

Supplemental Digital Content 2

Polygenic scoring on multi-trait analysis of GWAS (MTAG)-estimated effects

Methods: We constructed a new PRS_{reported MTAG} for self-reported PA using UK Biobank GWAS for “number of days/week of moderate PA 10+ minutes”) and for “number of days/week of vigorous PA 10+ minutes” (N=321,533) as another set of summary statistics to estimate the genetic correlation between these two PA measures and used it to obtain the new multi-trait analysis of GWAS (MTAG)-estimated effect sizes for PRS calculation (1). The new effective sample size for this new GWAS estimated by MTAG was 352,429. MTAG analyses were ran using Complex-Traits Genetics Virtual Lab –platform (Complex-Traits Genetics Virtual Lab (CTG-VL) — <https://genoma.io>).

Results: Compared to the PRS_{reported} (as also reported also in our manuscript) constructed on the basis of the self-reported “number of days/week of moderate PA 10+ minutes” question, the new PRS_{reported, MTAG} accounted for slightly higher variation (ΔR^2 0.32% vs. 0.25%) in the reported daily MET score in FTC (Supplemental Table 2).

Reference

1. Turley P, Walters RK, Maghzian O, et al. Multi-trait analysis of genome-wide association summary statistics using MTAG. *Nature Genetics*. 2018;50(2):229-237.

Supplemental Table 2. Associations between PRSs constructed on the basis of reported PA variables in UK Biobank and reported daily MET score in FTC.

Variables	β (SE)*	P*	R ² % (95% CI) [†]	ΔR^2 % [‡]	N
PRS for number of days/week of moderate PA 10+ minutes (variable 884) in UK Biobank (PRS_{reported moderate activity})					
Reported daily MET score in FTC	0.1717 (0.0323)	<0.0001	5.38 (4.50-6.25)	0.25	11,528
PRS for number of days/week of vigorous PA 10+ minutes (variable 904) in UK Biobank (PRS_{reported vigorous activity})					
Reported daily MET score in FTC	0.1924 (0.0321)	<0.0001	5.40 (4.56-6.33)	0.03	11,528
PRS for reported moderate and vigorous PA 10+ minutes (PRS_{reported MTAG})					
Reported daily MET score in FTC	0.1934 (0.0323)	<0.0001	5.45 (4.55-6.34)	0.32	11,528

PRS; polygenic risk score.

*Effect and P value adjusted for age, sex and 4 genetic principal components.

[†]Variation accounted for by age, sex and the PRS with family number as random effect of the linear mixed model in FTC.

[‡] ΔR^2 = difference of R-squared between models with and without PRS included.