The Gender-Specific Effects of Statin Use on Lipid and Inflammatory Markers

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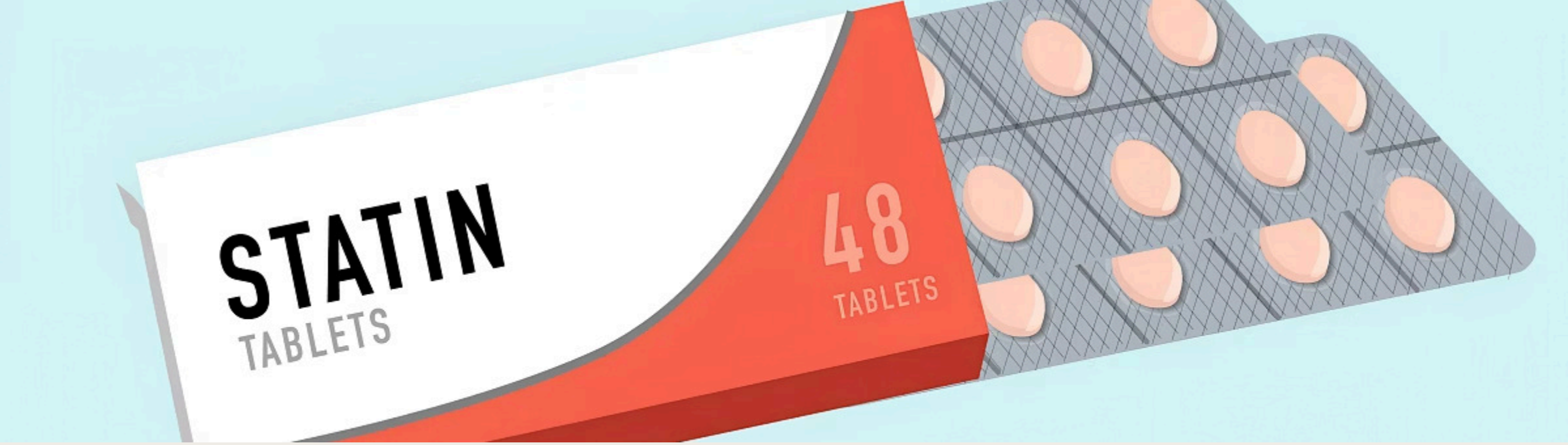
Background

- Clinical studies tend to be more men-focused
- This can lead to unknown or different effects in women
- We examine statins to explore gender-specific responses



Statin Therapy Effects

- Primarily prescribed to reduce Low-Density Lipoprotein (LDL)
- May influence other lipid and inflammatory markers
- Gender-specific responses remain inadequately characterized

Literature Review

Zhang et al. (2022)
"Association of statin use with lipid levels and cardiovascular risk among older adults"
PMID: 35029178

- Statins decrease LDL-C and increase HDL-C in both genders
- **Women showed a greater increase in HDL-C** than men

Moriarty et al. (2017)
"Effects of age, gender, and statin dose on lipid levels: Results from the VOYAGER meta-analysis database"
PMID: 28863328

- Statins decrease LDL-C more in women than male
- **HDL increase was greater in men than in women**
- Found that **age and gender both affect statin response**

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Research Analysis Platform

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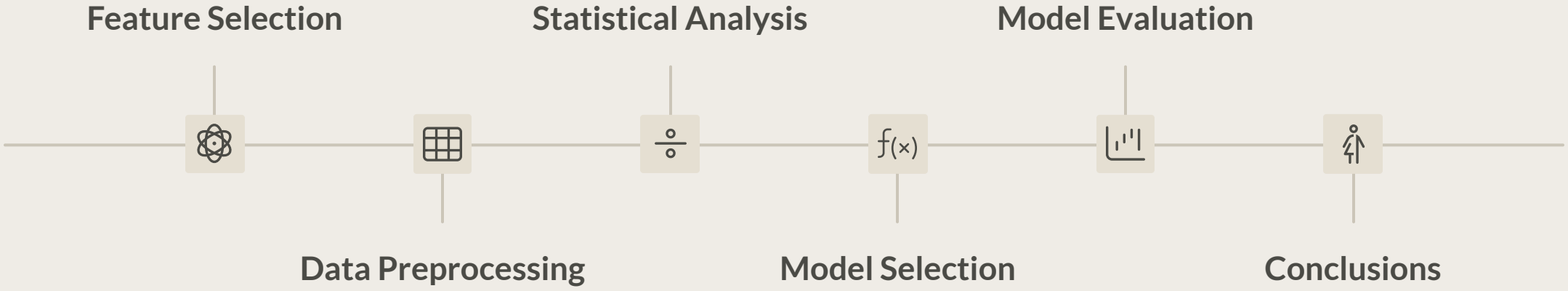
UK Biobank

