**Supplementary Materials**

**Physical activity attenuates but does not eliminate coronary heart disease risk amongst adults with risk factors: EPIC-CVD case-cohort study**

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**Tables**

**Supplementary Table S1.** Comparison of participants included in the complete case analysis and those excluded due to missing values in the sub-cohort and amongst those with CHD events outside the sub-cohort

**Supplemental Table S2** Characteristics of CHD cases outside the sub-cohort (N=8,393) stratified by physical activity and sex

**Supplementary Table S3**. Sensitivity analysis: Hazard ratio for coronary heart disease (CHD) across physical activity levels amongst participants, excluding those with a BMI <18.5kg/m2, with CHD risk factors defined by body mass index (BMI), total cholesterol, hypertension (clinically and/or history), history of diabetes and smoking status and with those without the specific risk factor and inactive as the reference group (Ref).

**Figures**

**Supplementary Figure S1.** Sensitivity analysis:Estimates of coronary heart disease (CHD) across physical activity levels amongst participants with CHD risk factors defined by body mass index (BMI), non-HDL cholesterol, history of diabetes, hypertension (clinically and/or history) and smoking status and with those without the risk factor and inactive as the reference group (REF). The model for each risk factor was adjusted for age at baseline, alcohol consumption, educational level, fruit intake, vegetable intake, the other risk factors and stratified by sex and centre.

**Supplementary Figure S2.** Sensitivity analysis: Estimates of coronary heart disease (CHD) across physical activity levels amongst men with CHD risk factors defined by body mass index (BMI), total cholesterol, history of diabetes, hypertension (clinically and/or history) and smoking status and with those without the risk factor and inactive as the reference group (REF). The model for each risk factor was adjusted for age at baseline, alcohol consumption, educational level, fruit intake, vegetable intake, the other risk factors, and stratified by centre.

**Supplementary Figure S3.** Sensitivity analysis: Estimates of coronary heart disease (CHD) across physical activity levels amongst women with CHD risk factors defined by body mass index (BMI), total cholesterol, history of diabetes, hypertension (clinically and/or history) and smoking status and with those without the risk factor and inactive as the reference group (REF). The model for each risk factor was adjusted for age at baseline, alcohol consumption, educational level, fruit intake, vegetable intake, the other risk factors and stratified by centre.

**Supplemental Table S1**. Comparison of included and excluded participants from the case-cohort study by location in or outside the sub-cohort

