A Prospective Study of Physical Activity and Cardiometabolic Diseases in association with Cancer Risk.

**Gebremariam et al.**

**Additional File 1**

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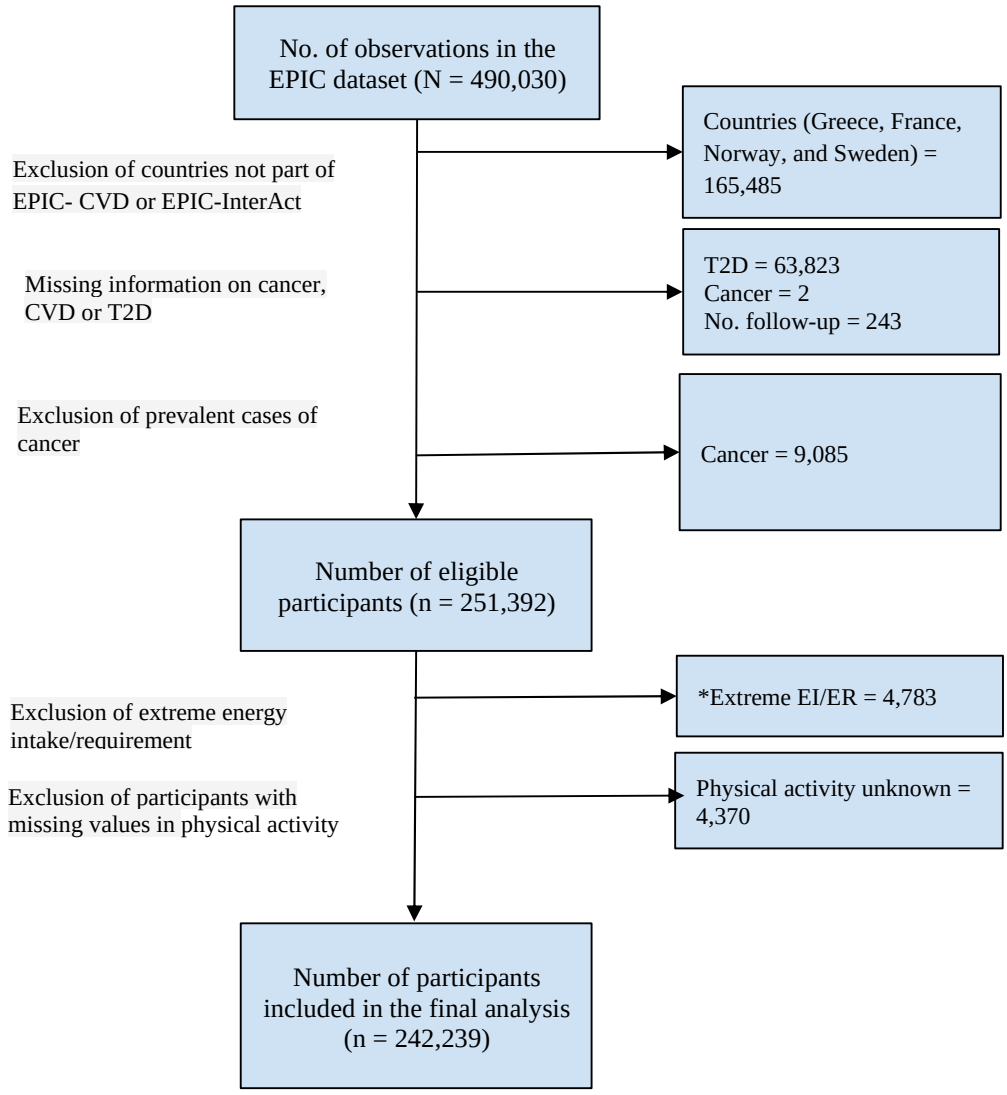
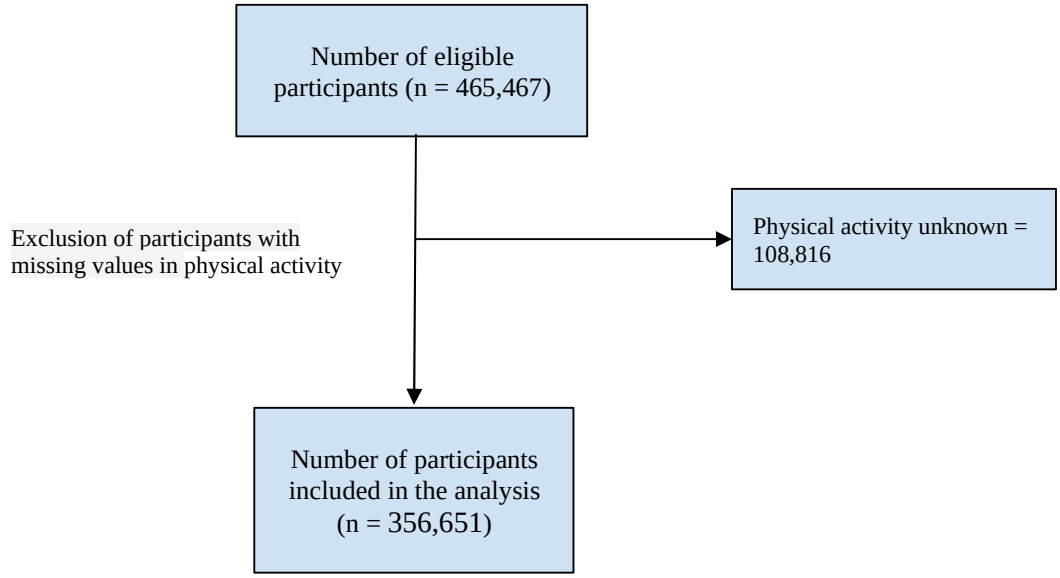
**Supplementary Figure 1: Flow chart with inclusion and exclusion criteria of the study population in EPIC.**




*Energy intake-to-energy requirement (EI/ER) calculated as the ratio of reported daily energy intake (from dietary assessment) to estimated energy requirement based on age, sex, body size, and physical activity. Participants in the top and bottom 1% of EI/ER values were excluded.
Abbreviations: CVD, cardiovascular diseases; EI/ER, energy intake/energy requirement; EPIC, European Prospective Investigation into Cancer and Nutrition; No., number; T2D, type 2 diabetes.

**Supplementary Figure 2: Flow chart with inclusion and exclusion criteria of the study population in UK Biobank.**




Abbreviations: CVD, cardiovascular diseases; No., number; T2D, type 2 diabetes.