- A large-scale biomedical database from **500,000+ UK participants**
- Includes health, genetic, and lifestyle data
- Ages - 37+
- Enables research on disease risk factors, treatment effects, and population health

Process


Feature Selection
Statistical Analysis
Model Evaluation
Data Preprocessing
Model Selection
Conclusions

Feature Selection

Demographic Data

- Gender
- Age

Lifestyle Factors

- Smoking status
- Pack years (cumulative smoking exposure)
- Walking activity
- Moderate activity
- BMI (Body Mass Index)

Clinical Measurements

- SBP (Systolic Blood Pressure)
- DBP (Diastolic Blood Pressure)
- Diabetes status

Lipid Profile

- Total cholesterol
- HDL cholesterol (High-Density Lipoprotein)
- LDL cholesterol (Low-Density Lipoprotein)
- Triglycerides
- Apolipoprotein A
- Apolipoprotein B

Liver Function Markers

- Albumin
- ALP (Alkaline Phosphatase)
- ALT (Alanine Transaminase)
- AST (Aspartate Aminotransferase)
- GGT (Gamma-Glutamyl Transferase)
- Total bilirubin

Inflammatory & Medication

- CRP (C-Reactive Protein) - inflammatory marker
- Statin use - medication status

Data Preprocessing

Reducing co-linearity

feature removal according to VIF test

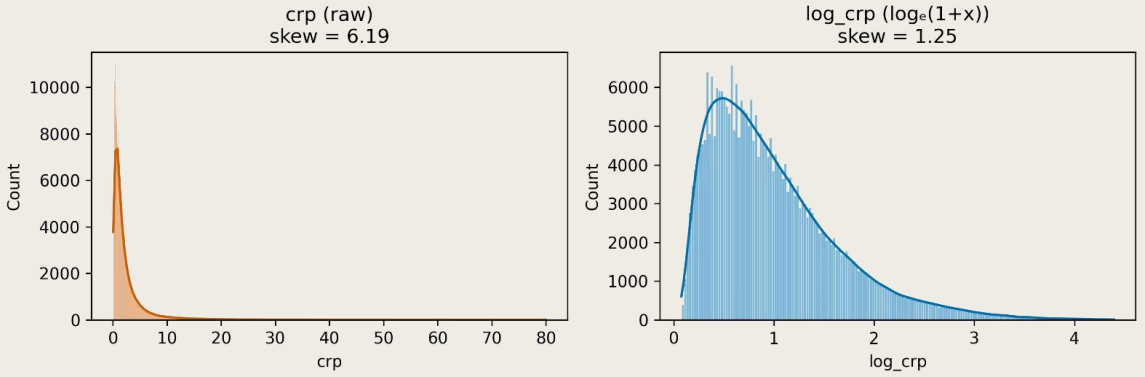
Missing values

Imputing and removing samples according to null count

Categorical Features

Using **One Hot Encoding**

Log transformation

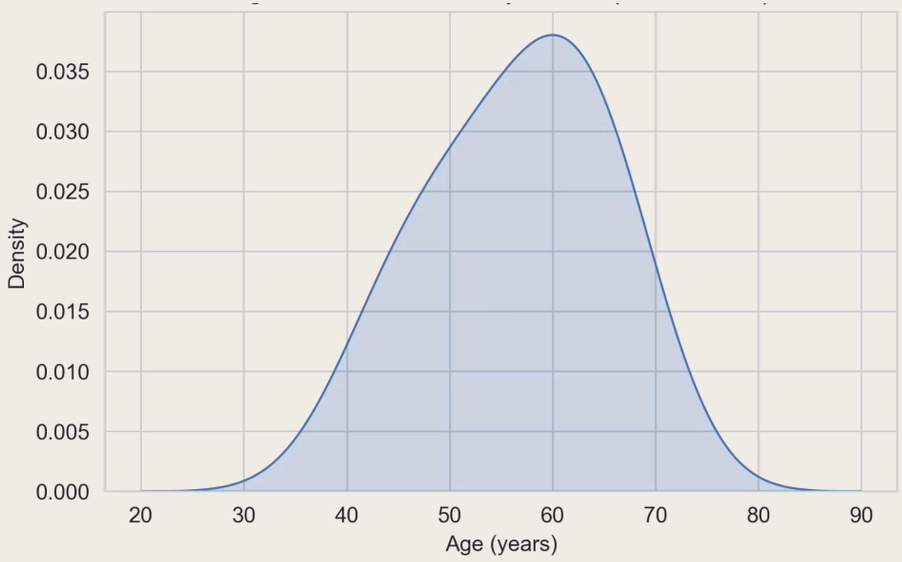


Our Dataset

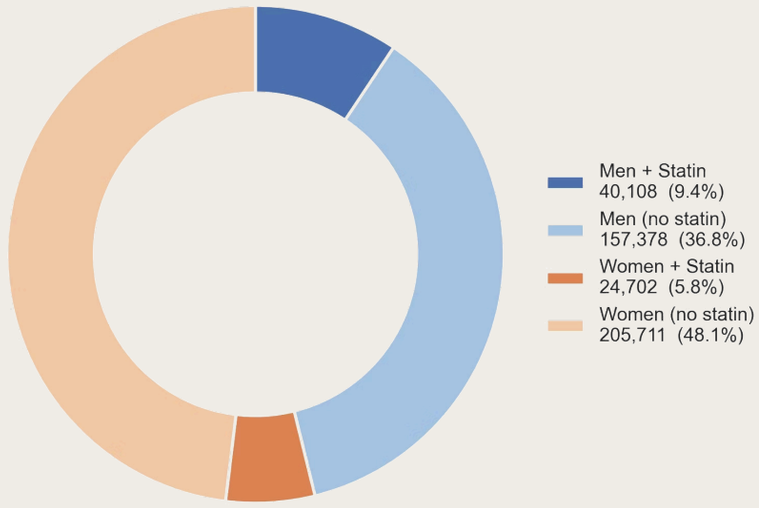
Derived from UK Biobank cohort

n ≈ 430,000 participants

Age Distribution of Study Cohort



Gender & Statin-Use Breakdown



Our Dataset

Derived from UK Biobank cohort

n ≈ 430,000 participants

⚠

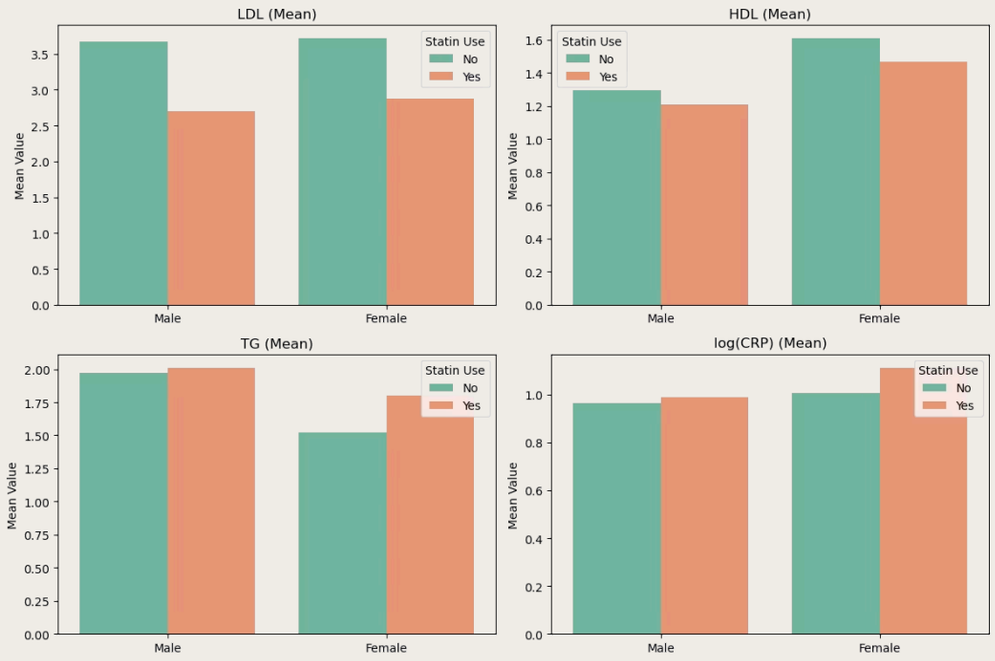
Dataset doesn't include before-and-after data regarding statin use.
We compare statin users and non-users.
While this limits causal interpretation, it's a valid and widely used approach in large-scale observational studies.

