# Abstract

# Introduction

# Methods

## Diversity Outbred Data

The phenotype data for diversity outbred mice was described in and contains data on 843 mice from the diversity outbred collection of both sexes. These data were downloaded from the Diversity Outbred Database. The phenotype file includes at least partial data for 165 phenotypes, measured once, twice, or weekly in the case of body weights. At week XXX mice were placed on a high fat high sucrose (HFHS) diet, or kept on a normal chow diet (NCD). In the final dataset there were 225 female mice on NCD, 223 male mice on NCD, 200 female mice on HFHS, and 196 male mice on HFHS.

## Statistics

All statistical analyses were performed using R version 4.2.0 [1]. Cholesterol data were not normally distributed within groups (p<0.05 by sex and diet stratified Shapiro-Wilk tests), so non-parametric pairwise tests were used. Summarized data is reported as mean +/- standard error of the mean. For all comparisons sex was first tested as a modifier, and then as a covariate. If there was significant evidence of sex modification, pairwise sex-stratified analyses are also reported. Statistical significance was set at an alpha of 0.05. All data and reproducible code are available for this manuscript at <https://github.com/BridgesLab/PrecisionNutrition>.

# Results

We first evaluated the cholesterol levels in the diversity outbred mice measured at 8 and 19 weeks. Cholesterol levels for each group were similar at both time points (p=0.465 by pairwise Wilcoxon test, see Supplementary Figure 1). This indicates that cholesterol levels are stable between both time points. As such, we calculated the average cholesterol of the two time points and used this for further analyses. We stratified these averaged cholesterol levels by sex and diet. We found the expected cholesterol elevations in mice on a HFHS diet (31.6 +/- 1.6 mg/dL, p=3.2 x 10-72 from a 2x2 ANOVA), and male sex (17.9 +/- 1.6 mg/dL, p=1.45 x 10-27; Figure 1). There was no evidence of a significant interaction between diet and sex (p=0.248).