Supplementary Table 1: Associations between estimated VO2 max and risk markers for type 2 diabetes and cardiovascular disease (differences per one unit increase in estimated VO2 max in ml O2/min/kg) with adjustments for fat mass index: by sex

|  |  |  |  |
| --- | --- | --- | --- |
| Risk markers (N = 1445) | Adjustments | % difference/difference\* (95% CI) for a one IQR increase in estimated VO2 max  | p(sex difference in association) |
| Boys (n=723) | Girls (n=722) |
| Insulin (mU/l) | Standard | -17.99 | (-22.54, -13.18) | -19.87 | (-24.61, -14.84) | 0.58 |
| Standard + FMI | -6.04 | (-10.91, -0.90) | -9.52 | (-14.46, -4.30) | 0.31 |
| HOMA Insulin resistance | Standard | -17.79 | (-22.38, -12.93) | -19.94 | (-24.71, -14.88) | 0.53 |
| Standard + FMI | -5.88 | (-10.81, -0.68) | -9.67 | (-14.66, -4.39) | 0.27 |
| HbA1c (%) | Standard | -0.87 | (-1.49, -0.25) | -0.20 | (-0.87, 0.46) | 0.14 |
| Standard + FMI | -0.64 | (-1.28, 0.00) | 0.00 | (-0.68, 0.69) | 0.16 |
| Glucose (mmol/l) | Standard | -1.23 | (-1.95, -0.50) | -0.72 | (-1.49, 0.07) | 0.34 |
| Standard + FMI | -0.89 | (-1.64, -0.13) | -0.42 | (-1.21, 0.39) | 0.38 |
| Urate (mmol/l) | Standard | -6.18 | (-8.46, -3.84) | -5.46 | (-7.92, -2.94) | 0.68 |
| Standard + FMI | -2.33 | (-4.69, 0.09) | -2.03 | (-4.53, 0.54) | 0.87 |
| C-reactive protein (mg/l) | Standard | -40.33 | (-47.37, -32.36) | -41.42 | (-48.78, -33.01) | 0.83 |
| Standard + FMI | -18.83 | (-27.70, -8.87) | -23.04 | (-31.90, -13.03) | 0.49 |
| Triglyceride (mmol/l) | Standard | -11.93 | (-15.16, -8.59) | -7.26 | (-10.88, -3.49) | 0.05 |
| Standard + FMI | -7.27 | (-10.68, -3.73) | -2.92 | (-6.69, 1.00) | 0.07 |
| HDL cholesterol (mmol/l) | Standard | 3.80 | (1.66, 5.99) | 3.76 | (1.47, 6.10) | 0.94 |
| Standard + FMI | 0.62 | (-1.46, 2.74) | 0.95 | (-1.25, 3.20) | 0.85 |
| LDL cholesterol (mmol/l) | Standard | -4.04 | (-6.53, -1.48) | -2.82 | (-5.51, -0.04) | 0.51 |
| Standard + FMI | -2.28 | (-4.90, 0.41) | -1.26 | (-4.05, 1.61) | 0.59 |
| Systolic blood pressure (mmHg)\* | Standard | -2.47 | (-3.49, -1.46) | -2.44 | (-3.52, -1.35) | 0.97 |
| Standard + FMI | -1.66 | (-2.70, -0.62) | -1.71 | (-2.82, -0.61) | 0.93 |
| Diastolic blood pressure (mmHg)\* | Standard | -2.64 | (-3.55, -1.73) | -3.79 | (-4.76, -2.81) | 0.09 |
| Standard + FMI | -2.10 | (-3.04, -1.15) | -3.30 | (-4.30, -2.31) | 0.07 |

\* Absolute differences are shown for untransformed variables

Percentage differences are shown for all other variables which are log transformed

Associations are adjusted for age (in quartiles), ethnic group, month of measurement, height, sex, an interaction between VO2 max and sex and school (random effect). P-values are for interaction between VO2 max and sex.

