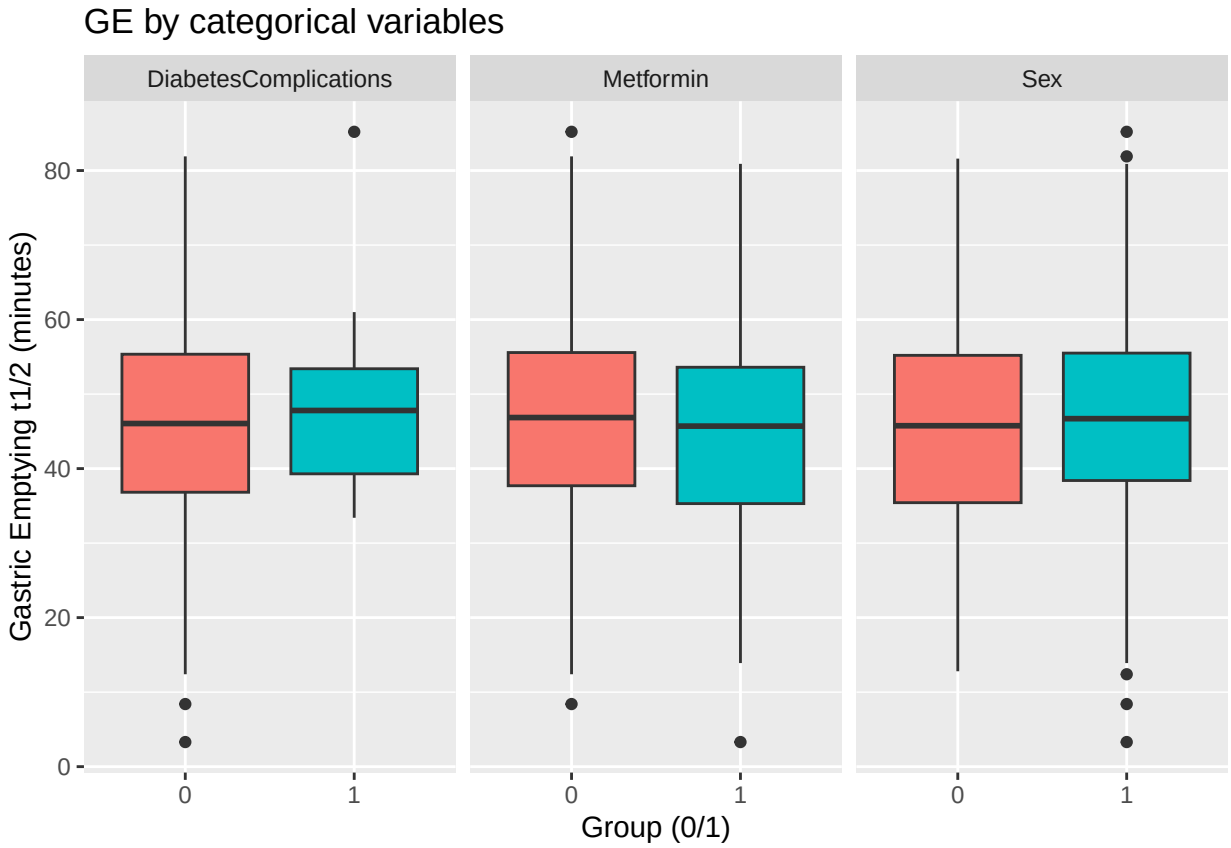


```
dat %>%
  pivot_longer(cols = all_of(continuous_vars), names_to = "variable", values_to = "value") %>%
  ggplot(aes(x = value, y = GE)) +
  geom_point(alpha = 0.5) +
  geom_smooth(method = "lm", se = FALSE, color = "blue") +
  facet_wrap(~variable, scales = "free_x") +
  labs(x = "Continuous Variables", y = "Gastric Emptying t1/2 (minutes)")
```

```
## `geom_smooth()` using formula = 'y ~ x'
```




```
# GE-Categorical
dat_long <- dat %>%
  pivot_longer(cols = all_of(categorical_vars), names_to = "variable", values_to = "group")
ggplot(dat_long, aes(x = factor(group), y = GE, fill = factor(group))) +
  geom_boxplot() +
  facet_wrap(~variable, scales = "free_x") +
  labs(x = "Group (0/1)", y = "Gastric Emptying t1/2 (minutes)",
       title = "GE by categorical variables") +
  theme(legend.position = "none")
```



The dataset contained very few missing values, which were removed without affecting the overall analysis.

Several continuous variables showed slight skewness, highlighting the need to check the normality of model residuals.

Sex was found to significantly influence Glucagon and PYY levels, suggesting it should be included as a covariate in modeling.

Strong correlations were observed between certain variables (e.g., BMI–BW, HbA1c–GlucoseFasting), indicating potential multicollinearity that should be controlled for during model construction.

Most biomarkers showed weak to moderate linear relationships with GE, supporting the use of a multivariable linear or generalized linear model to evaluate their combined effects. appropriately checked.

Model Fitting

First, we fitted all variables into the model, as model 1.

```
library(car)
```

```
## Loading required package: carData

##
## Attaching package: 'car'

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

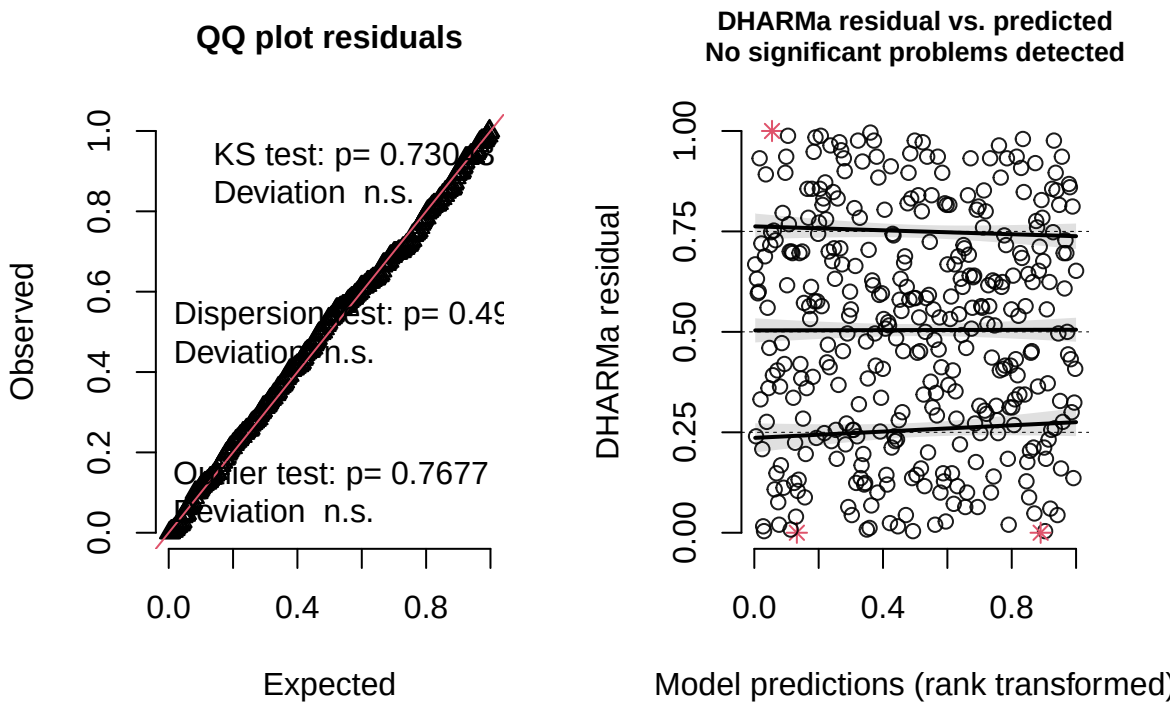
```r
library(DHARMa)
```

```
## This is DHARMa 0.4.7. For overview type '?DHARMa'. For recent changes, type news(package = 'DHARMa')
```

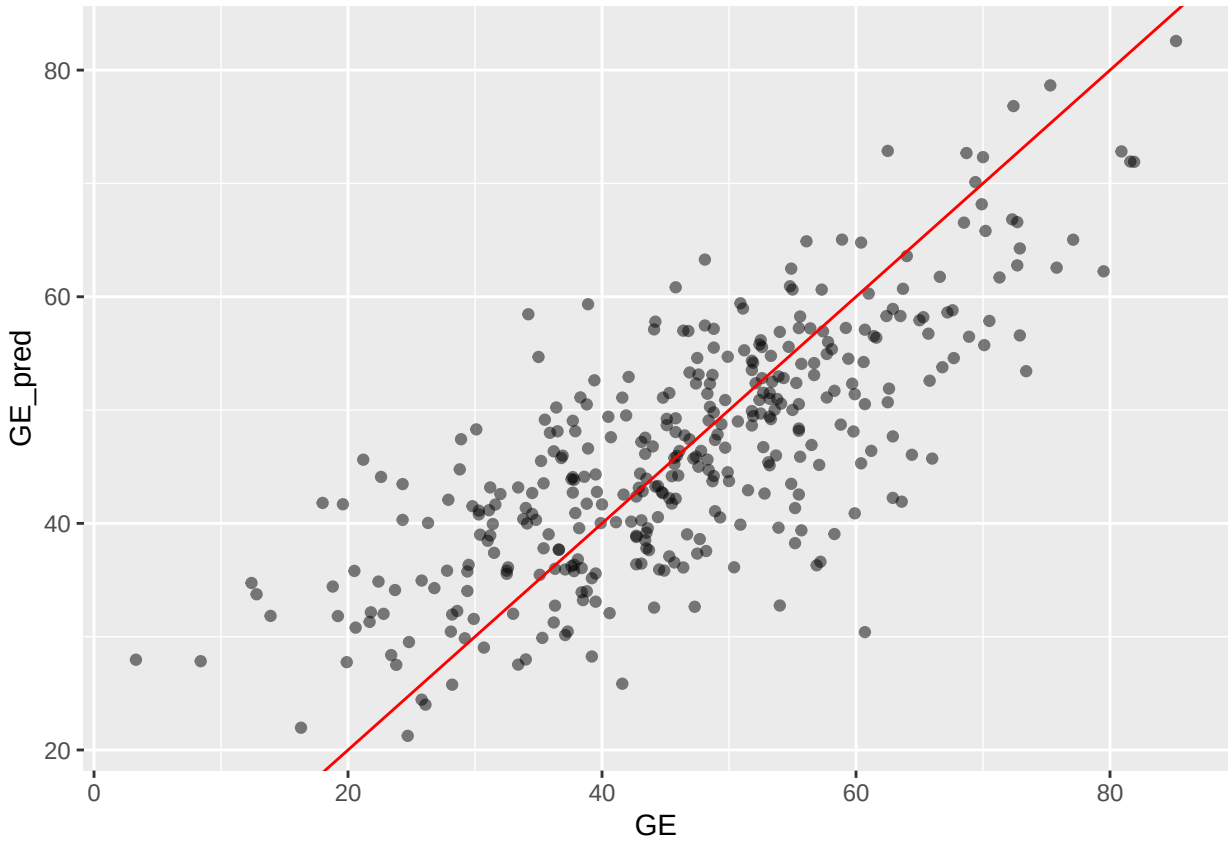
```r
library(interactions)
library(rsq)
model1 <- glm(GE ~ Sex + Age + Height + BW + BMI + GlucoseFasting + InsulinFasting + HbA1c + MatsudaIdx
              data = dat, family = gaussian)
summary(model1)
```

