

# Review of: "Signals of Human Polygenic Adaptation: Moving Beyond Single-Gene Methods and Controlling for Population-Specific Linkage Disequilibrium"

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Potential competing interests: No potential competing interests to declare.

This is certainly an important paper. The main problem, however, is that maybe only 10 to 100 people worldwide can really understand and evaluate the topic and the manuscript. It is a specialist paper with great potential if rewritten.

E.g. (p. 23): "In fact, as shown in the introduction,  $Q_{st}$  (erroneously named "phenotypic  $F_{st}$ " by Bird) is often much higher than  $F_{st}$  as shown by mathematical modeling (Kremer and Le Corre, 2013) and empirical results (Berg and Coop, 2014). The equivalence between  $Q_{st}$  and  $F_{st}$  ( $Q_{st} = F_{st}$ ) is expected under neutrality, and higher values of  $Q_{st}$  ( $Q_{st} > F_{st}$ ) indicate divergent selection (Leinonen et al., 2013). Bird's failure to acknowledge the difference between  $Q_{st}$  and  $F_{st}$  leads him to expect  $Q_{st} = F_{st}$  and to discard deviations from this equivalence as due to environmental factors or erroneous estimates of average IQ (Bird, 2021)."

Who can really judge whether this is an error on the part of Bird or a misjudgment on the part of Piffer?

My suggestions are aimed at making the content easier to understand so that more scientists (also outside a small circle of specialists) and maybe a broader audience (e.g., the average biology teacher at school) can benefit from it.

Use like PNAS boxes to explain all major terms and results and their significance for a broader audience:

- $F_{st}$
- $Q_{st}$  (and the difference between  $F_{st}$  and  $Q_{st}$ )
- candidate gene
- $F_{st}$  of background genetic variation
- allelic covariance
- add boxes significance
- SNPs
- GWAS
- polygenic score
- neutral SNPs
- individual loci
- COJO

- MTAG
- EA and educational attainment
- meaning of all figures (in the notes), e.g. "This Figure shows that ..."
- meaning of all tables (in the notes)
- Regarding Figures 5 to 8: Very good that a correlation is shown. But why  $R$  (in capital letters standing for a multiple correlation between various predictors and one criterion) and not a  $r$  (in lowercase meaning a bivariate between two variables as shown in the Figures 5 to 8)?
- Regarding Figures 5 to 8: Is it correct that the polygenic scores for education (what exactly is education here?) and for height were found in sample A and the presented correlations in the Figures 5 to 8 are found in an independent sample B, so it is an independent replication? Very important, stress this, explain this, this would be a very important finding if not one of revolutionary importance.
- Regarding Figures 5 to 8: Mention and discuss that correlations at the national data level are usually larger than correlations at the individual data level.

Consider controlling the correlations between polygenic scores and education/height for GDP/c and HDI. Mention that you overcontrol here as GDP/c and HDI depend on education (cognitive ability and somewhat conscientiousness).