Supplementary Table 2: Associations between estimated VO2 max and risk markers for type 2 diabetes and cardiovascular disease (differences per one unit increase in estimated VO2 max in ml O2/min/kg) with adjustments for fat mass index: by ethnic group

|  |  |  |  |
| --- | --- | --- | --- |
| Risk markers (N = 1445) | Adjustments | % difference/difference\* (95% CI) for a one IQR increase in estimated VO2 max  | p(ethnic difference in association) |
| White European (n=389) | South Asian (n=373) | Black African-Caribbean (n=346) | Other (n=337) |
| Insulin (mU/l) | Standard | -17.68 | (-23.57, -11.33) | -22.49 | (-28.41, -16.08) | -17.72 | (-24.40, -10.45) | -17.36 | (-23.87, -10.29) | 0.61 |
| Standard + FMI | -5.49 | (-11.73, 1.19) | -10.64 | (-16.93, -3.88) | -7.52 | (-14.38, -0.11) | -7.37 | (-14.04, -0.18) | 0.73 |
| HOMA Insulin resistance | Standard | -17.88 | (-23.80, -11.50) | -22.43 | (-28.40, -15.96) | -17.29 | (-24.05, -9.92) | -17.25 | (-23.81, -10.12) | 0.61 |
| Standard + FMI | -5.84 | (-12.12, 0.90) | -10.61 | (-16.97, -3.77) | -7.11 | (-14.08, 0.42) | -7.32 | (-14.06, -0.05) | 0.77 |
| HbA1c (%) | Standard | 0.00 | (-0.80, 0.82) | -0.98 | (-1.83, -0.12) | -1.16 | (-2.08, -0.24) | -0.28 | (-1.17, 0.62) | 0.16 |
| Standard + FMI | 0.24 | (-0.59, 1.07) | -0.73 | (-1.60, 0.15) | -0.96 | (-1.89, -0.03) | -0.08 | (-0.98, 0.83) | 0.16 |
| Glucose (mmol/l) | Standard | -1.59 | (-2.52, -0.64) | -0.69 | (-1.70, 0.33) | -0.83 | (-1.91, 0.26) | -0.71 | (-1.76, 0.34) | 0.51 |
| Standard + FMI | -1.24 | (-2.20, -0.28) | -0.32 | (-1.36, 0.72) | -0.54 | (-1.63, 0.57) | -0.43 | (-1.49, 0.64) | 0.52 |
| Urate (mmol/l) | Standard | -4.68 | (-7.69, -1.57) | -7.14 | (-10.27, -3.90) | -5.22 | (-8.63, -1.68) | -6.46 | (-9.71, -3.09) | 0.72 |
| Standard + FMI | -0.71 | (-3.77, 2.46) | -3.20 | (-6.39, 0.10) | -1.81 | (-5.23, 1.74) | -3.26 | (-6.52, 0.12) | 0.63 |
| C-reactive protein (mg/l) | Standard | -40.66 | (-49.58, -30.15) | -47.44 | (-55.83, -37.45) | -44.43 | (-53.89, -33.04) | -28.54 | (-40.30, -14.46) | 0.07 |
| Standard + FMI | -18.80 | (-29.98, -5.83) | -26.99 | (-37.68, -14.46) | -27.88 | (-39.01, -14.71) | -8.82 | (-22.46, 7.22) | 0.11 |
| Triglyceride (mmol/l) | Standard | -11.54 | (-15.73, -7.14) | -12.54 | (-16.96, -7.88) | -4.26 | (-9.42, 1.19) | -9.41 | (-14.13, -4.42) | 0.07 |
| Standard + FMI | -6.83 | (-11.20, -2.25) | -7.66 | (-12.28, -2.80) | 0.05 | (-5.24, 5.63) | -5.44 | (-10.28, -0.34) | 0.12 |
| HDL cholesterol (mmol/l) | Standard | 2.67 | (-0.08, 5.50) | 4.56 | (1.57, 7.64) | 4.68 | (1.48, 7.97) | 3.54 | (0.48, 6.69) | 0.78 |
| Standard + FMI | -0.52 | (-3.14, 2.18) | 1.21 | (-1.64, 4.14) | 1.93 | (-1.10, 5.06) | 0.88 | (-2.02, 3.88) | 0.67 |
| LDL cholesterol (mmol/l) | Standard | -5.84 | (-9.00, -2.57) | -4.68 | (-8.09, -1.15) | 1.36 | (-2.53, 5.41) | -3.41 | (-6.99, 0.30) | 0.03 |
| Standard + FMI | -4.15 | (-7.42, -0.77) | -2.84 | (-6.37, 0.82) | 2.92 | (-1.05, 7.05) | -1.97 | (-5.62, 1.81) | 0.04 |
| Systolic blood pressure (mmHg)\* | Standard | -2.37 | (-3.69, -1.05) | -3.10 | (-4.52, -1.69) | -1.66 | (-3.17, -0.15) | -2.58 | (-4.04, -1.12) | 0.55 |
| Standard + FMI | -1.55 | (-2.89, -0.21) | -2.26 | (-3.69, -0.83) | -0.97 | (-2.48, 0.54) | -1.91 | (-3.37, -0.44) | 0.61 |
| Diastolic blood pressure (mmHg)\* | Standard | -2.87 | (-4.06, -1.68) | -3.81 | (-5.08, -2.53) | -2.66 | (-4.02, -1.30) | -3.34 | (-4.65, -2.02) | 0.57 |
| Standard + FMI | -2.33 | (-3.54, -1.11) | -3.24 | (-4.54, -1.95) | -2.20 | (-3.57, -0.83) | -2.88 | (-4.21, -1.56) | 0.61 |