```
##
## Call:
## glm(formula = GE ~ Sex + Age + Height + BW + BMI + GlucoseFasting +
##     InsulinFasting + HbA1c + MatsudaIdx + HOMAB + DiabetesComplications +
##     Metformin + Gastrin + CCK + Ghrelin + Amylin + Glucagon +
##     GLP1 + PYY, family = gaussian, data = dat)
##
## Coefficients: (1 not defined because of singularities)
##                          Estimate Std. Error t value Pr(>|t|)
## (Intercept)           55.786887  59.176889   0.943  0.34649
## Sex                    3.276637   1.017970   3.219  0.00141 **
## Age                    0.077615   0.046367   1.674  0.09506 .
## Height                -0.287497   0.332842  -0.864  0.38832
## BW                     0.248418   0.357074   0.696  0.48708
## BMI                   -0.626067   1.744423  -0.359  0.71989
## GlucoseFasting        -0.649149   0.938698  -0.692  0.48969
## InsulinFasting        -0.124758   4.982047  -0.025  0.98004
## HbA1c                  0.372162   2.157608   0.172  0.86316
## MatsudaIdx            -0.827691   2.062192  -0.401  0.68840
## HOMAB                 -0.834878   7.335446  -0.114  0.90945
## DiabetesComplications  2.790453   2.102818   1.327  0.18539
## Metformin             -2.495386   1.127754  -2.213  0.02757 *
## Gastrin                0.061452   0.034619   1.775  0.07677 .
## CCK                          NA         NA      NA       NA
## Ghrelin                0.048553   0.004158  11.678  < 2e-16 ***
## Amylin                -0.082151   0.144171  -0.570  0.56917
## Glucagon               0.120889   0.174980   0.691  0.49011
## GLP1                   5.736636   0.342377  16.755  < 2e-16 ***
## PYY                    0.091999   0.048907   1.881  0.06080 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for gaussian family taken to be 88.92623)
##
##     Null deviance: 71279  on 362  degrees of freedom
## Residual deviance: 30591  on 344  degrees of freedom
## AIC: 2679.7
##
## Number of Fisher Scoring iterations: 2
```

```r
simres1 <- simulateResiduals(model1)
plot(simres1)
```




```
dat$GE_pred <- predict(model1, newdata = dat, type = "response", na.action = na.pass)
ggplot(dat, aes(x = GE, y = GE_pred)) +
  geom_point(alpha = 0.5) +
  geom_abline(intercept = 0, slope = 1, color = "red")
```




```
rsq(model1, adj = TRUE)
```

```
## [1] 0.5483745
```

Sex is significantly associated with gastric emptying (GE) (p = 0.00141), indicating that males and females differ in GE.

Metformin usage shows a significant negative association with GE (p = 0.02757), suggesting slower GE in users.

Ghrelin and GLP1 have very strong positive effects on GE (p < 2e-16 for both), indicating higher levels correspond to longer GE half-life.

Gastrin and PYY show marginal associations (p = 0.06–0.077), suggesting a possible weak positive effect.

Age also shows a marginal effect (p = 0.095), with older age slightly increasing GE.

CCK is not defined due to singularity, which indicates perfect collinearity with another variable (likely Gastrin), so it was dropped from the model.

Other variables, including Height, BW, BMI, GlucoseFasting, InsulinFasting, HbA1c, MatsudaIdx, HOMAB, DiabetesComplications, Amylin, Glucagon, do not show significant associations with GE in this model.

```
model2 <- glm(GE ~ Sex + Age + Height + BW + BMI + GlucoseFasting + InsulinFasting + HbA1c + MatsudaIdx
              data = dat, family = gaussian)
summary(model2)
```

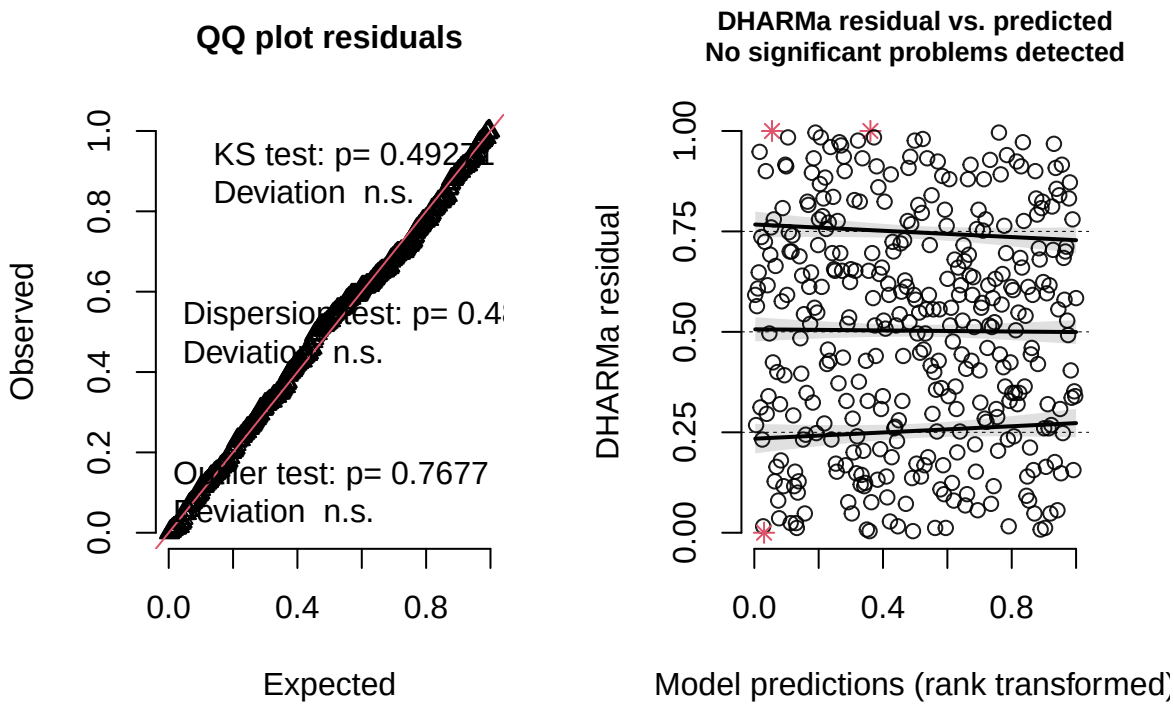
```
##
```

```
## Call:
## glm(formula = GE ~ Sex + Age + Height + BW + BMI + GlucoseFasting +
##     InsulinFasting + HbA1c + MatsudaIdx + HOMAB + DiabetesComplications +
##     Metformin + Gastrin + Ghrelin + Amylin + Glucagon + GLP1 +
##     PYY, family = gaussian, data = dat)
##
## Coefficients:
##                          Estimate Std. Error t value Pr(>|t|)
## (Intercept)           55.786887  59.176889   0.943  0.34649
## Sex                    3.276637   1.017970   3.219  0.00141 **
## Age                    0.077615   0.046367   1.674  0.09506 .
## Height                -0.287497   0.332842  -0.864  0.38832
## BW                     0.248418   0.357074   0.696  0.48708
## BMI                   -0.626067   1.744423  -0.359  0.71989
## GlucoseFasting        -0.649149   0.938698  -0.692  0.48969
## InsulinFasting        -0.124758   4.982047  -0.025  0.98004
## HbA1c                  0.372162   2.157608   0.172  0.86316
## MatsudaIdx            -0.827691   2.062192  -0.401  0.68840
## HOMAB                 -0.834878   7.335446  -0.114  0.90945
## DiabetesComplications  2.790453   2.102818   1.327  0.18539
## Metformin             -2.495386   1.127754  -2.213  0.02757 *
## Gastrin                0.061452   0.034619   1.775  0.07677 .
## Ghrelin                0.048553   0.004158  11.678  < 2e-16 ***
## Amylin                -0.082151   0.144171  -0.570  0.56917
## Glucagon               0.120889   0.174980   0.691  0.49011
## GLP1                   5.736636   0.342377  16.755  < 2e-16 ***
## PYY                    0.091999   0.048907   1.881  0.06080 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for gaussian family taken to be 88.92623)
##
##     Null deviance: 71279  on 362  degrees of freedom
## Residual deviance: 30591  on 344  degrees of freedom
## AIC: 2679.7
##
## Number of Fisher Scoring iterations: 2
```

```
rsq(model2, adj = TRUE)
```

```
## [1] 0.5483745
```

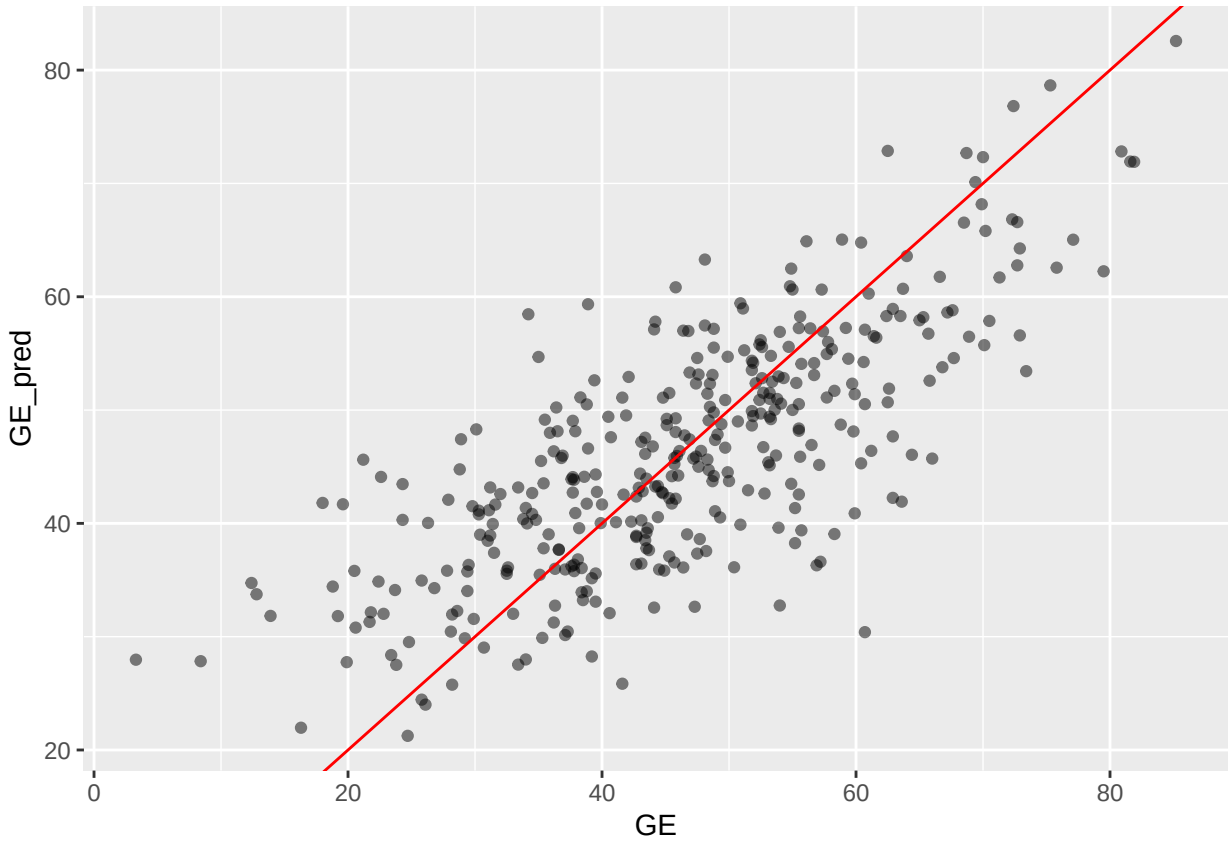
```
simres2 <- simulateResiduals(model2)
plot(simres2)
```




```
vif(model2)
```

```
##                  Sex                  Age               Height
##             1.056865             1.107838            41.884468
##                   BW                  BMI       GlucoseFasting
##            54.107466           284.271801            16.169906
##       InsulinFasting                HbA1c          MatsudaIdx
##           665.708971            16.224913            29.700250
##                HOMAB DiabetesComplications            Metformin
##           852.264193             1.071208             1.042593
##              Gastrin              Ghrelin               Amylin
##             1.046581             1.040432             1.033650
##             Glucagon                 GLP1                  PYY
##             1.047848             1.084886             1.069794
```