Statistical Analysis

Comparing Statin Users vs Non-Users: T-Tests and Effect Sizes

- **null hypothesis -** statins have no effect on mean values
- **alternative hypothesis -** statins do change the values

Marker	Gender	t-stat	p-value	Cohen's d
LDL	Female	-177.477	0.0	-1.093
LDL	Male	-253.317	0.0	-1.340
HDL	Female	-56.618	0.0	-0.378
HDL	Male	-53.415	0.0	-0.296
TG	Female	43.967	0.0	0.310
TG	Male	6.924	0.0	0.039
log(CRP)	Female	23.193	0.0	0.156
log(CRP)	Male	7.415	0.0	0.042



Model Selection

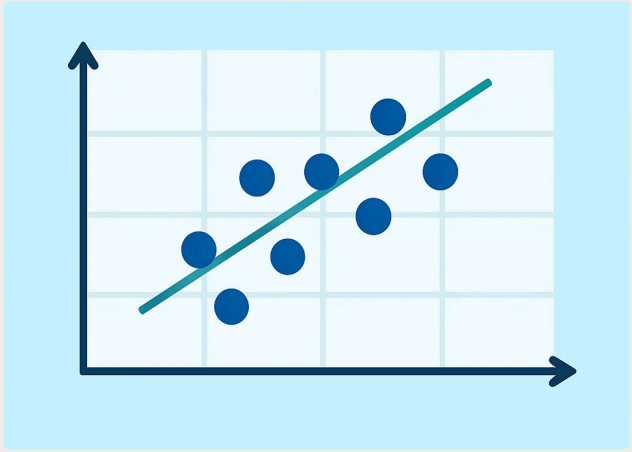
Linear Regression

- Continuous target variables
- Interpretable coefficients

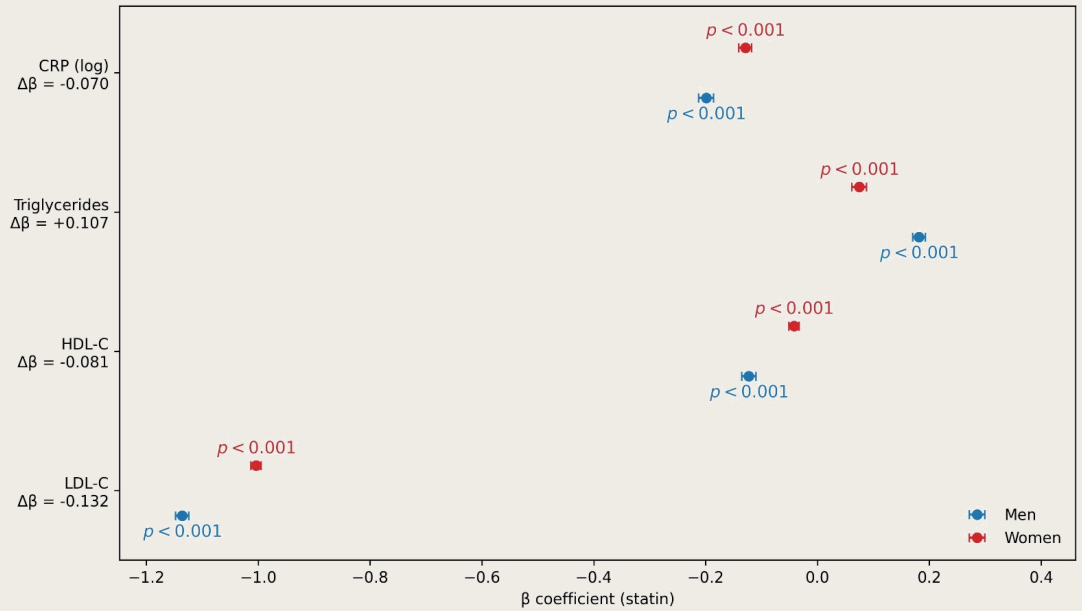
Four sex-stratified models targeting different markers:

- LDL cholesterol
- HDL cholesterol
- Triglycerides
- CRP (log-transformed)

