The Impact of High-Density Lipoproteins and Sex on the Frequency of Blood Monocytes in Older Adults.

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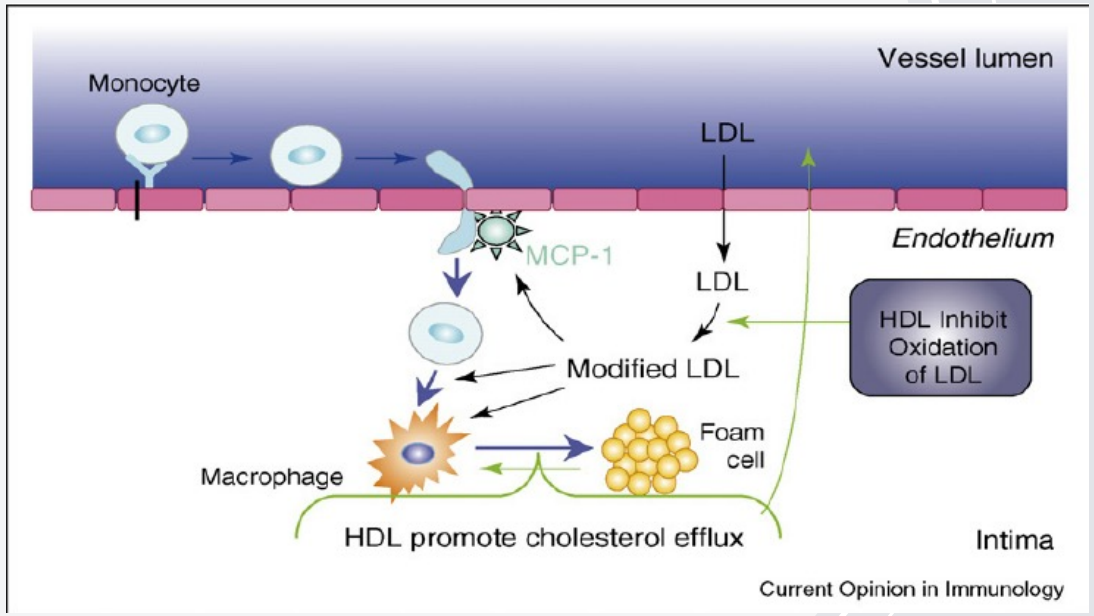
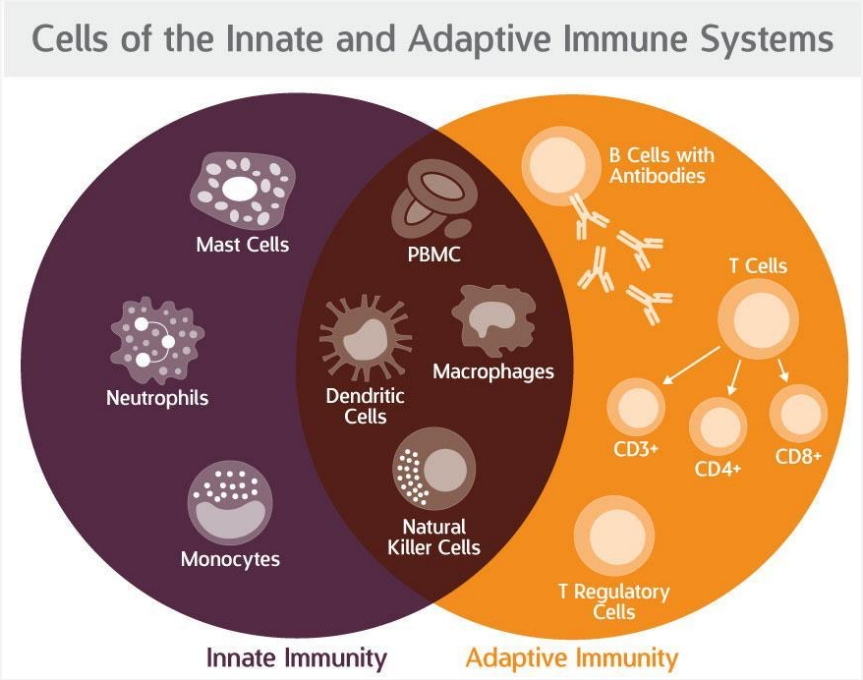


Background

- Foam cells are **a type of macrophage** that localize to fatty deposits on blood vessel walls, where they ingest low-density lipoproteins and become laden with lipids, giving them a foamy appearance. These can form a plaque that **can lead to atherosclerosis and trigger heart attacks and stroke**.
- HDL (high-density lipoprotein), or “good” cholesterol, **absorbs cholesterol and carries it back to the liver**. The liver then flushes it from the body.