|  |  |  |  |
| --- | --- | --- | --- |
|  | Included | Excludeda | P valueb |
| *Sub-cohort n (%)* | 14,663(89.6) | 1,701(10.4) |  |
| Age (years)c | 52.1±9.1 | 54.5±9.0 | <0.001 |
| Follow-up (years)d | 12.8(3.5) | 13.1(3.8) | <0.001 |
| Sex n (%) |  |  | <0.001 |
| Men (n=6,163) | 5,436(37.1) | 727(42.7) |  |
| Women (n=10,201) | 9,227(62.9) | 974(57.3) |  |
| Educational level n (%) |  |  | <0.001 |
| No schooling (n=1,290) | 1,248(8.5) | 42(3.0) |  |
| Primary (n=5,373) | 4,848(33.1) | 525(37.6) |  |
| Secondary (n=2,452) | 2,265(15.4) | 187(13.4) |  |
| Vocational/University(n=6,945) | 6,302(43.0) | 643(46.0) |  |
| Cambridge physical activity index n (%) |  |  | <0.001 |
| Inactive (n=3,743) | 3,362(22.9) | 381(26.8) |  |
| Moderately inactive (n=5,485) | 4,987(34.0) | 498(35.1) |  |
| Moderately active (n=36,46) | 3,342(22.8) | 304(21.4) |  |
| Active (n=3,209) | 2,972(20.3) | 237(16.7) |  |
| Alcohol consumption n (%) |  |  | <0.001 |
| None (n=2,713) | 2,438(16.6) | 275(16.6) |  |
| 1 to ≤5 g/day (n=4,917) | 4,394(30.0) | 523(31.5) |  |
| >5 to ≤10 g/day (n=2,341) | 2,055(14.0) | 286(17.2) |  |
| >10 to ≤40 g/day (n=4,956) | 4,480(30.6) | 476(28.7) |  |
| >40 g/day (n=1,396) | 1,296(8.8) | 100(6.0) |  |
| Fruit (g/day)d | 196.7(217.3) | 175.0(185.9) | <0.001 |
| Vegetables (g/day)d | 157.0(140.6) | 154.7(137.3) | 0.084 |
| Body mass index category n (%) |  |  | 0.011 |
| <25 kg/m2 (n=7,153) | 6,405(43.7) | 748(46.9) |  |
| 25-29.9 kg/m2 (n=6,410) | 5,791(39.5) | 619(38.8) |  |
| ≥30 kg/m2 (n=2,695) | 2,467(16.8) | 228(14.3) |  |
| Total cholesterol category n (%) |  |  | 0.249 |
| <5.2 mmol/l (n=4,314) | 4,086(27.9) | 228(25.3) |  |
| 5.2-6.1 mmol/l (n=5,640) | 5,303(36.2) | 337(37.4) |  |
| ≥6.2 mmol/l (n=5,610) | 5,274(36.0) | 336(37.3) |  |
| Hypertension n (%) |  |  | <0.001 |
| No (n=10,406) | 9,505(64.8) | 901(59.0) |  |
| Yes (n=5,783) | 5,158(35.2) | 625(41.0) |  |
| History of diabetes n (%) |  |  | <0.001 |
| No (n=15,505) | 14,264(97.3) | 1,241(94.4) |  |
| Yes (n=472) | 399(2.7) | 73(5.6) |  |
| Smoking status n (%) |  |  | <0.001 |
| Never (n=7,610) | 6,948(47.4) | 662(42.3) |  |
| Former(n=4,419) | 3,938(26.9) | 481(30.7) |  |
| Current (n=4,200) | 3,777(25.8) | 423(27.0) |  |
| *CHD cases outside sub-cohort* |  |  |  |
| n (%) | 8,393(64.7) | 4,576(35.3) |  |
| Age (years)c | 58.5±8.2 | 60.4±9.8 | <0.001 |
| Follow-up (years)d | 6.9(5.5) | 7.6(5.8) | <0.001 |
| Sex n (%) |  |  | <0.001 |
| Men (n=7,577) | 5,087(60.6) | 2,490(54.4) |  |
| Women (n=5,392) | 3,306(39.4) | 2,086(45.6) |  |
| Educational level n (%) |  |  | <0.001 |
| No schooling (n=464) | 410(4.9) | 54(1.62) |  |
| Primary (n=4,920) | 3,551(42.3) | 1,369(39.6) |  |
| Secondary (n=1,344) | 948(11.3) | 396(11.5) |  |
| Vocational/University (n=5,122) | 3,484(41.5) | 1,638(47.4) |  |
| Cambridge physical activity index n (%) |  |  | <0.001 |
| Inactive (n=3,906) | 2,392(28.5) | 1,514(37.4) |  |
| Moderately inactive (n=3,863) | 2,648(31.6) | 1,215(30.0) |  |
| Moderately active (n=2,436) | 1,716(20.4) | 720(17.8) |  |
| Active (n=2,239) | 1,637(19.5) | 602(14.9) |  |
| Alcohol consumption n (%) |  |  | <0.001 |
| None (n=2,293) | 1,466(17.5) | 827(18.6) |  |
| 1 to ≤5 g/day (n=4,098) | 2,407(28.7) | 1,691(38.0) |  |
| >5 to ≤10 g/day (n=1,811) | 1,111(13.2) | 700(15.8) |  |
| >10 to ≤40 g/day (n=3,516) | 2,525(30.1) | 991(22.3) |  |
| >40 g/day (n=1,111) | 884(10.5) | 227(5.1) |  |
| Fruit (g/day)d | 172.5(195.9) | 171.2(184.8) | 0.271 |
| Vegetables (g/day)d | 151.8(132.5) | 165.1(163.8) | <0.001 |
| Body mass index category n (%) |  |  | <0.001 |
| <25 kg/m2 (n=4,282) | 2,592(30.9) | 1,690(38.4) |  |
| 25-29.9 kg/m2 (n=5,979) | 4,042(48.2) | 1,937(44.0) |  |
| ≥30 kg/m2 (n=2,535) | 1,759(21.0) | 776(17.6) |  |
| Total cholesterol category n (%) |  |  | 0.945 |
| <5.2 mmol/l (n=1,485) | 1,283(15.3) | 202(15.6) |  |
| 5.2-6.1 mmol/l (n=3,081) | 2,670(31.8) | 411(31.8) |  |
| ≥6.2 mmol/l (n=5,119) | 4,440(52.9) | 679(52.6) |  |
| Hypertension n (%) |  |  | <0.001 |
| No (n=5,191) | 3,269(38.9) | 1,922(46.9) |  |
| Yes (n=7,302) | 5,124(61.1) | 2,178(53.1) |  |
| History of diabetes n (%) |  |  | 0.744 |
| No (n=11,523) | 7,800(92.9) | 3,723(92.8) |  |
| Yes (n=883) | 593(7.1) | 290(7.2) |  |
| Smoking status n (%) |  |  | <0.001 |
| Never (n=4,080) | 2,552(30.4) | 1,528(34.9) |  |
| Former (n=4,313) | 2,751(32.8) | 1,562(35.7) |  |
| Current (n=4,381) | 3,090(36.8) | 1,291(29.5) |  |