```
dat$GE_pred <- predict(model2, newdata = dat, type = "response", na.action = na.pass)
ggplot(dat, aes(x = GE, y = GE_pred)) +
  geom_point(alpha = 0.5) +
  geom_abline(intercept = 0, slope = 1, color = "red")
```




```
# examine model
# analyze_model <- function(model, data, pred_var=NULL, modx_var=NULL) {
#   print(summary(model))
#   print(rsq(model, adj = TRUE))
#
#   simres <- DHARMa::simulateResiduals(model)
#   plot(simres)
#
#   data$GE_pred <- predict(model, newdata = data, type = "response", na.action = na.pass)
#   ggplot(data, aes(x = GE, y = GE_pred)) +
#     geom_point(alpha = 0.5) +
#     geom_abline(intercept = 0, slope = 1, color = "red") +
#     ggtitle(deparse(substitute(model)))
#
#   if (!is.null(pred_var) & !is.null(modx_var)) {
#     interactions::interact_plot(model, pred = pred_var, modx = modx_var)
#   }
# }
# analyze_model(model1, dat[common_rows, ])
# analyze_model(model2, dat[common_rows, ])
#
# compare_models <- function(model1, model2) {
#   print(AIC(model1))
#   print(AIC(model2))
#   print(BIC(model1))
#   print(BIC(model2))
#   print(anova(model1, model2, test = "Chisq"))
```

```
# }
# compare_models(model2, model3)
# models
```

When deleted CCK, the model remained exactly the same.

Moreover, we can see that Height, BW, BMI, GlucoseFasting, InsulinFasting, HOMAB have significantly high VIF, indicating colinearality. MatsudaIdx, HbA1c, GlucoseFasting also showed relatively high VIF.

Because BMI contains information about both height and BodyWeight, we delete height and BW in the following model. HOMA-B is an index used to estimate pancreatic β -cell function based on fasting plasma glucose and fasting insulin levels. Thus, we delete InsulinFasting and only keep HOMAB. GlucoseFasting refers to the blood glucose concentration measured after at least 8 hours of fasting and is an important indicator for assessing glucose metabolism and diagnosing diabetes. HbA1c is a product of non-enzymatic glycation of hemoglobin by glucose in the blood, reflecting the average blood glucose level over the past 2-3 months. It is an important indicator for assessing diabetes control and long-term glycemic management. We chose Hb1Ac and deleted GlucoseFasting.

```
model3 <- glm(GE ~ Sex + Age + BMI + HbA1c + MatsudaIdx + HOMAB +
                DiabetesComplications + Metformin + Gastrin + Ghrelin + Amylin + Glucagon + GLP1 + PYY,
              data = dat, family = gaussian)
summary(model3)
```

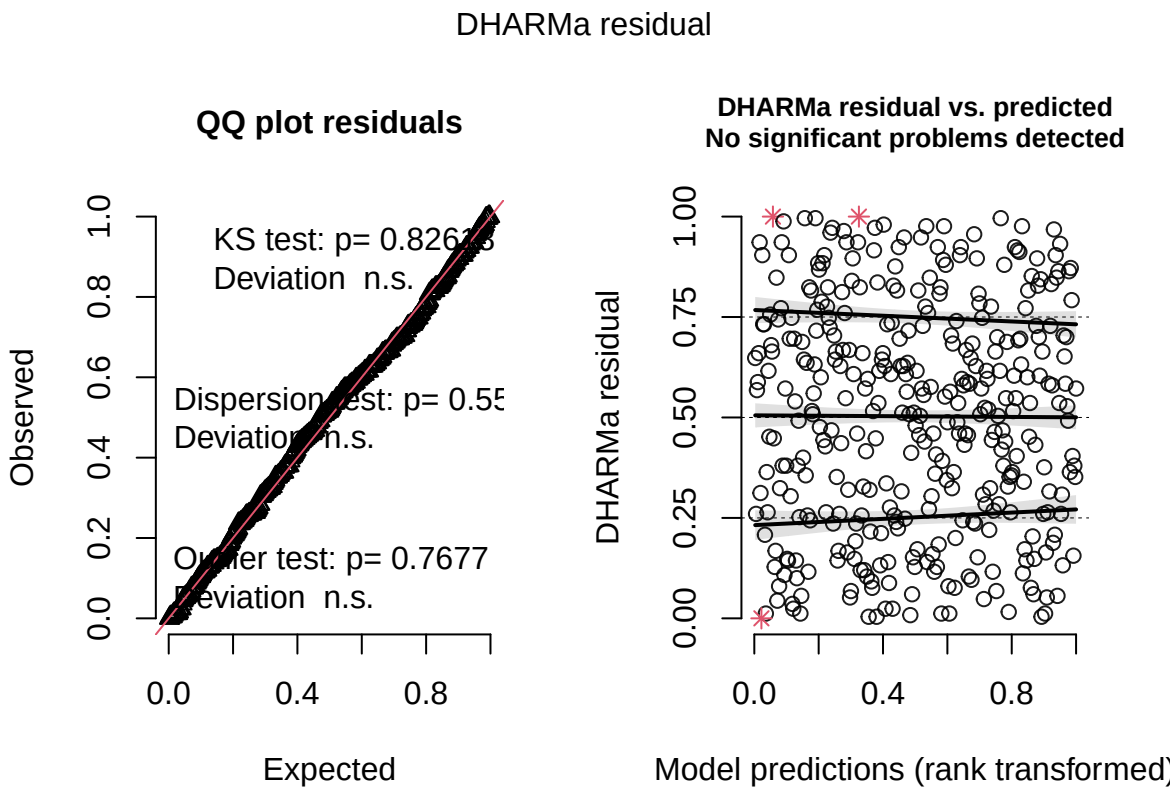
```
##
## Call:
## glm(formula = GE ~ Sex + Age + BMI + HbA1c + MatsudaIdx + HOMAB +
##     DiabetesComplications + Metformin + Gastrin + Ghrelin + Amylin +
##     Glucagon + GLP1 + PYY, family = gaussian, data = dat)
##
## Coefficients:
##                          Estimate Std. Error t value Pr(>|t|)
## (Intercept)           11.456380  19.585200   0.585  0.55896
## Sex                    3.168883   1.009710   3.138  0.00184 **
## Age                    0.078960   0.044737   1.765  0.07844 .
## BMI                    0.188169   0.304308   0.618  0.53675
## HbA1c                 -1.081421   0.544892  -1.985  0.04797 *
## MatsudaIdx            -0.872763   2.017074  -0.433  0.66551
## HOMAB                 -1.021323   1.528502  -0.668  0.50446
## DiabetesComplications  2.948125   2.078970   1.418  0.15707
## Metformin             -2.358375   1.112575  -2.120  0.03473 *
## Gastrin                0.060547   0.034420   1.759  0.07944 .
## Ghrelin                0.047948   0.004107  11.674  < 2e-16 ***
## Amylin                -0.087973   0.143099  -0.615  0.53911
## Glucagon               0.144054   0.173282   0.831  0.40636
## GLP1                   5.724822   0.337153  16.980  < 2e-16 ***
## PYY                    0.092356   0.048539   1.903  0.05790 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for gaussian family taken to be 88.31691)
##
##     Null deviance: 71279  on 362  degrees of freedom
## Residual deviance: 30734  on 348  degrees of freedom
## AIC: 2673.4
```

```
##
## Number of Fisher Scoring iterations: 2
```

```
rsq(model3, adj = TRUE)
```

```
## [1] 0.551469
```

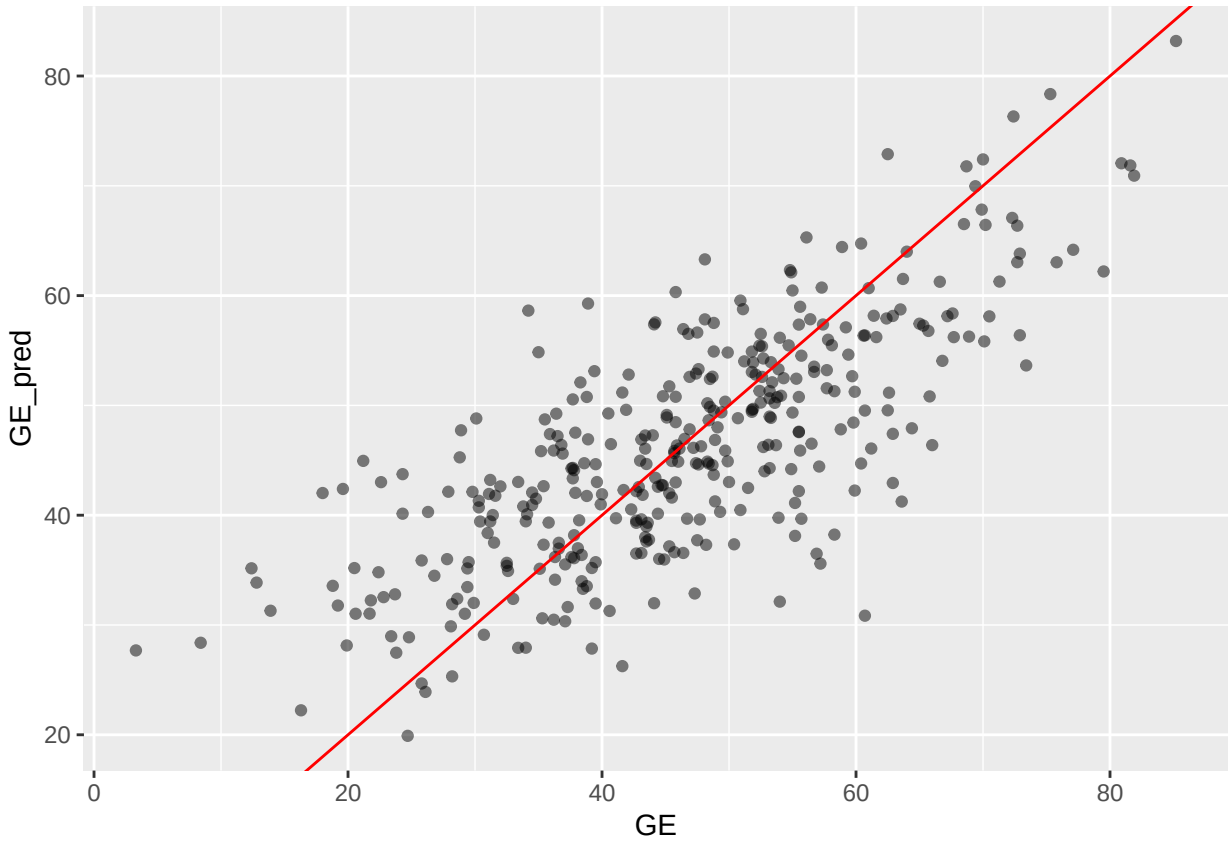
```
simres3 <- simulateResiduals(model3)
plot(simres3)
```




```
vif(model3)
```

```
##                    Sex                    Age                    BMI
##               1.046957               1.038397               8.710514
##                  HbA1c             MatsudaIdx                  HOMAB
##               1.041944              28.610909              37.259663
## DiabetesComplications              Metformin                Gastrin
##               1.054272               1.021717               1.041674
##                Ghrelin                 Amylin               Glucagon
##               1.022247               1.025364               1.034700
##                   GLP1                    PYY
##               1.059292               1.061018
```

```
dat$GE_pred <- predict(model3, newdata = dat, type = "response", na.action = na.pass)
ggplot(dat, aes(x = GE, y = GE_pred)) +
  geom_point(alpha = 0.5) +
  geom_abline(intercept = 0, slope = 1, color = "red")
```



The AIC value indicates that model3 has a slight improve on the model. Though Residual deviance rised slightly, the model is more stable. However, MatsudaIdx and HOMAB still has high VIF. The two variable represent different biological matters, so we look for ways to keep them both while dealing with the colinearality.

Standardization can improve coefficient stability. After standardization, variables are on a similar scale and numerical range, which makes the algorithm more stable when calculating the inverse matrix or least squares, reducing the impact of multicollinearity.

