The relationship between high-density lipoproteins and monocytes in older adults.

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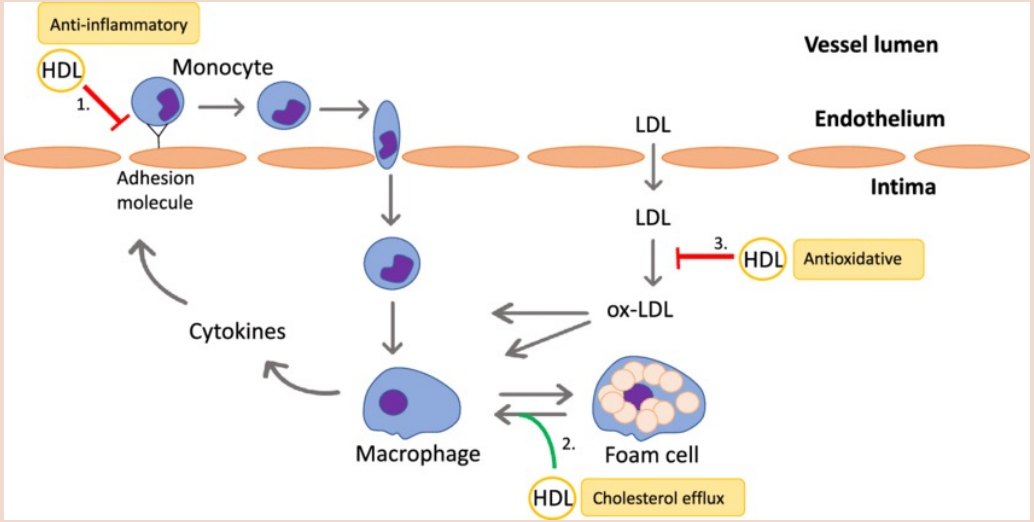
BIOL-606

Background

Atherosclerosis is caused by the accumulation and subsequent oxidation of LDL in the arterial intima

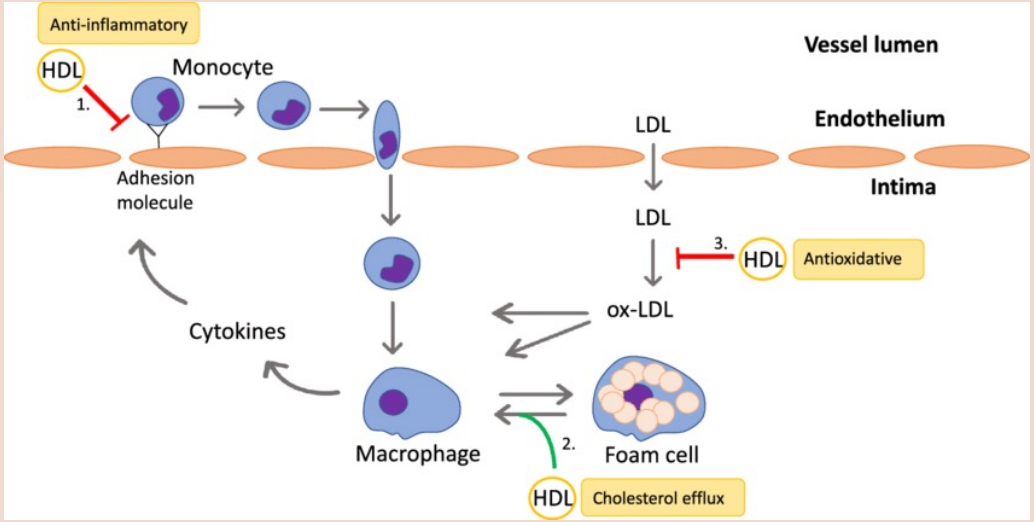
Ox-LDL promotes differentiation of monocytes into macrophages that scavenge ox-LDL and transform into foam cells.

Macrophages express cytokines which stimulate the endothelium to express adhesion molecules leading to interaction with circulating monocytes.