**Supplementary Table 1: Comparison of non-occupational physical activity measurements in EPIC and UK Biobank and assigned MET values**

| **EPIC** | | | **UK Biobank*** | | |
|---|---|---|---|---|---|
| **Activity type** | **MET values** | **Comments** | **Activity type** | **MET values** | **Comments** |
| Walking | 3.0 | For pleasure, shopping, to work | Walking for pleasure | 3.3 | For pleasure only |
| Housework | 3.0 | Cleaning, cooking,… | Light DIY | 2.25 | E.g., gardening |
| Gardening | 4.0 | | Heavy DIY | 4.5 | E.g., carpentry |
| Do-it-yourself | 4.5 | | Other exercises | 4.5 | E.g., swimming, cycling, keep fit, bowling |
| Physical exercise | 6.0 | Aerobics, swimming, jogging, cycling? | Strenuous sports | 8.0 | E.g., sports that make you sweat or breathe hard |
| Stair climbing | 8.0 | Flight of stairs climbed | | | |

*UKB refers to those who had a paid job and is derived from the Recent Physical Activity Questionnaire (RPAQ), as previously done by Pearce M et al. (2020) (1) and Chudasama Y et al. (2019) (2). For participants not in a paid job, occupational activity could not contribute to the total MET-h/week score (walking minutes × 3.3 METs + moderate-activity minutes × 4.0 METs + vigorous-activity minutes × 8.0 METs) obtained from the International Physical Activity Questionnaire (IPAQ) (3). Therefore, we considered the total MET-h/week score as a non-occupational physical activity.

**Supplementary Table 2: List of physical activity-related cancers with risk estimates or evaluation from the considered literature**

| Cancer Type/Site | Moore et al., 2016 (4); HR (95% CI) | Matthews et al., 2020 (5); HR (95% CI) | McTiernan et al., 2019 (6) | Friedenreich et al., 2021 (7) | World Cancer Research Fund, 2018 (8) |
|---|---|---|---|---|---|
| Colon | 0.87 (0.80, 0.94) | 0.84 (0.77, 0.92) | Strong | Strong | Strong |
| Breast: postmenopausal | 0.93 (0.90, 0.96) | 0.92 (0.88, 0.97) | Strong | Strong | Probable |
| Endometrial | 0.98 (0.89, 1.09) | 1.02 (0.91, 1.14) | Strong | Strong | Probable |
| Oesophageal adenocarcinoma | 0.62 (0.40, 0.97) | 0.90 (0.70, 1.16) | Strong | Strong | Limited-suggestive |
| Urinary Bladder | 0.88 (0.83, 0.94) | 0.95 (0.87, 1.03) | Strong | Strong | NE |
| Gastric Cardia | 0.85 (0.69, 1.04) | 0.81 (0.61, 1.08) | Strong | Strong | NE |
| Kidney: renal cell | 0.84 (0.77, 0.91) | 0.90 (0.80, 1.01) | Strong | Strong | NE |
| Lung | 0.73 (0.70, 0.76) | NE | Moderate | Moderate | Limited-suggestive |
| Head and neck | 0.85 (0.77, 0.94) | 0.94 (0.83, 1.07) | Limited | Limited | NE |
| Rectum | 0.88 (0.81, 0.96) | 0.93 (0.83, 1.05) | Limited | Limited | NE |
| Liver | 0.81 (0.61, 1.09) | 0.79 (0.64, 0.99) | NE | NE | Limited-suggestive |
| Gallbladder | 0.78 (0.57, 0.97) | 0.76 (0.51, 1.14) | NE | NE | NE |
| Small intestine | 0.81 (0.62, 1.05) | 0.83 (0.59, 1.16) | NE | NE | NE |
| Multiple Myeloma | 0.87 (0.77, 0.98) | 0.83 (0.71, 0.98) | NE | NE | NE |
| Myeloid leukaemia | 0.85 (0.73, 0.97) | 0.93 (0.77, 1.13) | NE | NE | NE |

NE, not evaluated.

**Supplementary Table 3: Diagnostic codes for the definition of cancer, type 2 diabetes, and cardiovascular diseases**

| **Physical activity-related cancers** | **ICD10 code** | **ICDO-3 code-histology** |
|---|---|---|
| Breast cancer | C50 | |
| Lung cancer | C34 | Excludes: 9050, 9051, 9052, 9053, 9054, 9055, 9140, 9590:9992 |
| Colon cancer | C18, C26.0 | |
| Rectal cancer | C19, C20 | Excludes: 9050/3–9055/3, 9140/3 |
| Oesophageal adenocarcinoma | C15 | 8140/3, 8144/3, 8480/3, 8481/3 & 8490/3 |
| Bladder cancer | C67 | |
| Endometrial cancer | C54–C55 | |
| Kidney | C64, C65 | |
| Multiple myeloma | C90 | 9731/3, 9732/3, 9734/3 |
| Myeloid leukemia | C92 | 9840/3, 9860/3, 9861/3, 9863/3, 9865/3, 9866/3, 9867/3, 9869/3, 9871/3–9876/3, 9891/3, 9895/3–9898/3, 9910/3, 9911/3, 9920/3, 9930/3, 9945/3, 9946/3 |
| Liver cancer | C22 | |
| Gastric cardia cancer | C16.0 | |
| Small intestine cancer | C17 | |
| Gallbladder cancer | C23 | |
| Head and neck cancer | C00-C14, C30-C33 | |
| **Overall cancer** | C00-C96, except C44 (non-melanoma skin cancer) | |
| **Type 2 diabetes** | E11 | |
| **Cardiovascular diseases** | | |
| Stroke | I60:I69 | |
| Coronary artery disease | I20:I25 | |

ICD, International Classification of Diseases; ICDO, International Classification of Diseases for Oncology, Third Edition

**Supplementary Table 4: Missing data distribution of covariates and outcome variables in EPIC and UKB cohorts.**

| EPIC (N = 242,239) | | | UKB (N = 334,596) | | |
|---|---|---|---|---|---|
| **Variable** | **Number of missing** | **Missing %** | **Variable** | **Number of missing** | **Missing %** |
| **Highest school level** (None, Primary school completed, Technical/professional school, Secondary school, longer education (incl. University deg.), Not specified/missing) | 4,594 | 1.9 | **Qualifications** (College or university degree, A levels/AS levels or equivalent, O levels/GCSEs or equivalent, CSES or equivalent, NVQ or HND or HNC or equivalent, other professional qualifications, none of the above, prefer not to answer/missing) | 2,267 | 0.6 |
| **Physical activity at work** (Sedentary, standing, manual work, heavy manual work, non-worker, missing) | 3,3642 | 1.5 | **Current employment status** (In paid employment or self-employed, retired, looking after home and/or family, unable to work because of sickness or disability, unemployed, doing unpaid or voluntary work, full or part-time student, none of the above, prefer not to answer/missing) | 1,218 | 0.3 |
| **Use of hormones for menopause*** (No, Yes, Missing) | 2,016 | 1.3 | **Ever used hormone-replacement therapy*** (No, Yes, do not know, Prefer not to answer/Missing) | 500 | 0.3 |
| **Smoking status** (Never, Former, Current, Unknown/Missing) | 743 | 0.3 | **Smoking status** (Never, Previous, Current, prefer not to answer/missing) | 877 | 0.23 |
| **Alcohol at recruitment** (g/d) | 445 | 0.18 | **Alcohol drinker status** (Never, previous, current, prefer not to answer/missing) | 227 | 0.06 |
| **Modified Relative Mediterranean diet score** (Low, Medium, High, Missing) | 445 | 0.18 | **Diet score** (scored 0 to 6) | 0 | 0 |
| **Body mass index** ($kg/m^2$) | 0 | 0 | **Body mass index** ($kg/m^2$) | 1,501 | 0.4 |
| **Height** (cm) | 0 | 0 | **Height** (cm) | 1,185 | 0.3 |
| **Menopausal status*** (Premenopausal, postmenopausal, Perimenopausal, Surgical postmen (bilateral ovariectomy)) | 0 | 0 | **Had menopause*** (Yes, No, had a hysterectomy, Not sure-other reasons, prefer not to answer/missing) | 6,763 | 3.8 |
| **Sex** (Male, Female) | 0 | 0 | **Sex** (Female, Male) | 0 | 0 |