```
dat_scaled <- dat
dat_scaled[all_vars] <- scale(dat[all_vars])

model4 <- glm(GE ~ Sex + Age + BMI + HbA1c + MatsudaIdx + HOMAB +
                DiabetesComplications + Metformin + Gastrin + Ghrelin + Amylin + Glucagon + GLP1 + PYY,
              data = dat_scaled, family = gaussian)
summary(model4)
```

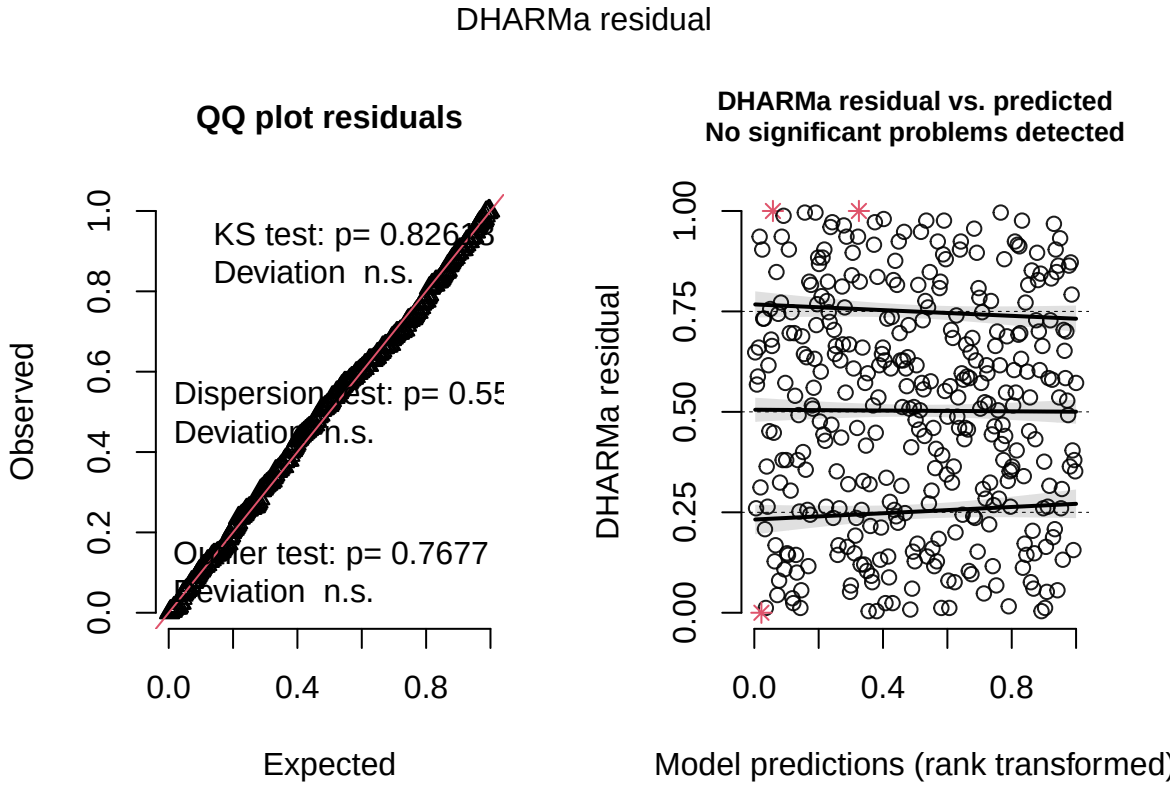
```
##
## Call:
## glm(formula = GE ~ Sex + Age + BMI + HbA1c + MatsudaIdx + HOMAB +
##     DiabetesComplications + Metformin + Gastrin + Ghrelin + Amylin +
##     Glucagon + GLP1 + PYY, family = gaussian, data = dat_scaled)
##
## Coefficients:
##                       Estimate Std. Error t value Pr(>|t|)
## (Intercept)            45.1881     0.7741  58.376  < 2e-16 ***
## Sex                     3.1689     1.0097   3.138  0.00184 **
## Age                     0.8884     0.5033   1.765  0.07844 .
```

```
## BMI                       0.9014     1.4578   0.618  0.53675
## HbA1c                    -1.0006     0.5042  -1.985  0.04797 *
## MatsudaIdx               -1.1432     2.6420  -0.433  0.66551
## HOMAB                    -2.0146     3.0150  -0.668  0.50446
## DiabetesComplications     2.9481     2.0790   1.418  0.15707
## Metformin                -2.3584     1.1126  -2.120  0.03473 *
## Gastrin                   0.8868     0.5041   1.759  0.07944 .
## Ghrelin                   5.8302     0.4994  11.674  < 2e-16 ***
## Amylin                   -0.3075     0.5002  -0.615  0.53911
## Glucagon                  0.4177     0.5024   0.831  0.40636
## GLP1                      8.6320     0.5084  16.980  < 2e-16 ***
## PYY                       0.9681     0.5088   1.903  0.05790 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for gaussian family taken to be 88.31691)
##
##     Null deviance: 71279  on 362  degrees of freedom
## Residual deviance: 30734  on 348  degrees of freedom
## AIC: 2673.4
##
## Number of Fisher Scoring iterations: 2
```

```
rsq(model4, adj = TRUE)
```

```
## [1] 0.551469
```

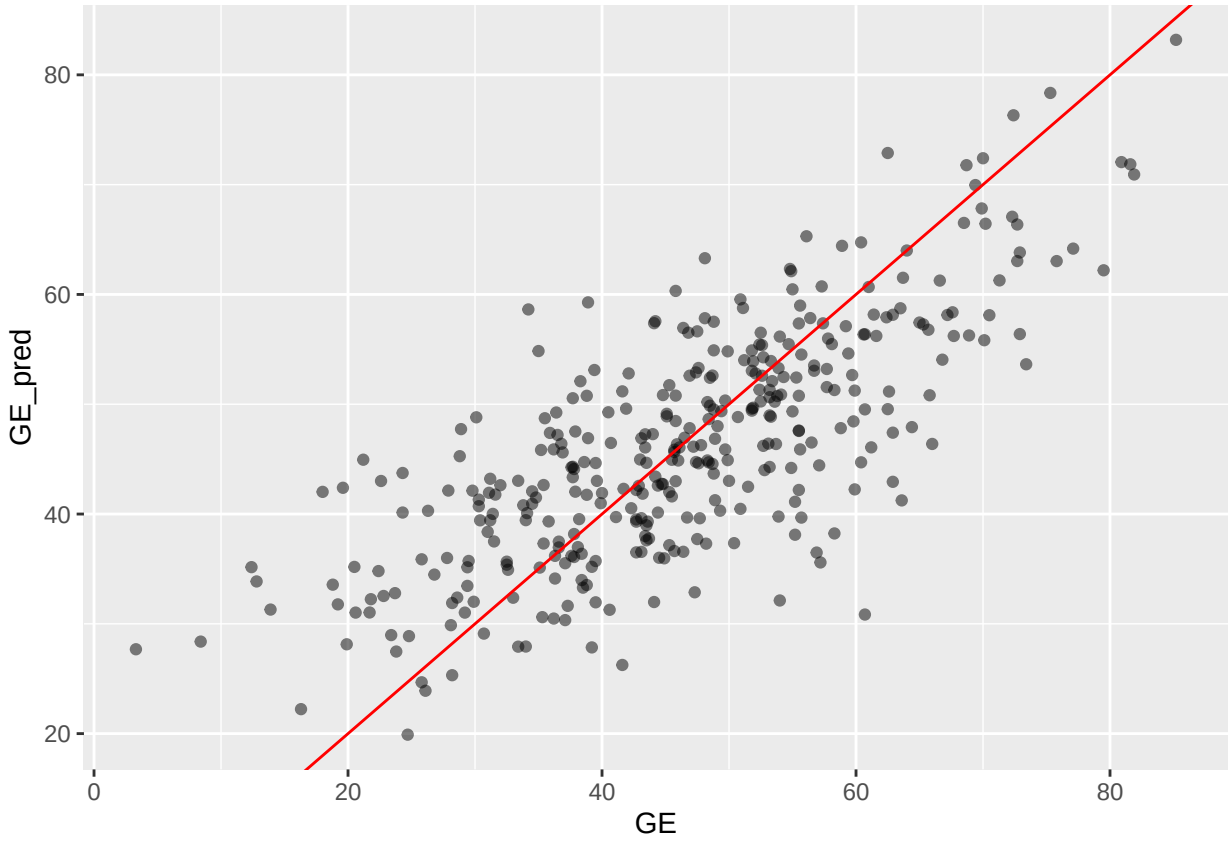
```
simres4 <- simulateResiduals(model4)
plot(simres4)
```



```r
vif(model4)
```

```
##                    Sex                    Age                    BMI
##               1.046957               1.038397               8.710514
##                  HbA1c             MatsudaIdx                  HOMAB
##               1.041944              28.610909              37.259663
## DiabetesComplications              Metformin                Gastrin
##               1.054272               1.021717               1.041674
##                Ghrelin                 Amylin               Glucagon
##               1.022247               1.025364               1.034700
##                   GLP1                    PYY
##               1.059292               1.061018
```

```r
dat$GE_pred <- predict(model4, newdata = dat_scaled, type = "response", na.action = na.pass)
ggplot(dat, aes(x = GE, y = GE_pred)) +
  geom_point(alpha = 0.5) +
  geom_abline(intercept = 0, slope = 1, color = "red")
```



After Standerdization, the parameter changed slightly.

Next, we add covariates to the model, according to early data exploration. A covariate is a variable that is potentially related to both the dependent variable (outcome) and one or more independent variables (predictors) in a statistical model.Including covariates allows us to control for confounding, reduce error variance, and obtain a more accurate estimate of the main effect of interest.

We first try to time PYY with Sex, since they both have significant impact on the model.

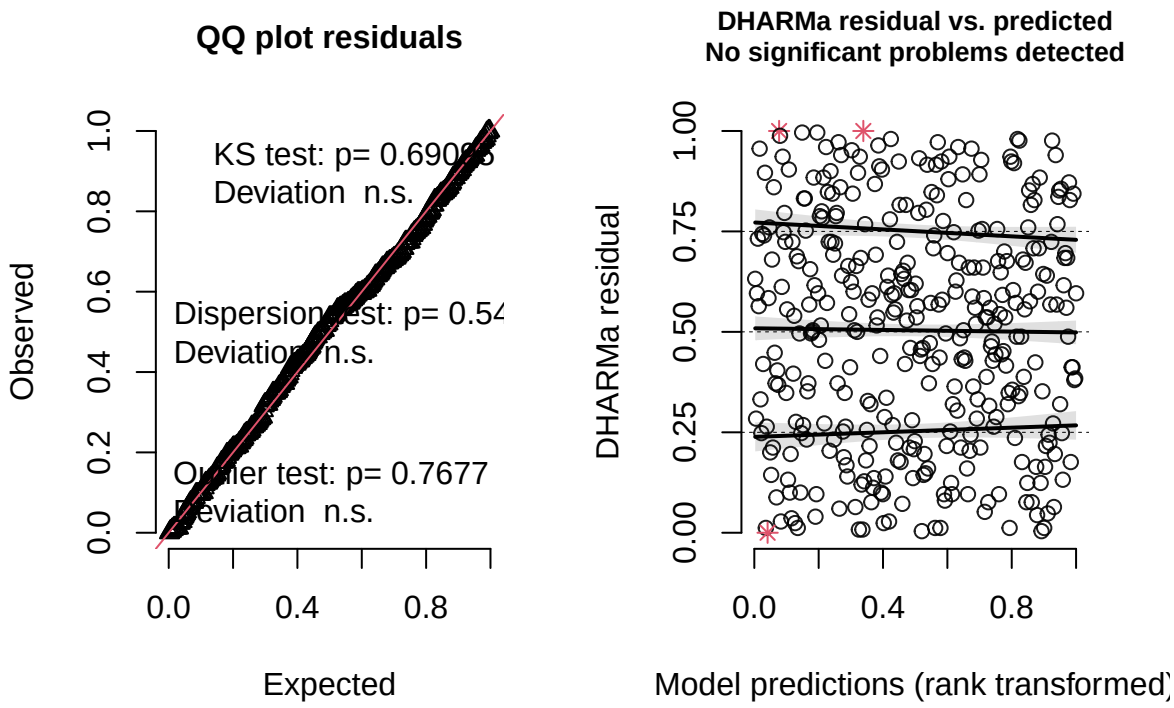
```r
# model
model5 <- glm(GE ~ Sex * PYY + Age + BMI + HbA1c + MatsudaIdx + HOMAB +
                DiabetesComplications + Metformin + Gastrin + Ghrelin + Amylin + Glucagon + GLP1,
              data = dat_scaled, family = gaussian)
summary(model5)
```