Background

- An *in vitro* study by Murphy et al. (2008) showed that high-density lipoprotein (HDL) caused a dose-dependent reduction in the activation of human monocytes.

- There are conflicting studies on the sexual-dimorphism of the immune system in older adults.

- A study by Marquez et al. (2020) concluded that older men had a higher innate and pro-inflammatory activity than older women. Conversely, So et al. (2021) found that innate immune functions in older women were more activated than in men.

Hypotheses

H0: High-density lipoproteins have no association with the blood monocyte frequencies of older adults.

H1: High-density lipoproteins are negatively associated with the blood monocyte frequencies of older adults.

H0: There is no difference between the blood monocyte frequencies of older men and older women.

H1: There is a difference between the blood monocyte frequencies of older men and older women.

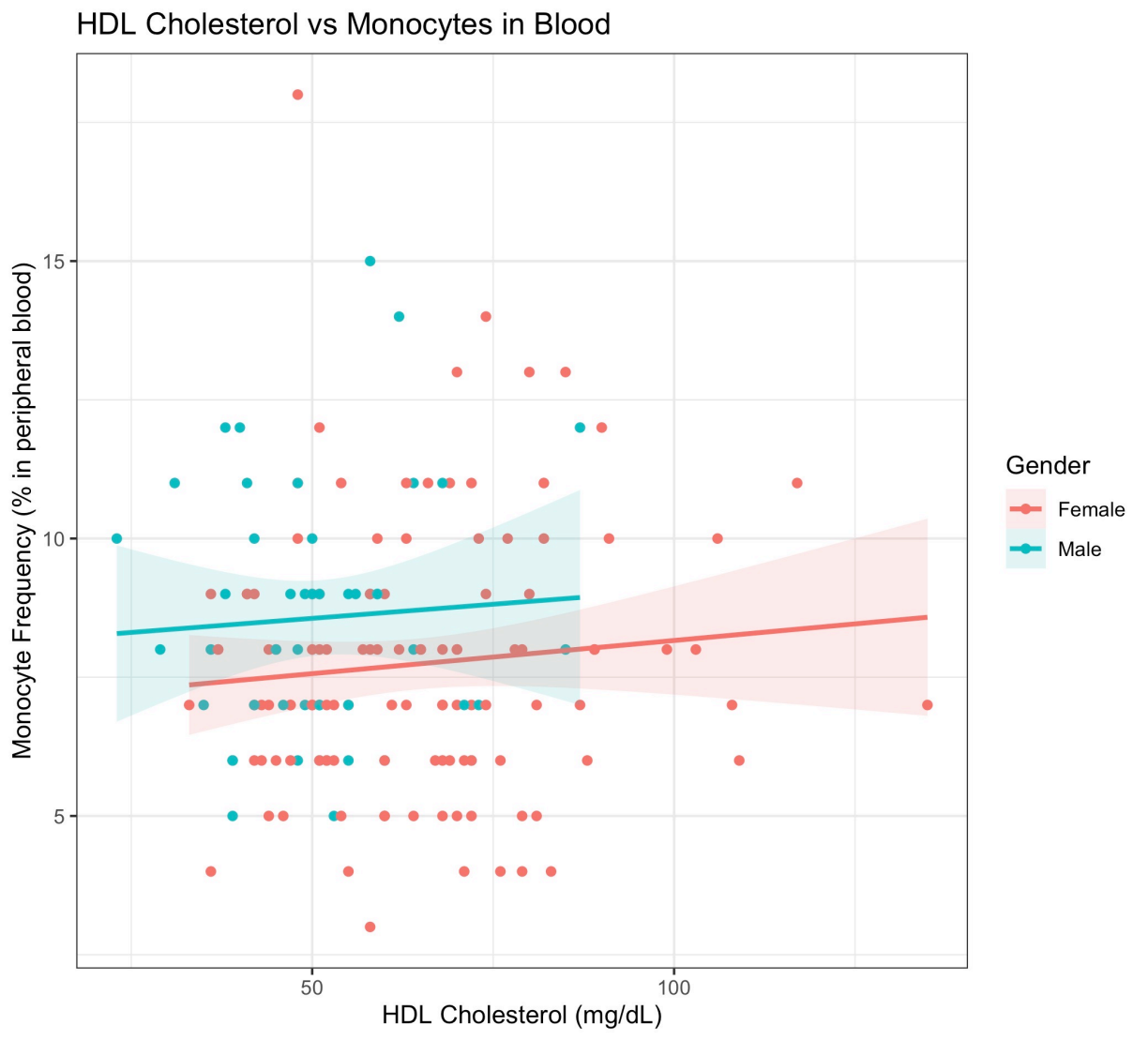
Experimental Design

- Older adults (between ages 65-85) were recruited from the San Diego area to participate in a clinical trial (2015-2021) involving 12 weeks of instructor-led Tai-Chi practice.
- The goal of the trial was to investigate the effects of Tai-Chi on the blood pressure and immune function of older adults.