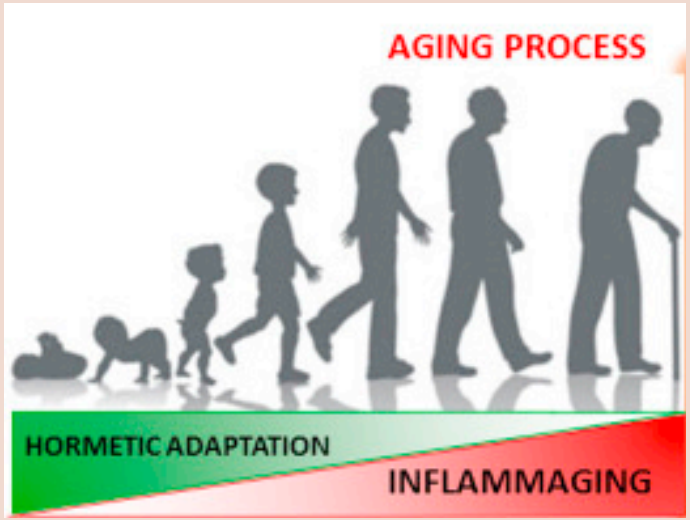
The effects of HDL on monocytes

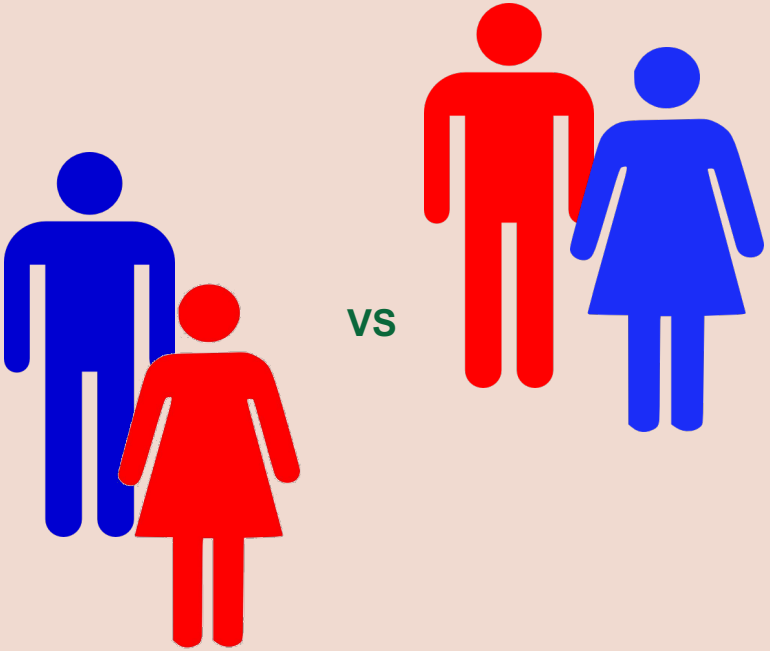
1) HDL inhibits expression of adhesion molecules on the epithelium and thereby inhibits monocyte chemotaxis and formation of foam cells.
2) HDL mediates cholesterol efflux and thereby decreases the accumulation of foam cells.
3) The primarily antioxidative effect of HDL is inhibition of oxidation of LDL.



Source: https://www.researchgate.net/publication/343441043/figure/fig1/AS:922664256405504@1596991709020/Anti-atherogenic-features-of-HDL-Atherosclerosis-is-an-inflammatory-condition-initiated.png

Age and Sex Differences in Inflammation





HAPI-CHI
A healthy aging study

Quick Overview

UC San Diego
School of Medicine

Lab Session Overview:

10:30 AM - 4PM – transportation provided by HAPI-CHI

Morning

Blood & Urine Sample Collection
Health History Interview
Balance & Posture Tests

Lunch – Meal is provided by HAPI-CHI

Blood Pressure & Blood Flow Testing

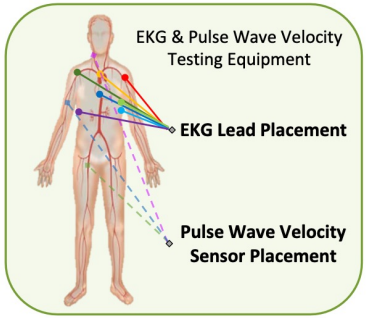
- EKG measurements various positions
- Pulse Wave Velocity
- Stationary Bicycle Test

Randomization: By participating in the HAPI-CHI research study, you are agreeing to participate in an assigned program. Your assignment will be ***based on chance*** and is ***randomly*** assigned to you.