```
##
## Call:
## glm(formula = GE ~ Sex * PYY + Age + BMI + HbA1c + MatsudaIdx +
##     HOMAB + DiabetesComplications + Metformin + Gastrin + Ghrelin +
##     Amylin + Glucagon + GLP1, family = gaussian, data = dat_scaled)
##
## Coefficients:
##                         Estimate Std. Error t value Pr(>|t|)
## (Intercept)              45.1077     0.7732  58.340  < 2e-16 ***
## Sex                       3.1610     1.0068   3.140  0.00184 **
## PYY                       1.8949     0.7339   2.582  0.01023 *
## Age                       0.8451     0.5025   1.682  0.09349 .
## BMI                       0.5733     1.4656   0.391  0.69591
## HbA1c                    -0.9721     0.5030  -1.933  0.05409 .
## MatsudaIdx               -0.6303     2.6505  -0.238  0.81218
## HOMAB                    -1.4152     3.0256  -0.468  0.64026
## DiabetesComplications     2.6135     2.0817   1.255  0.21015
## Metformin                -2.3474     1.1093  -2.116  0.03505 *
## Gastrin                   0.8577     0.5029   1.706  0.08899 .
## Ghrelin                   5.8821     0.4988  11.792  < 2e-16 ***
## Amylin                   -0.3060     0.4987  -0.614  0.53990
## Glucagon                  0.4297     0.5010   0.858  0.39162
## GLP1                      8.6253     0.5069  17.016  < 2e-16 ***
## Sex:PYY                  -1.7622     1.0084  -1.748  0.08142 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for gaussian family taken to be 87.7987)
##
##     Null deviance: 71279  on 362  degrees of freedom
## Residual deviance: 30466  on 347  degrees of freedom
## AIC: 2672.2
##
## Number of Fisher Scoring iterations: 2
```

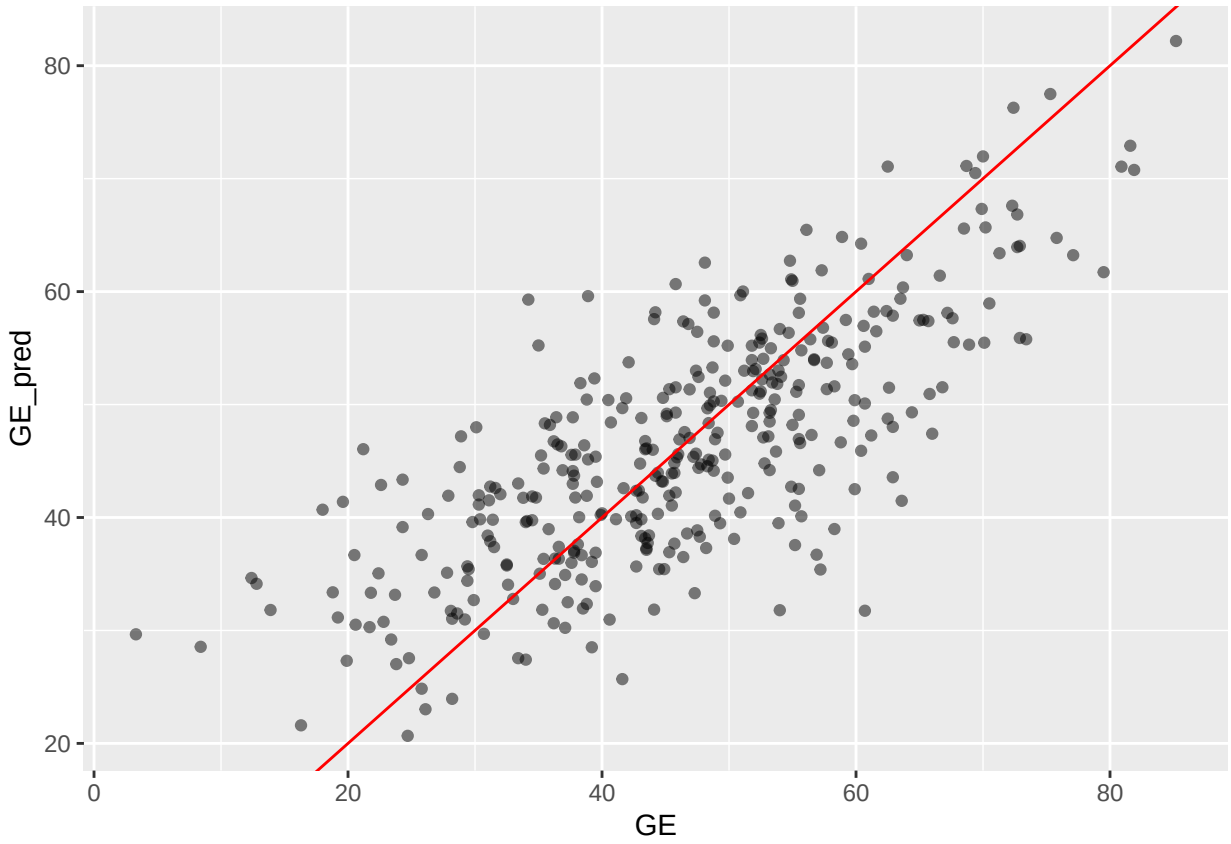
```r
rsq(model5, adj = TRUE)
```

```
## [1] 0.5541008
```

```r
simres5 <- simulateResiduals(model5)
plot(simres5)
```




```r
dat$GE_pred <- predict(model5, newdata = dat_scaled, type = "response", na.action = na.pass)
ggplot(dat, aes(x = GE, y = GE_pred)) +
  geom_point(alpha = 0.5) +
  geom_abline(intercept = 0, slope = 1, color = "red")
```



The results showed that model5 has a lower AIC and Residual deviance, which indicate a higher performance.

The interaction term Sex:PYY (β = -1.76, p = 0.081) shows a trend-level effect, meaning that it is not statistically significant at the conventional 0.05 level, but it approaches significance.In females (reference group), PYY has a positive association with GE (β = +1.89, p = 0.010), indicating that higher PYY levels are related to faster or greater gastric emptying. In males, the total effect of PYY becomes much weaker, suggesting that the positive relationship between PYY and GE observed in females is largely diminished or absent in males. Thus, the trend-level interaction implies that sex may modulate the physiological effect of PYY, but the evidence is not strong enough to claim a definitive moderating effect.

We move on to comparing model5 with model4.

```
# examine
AIC(model4, model5)
```

```
##        df      AIC
## model4 16 2673.409
## model5 17 2672.228
```

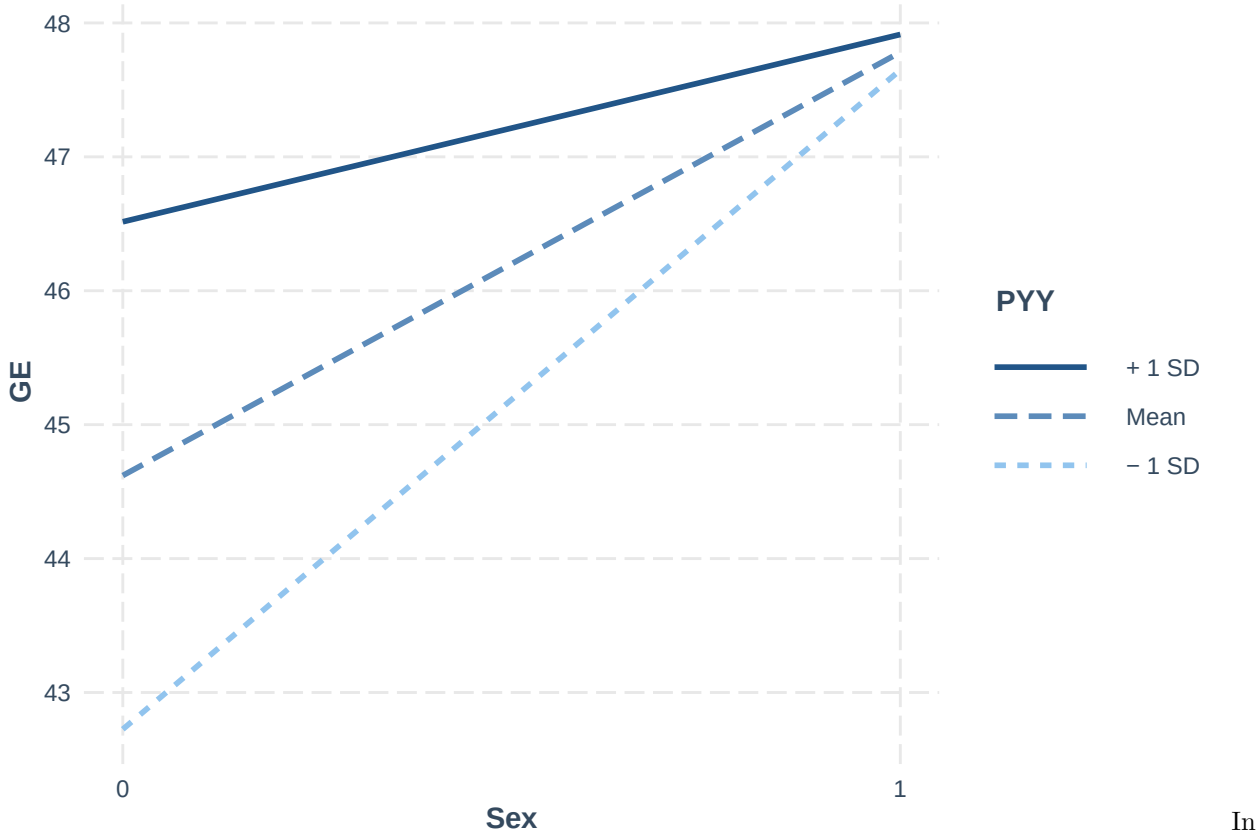
```
BIC(model4, model5)
```

```
##        df      BIC
## model4 16 2735.719
## model5 17 2738.433
```

```
anova(model4, model5, test = "Chisq")
```

```
## Analysis of Deviance Table
##
## Model 1: GE ~ Sex + Age + BMI + HbA1c + MatsudaIdx + HOMAB + DiabetesComplications +
##     Metformin + Gastrin + Ghrelin + Amylin + Glucagon + GLP1 +
##     PYY
## Model 2: GE ~ Sex * PYY + Age + BMI + HbA1c + MatsudaIdx + HOMAB + DiabetesComplications +
##     Metformin + Gastrin + Ghrelin + Amylin + Glucagon + GLP1
##   Resid. Df Resid. Dev Df Deviance Pr(>Chi)
## 1       348      30734
## 2       347      30466  1   268.14  0.08054 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
library(interactions)
interact_plot(model5, pred = "Sex", modx = "PYY")
```



In regression models, an interaction term such as A × B represents the idea that the effect of variable A on the outcome depends on variable B, and vice versa.

However, if one of these variables has no main effect - meaning it does not show any significant relationship with the dependent variable - then adding an interaction term is often statistically and conceptually unstable.

But in this work we are going to try and see the result of these interaction terms. Metformin has a significant impact, but HOMAB doesn't.