\* Absolute differences are shown for untransformed variables

Percentage differences are shown for all other variables which are log transformed

Associations are adjusted for sex, age (in quartiles), ethnic group, month of measurement, height, an interaction between VO2 max and ethnic group and school (random effect). P-values are for interaction between VO2 max and ethnic group.

Supplementary Table 3: Associations between estimated VO2 max, physical activity and risk markers for type 2 diabetes and cardiovascular disease (differences per one IQR increase in estimated VO2 max or counts), with adjustment for fat mass index

|  |  |  |
| --- | --- | --- |
|   |   | % difference / difference\* (95% CI) for a one IQR increase in estimated VO2 max or counts, p-value |
| Risk markers (N = 1083) | Variable | Standard adjustment | Standard + fat mass index adjustment |
| Insulin (mU/l) | Estimated VO2 max | -18.11 | (-21.99, -14.04) | <0.0001 | -6.43 | (-10.67, -1.98) | 0.005 |
| Counts | -16.60 | (-21.34, -11.57) | <0.0001 | -7.68 | (-12.45, -2.65) | 0.003 |
| HOMA Insulin resistance | Estimated VO2 max | -17.79 | (-21.67, -13.72) | <0.0001 | -6.23 | (-10.48, -1.77) | 0.01 |
| Counts | -16.28 | (-21.02, -11.25) | <0.0001 | -7.45 | (-12.23, -2.41) | 0.004 |
| HbA1c (%) | Estimated VO2 max | -0.64 | (-1.17, -0.10) | 0.02 | -0.38 | (-0.95, 0.19) | 0.19 |
| Counts | -0.22 | (-0.86, 0.42) | 0.50 | 0.00 | (-0.65, 0.65) | 1.00 |
| Glucose (mmol/l) | Estimated VO2 max | -0.95 | (-1.57, -0.33) | 0.003 | -0.64 | (-1.30, 0.03) | 0.06 |
| Counts | -0.12 | (-0.86, 0.63) | 0.76 | 0.18 | (-0.58, 0.94) | 0.64 |
| Urate (mmol/l) | Estimated VO2 max | -5.61 | (-7.60, -3.58) | <0.0001 | -1.94 | (-4.06, 0.23) | 0.08 |
| Counts | -2.82 | (-5.26, -0.31) | 0.03 | 0.14 | (-2.32, 2.67) | 0.91 |
| C-reactive protein (mg/l) | Estimated VO2 max | -43.95 | (-49.78, -37.44) | <0.0001 | -23.65 | (-31.22, -15.24) | <0.0001 |
| Counts | -28.20 | (-37.16, -17.97) | <0.0001 | -8.01 | (-18.39, 3.68) | 0.17 |
| Triglyceride (mmol/l) | Estimated VO2 max | -10.38 | (-13.25, -7.41) | <0.0001 | -5.54 | (-8.65, -2.31) | <0.001 |
| Counts | -9.33 | (-12.79, -5.74) | <0.0001 | -5.52 | (-9.06, -1.85) | 0.004 |
| HDL cholesterol (mmol/l) | Estimated VO2 max | 3.84 | (1.99, 5.73) | <0.0001 | 0.86 | (-0.99, 2.76) | 0.36 |
| Counts | 2.44 | (0.27, 4.67) | 0.03 | 0.23 | (-1.87, 2.37) | 0.83 |
| LDL cholesterol (mmol/l) | Estimated VO2 max | -3.06 | (-5.20, -0.87) | 0.01 | -1.22 | (-3.53, 1.14) | 0.31 |
| Counts | -2.71 | (-5.23, -0.12) | 0.04 | -1.34 | (-3.93, 1.32) | 0.32 |
| Systolic blood pressure (mmHg)\* | Estimated VO2 max | -2.56 | (-3.42, -1.69) | <0.0001 | -1.74 | (-2.66, -0.83) | <0.001 |
| Counts | -0.37 | (-1.42, 0.67) | 0.48 | 0.41 | (-0.64, 1.45) | 0.45 |
| Diastolic blood pressure (mmHg)\* | Estimated VO2 max | -3.40 | (-4.17, -2.62) | <0.0001 | -2.90 | (-3.73, -2.08) | <0.0001 |
| Counts | -1.67 | (-2.62, -0.72) | <0.001 | -1.09 | (-2.05, -0.13) | 0.03 |