aExcluded due to missing data: Number and percentage of participants (n, %) in the sub-cohort (N=16,364) with missing data per variable: Age (0), sex (0), duration of follow-up (1, 0.01%), body mass index (106, 0.7%), total cholesterol (800, 4.9%), educational level (304, 1.9%), alcohol consumption (41, 0.3%), hypertension (175, 1.1%), history of diabetes (387, 2.4%), physical activity index (281, 1.7%), fruit intake (51, 0.3%), vegetable intake (51, 0.3%). Number and percentage of participants (n) with CHD events outside the sub-cohort (N=12,969) with missing data per variable: Age (0), sex (0), duration of follow-up (0), body mass index (137, 1.3%), total cholesterol (3,284, 25.3%), educational level (1,119, 8.6%), alcohol consumption (140, 1.1%), hypertension (476, 3.7%), history of diabetes (5632, 4.3%), physical activity index (525, 4.1%), fruit intake (470, 3.6%), vegetable intake (470, 3.6%).

bP-values are derived from unpaired t-tests or Mann-Whitney tests for normal and non-normal distributed continuous variables, respectively, or derived from Chi2 tests for categorical variables.

cValues for normally distributed variables are expressed as mean ±standard deviation.

dValues from non-normally distributed variables are expressed as median (interquartile range).

**Supplemental Table S2** Characteristics of CHD cases outside the sub-cohort (N=8,393) stratified by physical activity and sex