```
# model
model6 <- glm(GE ~ Metformin * HOMAB + Sex + PYY + Age + BMI + HbA1c + MatsudaIdx +
                DiabetesComplications + Gastrin + Ghrelin + Amylin + Glucagon + GLP1,
```

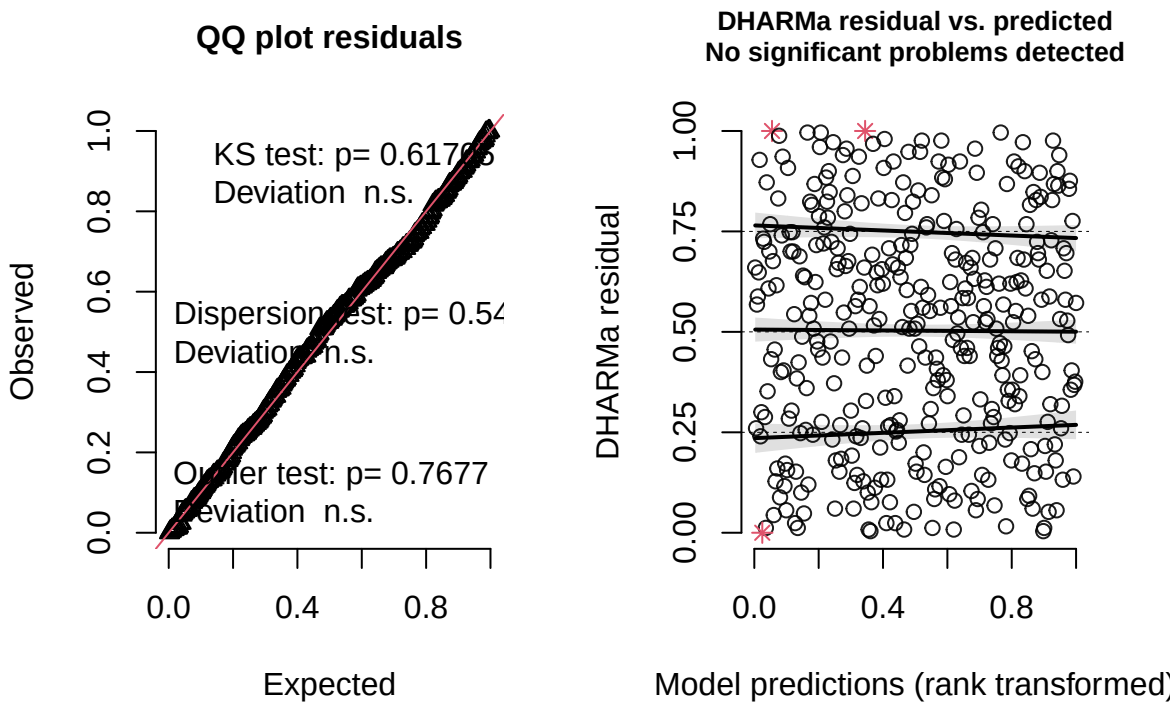
```
              data = dat_scaled, family = gaussian)
summary(model6)
```

```
##
## Call:
## glm(formula = GE ~ Metformin * HOMAB + Sex + PYY + Age + BMI +
##     HbA1c + MatsudaIdx + DiabetesComplications + Gastrin + Ghrelin +
##     Amylin + Glucagon + GLP1, family = gaussian, data = dat_scaled)
##
## Coefficients:
##                       Estimate Std. Error t value Pr(>|t|)
## (Intercept)            45.2270     0.7756  58.314  < 2e-16 ***
## Metformin              -2.2498     1.1197  -2.009  0.04528 *
## HOMAB                  -2.1899     3.0225  -0.725  0.46923
## Sex                     3.1256     1.0112   3.091  0.00216 **
## PYY                     0.9697     0.5089   1.905  0.05757 .
## Age                     0.8704     0.5039   1.727  0.08499 .
## BMI                     0.8506     1.4594   0.583  0.56036
## HbA1c                  -0.9616     0.5063  -1.899  0.05835 .
## MatsudaIdx             -1.0979     2.6433  -0.415  0.67815
## DiabetesComplications   2.8834     2.0809   1.386  0.16675
## Gastrin                 0.9113     0.5050   1.804  0.07205 .
## Ghrelin                 5.8303     0.4996  11.671  < 2e-16 ***
## Amylin                 -0.2704     0.5021  -0.539  0.59055
## Glucagon                0.3870     0.5038   0.768  0.44284
## GLP1                    8.6377     0.5086  16.984  < 2e-16 ***
## Metformin:HOMAB         1.0707     1.2117   0.884  0.37753
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for gaussian family taken to be 88.37259)
##
##     Null deviance: 71279  on 362  degrees of freedom
## Residual deviance: 30665  on 347  degrees of freedom
## AIC: 2674.6
##
## Number of Fisher Scoring iterations: 2
```

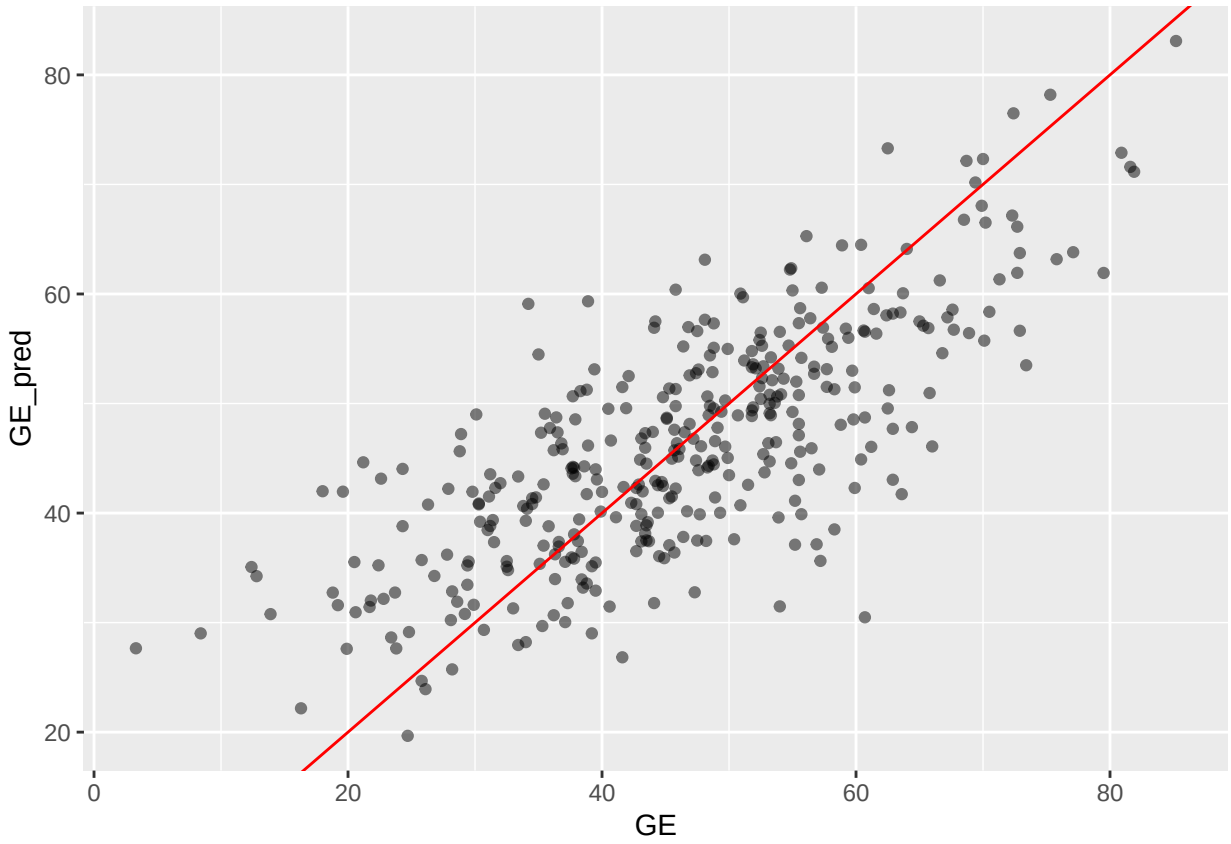
```
rsq(model6, adj = TRUE)
```

```
## [1] 0.5511862
```

```
simres6 <- simulateResiduals(model6)
plot(simres6)
```




```r
dat$GE_pred <- predict(model6, newdata = dat_scaled, type = "response", na.action = na.pass)
ggplot(dat, aes(x = GE, y = GE_pred)) +
  geom_point(alpha = 0.5) +
  geom_abline(intercept = 0, slope = 1, color = "red")
```



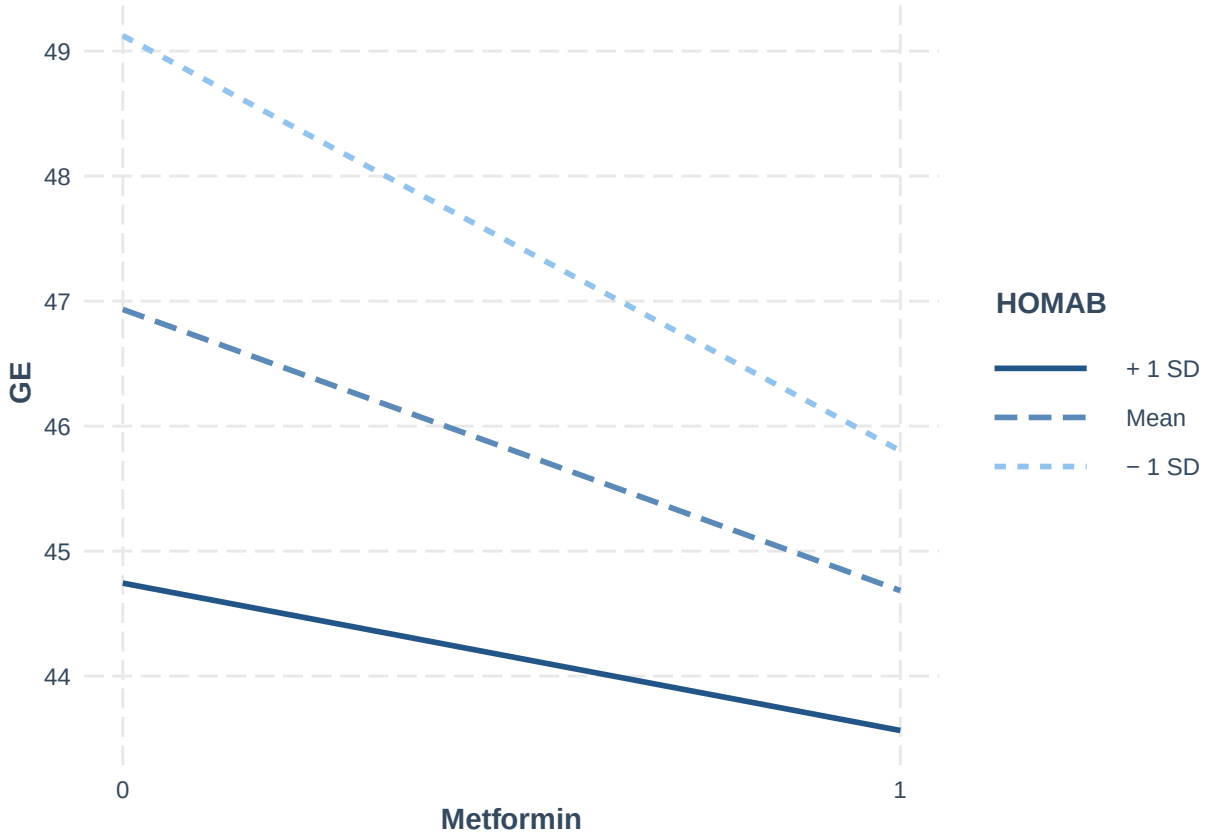

```
AIC(model4, model6)
```

```
##        df      AIC
## model4 16 2673.409
## model6 17 2674.593
```

```
BIC(model4, model6)
```

```
##        df      BIC
## model4 16 2735.719
## model6 17 2740.798
```

```
interact_plot(model6, pred = "Metformin", modx = "HOMAB")
```



From the result we can see that the interaction term did not work on improving the model.

Let's try DiabetesComplications-GLP1, in which DiabetesComplications does not have significant impact and GLP1 does.

