**Supplement to Paper 3**

**eTable 1:** Equation Converting ENMO into PAEE and Derivation of Percent MVPA

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| **Physical Activity Exposure** | **Definition** |
| Physical Activity Energy Expenditure (PAEE) | Following the work of Demspey, *et al*.1, we apply the quadratic equation from White, *et al.*2 to convert ENMO from wrist-worn accelerometer on dominant hand to PAEE with:  where x is the midpoint of one of UK Biobank’s predefined categories in milligravities. We then convert from J/min/kg into J/kg/day by multiplying by 1.44. We then sum over all of the intervals to get cumulative PAEE. |
| Percent MVPA | We divide PAEE spent above 125 mgs (equivalent to 3 METs) by overall PAEE to get the proportion of PAEE from moderate-to-vigorous physical activity and multiply this by 100 to yield the percent MVPA. |

**eTable 2:** Definitions and Conversions for Covariates in Model 1

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| **Covariate** | **Final Definition** | **UK Biobank Definition** | **Conversion** |
| Smoking Status | Categorical Variable with categories of Current, Never, and Previous following UK Biobank definition. | Categories of Current, Never, and Previous following UK Biobank definition. Derived from Current tobacco smoking and Past tobacco smoking fields. | None |
| Educational Attainment | Categorical variable with University Degree, Other Degree, and No Degree as levels. | Question asked: “which of the following qualifications do you have?” | Converted to University if “College or University Degree” selected, “None” if “None of the above” selected, and “Other” otherwise. |
| Employment Status | Binary variable with employment = 1 and other = 0. | Question asked: “which of the following describes your current situation?” | Converted to binary variable that equals 1 if “in paid employment or self-employed” and 0 if not. |
| Mobility Problems | Binary variable with mobility problems = 1 and no mobility problems = 0. | Question asked “Please click the ONE box that best describes your health TODAY.” | Converted to binary variable that equals 1 if they indicate any issues walking and 0 otherwise. |
| Parental History of Heart Disease | Binary variable with existence of history = 1 and no history = 0. | Question asked “Has/did your mother ever suffer from?” and “Has/did your father ever suffer from?” | Converted to binary variable that equals 1 if they indicate the mother OR father suffered from heart disease and 0 otherwise. |
| Weekly Processed Consumption | Numeric variable on frequency of processed meat consumption. | Question asked “How often do you eat processed meats?” and lists options as never, less than once a week, once a week, 2-4 times a week, 5-6 times a week, once or more daily. | Converted to numeric variable with never = 0, less than once a week = 0.5, once a week = 1, 2-4 times a week = 3, 5-6 times a week = 5.5, once or more daily = 7. |
| Fruit & Vegetable Consumption Quartile | Quartiles from 1 to 4 denoting total fruit and vegetable consumption. | Composite of four total questions. Combined cooked and raw vegetable intake “On average how many heaped tablespoons of COOKED(RAW) vegetables would you eat per day?” Combined dried and fresh fruit intake “On average how many pieces of DRIED(FRESH) fruit would you eat per day?” | Added fruit total and vegetable totals together and then split these totals into quartiles. |
| Weekly Oily Fish Consumption | Numeric variable on frequency of oily fish consumption per week. | Question asked “How often do you eat oily fish?” and lists options as never, less than once a week, once a week, 2-4 times a week, 5-6 times a week, once or more daily. | Converted to numeric variable with never = 0, less than once a week = 0.5, once a week = 1, 2-4 times a week = 3, 5-6 times a week = 5.5, once or more daily = 7. |
| Weekly Alcohol Consumption | Numeric variable on frequency of alcohol consumption per week. | Question asked “about how often do you drink alcohol?” and lists daily or almost daily, three or four times a week, once or twice a week, one to three times a month, special occasions only, never. | Converted to numeric variable with never = 0, daily or almost daily = 7, three or four times a week= 3.5, once or twice a week = 1.5, one to three times a month = 0.4, special occasions only = 0.03. |
| Added Salt Intake | Factor variable with four levels never/rarely, sometimes, usually, always. | Question asked “do you add salt to your food?” with options Never/rarely, sometimes, usually, always. | None |
| Season of Wear | Factor variable coded as Fall, Spring, Winter, or Summer based on date range. | Start time of wear denotes the date they began wearing an accelerometer. | Derived season ranges based on “Start time of wear” variable. |

**eFigure 1:** Kaplan-Meier survival estimates for main sample

Chart, diagram

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**eTable 3:** Quintiles of PAEE, % MVPA, and PGS