| | | | | | |
|---|---|---|---|---|---|
| **Center** (Florence, Varese, etc.) | 0 | 0 | **UK Biobank assessment centre** | 0 | 0 |
| **Any first CVD event (CHD/Stroke) (fatal/non-fatal)** (No, Yes) | 0 | 0 | **CVD Status** (No, Yes) | 0 | 0 |
| **InterAct diabetes status at completion of verification** (Non-case, Incident) | 0 | 0 | **T2D Status** (No, Yes) | 0 | 0 |
| **MET recreational and household activity** (MET-h/week) | 0 | 0 | **MET Total** (MET-h/week) | 0 | 0 |
| **Age at recruitment** (years) | 0 | 0 | **Age at recruitment** (years) | 0 | 0 |
| | | | **Average total household income before tax** (< £18,000; 18,000 to 30,999; 31,000 to 51,999; 52,000 to 100,000; >£100,000; do not know; prefer not to answer/missing) | 35,494 | 10.6 |
| | | | **Townsend deprivation index at recruitment** (scores) | 451 | 0.13 |
| | | | **Overall health rating** (Excellent, Good, Fair, Poor, Do not know, Prefer not to answer/missing | 1,224 | 0.34 |
| | | | **Sedentary behaviour (hours/day)** | 361 | 0.1 |
| | | | **Medication for cholesterol, blood pressure or diabetes** (Blood pressure medication, Cholesterol lowering medication, Insulin, None of the above, Do not know, Prefer not to answer, missing) | 181,737 | 50.9 |

*Only in women, EPIC, European Prospective Investigation into Cancer and Nutrition; MET-h/week: metabolic equivalent task hours per week; CVD, cardiovascular diseases; T2D, type 2 diabetes; UKB, UK Biobank.

**Supplementary Table 5: Baseline characteristics of the study population in EPIC by level of non-occupational physical activity (sex-specific quartiles)**

| Characteristics | Non-occupational physical activity level | | | | |
|---|---|---|---|---|---|
| | **Quartile 1** | **Quartile 2** | **Quartile 3** | **Quartile 4** | **Overall** |
| N (%) | 60,586 (25.0) | 60,593 (25.0) | 60,510 (25.0) | 60,550 (25.0) | 242,239 (100) |
| Non-occupational physical activity, MET-h/week | | | | | |
| Median (IQR) | 32.5 (21.5, 47.5) | 70.1 (50.1, 83.6) | 104.7 (76.7, 120.6) | 153.6 (130.3, 178.0) | 81.0 (48.8, 122.9) |
| Sex, n (%) | | | | | |
| Male | 23,311 (38.5) | 23,330 (38.5) | 23,257 (38.4) | 23,292 (38.5) | 93,190 (38.5) |
| Female | 37,275 (61.5) | 37,263 (61.5) | 37,253 (61.6) | 37,258 (61.5) | 149,049 (61.5) |
| Physical activity at work, n (%) | | | | | |
| Non-worker | 12,133 (20.0) | 15,131 (25.0) | 21,875 (36.2) | 32,381 (53.5) | 81,520 (33.7) |
| Sedentary occupation | 25,083 (41.4) | 22,371 (36.9) | 17,153 (28.3) | 10,334 (17.1) | 74,941 (30.9) |
| Standing occupation | 13,193 (21.8) | 13,923 (23.0) | 12,774 (21.1) | 8,815 (14.6) | 48,705 (20.1) |
| Manual work | 7,701 (12.7) | 6,727 (11.1) | 6,126 (10.1) | 5,775 (9.5) | 26,329 (10.9) |
| Heavy manual work | 1,759 (2.9) | 1,650 (2.7) | 1,654 (2.7) | 2,039 (3.4) | 7,102 (2.9) |
| Unknown | 717 (1.2) | 791 (1.3) | 928 (1.5) | 1,206 (2.0) | 3,642 (1.5) |
| Age at recruitment, years | | | | | |
| Median (IQR) | 53.0 (47.1, 58.3) | 52.8 (46.3, 58.5) | 52.8 (46.0, 59.0) | 52.9 (45.7, 59.3) | 52.9 (46.3, 58.8) |
| Height, cm | | | | | |
| Median (IQR) | 166(161, 173) | 166 (160, 173) | 166 (159, 173) | 165 (158, 173) | 166 (160, 173) |
| Body mass index, kg/m$^2$ | | | | | |
| Median (IQR) | 25.7 (23.2, 28.6) | 25.4 (23.1, 28.2) | 25.6 (23.3, 28.4) | 25.9 (23.5, 28.7) | 25.6 (23.2, 28.5) |
| Alcohol consumption, g/d | | | | | |
| Median (IQR) | 9 (2, 23) | 8 (2, 21) | 7 (1, 20) | 6 (1, 18) | 8 (1, 20) |
| Education, n (%) | | | | | |
| None | 2,381 (3.9) | 2,102 (3.5) | 4,266 (7.1) | 4,801 (7.9) | 13,550 (5.6) |
| Primary school completed | 17,886 (29.5) | 17,316 (28.6) | 18,636 (30.8) | 21,843 (36.1) | 75,681 (31.2) |
| Technical school | 17,497 (28.9) | 17,065 (28.2) | 16,002 (26.4) | 15,275 (25.2) | 65,839 (27.2) |
| Secondary school | 9,198 (15.2) | 8,757 (14.5) | 7,950 (13.1) | 7,452 (12.3) | 33,357 (13.8) |
| Longer education (incl. University) | 12,780 (21.1) | 14,272 (23.6) | 12,364 (20.4) | 9,802 (16.2) | 49,218 (20.3) |
| Missing | 844 (1.4) | 1,081 (1.8) | 1,292 (2.1) | 1,377 (2.3) | 4,594 (1.9) |
| Smoking status, n (%) | | | | | |
| Never | 24,302 (40.1) | 26,422 (43.6) | 28,126 (46.5) | 29,170 (48.2) | 108,020 (44.6) |