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Physical activity | | | | |
|  | Inactive | Moderately inactive | Moderately active | Active | P valuea |
| *Men (n=5,087)* |  |  |  |  |  |
| n (%) | 1,312(25.8) | 1,541(30.3) | 1,127(22.2) | 1,107(21.8) |  |
| Age (years)b | 61.1±8.7 | 57.9±7.8 | 56.2±7.5 | 55.3±7.2 | <0.001 |
| Educational level n (%) |  |  |  |  | 0.012 |
| No schooling (n=234) | 56(4.3) | 84(5.5) | 58(5.1) | 36(3.3) |  |
| Primary (n=2,027) | 531(40.5) | 566(36.7) | 451(40.0) | 479(43.3) |  |
| Secondary (n=561) | 144(11.0) | 189(12.3) | 126(11.2) | 102(9.2) |  |
| Vocational/University (n=2,265) | 581(44.3) | 702(45.6) | 492(43.7) | 490(44.3) |  |
| Alcohol consumption n (%) |  |  |  |  | <0.001 |
| None (n=554) | 213(16.2) | 139(9.0) | 101(9.0) | 101(9.1) |  |
| 1 to ≤5 g/day (n=1,157) | 343(26.1) | 348(22.6) | 243(21.6) | 223(20.1) |  |
| >5 to ≤10 g/day (n=687) | 178(13.6) | 202(13.1) | 152(13.5) | 155(14.0) |  |
| >10 to ≤40 g/day (n=1,869) | 414(31.6) | 606(39.3) | 426(37.8) | 423(38.2) |  |
| >40 g/day (n=820) | 164(12.5) | 246(16.0) | 205(18.2) | 205(18.5) |  |
| Fruit (g/day)c | 146.0(192.2) | 150.0(180.5) | 151.7(197.5) | 148.6(184.9) | 0.498 |
| Vegetables (g/day)c | 160.9(156.5) | 149.3(128.9) | 144.1(135.6) | 148.7(124.5) | 0.021 |
| Body mass index n (%) |  |  |  |  | 0.332 |
| <25 kg/m2 (n=1,365) | 345(26.3) | 423(27.4) | 305(27.1) | 292(26.4) |  |
| 25-29.9 kg/m2 (n=2,701) | 672(51.2) | 823(53.4) | 605(53.7) | 601(54.3) |  |
| ≥30 kg/m2 (n=1,021) | 295(22.5) | 295(19.1) | 217(19.3) | 214(19.3) |  |
| Total cholesterol n (%) |  |  |  |  | 0.120 |
| <5.2 mmol/l (n=887) | 222(16.9) | 286(18.6) | 174(15.4) | 205(18.5) |  |
| 5.2-6.1 mmol/l (n=1,742) | 425(32.4) | 527(34.2) | 414(36.7) | 376(34.0) |  |
| ≥6.0 mmol/l (n=2,458) | 665(50.7) | 728(47.2) | 539(47.8) | 526(47.5) |  |
| Hypertensiond n (%) |  |  |  |  | <0.001 |
| No (n=2,064) | 463(35.3) | 619(40.2) | 478(42.4) | 504(45.5) |  |
| Yes (n=3,023) | 849(64.7) | 922(59.8) | 649(57.6) | 603(54.5) |  |
| History of diabetes n (%) |  |  |  |  | <0.001 |
| No (n=4,731) | 1,186(90.4) | 1,436(93.2) | 1,068(94.8) | 1,041(94.0) |  |
| Yes (n=356) | 126(9.6) | 105(6.8) | 59(5.2) | 66(6.0) |  |
| Smoking status n (%) |  |  |  |  | 0.664 |
| Never (n=1,071) | 271(20.7) | 323(21.0) | 245(21.7) | 232(21.0) |  |
| Former (n=1,927) | 518(39.5) | 594(38.5) | 414(36.7) | 401(36.2) |  |
| Current (n=2,089) | 523(39.9) | 624(40.5) | 468(41.5) | 474(42.8) |  |
| *Women (n=3,306)* |  |  |  |  |  |
| n (%) | 1,080(32.7) | 1,107(33.5) | 589(17.8) | 530(16.0) |  |
| Age (years)b | 61.4±8.7 | 59.8±7.6 | 58.8±7.3 | 57.1±7.5 | <0.001 |
| Educational level n (%) |  |  |  |  | <0.001 |
| No schooling (n=176) | 97(9.0) | 59(5.3) | 13(2.2) | 7(1.3) |  |
| Primary (n=1,524) | 587(54.4) | 481(43.5) | 261(44.3) | 195(36.8) |  |
| Secondary (n=387) | 107(9.9) | 135(12.2) | 67(11.4) | 78(14.7) |  |
| Vocational/University (n=1,219) | 289(26.8) | 432(39.0) | 248(42.1) | 250(47.2) |  |
| Alcohol consumption n (%) |  |  |  |  | <0.001 |
| None (n=912) | 401(37.1) | 289(26.1) | 124(21.1) | 98(18.5) |  |
| 1 to ≤5 g/day (n=1,250) | 402(37.2) | 402(36.3) | 227(38.5) | 219(41.3) |  |
| >5 to ≤10 g/day (n=424) | 118(10.9) | 148(13.4) | 88(14.9) | 70(13.2) |  |
| >10 to ≤40 g/day (n=656) | 140(13.0) | 243(22.0) | 142(24.1) | 131(24.7) |  |
| >40 g/day (n=64) | 19(1.8) | 25(2.3) | 8(1.4) | 12(2.3) |  |
| Fruit (g/day)c | 209.5(213.3) | 210.0(183.2) | 214.3(195.4) | 225.8(189.9) | 0.687 |
| Vegetables (g/day)c | 173.5(159.3) | 154.9(121.1) | 145.8(107.1) | 148.6(88.6) | <0.001 |
| Body mass index n (%) |  |  |  |  | <0.001 |
| <25 kg/m2 (n=1227) | 318(29.4) | 428(38.7) | 249(42.3) | 232(43.8) |  |
| 25-29.9 kg/m2 (n=1,341) | 450(41.7) | 434(39.2) | 244(41.4) | 213(40.2) |  |
| ≥30 kg/m2 (n=738) | 312(28.9) | 245(22.1) | 96(16.3) | 85(16.0) |  |
| Total cholesterol n (%) |  |  |  |  | 0.371 |
| <5.2 mmol/l (n=396) | 123(11.4) | 148(13.4) | 67(11.4) | 58(10.9) |  |
| 5.2-6.1 mmol/l (n=928) | 293(27.1) | 327(29.5) | 159(27.0) | 149(28.1) |  |
| ≥6.0 mmol/l (n=1,982) | 664(61.5) | 632(57.1) | 363(61.6) | 323(60.9) |  |
| Hypertensiond n (%) |  |  |  |  | <0.001 |
| No (n=1,205) | 341(31.6) | 414(37.4) | 236(40.1) | 214(40.4) |  |
| Yes (n=2,101) | 739(68.4) | 693(62.6) | 353(59.9) | 316(59.6) |  |
| History of diabetes n (%) |  |  |  |  | 0.001 |
| No (n=3,069) | 980(90.7) | 1026(92.7) | 555(94.2) | 508(95.8) |  |
| Yes (n=237) | 100(9.3) | 81(7.3) | 34(5.8) | 22(4.2) |  |
| Smoking status n (%) |  |  |  |  | <0.001 |
| Never (n=1,481) | 508(47.0) | 538(48.6) | 244(41.4) | 191(36.0) |  |
| Former (n=824) | 260(24.1) | 261(23.6) | 148(25.1) | 155(29.2) |  |
| Current (n=1,001) | 312(28.9) | 308(27.8) | 197(33.4) | 184(34.7) |  |

aP values are derived from a Kruskal Wallis or ANOVA test for continuous variables or from a Chi2 test for categorical variables;

bValues for normally distributed variables are expressed as mean ±standard deviation;

cValues from non-normally distributed variables are expressed as median (interquartile range);