Two age X sex startifeid models targeting only LDL



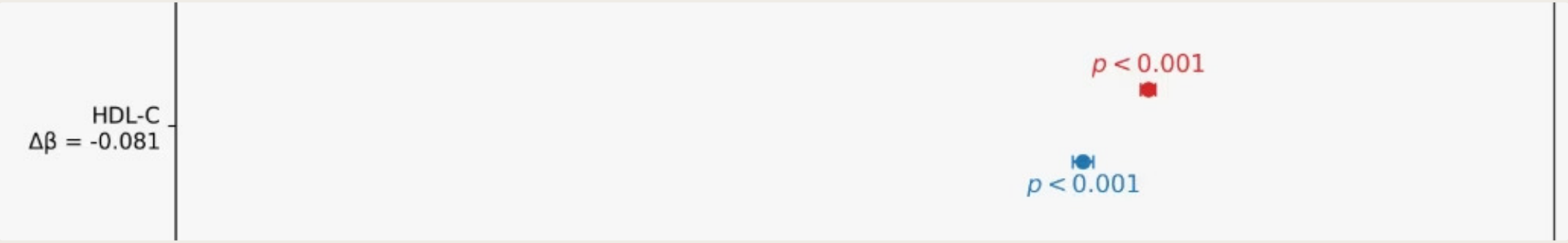
Model Analysis



- Anti-inflammatory benefit exists for both, yet is smaller in women
- Statin users have higher TG, especially men
- Both show lower HDL, fall ~x3 larger in men
- Larger LDL reduction in men

Model Analysis

Let’s revisit the literature and see whether our findings align



$$\beta_f = -0.12, \beta_m = -0.04$$

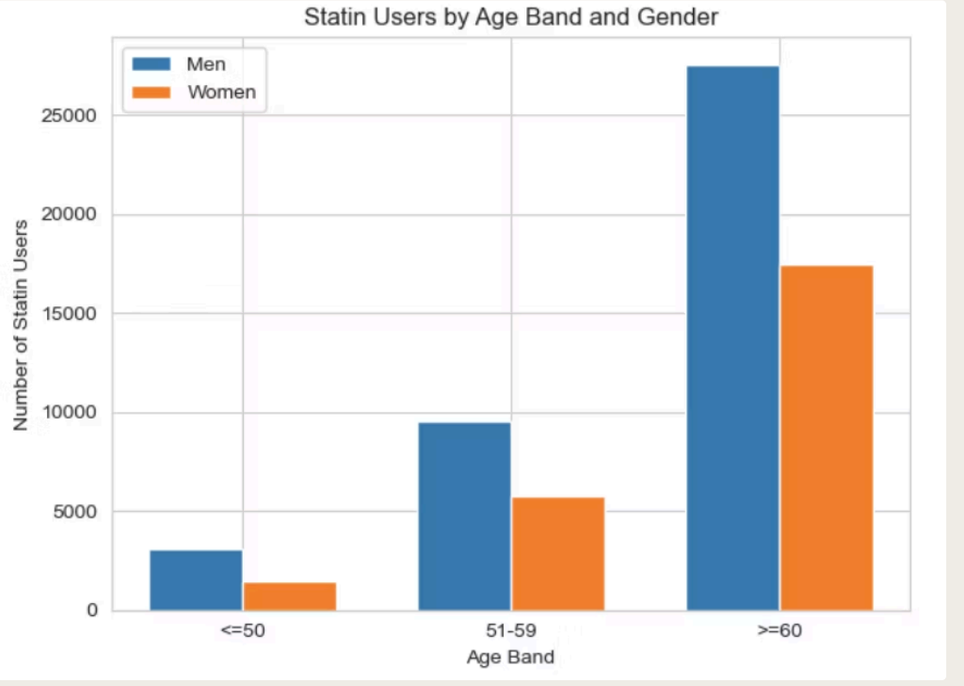
HDL levels in women on statins stay closer to non-users than in men

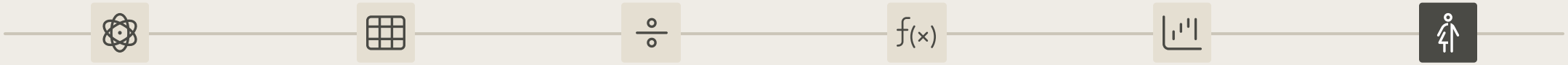
Model Analysis - Does Age Matter?

Two age bands were examined - <=50, >=60

- The model indicates statins reduce younger women LDL more effectively than men
  - A strong possibilty is that it is due to selective prescribing and not due to a clinical reason
- The older age band has about 10x more statin users than the younger band

Sex	Age Band	β (statin)
Men	<= 50	-0.694
Women	<= 50	-0.898
Men	>= 60	-1.216
Women	>= 60	-1.076





Conclusions

Some traditional drug studies have focused on men, leaving us with less knowledge about how medications affect women

Our study shows **clear differences** between men and women taking statins:

- Men's LDL drops more than women's
- Women get less anti-inflammation benefits than men
- Statins might have a greater positive effect on HDL in women rather than men

Conclusions

Future work

- Characterize Gender x Age effect
- Expand the research for other cholesterol reducing drugs

> **Good medicine needs to understand how drugs work differently in everyone - our research shows we still have work to do in order to figure out these differences between men and women**

Questions?