



# Predicting Statures and Comparing Genetic Effects on Height in Ancient and Modern European Populations

Penn Undergraduate Research Mentoring Program

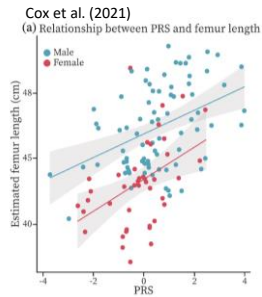
Kaeli Kaymak-Loveless<sup>1</sup>, Carson Shin<sup>2</sup>, Samantha Cox<sup>3</sup>, Iain Mathieson<sup>3</sup>

School of Engineering and Applied Science (2025)<sup>1</sup> | College of Arts and Sciences (2025)<sup>2</sup> | Department of Genetics, Perelman School of Medicine<sup>3</sup>

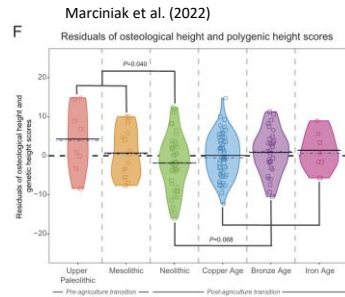
## Introduction

- Genome-wide association studies (GWAS) determine which genetic variants are associated with certain phenotypic traits
- A GWAS on height has been performed using data from present-day European populations
- Each variant in the GWAS has an effect size denoting how many standard deviations away from the mean height a person with that variant would be expected to be
- The effect sizes can be used to calculate a polygenic risk score (PRS) that combines the effects of the variants and can be used to predict stature
- We attempt to find a relationship between PRS from ancient genomes and the true statures from those ancient individuals
- What else can we predict in ancient humans?

## Background



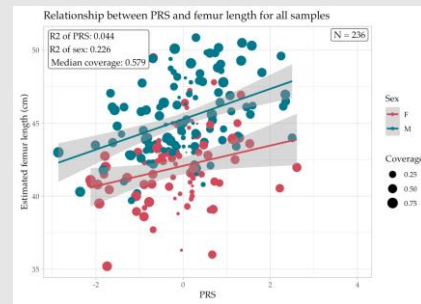
- Femur lengths calculated from given stature estimations and estimation methods
- Regression model compared femur length to PRS, sex, ancestry, and date;  $R^2$  of PRS was 0.063
- PRS able to predict some of the variation in femur length even with the effects of sex, date, and ancestry removed



- Plotted residuals by time period from a regression that compared stature to PRS and sex
- Average residual for the Neolithic period was negative
- Concluded that Neolithic humans must have suffered from poor health that impeded growth

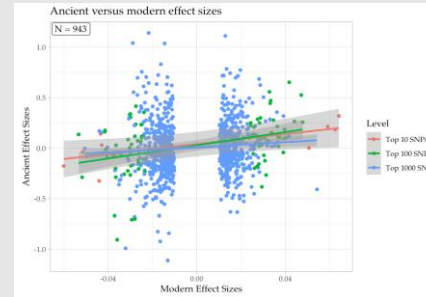
## Results

### Predicting Statures



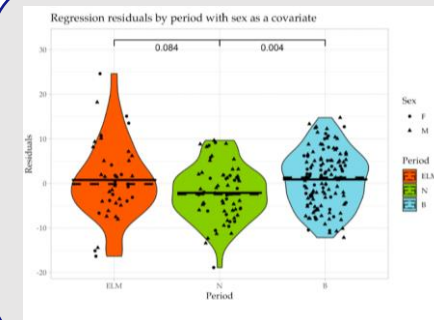
- Increased sample size
- Regression run as in Cox et al. (2021)
- $R^2$  of PRS decreased slightly, but still shows predictive power
- Lower coverage samples have PRS closer to 0 and could interfere with the regression

### Comparing Ancient and Modern Genetic Effects on Height



- Ancient effect sizes calculated by finding the slopes of the regressions on femur length and the presence of each variant
- 56 outliers with < 5 instances of the reference or alternate allele
- Without outliers, there is a significant positive correlation in every group of variants

### Analyzing Residuals



- Regression run as in Marciniak et al. (2022)
- Residuals plotted by time period, separating the pre-Neolithic (ELM), Neolithic (N), and post-Neolithic (B) periods
- Mean Neolithic residual is negative, suggesting stunted growth
- Environmental/social factors tend to affect the sexes differently, but there is no Neolithic sex difference
- Could be explained instead by a genetic shift that PRS does not pick up

## Conclusions

- Ancient statures can still be predicted to some extent by a combination of ancient genetics and modern genetic association studies
- We confirmed that Neolithic individuals seem to be shorter than expected
- Neolithic males and females are equally shorter than expected
- A significant positive correlation between ancient and modern genetic effects on height suggests little change in the effects of most variants over time, except for a few striking outliers

## Future Research

- Increase sample size
- Generate new PRS based upon adjusted ancient effect sizes and analyze predictive power of these new scores
- Determine correlation between ancient and modern effect sizes by time period to track changes over time and possibly explain the previously observed residual differences
- Investigate outlier variants that have significant effects on the correlation between ancient and modern effect sizes

## References

- Cox, S. L., Moots, H. M., Stock, J. T., Sibat, A., Bitarello, B. D., Nicklisch, N., Alt, K. W., Haak, W., Rosenstock, E., Ruff, C. B., & Mathieson, I. (2021). Predicting skeletal stature using ancient DNA. *American Journal of Biological Anthropology*, 177(1), 162–174.
- Cox, S. L., Ruff, C. B., Maier, R. M., & Mathieson, I. (2019). Genetic contributions to variation in human stature in prehistoric Europe. *Proceedings of the National Academy of Sciences*, 116(43), 21484–21492
- Marciniak, S., Bergøy, C. M., Silva, A. M., Hałuszko, A., Furmanek, M., et al. (2022). An integrative skeletal and paleogenomic analysis of stature variation suggests relatively reduced health for early European farmers. *Proceedings of the National Academy of Sciences*, 119(15).