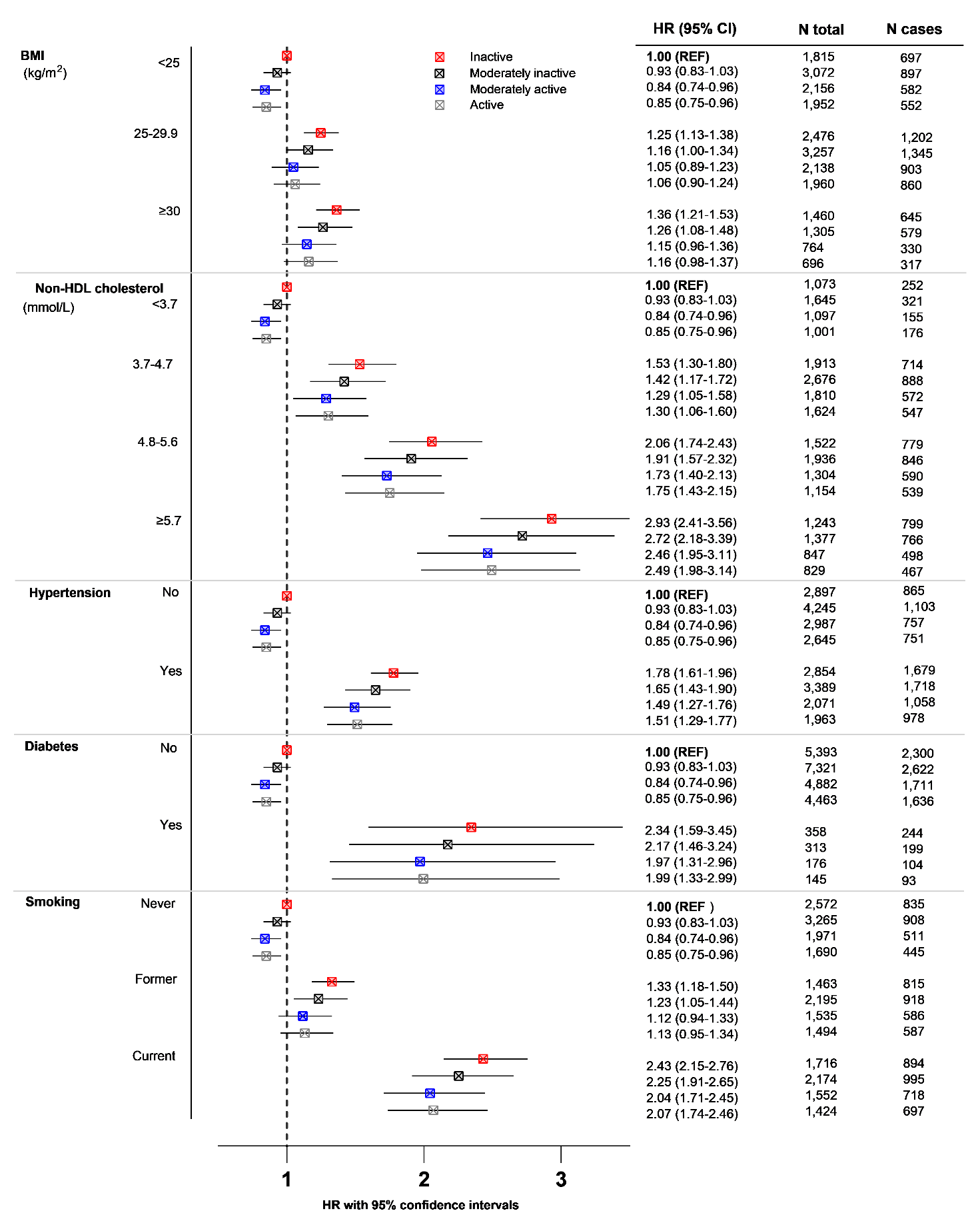
dHypertension definition is based on medical history and/or clinical measurements.

**Supplementary Table S3**. Sensitivity analysis: Hazard ratio for coronary heart disease across physical activity levels amongst participants, excluding those with a BMI <18.5kg/m2, with CHD risk factors defined by body mass index (BMI), total cholesterol, hypertension (clinically and/or history), history of diabetes and smoking status and with those without the specific risk factor and inactive as the reference group (REF).