- From a total of 191 participants that were enrolled, 159 participants were able to provide blood samples at the pre-intervention visit.
- These blood samples were sent to LabCorp for complete blood count tests and lipid panel tests.

Data Wrangling

```
hapi <- hapichi %>%
  filter(visit == 1) %>% # filter for baseline visit
  select(c("subject_id", "gender", "hdl_cholesterol", "monocytes")) %>%  #select variables of interest
  na.omit(TRUE) #omit participants that do not have complete clinical measurements


hapi['gender'][hapi['gender'] == '1'] <- 'Male’
hapi['gender'][hapi['gender'] == '2'] <- 'Female’


hapi$gender <- as.factor(hapi$gender)


hapi <- rename(hapi, Gender = gender)
```

subject_id	Gender	hdl_cholesterol	monocytes
1	Female	74	14
2	Female	70	13
3	Female	48	11
5	Female	88	6
7	Female	44	7
10	Male	60	6
11	Female	78	8
13	Female	103	8



Initial Graph

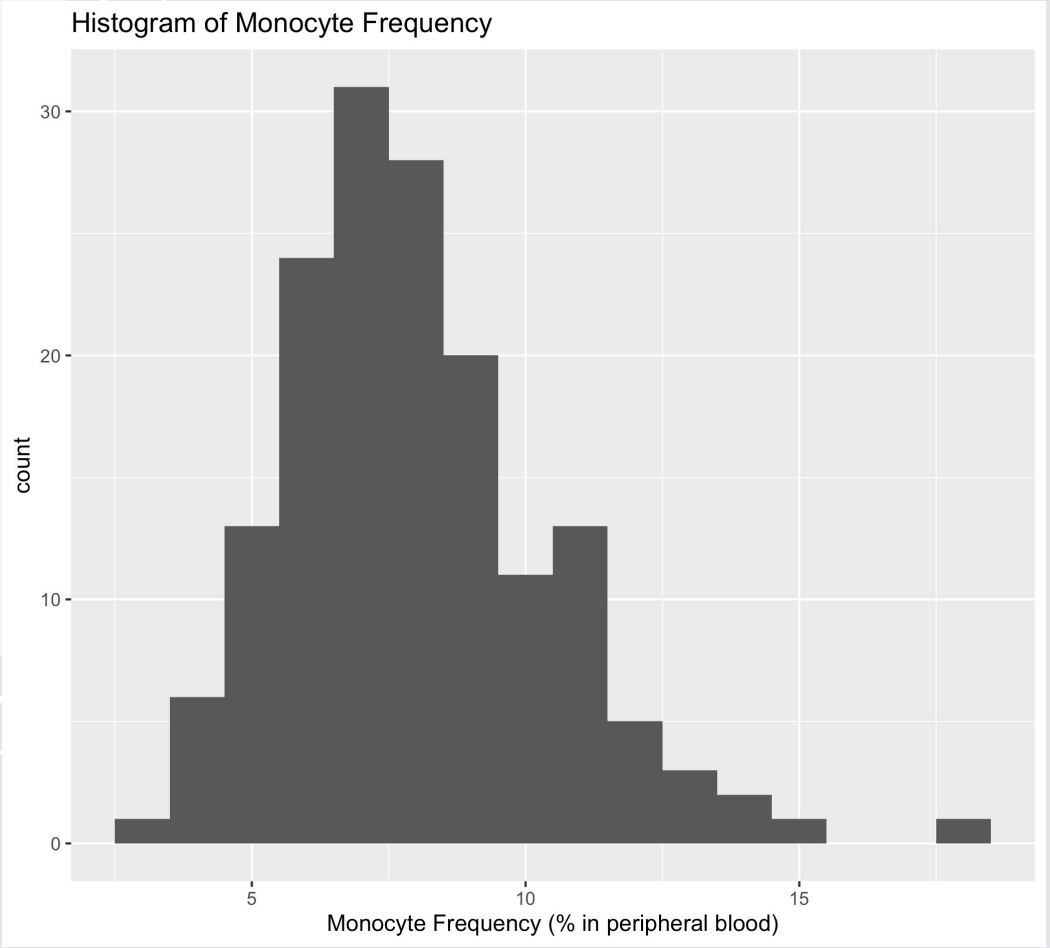
```
ggplot(data = hapi, aes(y = monocytes, x = hdl_cholesterol, group = Gender, colour = Gender)) +

  geom_point() +

  geom_smooth(method = "lm", alpha = .15, aes(fill = Gender)) +

  labs(title = "HDL Cholesterol vs Monocytes in Blood", x = "HDL Cholesterol (mg/dL)", y = "Monocyte Frequency (% in peripheral blood)") +

  theme_bw()
```