Interactive seminar series: 1 class per week – 2h each

Movement based Tai Chi: 2 class per week – 1h each

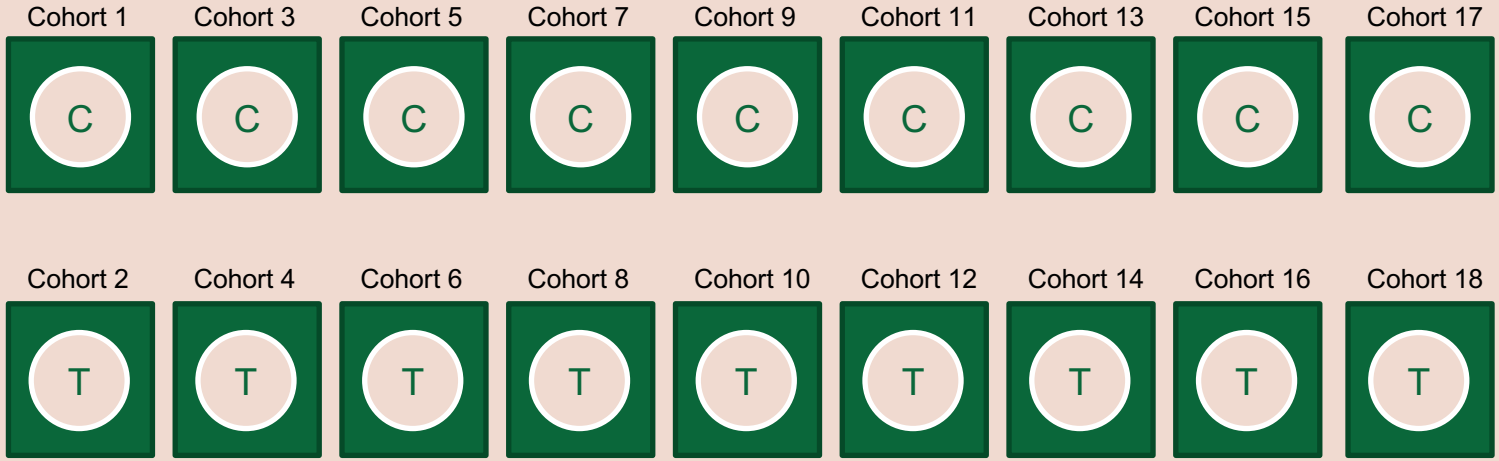
Participation in all aspects of this study are strictly voluntary. You may refuse to participate or withdraw at any time without penalty or loss of benefits to which you are entitled.



Consent Signing	Pre-value collection Hillcrest Lab Test V1	Week 6 Mid-session Test V2	Post-value collection Hillcrest Lab Test V3	3 Months Follow-up Test V4	6 Months Follow-up Test V5	9 Months Follow-up Test V6
	UCSD Hillcrest LAB	Program Site	UCSD Hillcrest LAB	Program Site	Program Site	Program Site
Earn up to:	$75	$50/$25	$100	$25	$25	$25

12 Week Program

STUDY DESIGN



Clinical population = 189 older adults (65-80 yrs)
C = control group [12 weeks of health instruction]
T = Tai-Chi group [12 weeks of instructor led Tai-Chi classes]
Group-Randomised Trials; each cohort progressed independently

Variables

Response

Frequency of circulating monocytes in whole blood

Predictor

High density lipoproteins (mg/dL), Age

Confounding

Sex at Birth

Random

Cohort group

HYPOTHESIS

Old Hypothesis

H_0: There is no inverse correlation between high-density lipoprotein levels and circulating monocyte frequencies in the blood of older adults.

H_A: There is an inverse correlation between high-density lipoprotein levels and circulating monocyte frequencies in the blood of older adults.