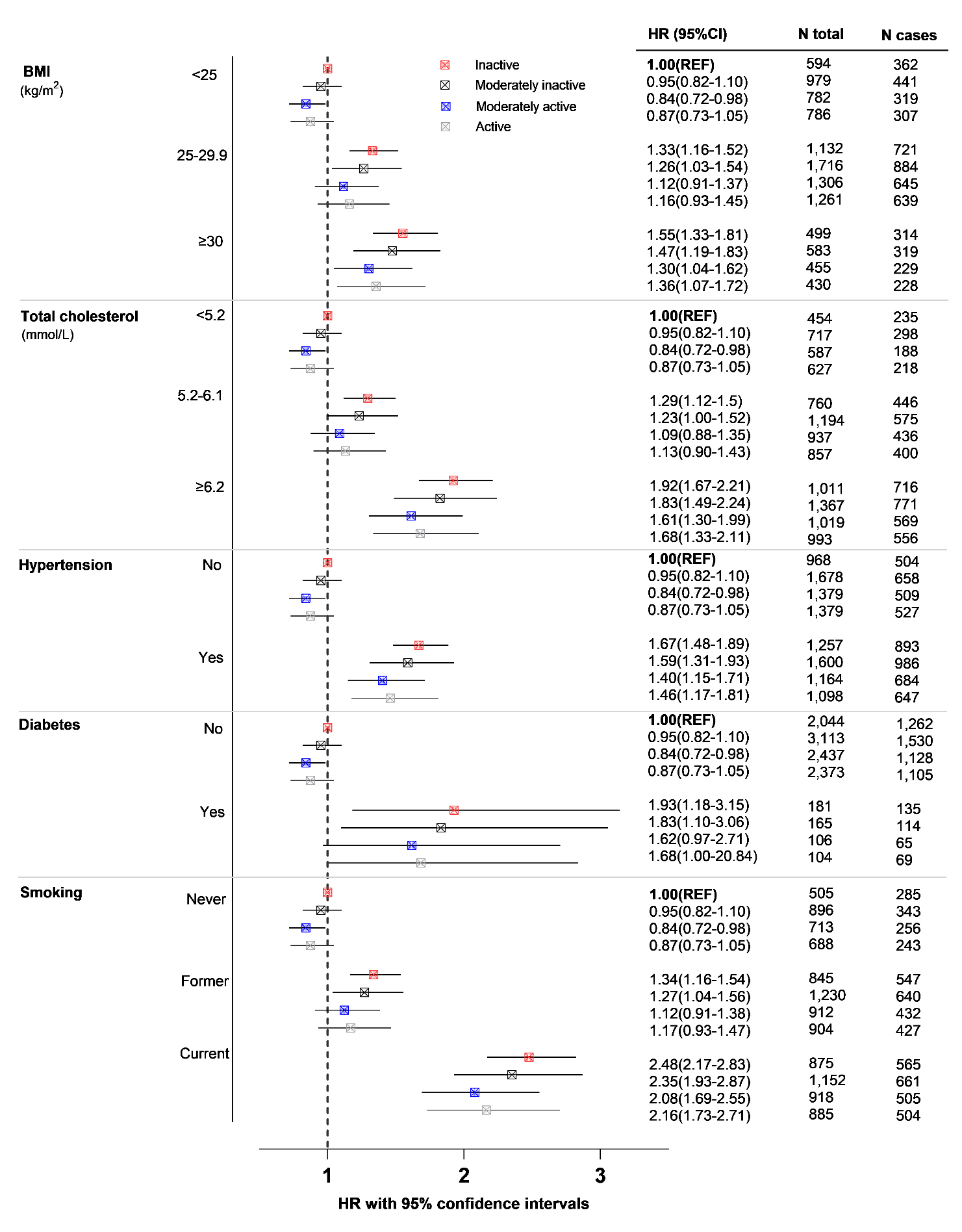
|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Risk factor category | Physical activity level | HRa (95% Cl) | N participants | N cases |
| BMI kg/m2 |  |  |  |  |
| 18.5-24.9 | **Inactive** | **1.0 (REF)** | 1,762 | 675 |
|  | Moderately inactive | 0.91 (0.82-1.01) | 3,010 | 875 |
|  | Moderately active | 0.84 (0.73-0.95) | 2,107 | 574 |
|  | Active | 0.84 (0.74 -0.95) | 1,917 | 545 |
| 25-29.9 | Inactive | 1.30 (1.18-1.43) | 2,477 | 1,202 |
|  | Moderately inactive | 1.19 (1.03 -1.37) | 3,257 | 1,345 |
|  | Moderately active | 1.09 (0.92-1.28) | 2,138 | 903 |
|  | Active | 1.09 (0.93-1.27) | 1,961 | 861 |
| ≥30 | Inactive | 1.48 (1.32 -1.65) | 1,461 | 646 |
|  | Moderately inactive | 1.35 (1.16 -1.57) | 1,305 | 579 |
|  | Moderately active | 1.24 (1.04 -1.46) | 764 | 330 |
|  | Active | 1.24 (1.05-1.46) | 696 | 317 |
| Total cholesterol mmol/l |  |  |  |  |
| <5.2 | Inactive | **1.0 (REF)** | 1,215 | 362 |
|  | Moderately inactive | 0.91 (0.82-1.01) | 1,790 | 452 |
|  | Moderately active | 0.84 (0.73-0.95) | 1,184 | 258 |
|  | Active | 0.84 (0.74 -0.95) | 1,112 | 273 |
| 5.2-6.1 | Inactive | 1.26 (1.10-1.44) | 1,912 | 754 |
|  | Moderately inactive | 1.15 (0.97 -1.36) | 2,617 | 907 |
|  | Moderately active | 1.05 (0.87-1.27) | 1,799 | 599 |
|  | Active | 1.06 (0.88 -1.26) | 1,572 | 560 |
| ≥6.2 | Inactive | 1.81 (1.56-2.11) | 2,573 | 1,407 |
|  | Moderately inactive | 1.66 (1.38-1.99) | 3,165 | 1,440 |
|  | Moderately active | 1.51 (1.24-1.85) | 2,026 | 950 |
|  | Active | 1.52 (1.25-1.85) | 1,890 | 890 |
| Hypertension |  |  |  |  |