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| **Quintiles** | **PAEE** | **% MVPA** | **Standardized PGS** |
| **20th Percentile** | **30.07 kJ/kg/day** | **25.97%** | **-0.83** |
| **40th Percentile** | **35.91 kJ/kg/day** | **32.65%** | **-0.26** |
| **60th Percentile** | **41.39 kJ/kg/day** | **38.53%** | **0.24** |
| **80th Percentile** | **48.50 kJ/kg/day** | **45.46%** | **0.81** |

**eTable 4:** Model 1 - controlling for full set of covariates in main analyses (Exposures Standardized)

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| **Exposure** | **Hazard Ratio** |
| PAEE | HR = 0.84 (95% CI: 0.79 to 0.89) |
| Standardized PGS (in PAEE eqtn) | HR = 1.49 (95% CI: 1.41 to 1.57) |
| % MVPA | HR = 0.80 (95% CI: 0.74 to 0.86) |
| Standardized PGS (in MVPA eqtn) | HR = 1.49 (95% CI: 1.41 to 1.575) |
| PAEE (in MVPA eqtn) | HR = 0.99 (95% CI: 0.91 to 1.07) |

**eTable 5:** Model 0 - controlling for age and biological sex (Exposures Standardized)

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| **Exposure** | **Hazard Ratio** |
| PAEE | HR = 0.82 (95% CI: 0.77 to 0.87) |
| Standardized PGS (in PAEE eqtn) | HR = 1.52 (95% CI: 1.44 to 1.6) |
| % MVPA | HR = 0.78 (95% CI: 0.72 to 0.84) |
| Standardized PGS (in MVPA eqtn) | HR = 1.51 (95% CI: 1.43 to 1.60) |
| PAEE (in MVPA eqtn) | HR = 0.97 (95% CI: 0.90 to 1.05) |

**eTable 6:** Interaction Results for PAEE and % MVPA

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| **Interaction between PAEE & % MVPA** |
| HR = 0.9999 (95% CI: 0.9995 to 1.0002) |
| **Interaction between PAEE & PGS** |
| HR = 1.0041 (95% CI: 0.9991 to 1.0092) |
| **Interaction between % MVPA & PGS** |
| HR = 1.0034 (95% CI: 0.9986 to 1.0083) |

**eTable 7:** Model 2 - Add BMI, Sleep Duration, Medication use to Model 1 (Exposures standardized)

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| --- | --- |
| **Exposure** | **Hazard Ratio** |
| **PAEE** | **HR = 0.90 (95% CI: 0.84 to 0.96)** |
| **Standardized PGS (in PAEE eqtn)** | **HR = 1.47 (95% CI: 1.39 to 1.55)** |
| **% MVPA** | **HR = 0.84 (95% CI: 0.77 to 0.90)** |
| **Standardized PGS (in MVPA eqtn)** | **HR = 1.47 (95% CI: 1.39 to 1.55)** |
| **PAEE (in MVPA eqtn)** | **HR = 1.01 (95% CI: 0.93 to 1.10)** |

**eTable 8:** Model 3 - Adding manual labor and whether individual is physically active in occupation to Model 2 (Exposures Standardized)

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| --- | --- |
| **Exposure** | **Hazard Ratio** |
| **PAEE** | **HR = 0.89 (95% CI: 0.84 to 0.95)** |
| **Standardized PGS (in PAEE eqtn)** | **HR = 1.47 (95% CI: 1.39 to 1.55)** |
| **% MVPA** | **HR = 0.84 (95% CI: 0.78 to 0.91)** |
| **Standardized PGS (in MVPA eqtn)** | **HR = 1.47 (95% CI: 1.39 to 1.55)** |
| **PAEE (in MVPA eqtn)** | **HR = 1.00 (95% CI: 0.92 to 1.09)** |

**eTable 9:** Overview of Physical Activity Volume and Genetic Susceptibility Results (First Year Excluded)

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| --- | --- | --- | --- | --- |
| **Genetic Risk Quintile** | **Physical Activity Energy Expenditure Risk Quintile** | | | |
| *20th Percentile* | *40th Percentile* | *60th Percentile* | *80th Percentile* |
| *20th Percentile* | 1 (Reference) | 1.09 (95% CI: 1.05-1.13) | 1.16 (95% CI: 1.09-1.25) | 1.25 (95% CI: 1.13-1.38) |
| *40th Percentile* | 1.26 (95% CI: 1.21-1.30) | 1.37 (95% CI: 1.30-1.44) | 1.46 (95% CI: 1.35-1.58) | 1.57 (95% CI: 1.41-1.75) |
| *60th Percentile* | 1.53 (95% CI: 1.44-1.63) | 1.68 (95% CI: 1.56-1.81) | 1.79 (95% CI: 1.63-1.97) | 1.92 (95% CI: 1.71-2.17) |
| *80th Percentile* | 1.93 (95% CI: 1.75-2.12) | 2.10 (95% CI: 1.89-2.33) | 2.24 (95% CI: 1.99-2.52) | 2.41 (95% CI: 2.09-2.77) |