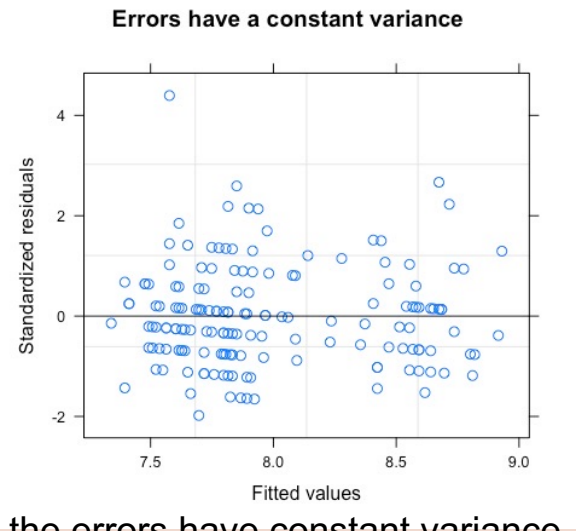
New Hypotheses:

H_0: There is no inverse correlation between high-density lipoprotein levels and circulating monocyte frequencies in the blood of older adults, when accounting for age, gender and cohort factors.

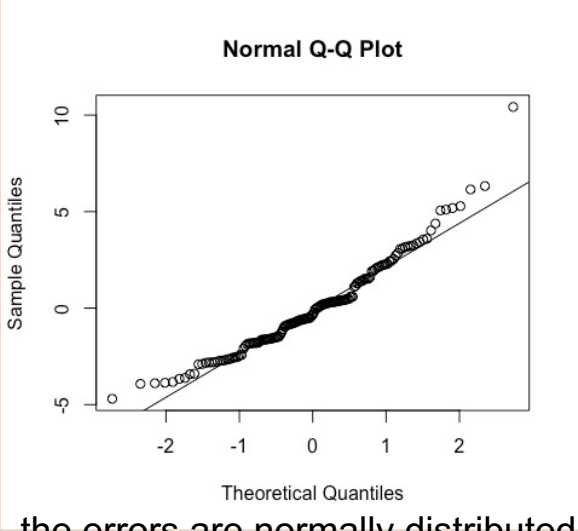
H_A: There is an inverse correlation between high-density lipoprotein levels and circulating monocyte frequencies in the blood of older adults, when accounting for age, gender and cohort factors.

Model 0 : Assumptions

mod0 <- lme(monocytes ~ log(hdl_cholesterol) + sex, random = ~1|cohort, data = df, method = "ML", na.action = na.omit)



the errors have constant variance



the errors are normally distributed

Model 0 : Stats Summary

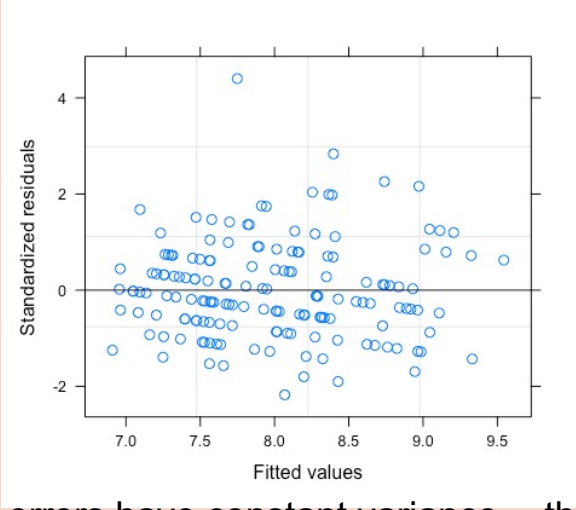
Analysis of Deviance Table (Type II tests)			
	Chisq	Df	Pr(>Chisq)
log(hdl_cholesterol)	0.8617	1	0.35326
sex	4.9262	1	0.02645 *

Summary Table of Fixed Effects		
	Value	p-value
Intercept	5.129	0.0739
log(hdl_cholesterol)	0.632	0.3594
sexMale	0.977	0.0295 *

```
Random effects:
 Formula: ~1 | cohort
         (Intercept) Residual
StdDev: 0.0001292081 2.371389
```