Data Inspection

```
hapi %>% group_by(Gender) %>%
summarise('Participant Count' = length(Gender))
#unbalanced data
```

```
shapiro.test(hapi$monocytes) #non-normal

ggplot(hapi, aes(monocytes)) +
  ggtitle("Histogram of Monocyte Frequency") +
  geom_histogram(binwidth = 1) +
  xlab("Monocyte Frequency (% in peripheral
blood)")  #right-skewed response data
```

	Gender	`Participant Count`
	<fct>	<int>
1	Female	112
2	Male	47

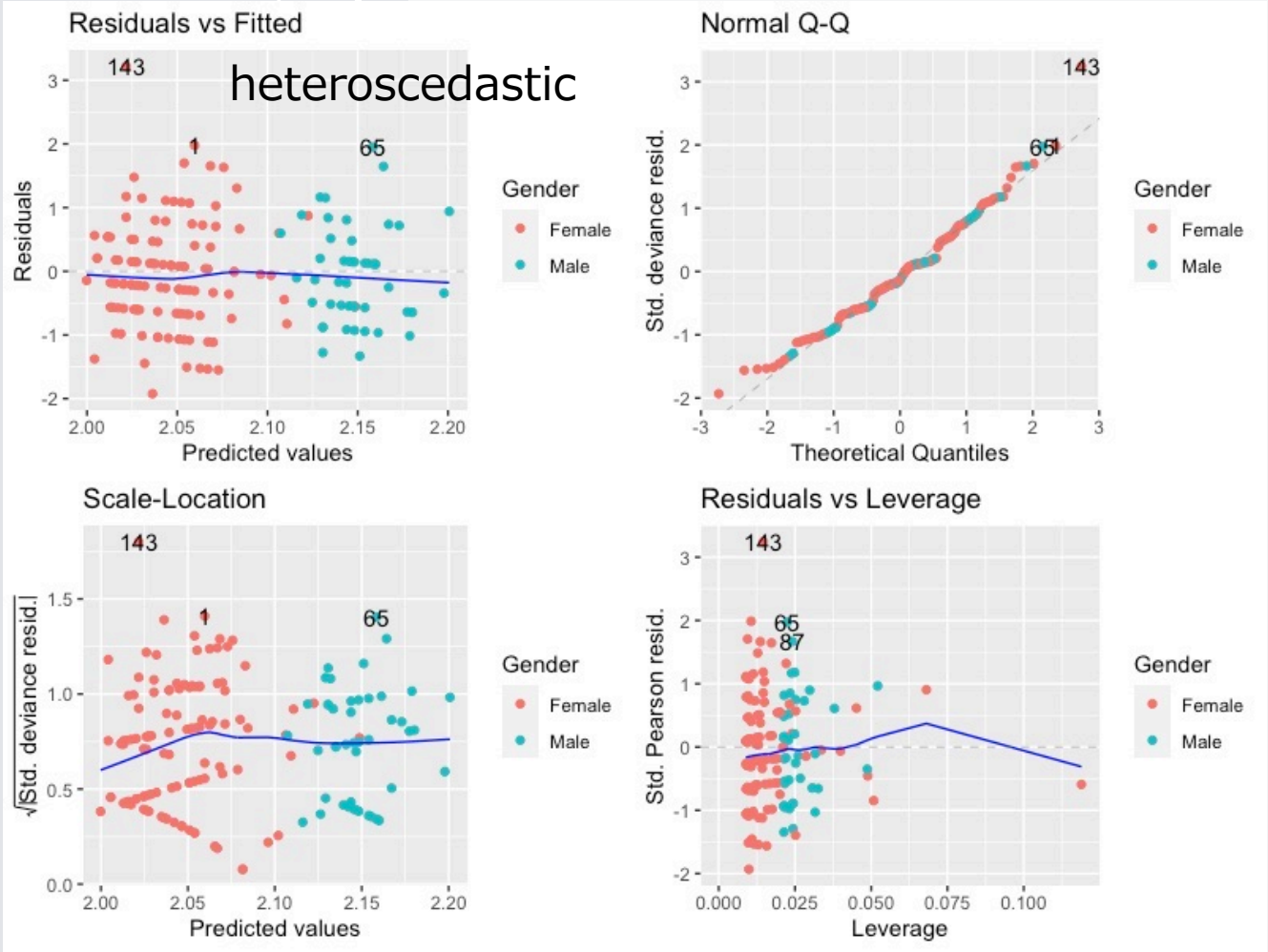


Data Inspection (cont.)

```
hapi.mod <- glm(monocytes ~ hdl_cholesterol + Gender, data = hapi, family = 'poisson')
```

```
AER::dispersiontest(hapi.mod)

# check dispersion: ~0.7057, data is underdispersed
```

```
autoplot(hapi.mod, colour = 'Gender')
```



Model Evaluation and Results

The sample sizes are unbalanced.

The response data is under-dispersed and heteroscedastic.

There is no interaction effect between the predictor variables.

