Task 2:

Q1. Model fasted gastric emptying (GE_fasted) to determine the rate and half-life of gastric emptying.

We start with looking at the data. We see that the median and mean deviate substantially for both GE_fasted and GE_fed suggesting skewness.

```
> summary(data_2)
       X                Time           GE_fasted           GE_fed
 Min.   : 1.00    Min.   : 1.00    Min.   :  7.23    Min.   : -2.99
 1st Qu.:15.75    1st Qu.:15.75    1st Qu.: 13.98    1st Qu.: 30.96
 Median :30.50    Median :30.50    Median : 26.02    Median : 80.47
 Mean   :30.50    Mean   :30.50    Mean   : 36.33    Mean   : 63.18
 3rd Qu.:45.25    3rd Qu.:45.25    3rd Qu.: 52.37    3rd Qu.: 94.06
 Max.   :60.00    Max.   :60.00    Max.   :100.00    Max.   :101.70
```

Plotting the fasted data reveals a decay trend, consistent with an exponential process. We therefore fit an exponential model.
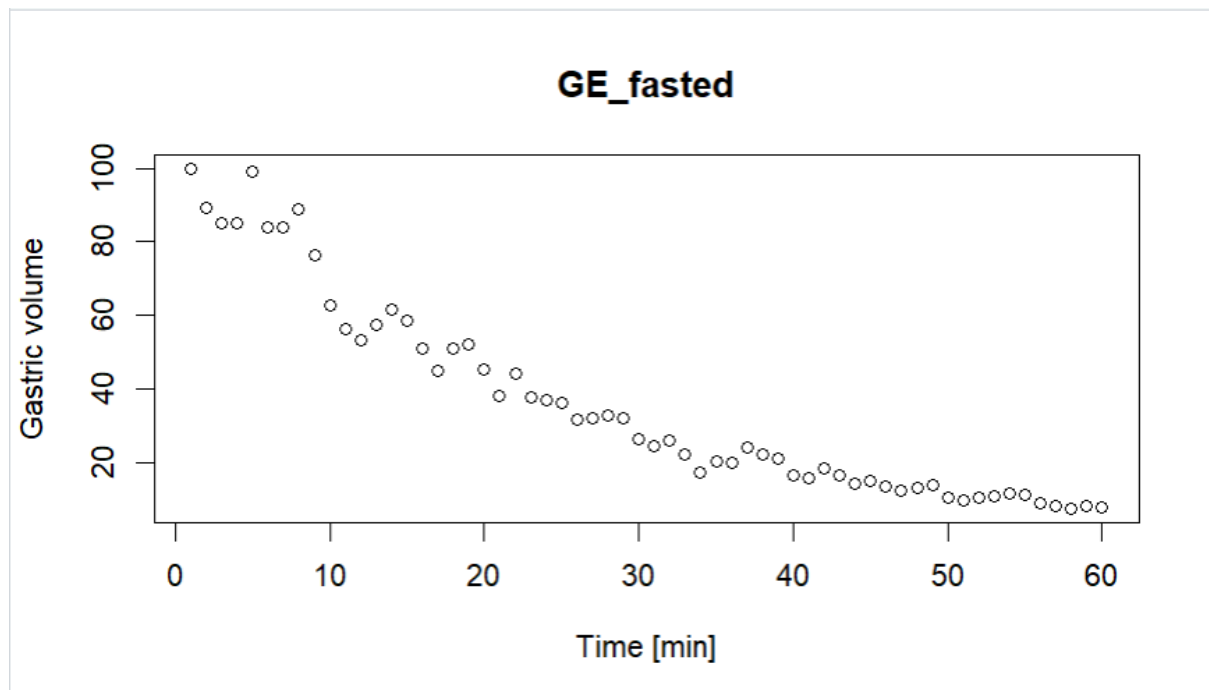
We assume the data to follow a decay curve, and we fit a model for it.

```
#we try to fit an exponential decay model
fasted_fit <- nls(GE_fasted ~ GE0 * exp(-k * X),
                  data = data_2,
                  start = list(GE0 = max(data_2$GE_fasted), k = 0.01))
```

```
> summary(fasted_fit)

Formula: GE_fasted ~ GE0 * exp(-k * X)

Parameters:
     Estimate Std. Error t value Pr(>|t|)
GE0 1.061e+02  1.964e+00   54.01   <2e-16 ***
k   4.416e-02  1.188e-03   37.17   <2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 4.337 on 58 degrees of freedom

Number of iterations to convergence: 5
Achieved convergence tolerance: 2.263e-06
```
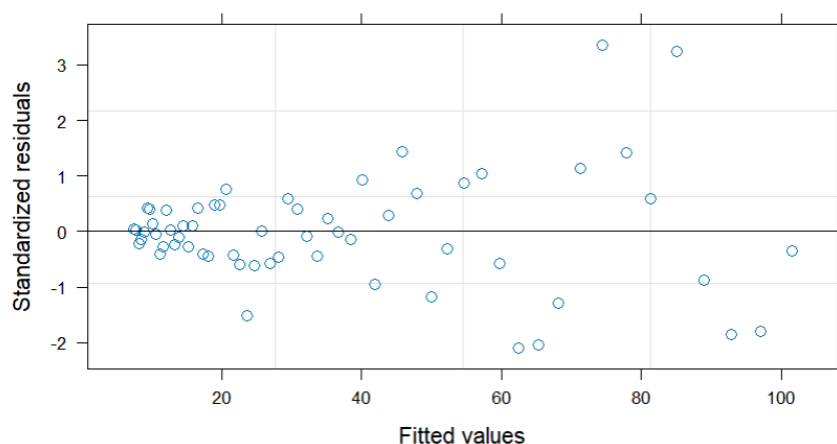
The model summary shows:

- Low standard errors
- High t-values
- Statistically significant p-values
- Low residuals

Together, these indicate a good model fit. A residuals vs. fitted plot confirms that residuals are small and evenly distributed.

Comparing predictions against observed data shows that the predicted curve (red line) closely follows the original data points (black dots).

```
time_seq <- seq(min(data_2$X), max(data_2$X), length.out = 60)
pred_fasted <- predict(fasted_fit, newdata_fasted = data.frame(X = time_seq))

plot(data_2$X, data_2$GE_fasted, pch = 16, main = "Observed vs Fitted_fasted",  xlab
lines(time_seq, pred_fasted, col = "red", lwd = 2)
```

Observed vs Fitted_fasted
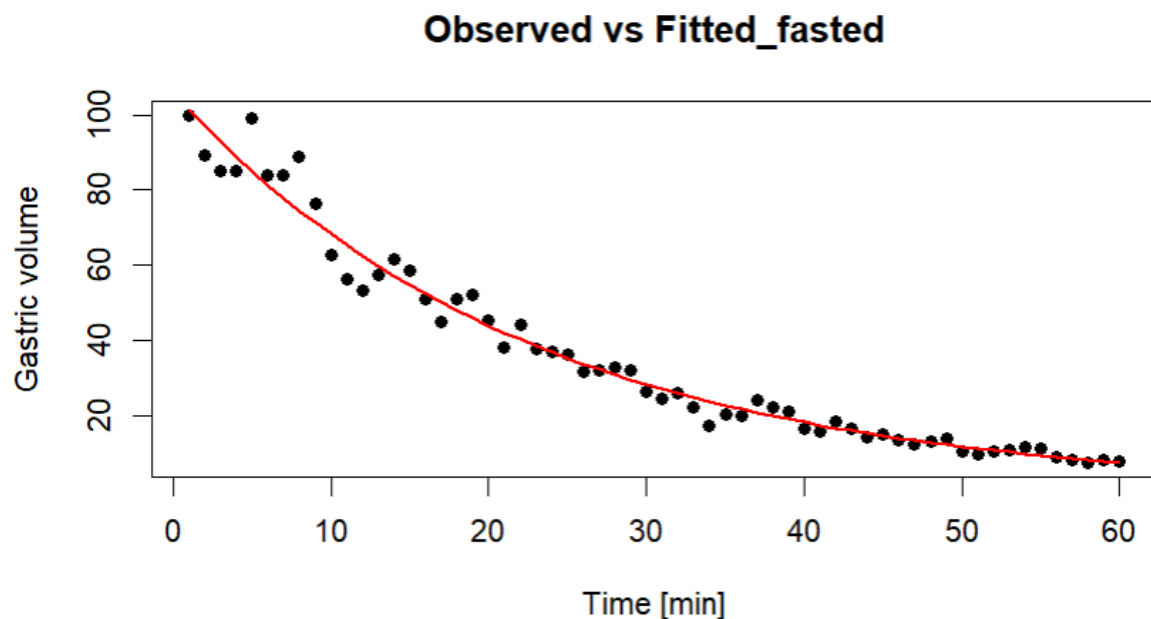

From this model we determine:

- **Rate constant (k):** 0.0044
- **Half-life ($t_{1/2}$):** 15.7

```
> coef_fasted <- coef(fasted_fit)
> t_half_fasted <- log(2)/coef_fasted["k"]
> print(t_half_fasted)
       k
15.69482
```

We could also use an alternative approach with log transforming the data.

```
log_GE_fasted <- log(data_2$GE_fasted)

#We see that we get a linear relationship
plot(data_2$X,log_GE_fasted, main = "Log GE_fasted", xlab = "Time [min]", ylab = "Ga
```
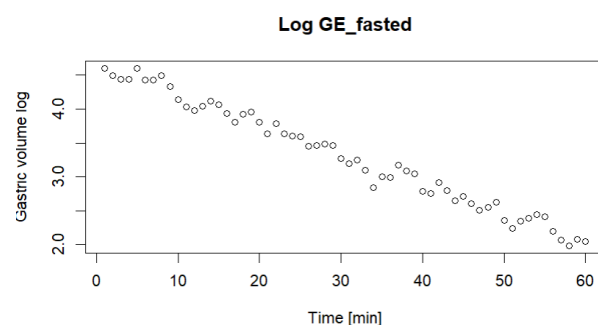

We can now plot the log data, we see that the data seem to follow a more linear trend. We can now fit a linear model to the data.

```
> lm_GE_fasted <- lm(formula = log_GE_fasted ~ X, data=data_2)
> summary(lm_GE_fasted)

Call:
lm(formula = log_GE_fasted ~ X, data = data_2)

Residuals:
     Min       1Q    Median       3Q       Max
-0.315603 -0.079253  0.001673  0.073441  0.185133

Coefficients:
             Estimate Std. Error t value Pr(>|t|)
(Intercept)  4.6576842  0.0266059   175.1   <2e-16 ***
X           -0.0442232  0.0007586   -58.3   <2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 0.1018 on 58 degrees of freedom
Multiple R-squared:  0.9832,    Adjusted R-squared:  0.9829
F-statistic:  3399 on 1 and 58 DF,  p-value: < 2.2e-16
```

The residuals are normally distributed, standard errors are low, and the R^2 value is close to 1, confirming a strong fit. The estimated rate and half-life are nearly identical to the exponential fit.

```
> AIC(fasted_fit)
[1] 350.2964
> AIC(lm_GE_fasted)
[1] -99.97951
```

We can also compare the models with the AIC values for the models. Since lm_GE_fasted has a lower AIC value the model is a better fit.

Q2. Model the fed state gastric emptying profile.