Model 1: Assumptions

mod1 <- lme(monocytes ~ log(hdl_cholesterol) + age + sex, random = ~1|cohort, data = df, method = "ML", na.action = na.omit)



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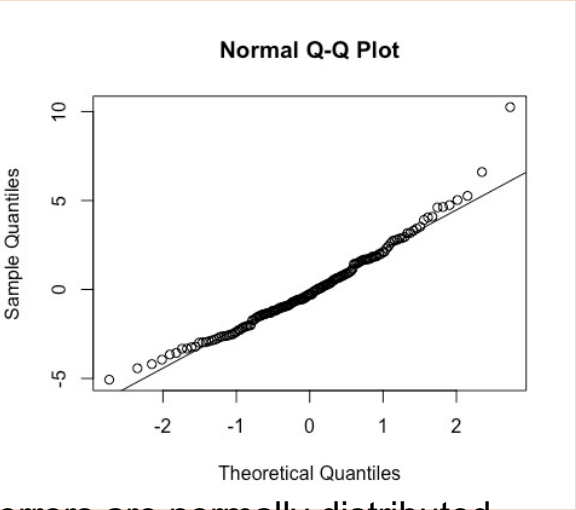


the errors are normally distributed

Model 1: Stats Summary

Analysis of Deviance Table (Type II tests)			
	Chisq	Df	Pr(>Chisq)
log(hdl_cholesterol)	0.251	1	0.617
age	5.848	1	0.016 *
sex	4.836	1	0.028 *

anova (mod 0 vs mod 1)

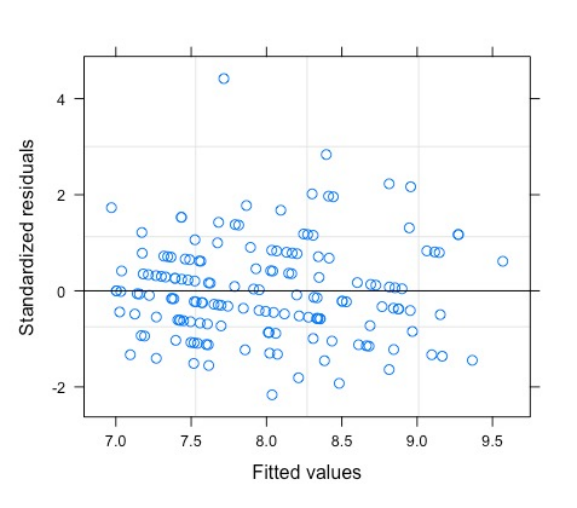
p-value = 0.0166
#model 1 fits the data better than model 0

Summary Table of Fixed Effects		
	Value	p-value
Intercept	2.0323894	0.5121
log(hdl)	0.3402411	0.6219
age	0.0593750	0.0183 *
sexMale	0.9513485	0.0316 *

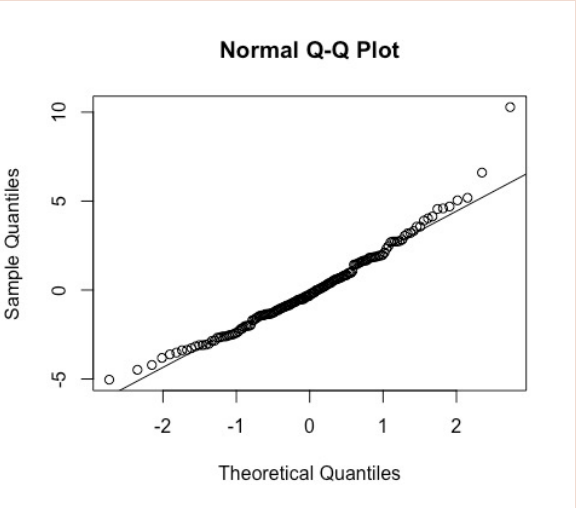
```
Random effects:
 Formula: ~1 | cohort
        (Intercept) Residual
StdDev: 0.0001067637 2.328944
```