| | | | | | |
|---|---|---|---|---|---|
| Previous | 17,542 (29.0) | 18,356 (30.3) | 17,915 (29.6) | 17,155 (28.3) | 70,968 (29.3) |
| Current | 18,519 (30.6) | 15,622 (25.8) | 14,276 (23.6) | 14,091 (23.3) | 62,508 (25.8) |
| Missing | 223 (0.4) | 193 (0.3) | 193 (0.3) | 134 (0.2) | 743 (0.3) |
| Med. diet, n (%) | | | | | |
| Low | 15,967 (26.4) | 15,785 (26.1) | 14,627 (24.2) | 14,572 (24.1) | 60,951 (25.2) |
| Medium | 27,352 (45.1) | 28,290 (46.7) | 28,567 (47.2) | 27,229 (45.0) | 111,438 (46.0) |
| High | 17,116 (28.3) | 16,408 (27.1) | 17,220 (28.5) | 18,661 (30.8) | 69,405 (28.7) |
| Missing | 151 (0.2) | 110 (0.2) | 96 (0.2) | 88 (0.1) | 445 (0.2) |
| Country of recruitment, n (%) | | | | | |
| Italy | 12,064 (19.9) | 10,397 (17.2) | 9,475 (15.7) | 11,988 (19.8) | 43,924 (18.1) |
| Spain | 8,070 (13.3) | 7,130 (11.8) | 10,859 (17.9) | 11,592 (19.1) | 37,651 (15.5) |
| United Kingdom | 7,032 (11.6) | 8,275 (13.7) | 8,418 (13.9) | 7,935 (13.1) | 31,660 (13.1) |
| The Netherlands | 3,943 (6.5) | 6,883 (11.4) | 8,530 (14.1) | 10,500 (17.3) | 29,856 (12.3) |
| Germany | 8,137 (13.4) | 12,365 (20.4) | 12,794 (21.1) | 11,706 (19.3) | 45,002 (18.6) |
| Denmark | 21,340 (35.2) | 15,543 (25.7) | 10,434 (17.2) | 6,829 (11.3) | 54,146 (22.4) |
| Menopausal status [a], n (%) | | | | | |
| Pre-menopause | 11,005 (29.5) | 12,891 (34.6) | 13,283 (35.7) | 13,479 (36.2) | 50,658 (34.0) |
| Post-menopause | 19,187 (51.5) | 17,661 (47.4) | 17,558 (47.1) | 17,166 (46.1) | 71,572 (48.0) |
| Perimenopause | 5,612 (15.1) | 5,314 (14.3) | 5,034 (13.5) | 5,041 (13.5) | 21,001 (14.1) |
| Surgical menopause | 1,471 (3.9) | 1,397 (3.7) | 1,378 (3.7) | 1,572 (4.2) | 5,818 (3.9) |
| Use of hormones for menopause, n (%) | | | | | |
| No | 29,455 (79.0) | 30,616 (82.2) | 31,513 (84.6) | 32,328 (86.8) | 123,912 (83.1) |
| Yes | 7,300 (19.6) | 6,208 (16.7) | 5,287 (14.2) | 4,326 (11.6) | 23,121 (15.5) |
| Missing | 520 (1.4) | 439 (1.2) | 453 (1.2) | 604 (1.6) | 2,016 (1.4) |
| Ever use of oral contraceptives [a], n (%) | | | | | |
| No | 14,136 (37.9) | 14,126 (37.9) | 15,619 (41.9) | 17,826 (47.8) | 61,707 (41.4) |
| Yes | 22,835 (61.3) | 22,973 (61.7) | 21,507 (57.7) | 19,310 (51.8) | 86,625 (58.1) |
| Missing | 304 (0.8) | 164 (0.4) | 127 (0.3) | 122 (0.3) | 717 (0.5) |
| Family history of breast cancer [a], n (%) | | | | | |
| No | 7,059 (18.9) | 10,061 (27.0) | 14,794 (39.7) | 16,422 (44.1) | 48,336 (32.4) |
| Yes | 618 (1.7) | 920 (2.5) | 1,242 (3.3) | 1,309 (3.5) | 4,089 (2.7) |
| Uknown | 29,598 (79.4) | 26,282 (70.5) | 21,217 (57.0) | 19,527 (52.4) | 96,624 (64.8) |
| Age at first birth [a], n (%) | | | | | |

| | | | | | |
|---|---|---|---|---|---|
| <20 | 2,886 (7.7) | 2,631 (7.1) | 2,565 (6.9) | 2,379 (6.4) | 10,461 (7.0) |
| 20–24 | 12,526 (33.6) | 13,108 (35.2) | 13,828 (37.1) | 14,095 (37.8) | 53,557 (35.9) |
| 25–29 | 9,648 (25.9) | 10,888 (29.2) | 11,873 (31.9) | 12,991 (34.9) | 45,400 (30.5) |
| ≥ 30 | 3,756 (10.1) | 4,217 (11.3) | 4,311 (11.6) | 4,724 (12.7) | 17,008 (11.4) |
| Never pregnant | 6,672 (17.9) | 5,152 (13.8) | 3,720 (10.0) | 2,426 (6.5) | 17,970 (12.1) |
| Missing | 1,787 (4.8) | 1,267 (3.4) | 956 (2.6) | 643 (1.7) | 4,653 (3.1) |
| Breastfeeding duration [a], n (%) | | | | | |
| Never breastfed | 4,783 (12.8) | 4,878 (13.1) | 4,889 (13.1) | 4,720 (12.7) | 19,270 (12.9) |
| <6 months | 11,659 (31.3) | 12,594 (33.8) | 12,750 (34.2) | 11,725 (31.5) | 48,728 (32.7) |
| 6–11 months | 7,118 (19.1) | 6,994 (18.8) | 7,020 (18.8) | 7,339 (19.7) | 28,471 (19.1) |
| 12–23 months | 4,378 (11.7) | 4,510 (12.1) | 4,906 (13.2) | 5,725 (15.4) | 19,519 (13.1) |
| ≥ 24months | 1,283 (3.4) | 1,456 (3.9) | 1,957 (5.3) | 2,557 (6.9) | 7,253 (4.9) |
| Never pregnant | 6,672 (17.9) | 5,152 (13.8) | 3,720 (10.0) | 2,426 (6.5) | 17,970 (12.1) |
| Missing | 1,382 (3.7) | 1,679 (4.5) | 2,011 (5.4) | 2,766 (7.4) | 7,838 (5.3) |
| Parity [a], n (%) | | | | | |
| Nulliparous | 6,672 (17.9) | 5,152 (13.8) | 3,720 (10.0) | 2,426 (6.5) | 17,970 (12.1) |
| 1 | 6,458 (17.3) | 6,353 (17.0) | 5,884 (15.8) | 4,925 (13.2) | 23,620 (15.8) |
| 2 | 14,161 (38.0) | 14,919 (40.0) | 15,106 (40.5) | 14,663 (39.4) | 58,849 (39.5) |
| ≥3 | 7,884 (21.2) | 8,715 (23.4) | 10,256 (27.5) | 12,369 (33.2) | 39,224 (26.3) |
| Missing | 2,100 (5.6) | 2,124 (5.7) | 2,287 (6.1) | 2,875 (7.7) | 9,386 (6.3) |

Values are medians (interquartile range) unless otherwise stated.