**eTable 10:** Overview of Physical Activity Intensity and Genetic Susceptibility Results (First Year Excluded)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Genetic Risk Quintile** | **Percent Moderate-to-Vigorous Physical Activity Risk Quintile** | | | |
| *20th Percentile* | *40th Percentile* | *60th Percentile* | *80th Percentile* |
| *20th Percentile* | 1 (Reference) | 1.14 (95% CI: 1.09-1.20) | 1.28 (95% CI: 1.17-1.41) | 1.46 (95% CI: 1.26-1.69) |
| *40th Percentile* | 1.26 (95% CI: 1.21-1.30) | 1.44 (95% CI: 1.35-1.53) | 1.61 (95% CI: 1.46-1.78) | 1.83 (95% CI: 1.58-2.13) |
| *60th Percentile* | 1.54 (95% CI: 1.44-1.64) | 1.76 (95% CI: 1.62-1.91) | 1.97 (95% CI: 1.76-2.21) | 2.25 (95% CI: 1.92-2.63) |
| *80th Percentile* | 1.93 (95% CI: 1.75-2.12) | 2.20 (95% CI: 1.97-2.46) | 2.47 (95% CI: 2.16-2.83) | 2.81 (95% CI: 2.36-3.35) |

**eTable 11:** Overview of Physical Activity Volume and Genetic Susceptibility Results (MICE imputation)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Genetic Risk Quintile** | **Physical Activity Energy Expenditure Risk Quintile** | | | |
| *20th Percentile* | *40th Percentile* | *60th Percentile* | *80th Percentile* |
| *20th Percentile* | 1 (Reference) | 1.11 (95% CI: 1.07-1.15) | 1.21 (95% CI: 1.13-1.29) | 1.32 (95% CI: 1.20-1.45) |
| *40th Percentile* | 1.26 (95% CI: 1.22-1.30) | 1.40 (95% CI: 1.33-1.47) | 1.52 (95% CI: 1.41-1.63) | 1.66 (95% CI: 1.50-1.83) |
| *60th Percentile* | 1.53 (95% CI: 1.45-1.63) | 1.71 (95% CI: 1.60-1.84) | 1.86 (95% CI: 1.71-2.03) | 2.03 (95% CI: 1.82-2.27) |
| *80th Percentile* | 1.93 (95% CI: 1.76-2.11) | 2.14 (95% CI: 1.95-2.36) | 2.33 (95% CI: 2.09-2.60) | 2.54 (95% CI: 2.24-2.89) |

**eTable 12:** Overview of Physical Activity Intensity and Genetic Susceptibility Results (MICE imputation)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Genetic Risk Quintile** | **Percent Moderate-to-Vigorous Physical Activity Risk Quintile** | | | |
| *20th Percentile* | *40th Percentile* | *60th Percentile* | *80th Percentile* |
| *20th Percentile* | 1 (Reference) | 1.15 (95% CI: 1.09-1.20) | 1.29 (95% CI: 1.18-1.40) | 1.47 (95% CI: 1.29-1.68) |
| *40th Percentile* | 1.26 (95% CI: 1.22-1.30) | 1.44 (95% CI: 1.36-1.52) | 1.62 (95% CI: 1.47-1.77) | 1.84 (95% CI: 1.61-2.11) |
| *60th Percentile* | 1.54 (95% CI: 1.45-1.63) | 1.76 (95% CI: 1.64-1.90) | 1.98 (95% CI: 1.78-2.20) | 2.26 (95% CI: 1.95-2.62) |
| *80th Percentile* | 1.92 (95% CI: 1.76-2.10) | 2.20 (95% CI: 1.99-2.44) | 2.48 (95% CI: 2.19-2.81) | 2.83 (95% CI: 2.41-3.32) |

**eFigure 2:** Plots of CAD Events by Polygenic Risk Score and Physical Activity Volume for Black and Asian Participants

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| **Among Self-Reported Black Participants (n = 421; cases = 5)** |
| Chart, scatter chart  Description automatically generated |
| **Among Self-Reported Asian Participants (n = 1090; cases = 33)** |
| Chart, diagram  Description automatically generated |

**eFigure 3:** Objective PA vs Longitudinal Subjective PA Correlation

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| Chart, waterfall chart  Description automatically generated |
| Note: While correlation between self-reported MVPA and MVPA from accelerometer are low, this correlation changes relatively little between closer or farther visit from accelerometer wear start date and is in line with low correlations even between self-reported MVPA and MVPA from accelerometers measured contemporaneously.3 |

**References from the Appendix**

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