Model 2 : Assumptions

```
mod2 <- lme(monocytes ~ log(hdl_cholesterol) * age + sex,
random = ~1|cohort, data = df, method = "ML", na.action =
na.omit)
```



the errors have constant variance



the errors are normally distributed

Model 2 : Stats Summary

Analysis of Deviance Table (Type II tests)			
	Chisq	Df	Pr(>Chisq)
Intercept	0.2439	1	0.62138
log(hdl)	0.1261	1	0.72253
age	0.0575	1	0.81053
sex	4.8659	1	0.02739 *
log(hdl):age	0.1721	1	0.67828

Summary Table of Fixed Effects		
	Value	p-value
Intercept	12.203004	0.6277
log(hdl)	-2.118180	0.7273
age	-0.081809	0.8138
sexMale	0.953871	0.0316 *
log(hdl):age	0.034079	0.6837

```
Random effects:
 Formula: ~1 | cohort
        (Intercept) Residual
StdDev: 0.0001053432 2.327685
```

anova (mod 1 vs mod 2)

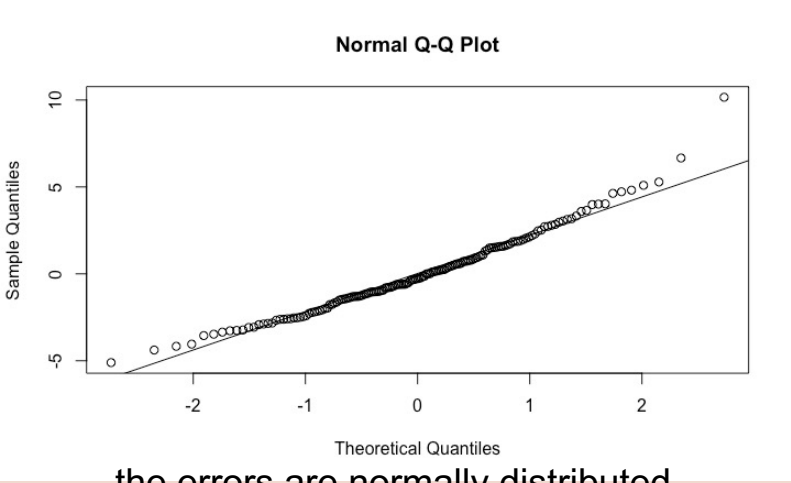
p-value = 0.6784

not significantly different and so the interaction effect will be dropped

Model 3 : Assumptions

mod3 <- lme(monocytes ~ age + sex, random = ~1|cohort, data = df, method = "ML", na.action = na.omit)

the errors have constant variance



the errors are normally distributed

Model 3 : Stats Summary

Analysis of Deviance Table (Type II tests)			
	Chisq	Df	Pr(>Chisq)
age	6.4810	1	0.01090 *
sex	4.6618	1	0.03084 *

Summary Table of Fixed Effects		
	Value	p-value
Intercept	3.279638	0.0680
age	0.061558	0.0128 *
sexMale	0.875341	0.0342 *

