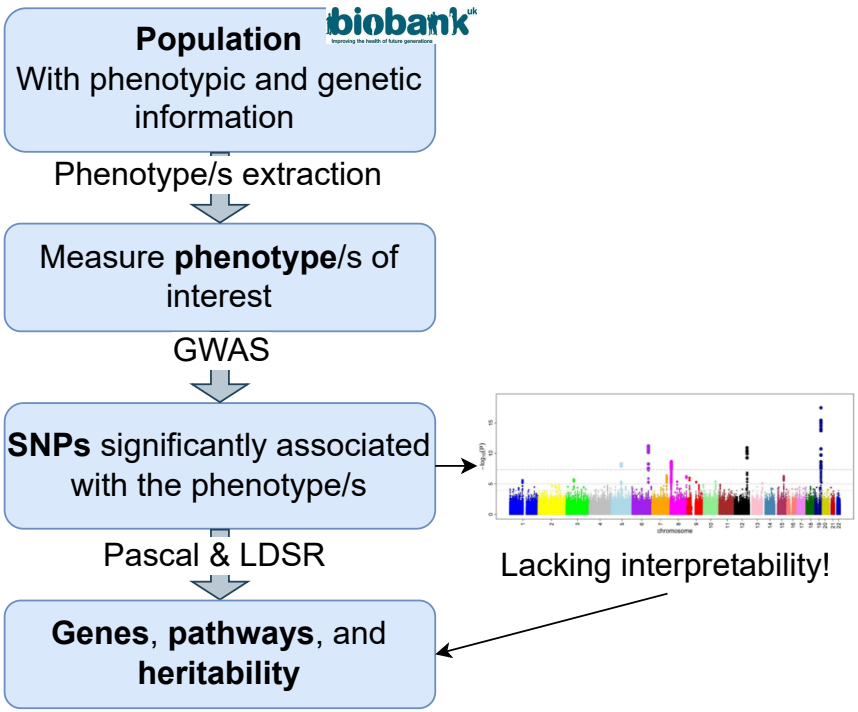
Genetics of different body mass measures

Sofía Ortín Vela
sofia.ortinvela@unil.ch

Course: Biological problems that require math
DBC - Groupe du Prof. Bergmann

March 4, 2022

Introduction



A *phenotype*: is an individual's observable trait. Ex: Binary phenotypes: cases-controls diabetes. Quantitave: height, ...

Heritability: measures how much of the variation of a trait can be attributed to variation of genetic factors, as opposed to variation of environmental factors. Ex: height or eye colour $\uparrow h^2$ traits VS weight more dependent of environmental factors.

This project: Perform GWAS on phenotypes based on body size measures (height, weight, and hips circumference), and compare their genetics (i.e. the genes, pathways and h^2 associated with the different phenotypes).

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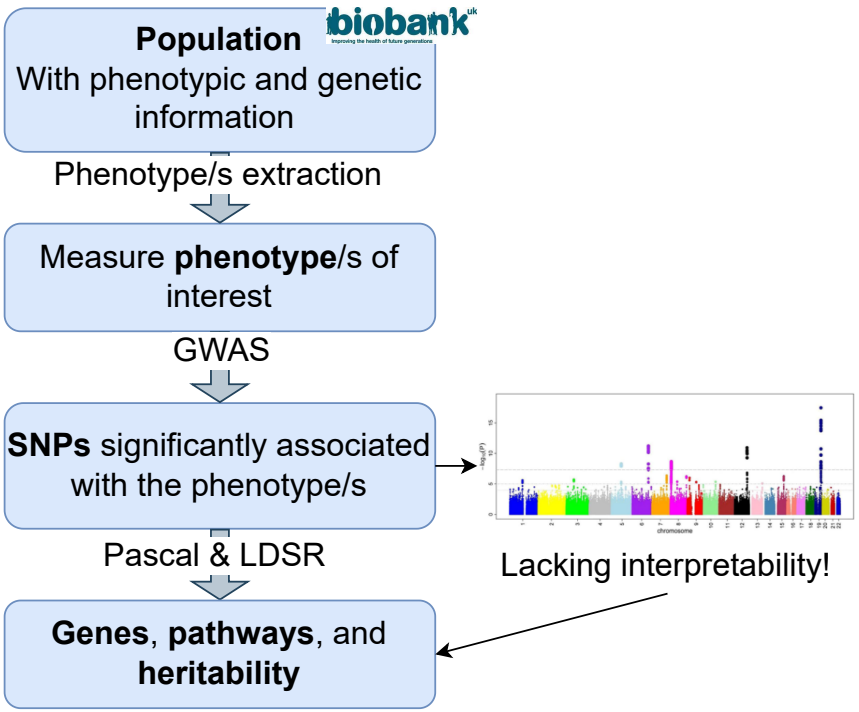

