**Paper meetings**

3/29/2022

* Figure 7, put together in nice layout, remove empty space, more compact
* Calcium look like outlier – more variants pass through in QC for NFE – larger distribution of z score
* Change to 90% confidence intervals – more bootstrap samples, from 100 to 1000 z-scores. Drop bottom and top 5%
* Methods section, together with derivation; put it together in the manuscript, then send to Arbel – top priority
* Matt is looking into biological info on sexual selection – down the hall
* ~~Put the new gen env figure in – change to +/-3 on each side~~
  + ~~Can change pgs one to +/- 3se on each side~~
  + ~~Keep 2 sample ttest for the pgs one~~
* ~~Change to genetic effect v testosterone level correlation (right side) to 90% confidence interval~~

4/5/2022

* Edits to selection figure done
* Do not have posterior estimate summary statistics at the moment
  + How should we store to them view? Very compressed zip files?
* Gen env pvalues: difference of ratio from 1:1
  + Z score = (ratio – 1) / ratio\_se
  + Ratio se from previous equation: (x/y)\*sqrt((x.se^2/x^2)+(y.se^2/y^2))
* Need z score table for supplement
* Choice of taking random SNPs per LD block is valid, but there are other methods that can be more powerful
  + Can use most common variants – if have higher af, have higher LD across the board
    - Can have small section: discuss in way that shows we thought about it
  + Our statements currently are about LD blocks only right now
* High variance, but might get high error for calcium; calcium has low polygenicity
* Fst looking at differences of m-f af
  + If we find variant where there is a difference
  + Variant affects longevity differently in males and females (selection)
  + Selection can be on other associated traits, trait has to affect longevity
    - Like diabetes
* Supplementary text files—corral, put in corral BOX
  + Need individual files for each figure
  + Make github available through website – make repository public
* Pvalue
  + No less or more accurate, easier to read
  + Color datapoints by whether they are significant
  + Detail method we are doing in methods
  + Don’t know if its normally distributed
  + Can look up distribution of ratio
  + Assume: Distance from 1:1 is normally distributed
  + Can make a diagram with 90% confidence interval

Supp tables needed

* Sex-specific gwas
* Posterior summary statistics
* Sex selection – filter gwas by pvalue
* Sex selection – results for other ancestry groups

4/12/2022

Matt

* Not much change in estimated A values even when remove mismatched sites
  + Each trait only had ~0-10 site removed
* Get final results from Matt – updated analysis, methods
* Papers (Kasimatis) finding sex-antagonistic selection based on M-F allele frequencies due to artifact
  + Getting mis-mapped from sex-chromosomes, high correlation between autosomes and sex chromosomes
  + Creates bias from Y chromosome (sex chromo) 🡪 mean diff in allele frequencies
  + Take out regions with sequence that maps to sex-chromosomes
  + Use BLAST
* Found overall age distribution for gnomAD – need across ancestries
* Have Fst and x-axis (gxsex genetic variance) which are both symmetric
  + Currently know for bmi, whole fat, the drive is opposite, but don’t know exact direction
  + Genetic variation selected, not focal traits; does not necessarily have to be sexually antagonistic selection
  + Simulation study – under model with different survivorship, don’t necessarily have sexually antagonistic selection, what would it look like if we performed our selection estimation
* Double check alpha – shouldn’t have female or male specific
* Testosterone mendelian randomization
  + When have actual measure of testosterone on x-axis, can’t tell for sure if it’s the cause for the genetic effect of the trait to change
  + A 🡪 B, wonder if there is causal relationship, look at correlation first
  + Mendelian randomization
    - May have confounder C that affects both A and C
    - Look at another variable D that you has causal relationship with A, therefore, the only relationship with B is if it is mediated by A, and then C will be random
    - D in this case if PGS for A bc it has causal relationship with A phenotype values \
    - PGS D may be confounded with PGS-traits B due to pleiotropy
  + Bin individuals by PGS
  + Expect to weaken relationships, can have a supplement or main
* Check correlation with age
* ~~Check how much space taking up on corral~~
* ~~T PGS, sex specific SD on x-axis or diff axes~~
* M-F effect estimate comparison
  + Split by MAF
  + Overall figure
  + LD blocks

4/19/2022

* May 6 talk at lab meeting: have a week to prepare, address her comments, be able to defend work
* Need to work on poster
* Keep prioritize manuscript
* Too long
  + Move PGS to supplement, figure not as interesting; replace with small paragraph in main text
* Kasimatis: sex-GWAS, see different hits, say due to mismapping
  + Just can exclude those sites
* Piratsu: say different hits due to recruitment bias by sex
  + If there is GxSex interaction on participation, can affect all of our results
  + Potential issue, but most likely very small effect
  + They found weak signals for recruitment bias
* Benonisdottir: don’t find significant sex specific genetics effects based on recruitment
* Expand discussion on recruitment bias in introduction
  + Read those papers, familiarize
* M-f effect plots
  + Smaller R^2 due to noise,
  + Mash reduce SNPs from noise to null
  + Check phenotypic variance, if male biased, slope will increase vice versa; check if going in direction of variance
  + Do overall plot
* Change urate to bmi or weight
* Figure 3: log scale y axis so that the male:female amplification are even
* Age as confounder – why is it weird with arm fat-free mass
  + Could try version of main figure corrected for age
  + Genetic effect ~ testosterone level + age used to get correlation R^2
  + Instead use est(y\_i) = y\_i – hat(y\_i)
    - Regress y\_i on mean age across bins
    - Get correlation of (est(y\_i), testosterone level)
* Bernabeau: Gwas on one site,
  + X: AA, AT, TT
  + Y = ex. Weight sex adjusted
* **Test idea of alpha (amplification)**
  + X = genotype, polygenic score in one sex;; male score on top plot, female score on bottom plot;; expect to see similar results
    - Bin individuals by PGS
  + Y = phenotype, adjusted for sex and can also test not adjusted for sex
* PGS – prediction
  + If multiplied by same constant across big part of genotype in males, prediction is gonna be same, but just better in males
* More comments to come 😊

4/20/2022

* Comments from Molly

version of equal amplification plot only with traits that show evidence for amplification, or instead have different symbols for traits with evidence and ones without.