| No | Inactive | **1.0 (REF)** | 2,864 | 856 |
|  | Moderately inactive | 0.91 (0.82-1.01) | 4,197 | 1,088 |
|  | Moderately active | 0.84 (0.73-0.95) | 2,947 | 751 |
|  | Active | 0.84 (0.74 -0.95) | 2,614 | 747 |
| Yes | Inactive | 1.80 (1.65-1.96) | 2,836 | 1,667 |
|  | Moderately inactive | 1.65 (1.44-1.89) | 3,375 | 1,711 |
|  | Moderately active | 1.51 (1.29-1.76) | 2,062 | 1,056 |
|  | Active | 1.51 (1.30-1.75) | 1,960 | 976 |
| History of diabetes |  |  |  |  |
| No | Inactive | **1.0 (REF)** | 5,342 | 2,279 |
|  | Moderately inactive | 0.91 (0.82-1.01) | 7,260 | 2,601 |
|  | Moderately active | 0.84 (0.73-0.95) | 4,833 | 1,703 |
|  | Active | 0.84 (0.74 -0.95) | 4,430 | 1,631 |
| Yes | Inactive | 2.41 (1.62-3.59) | 358 | 244 |
|  | Moderately inactive | 2.20 (1.46-3.33) | 312 | 198 |
|  | Moderately active | 2.01 (1.32-3.06) | 176 | 104 |
|  | Active | 2.02 (1.33-3.06) | 144 | 92 |
| Smoking status |  |  |  |  |
| Never | Inactive | **1.0 (REF)** | 2,560 | 833 |
|  | Moderately inactive | 0.91 (0.82-1.01) | 3,240 | 898 |
|  | Moderately active | 0.84 (0.73-0.95) | 1,950 | 509 |
|  | Active | 0.84 (0.74 -0.95) | 1,669 | 443 |
| Former | Inactive | 1.34 (1.19 -1.50) | 1,455 | 810 |
|  | Moderately inactive | 1.22 (1.05-1.43) | 2,179 | 912 |
|  | Moderately active | 1.12 (0.94-1.33) | 1,528 | 585 |
|  | Active | 1.12 (0.95-1.33) | 1,491 | 587 |
| Current | Inactive | 2.54 (2.23-2.88) | 1,685 | 880 |
|  | Moderately inactive | 2.32 (1.97-2.74) | 2,153 | 989 |
|  | Moderately active | 2.12 (1.77-2.54) | 1,531 | 713 |
|  | Active | 2.13 (1.78-2.53) | 1,414 | 693 |