```
# model
model7 <- glm(GE ~ DiabetesComplications * GLP1 + Metformin + HOMAB + Sex + PYY + Age + BMI + HbA1c +
                MatsudaIdx +Gastrin + Ghrelin + Amylin + Glucagon,
              data = dat_scaled, family = gaussian)
summary(model7)
```

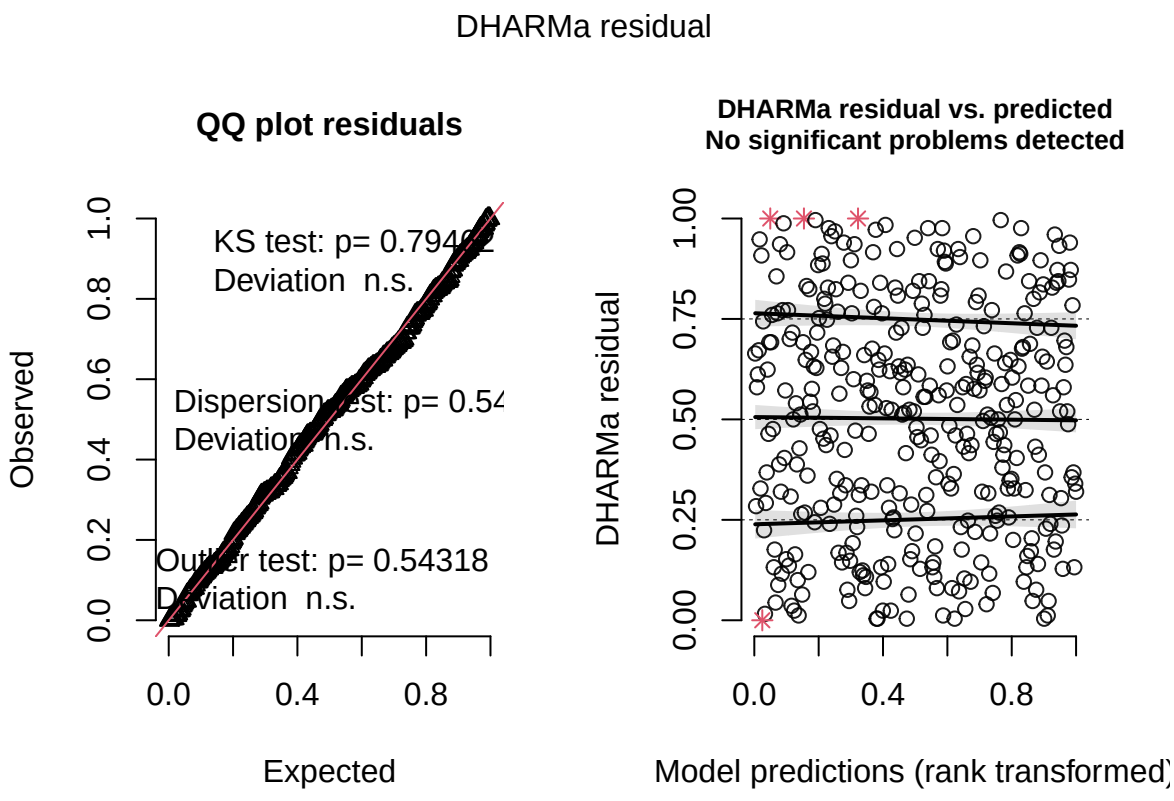
```
##
## Call:
## glm(formula = GE ~ DiabetesComplications * GLP1 + Metformin +
##     HOMAB + Sex + PYY + Age + BMI + HbA1c + MatsudaIdx + Gastrin +
##     Ghrelin + Amylin + Glucagon, family = gaussian, data = dat_scaled)
##
## Coefficients:
##                             Estimate Std. Error t value Pr(>|t|)
## (Intercept)                  45.1364     0.7699  58.629  < 2e-16 ***
## DiabetesComplications         1.6076     2.1497   0.748  0.45507
## GLP1                          8.9438     0.5238  17.076  < 2e-16 ***
## Metformin                    -2.1906     1.1085  -1.976  0.04893 *
## HOMAB                        -1.9431     2.9974  -0.648  0.51725
## Sex                           3.1653     1.0038   3.153  0.00175 **
## PYY                           0.9034     0.5066   1.783  0.07541 .
## Age                           0.8527     0.5006   1.703  0.08941 .
## BMI                           0.9198     1.4492   0.635  0.52604
```

```
## HbA1c                        -1.0214     0.5013  -2.038  0.04235 *
## MatsudaIdx                   -1.0384     2.6268  -0.395  0.69287
## Gastrin                       0.8686     0.5012   1.733  0.08399 .
## Ghrelin                       5.8836     0.4970  11.838  < 2e-16 ***
## Amylin                       -0.2793     0.4974  -0.562  0.57476
## Glucagon                      0.4654     0.4999   0.931  0.35252
## DiabetesComplications:GLP1   -4.4361     1.9571  -2.267  0.02403 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for gaussian family taken to be 87.27915)
##
##     Null deviance: 71279  on 362  degrees of freedom
## Residual deviance: 30286  on 347  degrees of freedom
## AIC: 2670.1
##
## Number of Fisher Scoring iterations: 2
```

```
rsq(model7, adj = TRUE)
```

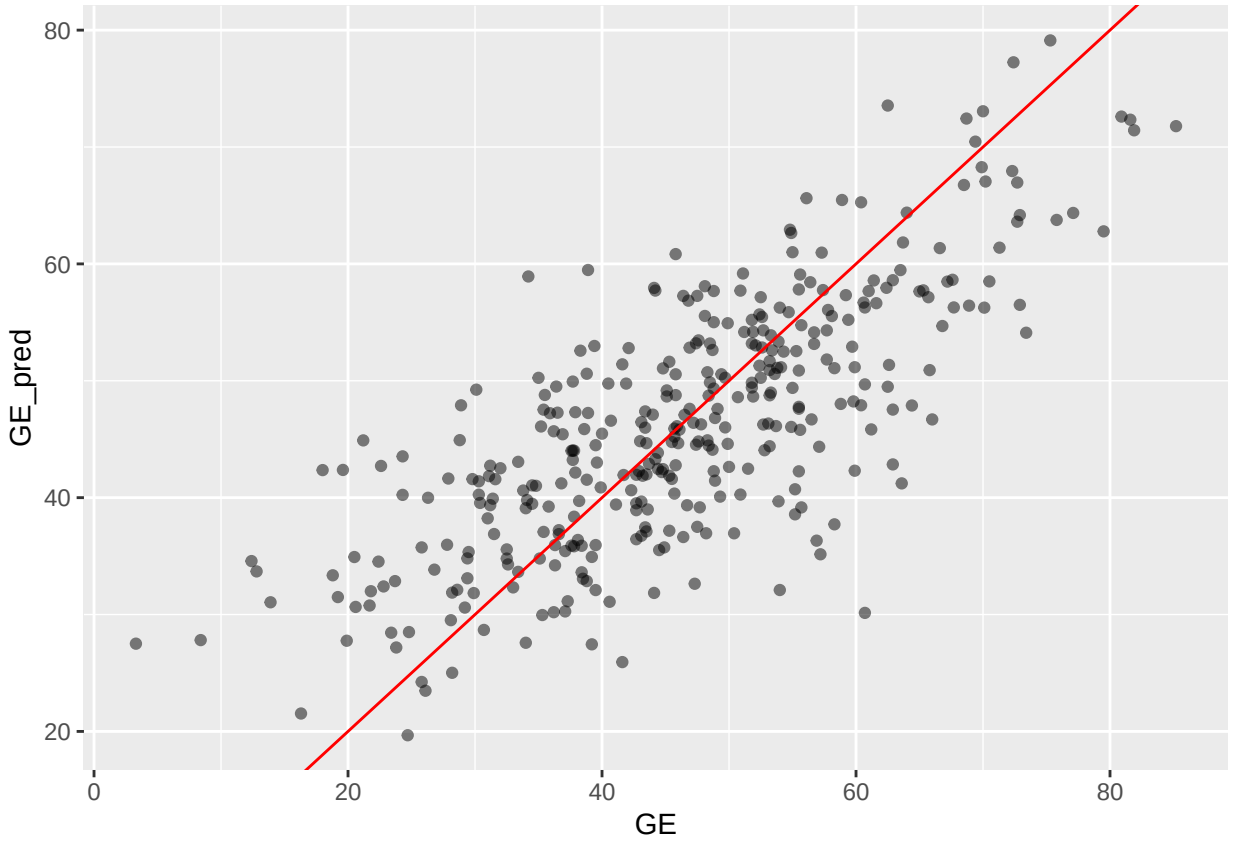
```
## [1] 0.5567395
```

```
simres7 <- simulateResiduals(model7)
plot(simres7)
```




```
dat$GE_pred <- predict(model7, newdata = dat_scaled, type = "response", na.action = na.pass)
ggplot(dat, aes(x = GE, y = GE_pred)) +
```

```
  geom_point(alpha = 0.5) +
  geom_abline(intercept = 0, slope = 1, color = "red")
```



Although DiabetesComplications itself is not a significant predictor of GE (p = 0.455), the interaction term DiabetesComplications × GLP1 is significant (p = 0.024).This indicates a moderation effect - the influence of GLP1 on GE differs depending on the presence of diabetes complications.

In individuals without complications, GLP1 has a strong positive association with GE ($\beta \approx 8.94$).

In individuals with complications, this effect is weakened ($\beta \approx 8.94$ - 4.44 ≈ 4.50).

Thus, GLP1's positive effect on GE is moderated by diabetes complications, suggesting that the physiological role of GLP1 may be partially impaired in patients with complications.

```
# examine
AIC(model4, model7)
```

```
##        df      AIC
## model4 16 2673.409
## model7 17 2670.074
```

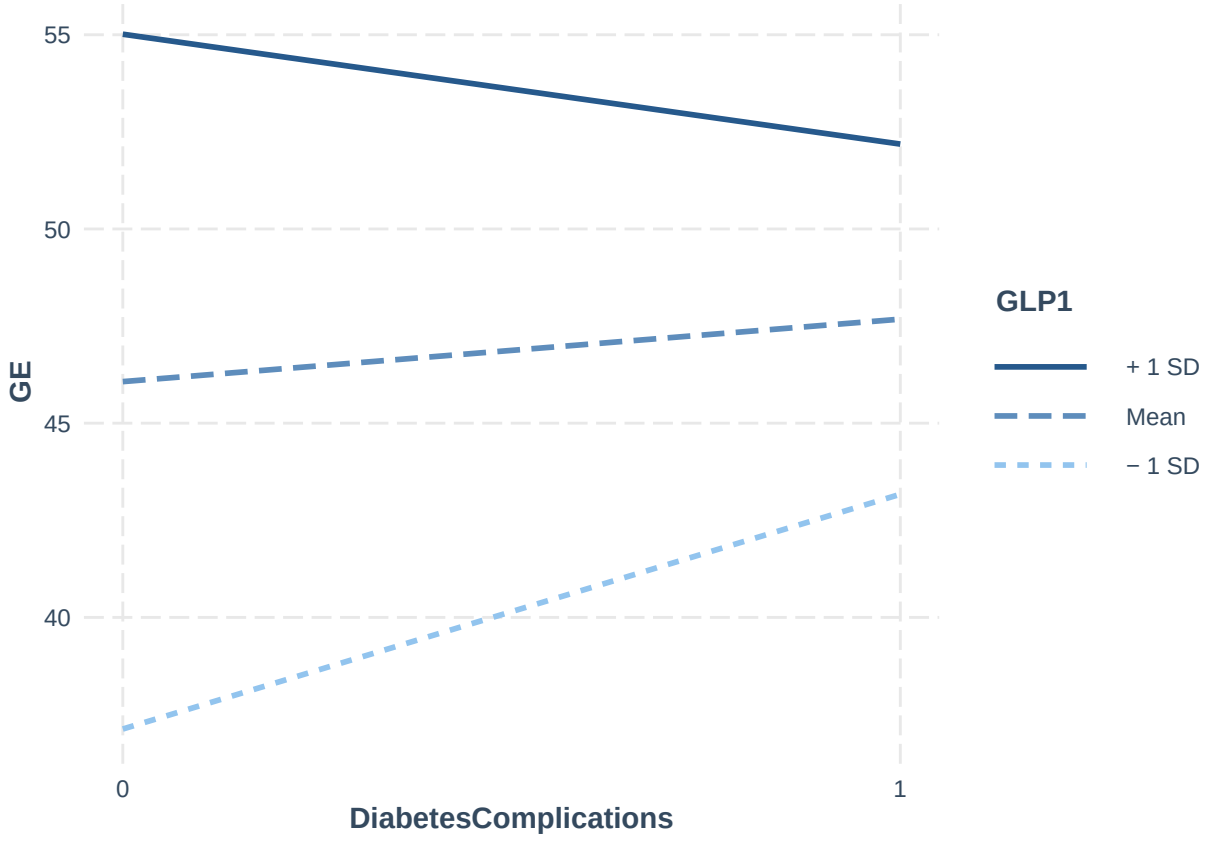
```
BIC(model4, model7)
```