[a] Only in women; Med. diet: Mediterranean diet; IQR, interquartile range; MET-h/week, metabolic equivalent task hours per week; EPIC: European Prospective Investigation into Cancer and Nutrition

**Supplementary Table 6: Baseline characteristics of the study population in UKB by levels of non-occupational physical activity (sex-specific quartiles)**

| Characteristics | Non-occupational physical activity level | | | | |
|---|---|---|---|---|---|
| | Quartile 1 | Quartile 2 | Quartile 3 | Quartile 4 | Overall |
| N (%) | 89,164 (25.0) | 89,163 (25.0) | 89,162 (25.0) | 89,162 (25.0) | 356,651 (100) |
| Total physical activity, MET-h/week | | | | | |
| Median (IQR) | 11.3 (4.2, 28.5) | 17.0 (11.0, 36.9) | 29.4 (21.6, 44.9) | 67.1 (47.3, 100.1) | 29.9 (13.7, 59.6) |
| Non-occupational physical activity, MET-h/week | | | | | |
| Median (IQR) | 2.8 (1.1, 4.4) | 10.7 (8.5, 13.3) | 23.8 (19.7, 29.2) | 60.2 (45.8, 88.8) | 16.2 (6.4, 36.1) |
| Sedentary behaviour, hours/day, n (%) | | | | | |
| 0-3 | 22,108 (24.8) | 25,276 (28.3) | 25,641 (28.8) | 24,856 (27.9) | 97,881 (27.4) |
| 4-5 | 32,794 (36.8) | 34,750 (39.0) | 35,435 (39.7) | 36,367 (40.8) | 139,346 (39.1) |
| 6-7 | 19,133 (21.5) | 18,132 (20.3) | 18,366 (20.6) | 19,524 (21.9) | 75,155 (21.1) |
| 8-24 | 15,083 (16.9) | 10,929 (12.3) | 9,614 (10.8) | 8,282 (9.3) | 43,908 (12.3) |
| Missing | 46 (0.1) | 76 (0.1) | 106 (0.1) | 133 (0.1) | 361 (0.1) |
| Sex, n (%) | | | | | |
| Male | 43,736 (49.1) | 43,735 (49.1) | 43,735 (49.1) | 43,735 (49.1) | 174,941 (49.1) |
| Female | 45,428 (50.9) | 45,428 (50.9) | 45,427 (50.9) | 45,427 (50.9) | 181,710 (50.9) |
| Employment, n (%) | | | | | |
| Unemployed | 779 (0.9) | 1,183 (1.3) | 1,755 (2.0) | 2,608 (2.9) | 6,325 (1.8) |
| Retired | 9,249 (10.4) | 18,151 (20.4) | 30,714 (34.4) | 53,109 (59.6) | 111,223 (31.2) |
| Unable to work because of sickness or disability | 2,780 (3.1) | 2,032 (2.3) | 2,032 (2.3) | 2,677 (3.0) | 9,521 (2.7) |
| Looking after home and/or family | 575 (0.6) | 1,263 (1.4) | 2,427 (2.7) | 4,514 (5.1) | 8,779 (2.5) |
| Full or part-time student | 99 (0.1) | 208 (0.2) | 337 (0.4) | 441 (0.5) | 1,085 (0.3) |
| Doing unpaid or voluntary work | 140 (0.2) | 260 (0.3) | 447 (0.5) | 754 (0.8) | 1,601 (0.4) |
| In paid employment or self-employed | 75,205 (84.3) | 65,591 (73.6) | 50,668 (56.8) | 23,750 (26.6) | 215,214 (60.3) |
| Missing | 184 (0.2) | 269 (0.3) | 466 (0.5) | 766 (0.9) | 1,685 (0.5) |
| Age at assessment, years | | | | | |
| Median (IQR) | 54.7 (48.2, 60.5) | 55.7 (48.8, 61.7) | 57.9 (49.9, 63.4) | 61.8 (54.6, 65.7) | 57.5 (49.8, 63.2) |
| Height, cm | | | | | |
| Median (IQR) | 169 (162, 176) | 169 (163, 176) | 169 (163, 176) | 168 (162, 175) | 169 (162, 176) |
| Body mass index, kg/m$^2$ | | | | | |
| Median (IQR) | 27.5 (24.6, 31.0) | 26.7 (24.1, 29.7) | 26.3 (23.9, 29.2) | 26.2 (23.8, 29.0) | 26.6 (24.1, 29.7) |
| Townsend deprivation, score | | | | | |

| | | | | | |
|---|---|---|---|---|---|
| Median (IQR) | -1.8 (-3.4, 1.1) | -2.3 (-3.7, 0.3) | -2.4 (-3.8, 0.0) | -2.4 (-3.8, 0.0) | -2.2 (-3.7, 0.3) |
| Qualifications, n (%) | | | | | |
| CSEs or equivalent | 6,059 (6.8) | 4,535 (5.1) | 4,064 (4.6) | 3,740 (4.2) | 18,398 (5.2) |
| O levels/GCSEs or equivalent | 19,669 (22.1) | 18,391 (20.6) | 18,290 (20.5) | 18,907 (21.2) | 75,257 (21.1) |
| A levels/AS levels or equivalent | 10,605 (11.9) | 11,251 (12.6) | 10,899 (12.2) | 9,594 (10.8) | 42,349 (11.9) |
| NVQ or HND or HNC or equivalent | 6,411 (7.2) | 5,421 (6.1) | 5,379 (6.0) | 6,071 (6.8) | 23,282 (6.5) |
| College or University degree | 30,070 (33.7) | 35,527 (39.8) | 34,758 (39.0) | 28,326 (31.8) | 128,681 (36.1) |
| Others [a] | 4,146 (4.6) | 4,083 (4.6) | 4,442 (5.0) | 5,224 (5.9) | 17,895 (5.0) |
| None of the above | 11,656 (13.1) | 9,525 (10.7) | 10,867 (12.2) | 16,474 (18.5) | 48,522 (13.6) |
| Missing | 548 (0.6) | 430 (0.5) | 463 (0.5) | 826 (0.9) | 2,267 (0.6) |
| Smoking status, n (%) | | | | | |
| Never | 46163 (55.9) | 48042 (57.3) | 47463 (56.5) | 45937 (54.6) | 187605 (56.1) |
| Previous | 26785 (32.5) | 28025 (33.4) | 28950 (34.5) | 29160 (34.6) | 112920 (33.7) |
| Current | 9369 (11.4) | 7629 (9.1) | 7412 (8.8) | 8885 (10.6) | 33295 (10.0) |
| Missing | 209 (0.3) | 187 (0.2) | 181 (0.2) | 199 (0.2) | 776 (0.2) |
| Alcohol status, n (%) | | | | | |
| Never | 48,624 (54.5) | 50,511 (56.7) | 49,788 (55.8) | 47,729 (53.5) | 196,652 (55.1) |
| Previous | 28,691 (32.2) | 29,871 (33.5) | 31,432 (35.3) | 33,303 (37.4) | 123,297 (34.6) |
| Current | 11,586 (13.0) | 8,608 (9.7) | 7,743 (8.7) | 7,888 (8.8) | 35,825 (10.0) |
| Missing | 263 (0.3) | 173 (0.2) | 199 (0.2) | 242 (0.3) | 877 (0.2) |
| Healthy diet Score [a] | | | | | |
| 6, healthier | 2,019 (2.3) | 2,299 (2.6) | 2,572 (2.9) | 2,893 (3.2) | 9,783 (2.7) |
| 5 | 14,946 (16.8) | 17,194 (19.3) | 18,582 (20.8) | 20,030 (22.5) | 70,752 (19.8) |
| 4 | 34,415 (38.6) | 37,713 (42.3) | 38,816 (43.5) | 39,376 (44.2) | 150,320 (42.1) |
| 3 | 25,627 (28.7) | 23,851 (26.7) | 22,488 (25.2) | 21,181 (23.8) | 93,147 (26.1) |
| 2 | 9,506 (10.7) | 6,724 (7.5) | 5,675 (6.4) | 4,760 (5.3) | 26,665 (7.5) |
| 1 | 2,307 (2.6) | 1,235 (1.4) | 929 (1.0) | 825 (0.9) | 5,296 (1.5) |
| 0, unhealthier | 344 (0.4) | 147 (0.2) | 100 (0.1) | 97 (0.1) | 688 (0.2) |
| Menopause [c], n (%) | | | | | |
| No | 15,143 (33.3) | 14,212 (31.3) | 11,936 (26.3) | 7,098 (15.6) | 48,389 (26.6) |
| Yes | 23,201 (51.1) | 24,986 (55.0) | 27,262 (60.0) | 32,320 (71.1) | 107,769 (59.3) |
| Had a hysterectomy | 4,805 (10.6) | 4,273 (9.4) | 4,590 (10.1) | 5,121 (11.3) | 18,789 (10.3) |