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Phenotype extraction: Literature

Body mass index (BMI) :

Most famous measure of body fat that applies to adult men and women

$$BMI = \frac{weight(kg)}{height^2(m^2)}$$

For more details about BMI at a phenotypic level: Olga's project

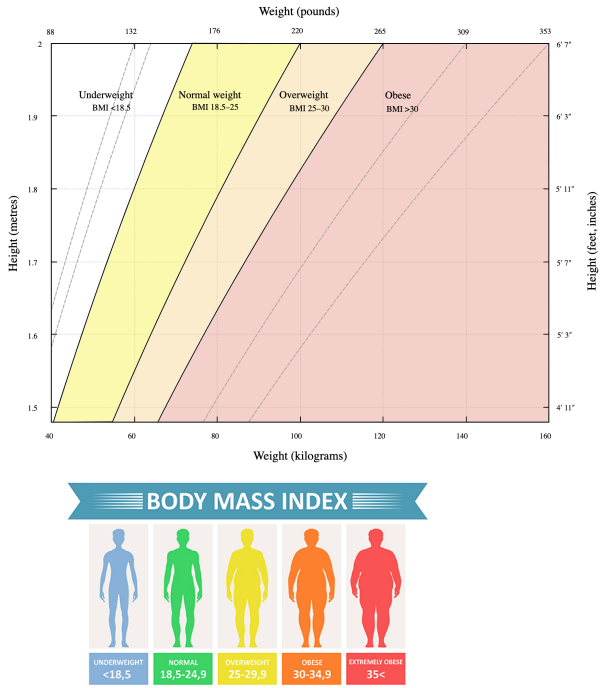


Figure: BMI: *By amfucla using gnuplot and inkscapeand*, and *cdc.gov/healthyweight*

Phenotype extraction: Literature

Body mass index (BMI) :

Most famous measure of body fat that applies to adult men and women

$$BMI = \frac{weight(kg)}{height^2(m^2)}$$

But ... Why squared?

Other measures: Ponderal index (PI)

$$PI = \frac{weight(kg)}{height^3(m^3)}$$

Mainly used to assess the pattern of fetal growth

For more details about BMI at a phenotypic level: Olga's project

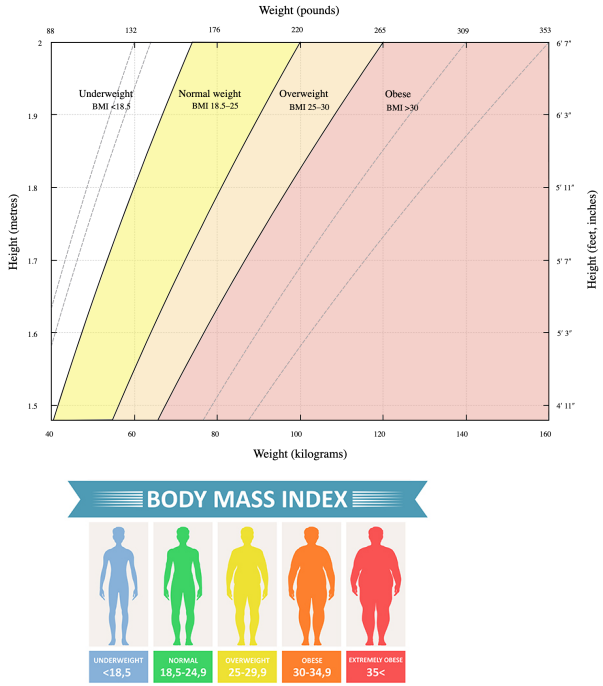


Figure: BMI: *By amfucla using gnuplot and inkscapeand*, and *cdc.gov/healthyweight*