```
##        df      BIC
## model4 16 2735.719
## model7 17 2736.278
```

```r
anova(model4, model7, test = "Chisq")
```

```
## Analysis of Deviance Table
##
## Model 1: GE ~ Sex + Age + BMI + HbA1c + MatsudaIdx + HOMAB + DiabetesComplications +
##     Metformin + Gastrin + Ghrelin + Amylin + Glucagon + GLP1 +
##     PYY
## Model 2: GE ~ DiabetesComplications * GLP1 + Metformin + HOMAB + Sex +
##     PYY + Age + BMI + HbA1c + MatsudaIdx + Gastrin + Ghrelin +
##     Amylin + Glucagon
##   Resid. Df Resid. Dev Df Deviance Pr(>Chi)
## 1       348      30734
## 2       347      30286  1   448.42  0.02341 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```r
interact_plot(model7, pred = "DiabetesComplications", modx = "GLP1")
```




```r
library(glmnet)
```

```
## Loading required package: Matrix

##
## Attaching package: 'Matrix'
```

```
## The following objects are masked from 'package:tidyr':
##
##     expand, pack, unpack

## Loaded glmnet 4.1-10
```

```
x <- model.matrix(GE ~ DiabetesComplications + GLP1 + Metformin + HOMAB + Sex + PYY + Age + BMI + HbA1c
                  data = dat_scaled)[, -1]
y <- dat_scaled$GE
lasso_fit <- cv.glmnet(x, y, alpha = 1, family = "gaussian")

lasso_fit$lambda.min
```

```
## [1] 0.04580325
```

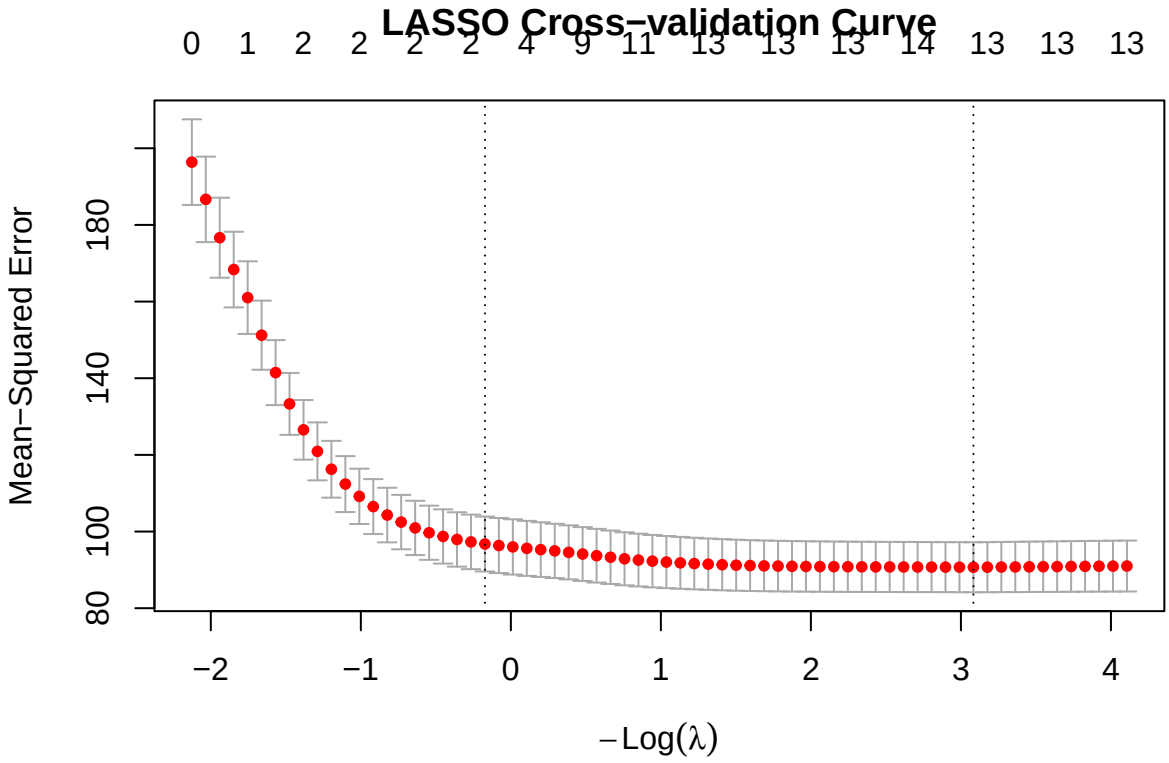
```
lasso_fit$lambda.1se
```

```
## [1] 1.188606
```

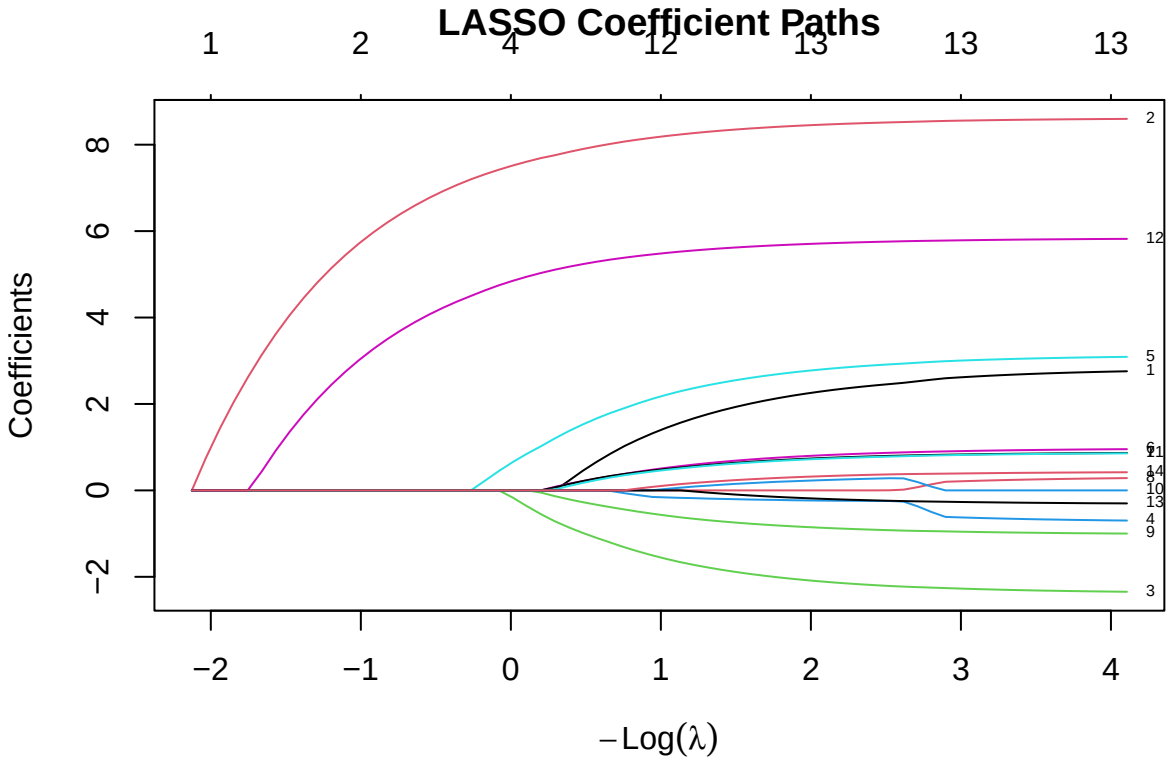
```
coef(lasso_fit, s = "lambda.min")
```

```
## 15 x 1 sparse Matrix of class "dgCMatrix"
##                         lambda.min
## (Intercept)           45.2619175
## DiabetesComplications  2.6340494
## GLP1                   8.5610646
## Metformin             -2.2810274
## HOMAB                 -0.6339552
## Sex                    3.0142631
## PYY                    0.9147268
## Age                    0.8356951
## BMI                    0.2198876
## HbA1c                 -0.9607997
## MatsudaIdx             .
## Gastrin                0.8241557
## Ghrelin                5.7910326
## Amylin                -0.2719751
## Glucagon               0.3952961
```

```
plot(lasso_fit)
title("LASSO Cross-validation Curve")
```




```
plot(glmnet(x, y, alpha=1), xvar="lambda", label=TRUE)
title("LASSO Coefficient Paths")
```



Compared to model4 of linear regression model, repid change occured in the estimated impact of vars that has colinear relation with others in normalized linear regression model.

Conclusion:

In this study, we investigated factors influencing gastric emptying (GE) in individuals with Type II Diabetes Mellitus using the DiGeHormone dataset. Our analysis combined extensive data exploration with multivariable regression modeling, including standardization, covariate adjustment, interaction assessment, and regularization techniques.

Data Exploration:

Initial data exploration showed minimal missing data (<1%), which were removed without affecting results. Most biomarkers exhibited approximately normal distributions, whereas some clinical variables were slightly skewed, highlighting the importance of checking model assumptions. Categorical data was found to affect levels of some of the continuous value, indicating its relevance as a covariate. Strong correlations were observed between BMI and body weight, HbA1c and fasting glucose, and other related measures, suggesting potential multicollinearity among predictors. Scatterplots indicated weak to moderate linear relationships between most biomarkers and GE, supporting the use of multivariable regression models.

Modeling Results:

Multivariable linear regression identified several key factors associated with GE. Sex and Metformin usage showed significant effects, with males and non-users having faster gastric emptying. Ghrelin and GLP1 were strongly positively associated with GE, while Gastrin and PYY demonstrated marginal associations. Covariate inclusion and standardization improved model stability and reduced collinearity effects, allowing retention of biologically relevant variables such as Matsuda Index and HOMA-B.

Interaction analyses revealed that sex modulates the effect of PYY on GE, with a trend-level interaction suggesting the positive association between PYY and GE is stronger in females. Furthermore, while DiabetesComplications alone was not a significant predictor, its interaction with GLP1 was significant, indicating a moderation effect where GLP1's positive impact on GE is attenuated in patients with complications.

Finally, regularization using LASSO confirmed the robustness of key predictors, highlighting the importance of Ghrelin, GLP1, Metformin, and Sex in explaining variability in GE while controlling for multicollinearity. LASSO coefficient paths and cross-validation curves provided additional insight into variable selection and model stability.

Overall, our results suggest that endogenous GI hormones, medication usage, and sex are important determinants of gastric emptying in T2DM. Interaction effects underscore the need to consider potential moderators in modeling physiological outcomes. Standardization and regularization techniques enhance model interpretability and reliability, particularly in the presence of collinear predictors.