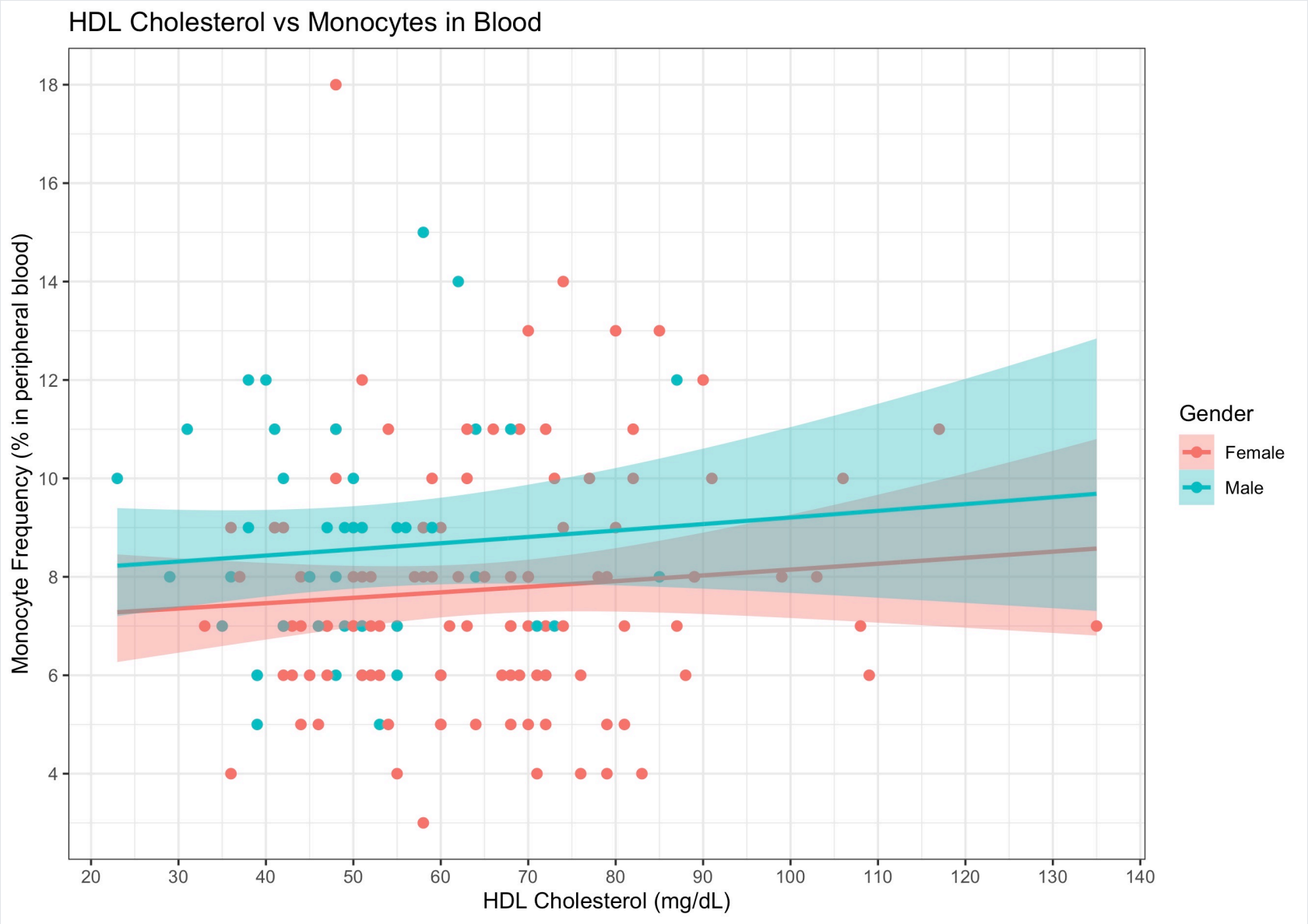
Therefore, analysed the model using a Type II ANOVA.

```
Analysis of Deviance Table (Type II tests)

Response: monocytes
                LR Chisq Df Pr(>Chisq)
hdl_cholesterol   0.8091  1    0.36839
Gender            3.5727  1    0.05874 .
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
```

Visual Model RCode

```
# Generate new explanatory variable values

new.x <- expand.grid(

  hdl_cholesterol = seq(from = 23, to = 135, length.out = 500), # range(hapi$hdl_cholesterol)

  Gender = levels(hapi$Gender))



# Generate new response variable values

new.y <- predict(hapi.mod, newdata = new.x, se.fit = TRUE)

new.y <- data.frame(new.y)



# Create a new datafame from these generated values

addThese <- data.frame(new.x, new.y)

addThese <- mutate(addThese, monocytes = exp(fit), lwr = exp(fit - 1.96 * se.fit), upr = exp(fit + 1.96 * se.fit))
```

```
# Add trend lines to the linear models using the predicted values with confidence intervals

midterm_1_plot <- ggplot(hapi, aes(x = hdl_cholesterol, y = monocytes, colour = Gender)) +

  geom_point(size = 2.0, aes(colour = Gender)) +

  geom_smooth(data = addThese, aes(ymin = lwr, ymax = upr, colour = Gender, fill = Gender), stat = 'identity') +

  scale_x_continuous(n.breaks = 10) +

  scale_y_continuous(n.breaks = 10) +

  labs(title = "HDL Cholesterol vs Monocytes in Blood", x = "HDL Cholesterol (mg/dL)", y = "Monocyte Frequency (% in peripheral blood)") +

  theme_bw()
```


HDL Cholesterol vs Monocytes in Blood
Monocyte Frequency (% in peripheral blood)
HDL Cholesterol (mg/dL)
Gender
Female
Male
18
16
14
12
10
8
6
4
20
30
40
50
60
70
80
90
100
110
120
130
140

Conclusion

- I failed to reject both null hypotheses.
- High-density lipoproteins have no effect on the blood monocyte frequencies of older adults.
- There is no difference between the blood monocyte frequencies of older men and older women.
- Consider re-analysis using a Conway-Maxwell distribution to better model the under-dispersed data
- A larger clinical sample size would also be ideal to increase statistical power and confidently derive any concrete conclusions of sexual dimorphism.

References

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