aHazard Ratio (HR) and 95% Confidence Intervals (CI) estimated from Prentice-weighted Cox proportional hazard models. The model for each risk factor was adjusted for age at baseline, alcohol consumption, educational level, fruit intake, vegetable intake, and all the other risk factors, stratified by sex and center. HRs were first estimated per center and then combined by multivariate random-effect meta-analysis. Analysis included 22,855 participants, including 8,852 incident CHD cases.

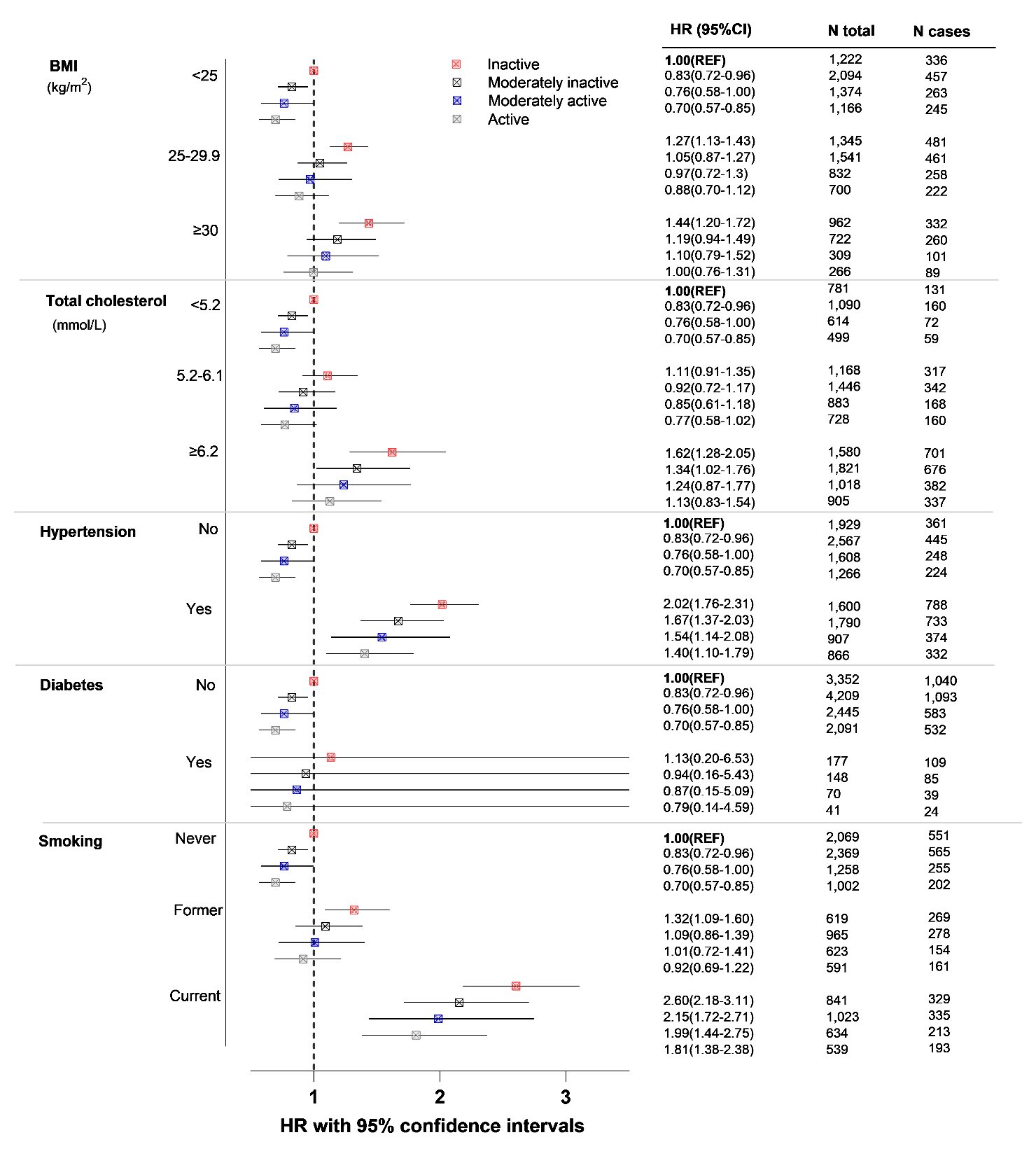
**Supplementary Figure S1.** Sensitivity analysis:Combinedestimates of coronary heart disease (CHD) across physical activity levels amongst participants with CHD risk factors defined by body mass index (BMI), non-HDL cholesterol, history of diabetes, hypertension (clinically and/or history) and smoking status and with those without the risk factor and inactive as the reference group (REF). The model for each risk factor was adjusted for age at baseline, alcohol consumption, educational level, fruit intake, vegetable intake, the other risk factors and stratified by sex and centre. N=23,051, including 8,389 CHD cases



**Supplementary Figure S2.** Sensitivity analysis: Combined estimates of coronary heart disease (CHD) across physical activity levels amongst men with CHD risk factors defined by body mass index (BMI), total cholesterol, history of diabetes, hypertension (clinically and/or history) and smoking status and with those without the risk factor and inactive as the reference group (REF). The model for each risk factor was adjusted for age at baseline, alcohol consumption, educational level, fruit intake, vegetable intake, the other risk factors, and stratified by centre. n=10,523 participants, including 5,408 CHD cases

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**Supplementary Figure S3.** Sensitivity analysis: Combined estimates of coronary heart disease (CHD) across physical activity levels amongst women with CHD risk factors defined by body mass index (BMI), total cholesterol, history of diabetes, hypertension (clinically and/or history) and smoking status and with those without the risk factor and inactive as the reference group (REF). The model for each risk factor was adjusted for age at baseline, alcohol consumption, educational level, fruit intake, vegetable intake, the other risk factors and stratified by centre. n=12,533 participants, including 3,306 CHD cases

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