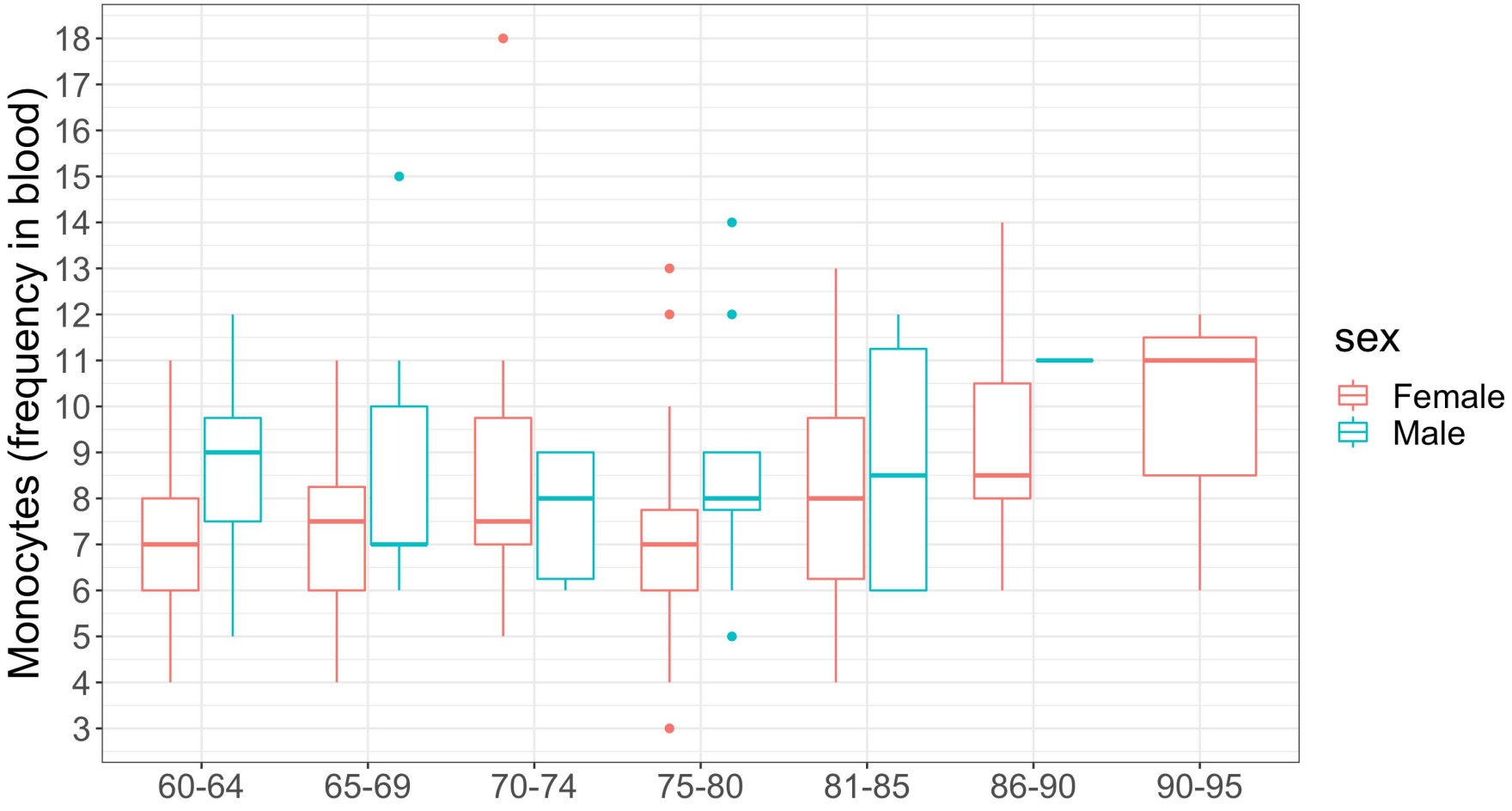
```
Random effects:
 Formula: ~1 | cohort
        (Intercept) Residual
StdDev: 0.0001072882 2.330779
```

anova (mod 1 vs mod 3)

p-value = 0.6168

not significantly different and so the conservative model 3 is preferred

Figure 1: Monocytes vs Subject Characteristics



CONCLUSIONS

Conclusion 1:
We fail to reject the null hypothesis

Conclusion 2:
High density lipoproteins is not correlated with the frequency of circulating monocytes.

Conclusion 3:
Males have a higher frequency of monocytes in blood compared to females.

Conclusion 4:
Age is significantly and positively correlated with the frequency of circulating monocytes.

OUR TEAM

Principal Investigator	Suzi Hong, PhD
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Clinical Research Associate	Amanda Walker
Clinical Research Associate	Chad Spoon
Funding	U.S. NIH R01 Grant

Resources

1. Fox J, Weisberg S (2019). An R Companion to Applied Regression, Third edition. Sage, Thousand Oaks CA. https://socialsciences.mcmaster.ca/jfox/Books/Companion/.
2. R Core Team (2021). *R: A language and environment for statistical computing*. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.
3. RStudio Team (2021). *RStudio: Integrated Development Environment for R*. RStudio, PBC, Boston, MA URL http://www.rstudio.com/.
4. https://pubmed.ncbi.nlm.nih.gov/18617650/
5. https://www.nature.com/articles/s41467-020-14396-9
6. https://bsd.biomedcentral.com/articles/10.1186/s13293-021-00387-y