\* Absolute differences are shown for untransformed variables

Percentage differences are shown for all other variables which are log transformed

Standard adjustment is for sex, age (in quartiles), ethnic group, month of measurement, height, and school (random effect)

Supplementary Table 4: Associations between estimated VO2 max and risk markers for type 2 diabetes and cardiovascular disease (differences per one IQR increase in estimated VO2 max) by tertiles of physical activity counts

|  |  |  |
| --- | --- | --- |
|   | % difference / difference\* (95% CI) for a one IQR increase in estimated VO2 max by tertiles of physical activity counts  | p (interaction) |
| Risk markers (N = 1083) | Lowest tertile of PA counts | Middle tertile of PA counts | Highest tertile of PA counts |
| Insulin (mU/l) | -21.27 | (-27.32, -14.72) | -18.39 | (-24.97, -11.22) | -9.03 | (-15.84, -1.66) | 0.03 |
| HOMA-IR | -20.99 | (-27.06, -14.42) | -18.01 | (-24.61, -10.82) | -8.88 | (-15.70, -1.51) | 0.03 |
| HbA1c (%) | -1.31 | (-2.21, -0.41) | 0.15 | (-0.79, 1.11) | -0.72 | (-1.59, 0.16) | 0.08 |
| Glucose (mmol/l) | -1.26 | (-2.31, -0.21) | -0.83 | (-1.92, 0.28) | -0.73 | (-1.75, 0.30) | 0.77 |
| Urate (mmol/l) | -6.73 | (-10.03, -3.31) | -5.98 | (-9.45, -2.39) | -3.30 | (-6.61, 0.14) | 0.36 |
| CRP (mg/l) | -42.22 | (-52.00, -30.45) | -42.55 | (-52.65, -30.31) | -41.64 | (-51.24, -30.16) | 0.99 |
| Triglyceride (mmol/l) | -13.04 | (-17.63, -8.19) | -10.31 | (-15.26, -5.07) | -4.34 | (-9.25, 0.83) | 0.04 |
| HDL cholesterol (mmol/l) | 6.47 | (3.29, 9.74) | 1.84 | (-1.34, 5.12) | 2.51 | (-0.47, 5.57) | 0.08 |
| LDL cholesterol (mmol/l) | -5.08 | (-8.61, -1.42) | -0.96 | (-4.78, 3.02) | -1.59 | (-5.13, 2.08) | 0.23 |
| Systolic BP (mmHg)\* | -3.15 | (-4.60, -1.71) | -1.83 | (-3.34, -0.31) | -2.54 | (-3.94, -1.13) | 0.47 |
| Diastolic BP (mmHg)\* | -3.80 | (-5.10, -2.49) | -3.00 | (-4.37, -1.63) | -3.04 | (-4.31, -1.77) | 0.61 |

\* Absolute differences are shown for untransformed variables

Percentage differences are shown for all other variables which are log transformed

Differences are adjusted for sex, age (quartiles), ethnic group, month, height, an interaction between estimated VO2 max and tertiles of PA and school (random effect)