| | | | | | |
|---|---|---|---|---|---|
| Missing | 2,279 (5.0) | 1,957 (4.3) | 1,639 (3.6) | 888 (2.0) | 6,763 (3.7) |
| Ever use of HRT [c], n (%) | | | | | |
| No | 31,263 (68.8) | 30,718 (67.6) | 28,695 (63.2) | 24,724 (54.4) | 115,400 (63.5) |
| Yes | 13,999 (30.8) | 14,578 (32.1) | 16,633 (36.6) | 20,600 (45.3) | 65,810 (36.2) |
| Missing | 166 (0.4) | 132 (0.3) | 99 (0.2) | 103 (0.2) | 500 (0.3) |
| Ever use of oral contraceptives [c], n (%) | | | | | |
| No | 6,606 (14.5) | 6,746 (14.8) | 7,969 (17.5) | 10,181 (22.4) | 31,502(17.3) |
| Yes | 38,709 (85.2) | 38,594 (85.0) | 37,362 (82.2) | 35,145 (77.4) | 149,810 (82.4) |
| Unknown | 113 (0.2) | 88 (0.2) | 96 (0.3) | 101 (0.2) | 398 (0.3) |
| Age at first birth [c], n (%) | | | | | |
| <20 | 3,222 (7.1) | 2,375 (5.2) | 2,488 (5.5) | 2,979 (6.6) | 11,064 (6.1) |
| 20–24 | 9,450 (20.8) | 8,881 (19.5) | 9,712 (21.4) | 12,010 (26.4) | 40,053 (22.0) |
| 25–29 | 10,681 (23.5) | 11,859 (26.1) | 12,127 (26.7) | 12,052 (26.5) | 46,719 (25.7) |
| ≥30 | 5,778 (12.7) | 6,555 (14.4) | 6,144 (13.5) | 4,923 (10.8) | 23,400 (12.9) |
| Never pregnant | 13,446 (29.6) | 13,142 (28.9) | 12,622 (27.8) | 11,449 (25.2) | 50,659 (27.9) |
| Unknown | 2,851 (6.3) | 2,616 (5.8) | 2,334 (5.1) | 2,014 (4.4) | 9,815 (5.4) |

MET-h/week, metabolic equivalent task hours per week; HRT: hormonal replacement therapy; IQR: interquartile range; AS: Advanced Subsidiary; GCSEs: General Certificate of Secondary Education; CSEs: Certificate of Secondary Education; NVQs: National Vocational Qualifications; HNDs: Higher National Diplomas; and HNCs: Higher National Certificates.

[a] Refers to other professions such as nursing, teaching.

[b] Scores are arranged from the healthier (6) to unhealthier (0)—Healthy diet score was calculated based on consumption of commonly eaten food groups following recommendations.

[c] Only in women.

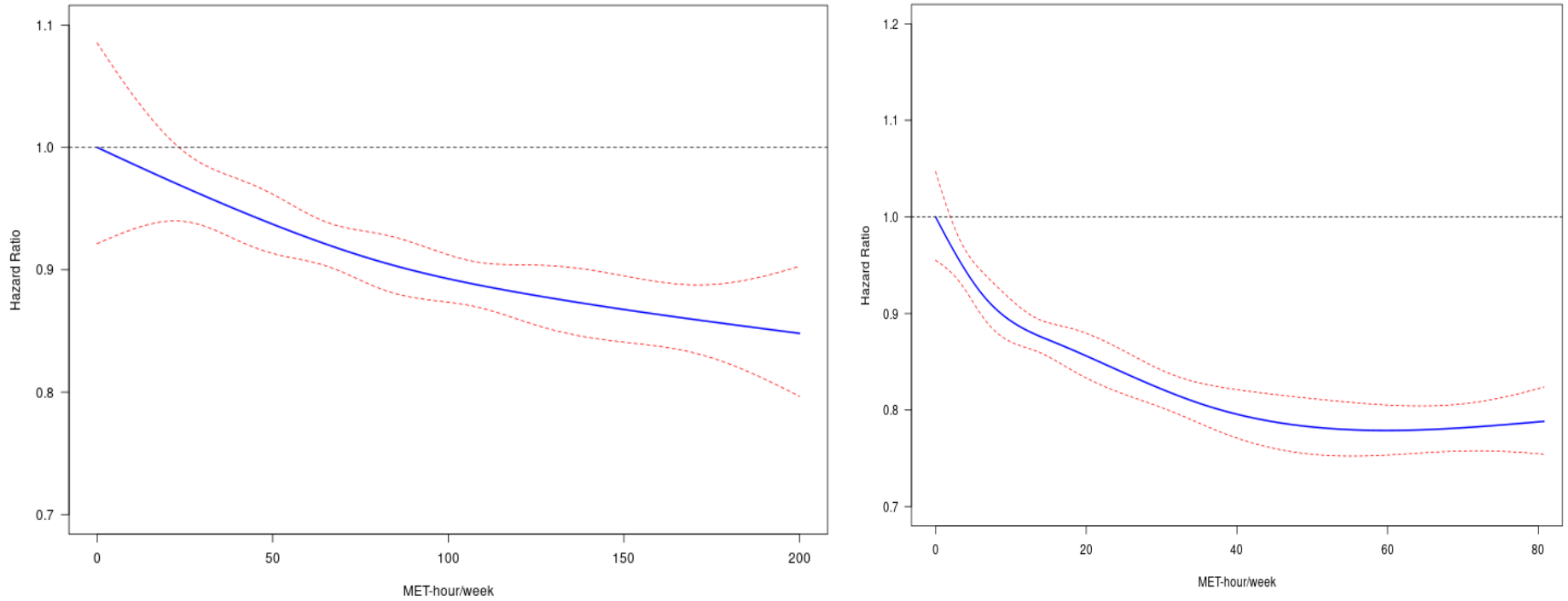
**Supplementary Table 7: The distribution of physical activity-related cancers and all cancers recorded in EPIC and UK Biobank.**

