

# Polygenic Basis of Diurnal Temperature Rhythms Predicts Cardiometabolic and Sleep-Related Susceptibility

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Circadian rhythms regulate many aspects of human physiology and are closely linked to cardiometabolic and cognitive health. Wrist temperature, measured through wearable devices, provides a scalable, non-invasive digital biomarker for peripheral circadian rhythms. Using UK Biobank accelerometer data on a 7-day Axivity wearable study collected in more than 80,000 white-British participants, circadian parameters (amplitude, acrophase) were modelled using cosinor wave and mixed effects approaches that account for seasonality and device variation. This framework enables robust characterisation of individual circadian profiles across days and seasons.

Preliminary genome-wide association analysis of diurnal wrist temperature rhythms revealed a modest SNP-heritability ( $h^2 = 0.1$ ) and one genome-wide locus (rs6433478) previously shown to be associated with physical activity and chronotype. Tissue enrichment based on GTEx highlighted differential expression in thyroid, blood vessels, and uterus, suggesting involvement of thermoregulatory and metabolic pathways. Genetic correlation analyses performed through bivariate LD-score regression indicated shared architecture with diabetes mellitus ( $r_c = -0.41$ ,  $p = 2.72 \times 10^{-13}$ ), congestive heart failure ( $r_c = -0.39$ ,  $p = 2.74 \times 10^{-11}$ ), sleep apnoea ( $r_c = -0.34$ ,  $p = 1.832 \times 10^{-10}$ ), obesity ( $r_c = -0.35$ ,  $p = 1.112 \times 10^{-13}$ ), and hypertension ( $r_c = -0.30$ ,  $p = 7.358 \times 10^{-10}$ ), reinforcing the physiological relevance of circadian thermoregulation. Finally, adjustment on seasonal variations and self-reported physical activity made no meaningful difference to the overall findings.

To the best of our knowledge, this study is the largest GWAS on diurnal temperature extracted through wearable technologies. Our work highlights both the opportunities and challenges of integrating large-scale digital biomarker data into genomic research. Our GWAS remains underpowered for downstream post-GWAS analyses, attributable to the intrinsic measurement heterogeneity; at the same time, warrant future investigations with larger sample sizes to fully unravel the complex polygenicity embedded in thermoregulation. Our work provides genetic evidence highlighting the role of wearable-based circadian measures in managing cardiometabolic and sleep disorders.

(290 words)

Keywords: Diurnal temperature, Digital omics, wearable technologies, GWAS, cardiometabolic outcomes