Supplementary Table 5: Ethnic differences in risk markers for type 2 diabetes and cardiovascular disease: effect of adjustment for estimated VO2 max and physical activity counts

|  |  |  |
| --- | --- | --- |
| Risk markers (N = 1083) | Adjustments | % difference / difference\* (95% CI), p-value, % reduction in ethnic difference following adjustment for estimated VO2 max  |
| South Asian - white European |
| Insulin (mU/l) | Standard | 44.49 | (30.34, 60.18) | <0.0001 |  |
| Standard + VO2 max  | 41.15 | (27.68, 56.04) | <0.0001 | 7.5 |
| Standard + VO2 max + counts | 38.24 | (25.09, 52.76) | <0.0001 | 14.0 |
| HOMA Insulin resistance | Standard | 44.03 | (30.00, 59.56) | <0.0001 |   |
| Standard + VO2 max  | 40.76 | (27.40, 55.53) | <0.0001 | 7.4 |
| Standard + VO2 max + counts | 37.94 | (24.88, 52.36) | <0.0001 | 13.8 |
| HbA1c (%) | Standard | 1.66 | (0.56, 2.76) | 0.003 |  |
| Standard + VO2 max  | 1.58 | (0.49, 2.69) | 0.004 | 4.8 |
| Standard + VO2 max + counts | 1.58 | (0.48, 2.68) | 0.005 | 4.8 |
| Glucose (mmol/l) | Standard | 1.60 | (0.32, 2.90) | 0.01 |  |
| Standard + VO2 max  | 1.49 | (0.22, 2.79) | 0.02 | 6.9 |
| Standard + VO2 max + counts | 1.52 | (0.23, 2.82) | 0.02 | 5.0 |
| Urate (mmol/l) | Standard | 0.87 | (-3.43, 5.35) | 0.70 |   |
| Standard + VO2 max  | 0.18 | (-4.03, 4.56) | 0.94 | 79.3 |
| Standard + VO2 max + counts | -0.01 | (-4.21, 4.38) | 1.00 | 101.1 |
| C-reactive protein (mg/l) | Standard | 20.11 | (-4.33, 50.81) | 0.11 |  |
| Standard + VO2 max  | 11.08 | (-10.93, 38.53) | 0.35 | 44.9 |
| Standard + VO2 max + counts | 8.35 | (-13.14, 35.16) | 0.48 | 58.5 |
| Triglyceride (mmol/l) | Standard | 17.50 | (9.85, 25.68) | <0.0001 |   |
| Standard + VO2 max  | 15.96 | (8.54, 23.90) | <0.0001 | 8.8 |
| Standard + VO2 max + counts | 14.73 | (7.39, 22.57) | <0.0001 | 15.8 |
| HDL cholesterol (mmol/l) | Standard | -5.76 | (-9.16, -2.24) | 0.002 |  |
| Standard + VO2 max  | -5.22 | (-8.63, -1.68) | 0.004 | 9.4 |
| Standard + VO2 max + counts | -4.96 | (-8.40, -1.39) | 0.01 | 13.9 |
| LDL cholesterol (mmol/l) | Standard | 1.68 | (-2.74, 6.30) | 0.46 |   |
| Standard + VO2 max  | 1.29 | (-3.10, 5.89) | 0.57 | 23.2 |
| Standard + VO2 max + counts | 1.04 | (-3.35, 5.64) | 0.65 | 38.1 |
| Systolic blood pressure (mmHg)\* | Standard | -0.57 | (-2.38, 1.23) | 0.53 |  |
| Standard + VO2 max  | -0.88 | (-2.66, 0.89) | 0.33 | -54.4 |
| Standard + VO2 max + counts | -0.83 | (-2.62, 0.95) | 0.36 | -45.6 |
| Diastolic blood pressure (mmHg)\* | Standard | 1.62 | (-0.01, 3.26) | 0.05 |   |
| Standard + VO2 max  | 1.24 | (-0.35, 2.83) | 0.13 | 23.5 |
| Standard + VO2 max + counts | 1.13 | (-0.46, 2.73) | 0.16 | 30.2 |

\* Absolute differences are shown for untransformed variables

Percentage differences are shown for all other variables which are log transformed. Standard adjustment is for sex, age (in quartiles), ethnic group, month of measurement, height, and school (random effect).

Supplementary Figure 1: Mean fasting insulin by tertiles of physical activity and physical fitness



Geometric means are adjusted for sex, age (in quartiles), ethnic group, month of measurement, height, and school (random effect)