| Types of cancer | EPIC | | UKB | |
|---|---|---|---|---|
| | Frequency | Percentage | | |
| Breast cancer | 6,772 | 22.4 | 6,285 | 17.8 |
| Lung cancer | 2,648 | 8.8 | 2,452 | 6.9 |
| Colon cancer | 2,582 | 8.5 | 2,642 | 7.5 |
| Rectal cancer | 1,397 | 4.5 | 1,369 | 3.9 |
| Oesophageal adenocarcinoma | 155 | 0.5 | 449 | 1.3 |
| Bladder cancer | 1,250 | 4.1 | 778 | 2.2 |
| Endometrial cancer | 998 | 3.3 | 971 | 2.7 |
| Head and neck cancer | 833 | 2.8 | 867 | 2.4 |
| Kidney cancer | 770 | 2.5 | 981 | 2.8 |
| Multiple myeloma | 375 | 1.2 | 606 | 1.7 |
| Myeloid leukemia | 260 | 0.9 | 300 | 0.8 |
| Liver cancer | 301 | 1.0 | 403 | 1.1 |
| Gastric cardia cancer | 170 | 0.6 | 193 | 0.5 |
| Small intestine cancer | 83 | 0.3 | 165 | 0.5 |
| Gallbladder cancer | 65 | 0.2 | 71 | 0.2 |
| Other cancers | 11,552 | 38.2 | 16,860 | 47.6 |
| **Total number of cancer cases** | **30,211** | **100.0%** | **35,392** | **100.0%** |

Cancers categorized as "other cancers" refer to those cancers not included in the physical activity-related cancers. EPIC, European Prospective Investigation into Cancer and Nutrition; UKB, UK Biobank.

**Supplementary Figure 3: The association between non-occupational physical activity and risk of physical activity-related cancers in the fully adjusted model of EPIC (a) and UKB (b) cohorts.**

a) b)



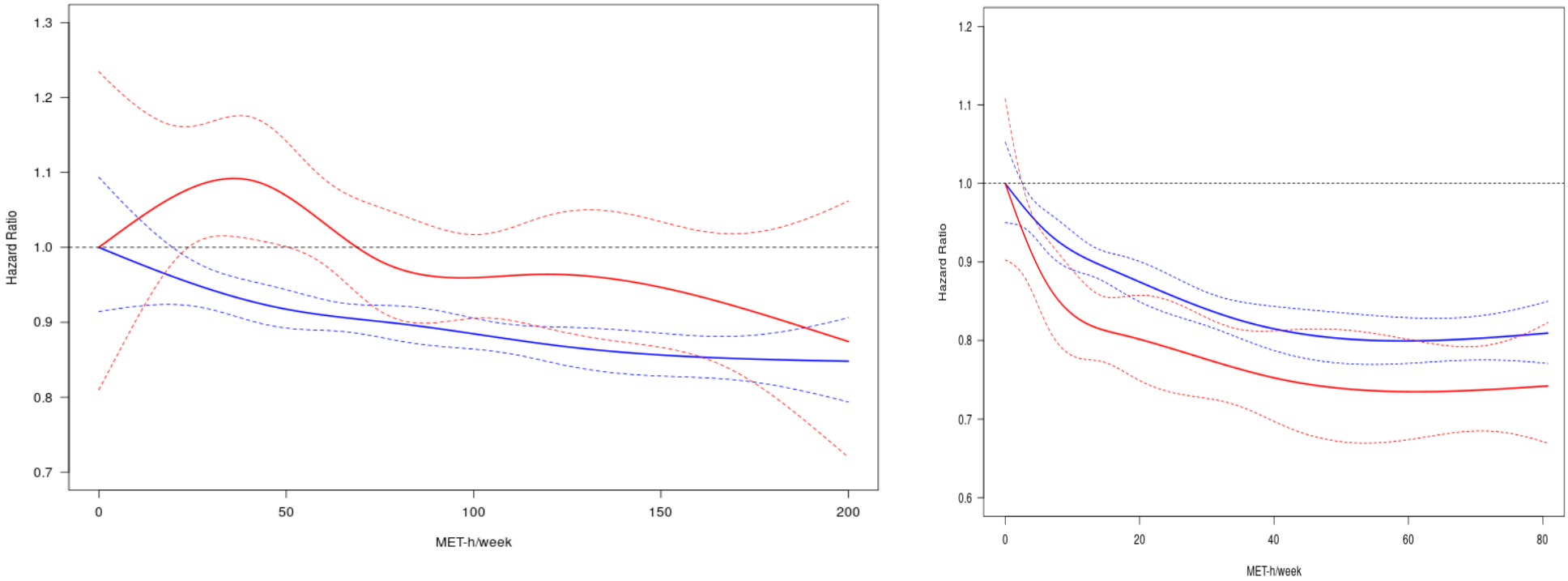

a) EPIC study; b) UK Biobank. The solid line represents the adjusted HRs, and the broken lines indicate the 95% CIs from the Cox regression with non-occupational physical activity (NOPA) modelled as a natural spline with three knots positioned at the 25$^{th}$, 50$^{th}$, and 75$^{th}$ percentiles of NOPA, measured in MET-hour/week. Reference = 0 MET-h/week. Evidence of non-linearity was assessed using a likelihood ratio test comparing the spline model with a linear model (p=0.706 in EPIC and p<0.001 in UKB).

The models were stratified by age (5-year categories), sex, and recruitment centre, and adjusted for education, BMI, height, smoking status, alcohol consumption, diet quality, occupational PA/employment, menopause status, and menopausal hormone use.

Abbreviations: BMI, body mass index; CI, confidence interval; EPIC, European Prospective Investigation into Cancer and Nutrition; MET-h/week, metabolic equivalent task hours per week; UKB, UK Biobank.