When looking at the data set for the fed_state we see two negative values. Negative volume is not possible so we remove them from the data.

```
GE_fed_data <- data_2$GE_fed[data_2$GE_fed >= 0]
length(GE_fed_data)
X_data <- data_2$X[data_2$GE_fed > 0]
```

Plotting the fed-state data shows that the profile does not follow a simple exponential decay. Instead, there is an initial lag phase before emptying begins. To account for this, we fit a Weibull model, which incorporates a lag parameter.
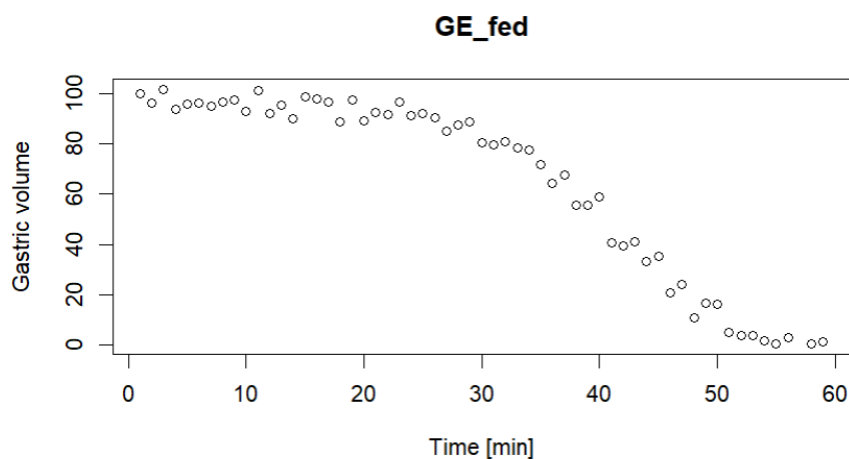
GE_fed

```
> summary(fed_fit)

Formula: GE_fed_data ~ GEO * exp(-(k * X_data)^b)

Parameters:
     Estimate Std. Error t value Pr(>|t|)
GEO 9.570e+01  7.172e-01  133.43   <2e-16 ***
k   2.296e-02  1.176e-04  195.27   <2e-16 ***
b   5.529e+00  2.159e-01   25.61   <2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 3.424 on 55 degrees of freedom

Number of iterations to convergence: 7
Achieved convergence tolerance: 1.058e-06
```
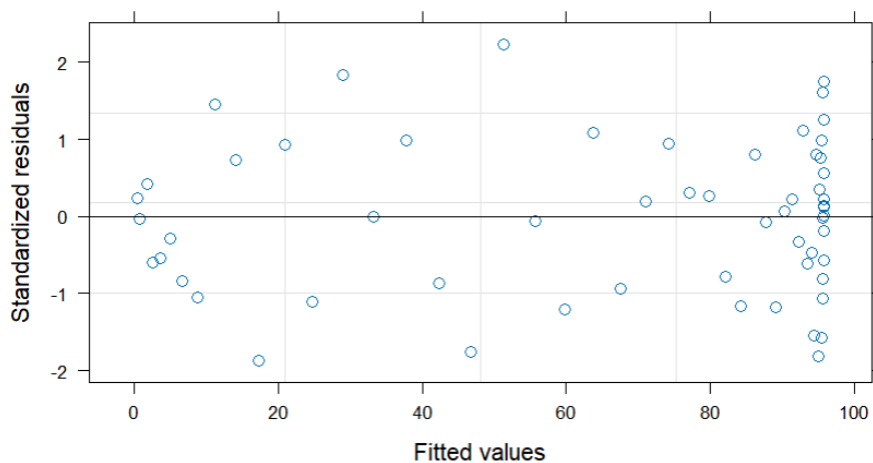
The Weibull model shows:

- Low standard errors
- Statistically significant p-values
- Low residuals


```
# Predictions
time_seq_fed <- seq(min(X_data), max(X_data), length.out = 58)
pred_fed <- predict(fed_fit, newdata = data.frame(X = time_seq_fed))

# Plot
plot(X_data, GE_fed_data, pch = 16, main = "Observed vs Fitted_fed",
     xlab = "Time [min]", ylab = "Gastric volume")
lines(time_seq_fed, pred_fed, col = "red", lwd = 2)
```

Predicted vs. observed plots demonstrate that the Weibull model fits the data well across the time course.