- Is the denominator's index that important?:

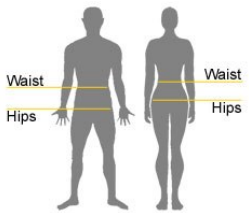
$$BMI_x = \frac{weight}{height^x}$$

When we perform the GWAS on $\neq$ x's values, are the same genes significants? If not, is there any biological justification? Is the heritability the same?

- Can we create a body mass measure more geneticaly relevant? Include not only height and weight, but also other body size measures (particularly hip circumference):

$$BM_{x,y} = \frac{weight}{height^x \cdot hip^y_{circumference}}$$

Do we have the same signicants genes?



Hypothesis

Question I: How sensitive is the BMI GWAS to small changes in the index?

$$BMI_{\epsilon} = \frac{weight}{height^{x}}$$

Where x ranges from 1 to 3. Particularly, $BMI_{x=2} = BMI$, and $BMI_{x=3} = PI$

Ex: If x = [1, 1.5, 2.5] $\rightarrow$ 3 phenotypes: $\frac{weight}{height}$, $\frac{weight}{height^{1.5}}$, and $\frac{weight}{height^{2.5}}$ $\rightarrow$ 3 GWAS' results $\rightarrow$ Compare the results

Question II: How the genetics differs between different body mass measures?

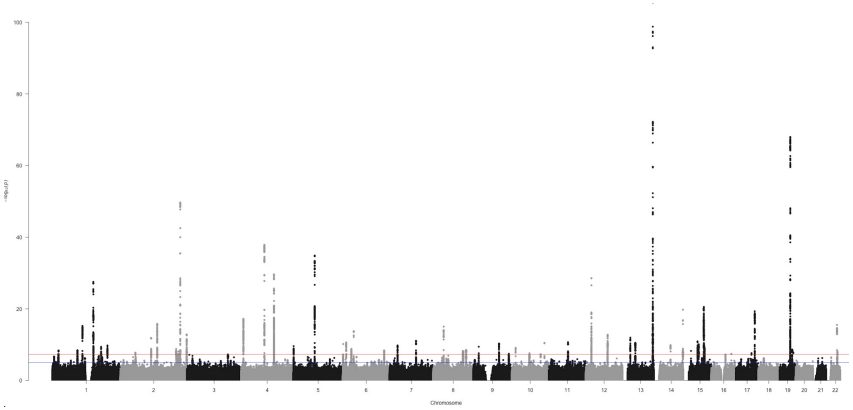
$$BM_{x,y} = \frac{weight}{height^{x} \cdot hip^{y}_{circumference}}$$

Where x ranges from 1 to 3, and y ranges from 0 to 1

How x and y choices' affects their genetics

Methodology

- Basic data exploration fields of interest in the UK Biobank (more extensively in Olga's project)
- Perform GWAS on these different phenotypes (different x and y values)
- Analyse significant SNPs for the different phenotypes: Manhattan and QQ plots
- Analyse the genes, pathways, and heritability ($h^2 = V_A/V_P$) of these phenotypes
- Compare genetics associated with each phenotype. If some genes are only present in some phenotypes, how can we explain it?



What you will learn in this course

- How to face a real project, facing troubles of not prepared experiments
- How to use basics mathematical concepts in favor of your biological knowledge

- Get more familiar with the terms: LD, h^2, additive model
- How to perform a GWAS; Manhattan and QQ plots
- How to compute heritability (h^2)

* Improve basic programming skills

email: sofia.ortinvela@unil.ch