Observed vs Fitted_fed
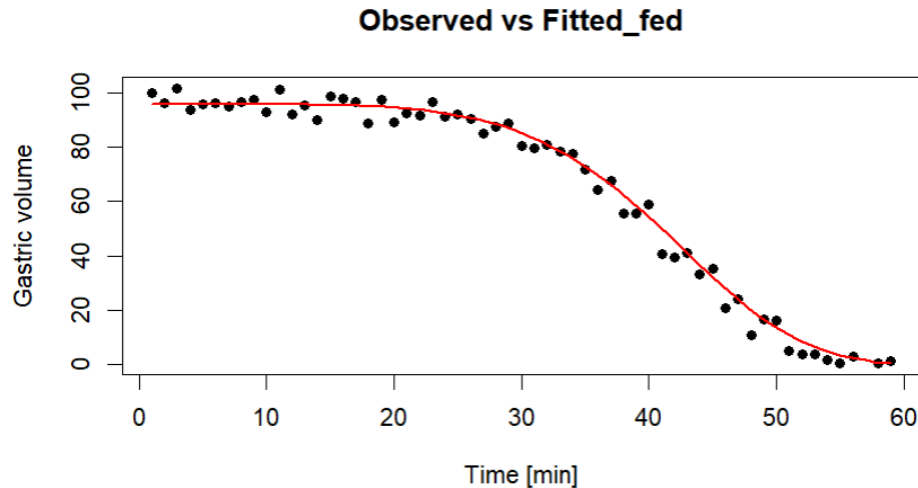
Q3. *In larger studies we normally depend on secondary parameters (such as half-life) rather than the time-dynamic profiles.*
For the fed state gastric emptying profile, how informative is half-life for describing the time-dynamics?
Can you propose alternative secondary parameters?

In larger studies, secondary parameters (such as half-life) are often used instead of full time-dynamic profiles. However, half-life is not always informative for the fed state because:

- Different curve shapes can yield the same t_{50}.
- Subjects may share identical t_{50} values but differ in early retention, which has important clinical implications.
- Half-life assumes exponential decay and does not account for the lag phase.

For example:

- **$T_{1/2}$ (fasted):** 15.7
- **$T_{1/2}$ (fed):** 30.2

This comparison suggests that fed emptying is only about twice as slow, when in fact the lag phase makes it much less representative.

```
> coef_fed <- coef(fed_fit)
> t_half_fed <- log(2)/coef_fed["k"]
> print(t_half_fed)
      k
30.19421
```

Example of another parameter.
T-lag25- time until 25% of gastric volume is emptied

```
> threshold_fed <- 0.75 * coef_fed["GE0"]
> idx_fed <- which.min(abs(pred_fed - threshold_fed))
> T25_fed<- time_seq_fed[idx_fed]
> print(T25_fed)
[1] 35.59649
```

.

```
> threshold_fasted <- 0.75 * coef_fasted["GE0"]
> idx_fasted <- which.min(abs(pred_fasted- threshold_fasted))
> T25_fasted <- time_seq[idx_fasted]
> print(T25_fasted)
[1] 7
```

Here we get a much better description of the lag in the fed state and how much faster the fasted state is.

Example of another parameter.

Time at Steepest decline (most negative derivate)

Conclusion

- **Fasted gastric emptying** is well described by an exponential (or log-linear) model with a half-life of ~15.7 minutes.
- **Fed gastric emptying** requires a Weibull model due to the initial lag phase; half-life (~30.2 minutes) is insufficient to describe its dynamics.
- **Half-life is not always informative** in the fed state. Alternative secondary parameters such as *T-lag25* and *time at steepest decline* provide a more accurate representation of gastric emptying dynamics.