**Supplementary Figure 4: The association between non-occupational physical activity and risk of physical activity-related cancers in the fully adjusted model of EPIC (a) and UK Biobank (b) by cardiometabolic disease status.**

a) b)



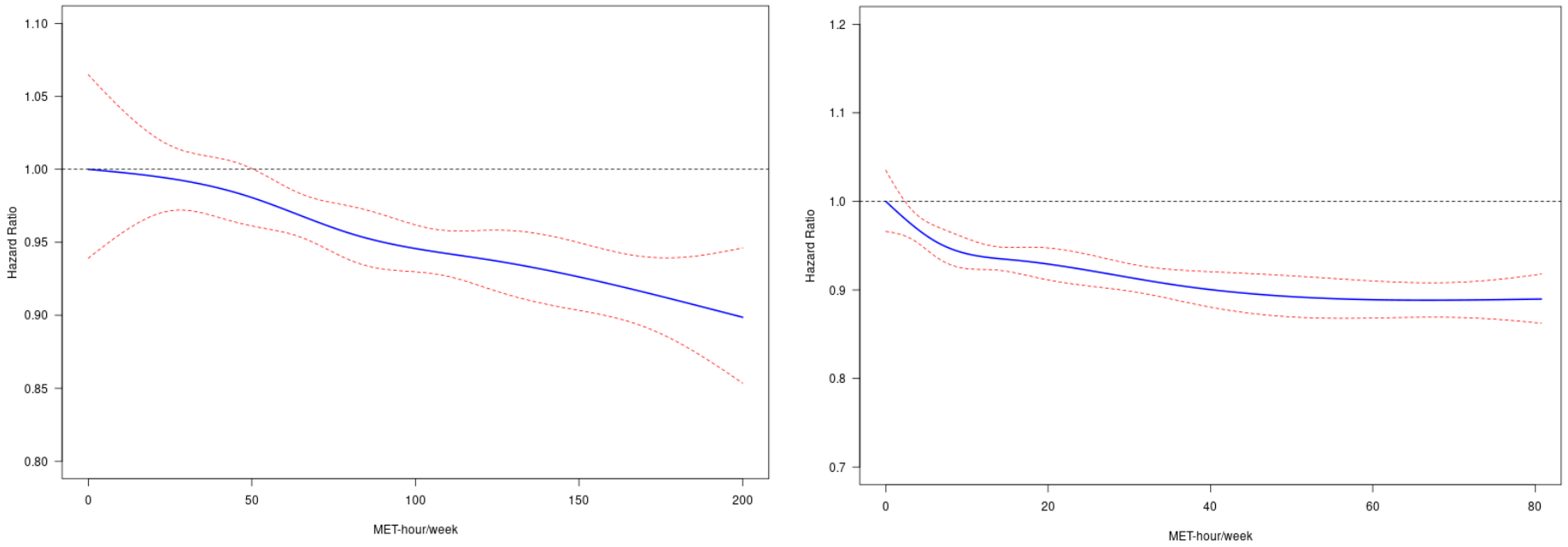

a) EPIC study; b) UK Biobank. The solid blue line represents the adjusted HRs for participants without cardiometabolic disease, while the red lines represent those with cardiometabolic disease, and the broken lines indicate the 95% CIs from the Cox regression with non-occupational physical activity (NOPA) modelled as a natural spline with three knots positioned at the 25$^{th}$, 50$^{th}$, and 75$^{th}$ percentiles of NOPA, measured in MET-hour/week. Reference = 0 MET-h/week.

The models were stratified by age (5-year categories), sex, and recruitment centre, and adjusted for education, BMI, height, smoking status, alcohol consumption, diet quality, occupational PA/employment, menopause status, and menopausal hormone use.

Abbreviations: BMI, body mass index; CI, confidence interval; CMD, T2D and/or CVD; CVD, cardiovascular disease; EPIC, European Prospective Investigation into Cancer and Nutrition; MET-h/week, metabolic equivalent task hours per week; T2D, type 2 diabetes; UKB, UK Biobank.

**Supplementary Figure 5: The association between non-occupational physical activity and risk of all cancers in the fully adjusted model of EPIC (a) and UKB (b) cohorts.**

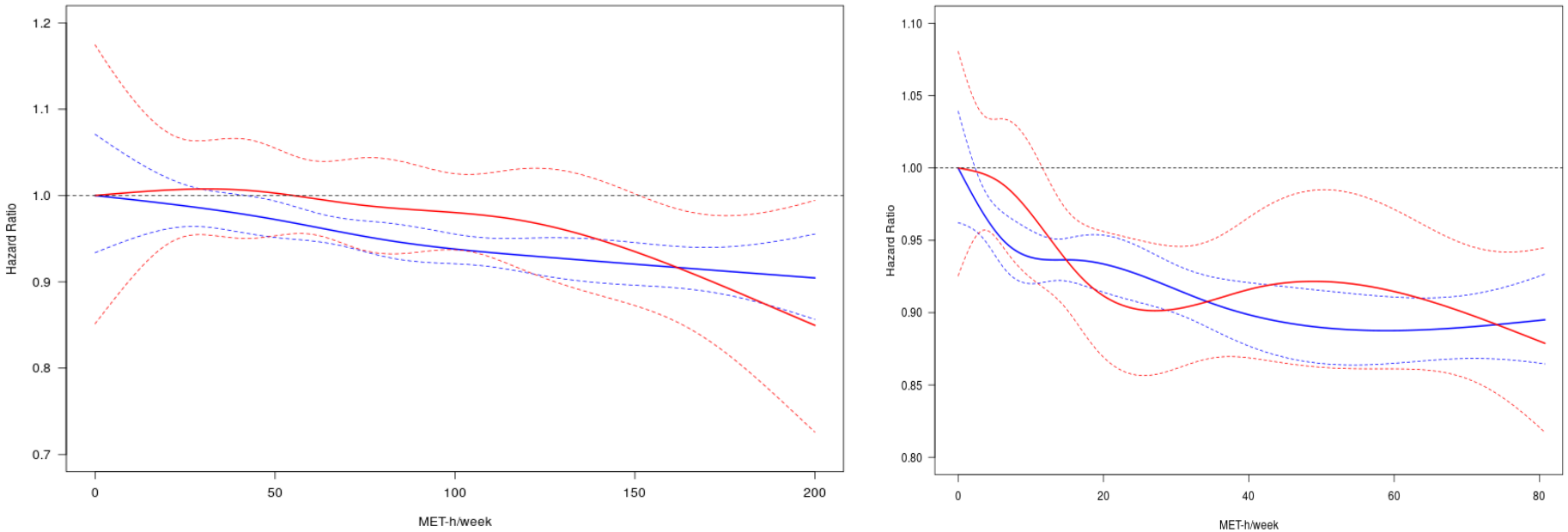
a) b)




a) EPIC study; b) UK Biobank. The solid line represents the adjusted HRs, and the broken lines indicate the 95% CIs from the Cox regression with non-occupational physical activity (NOPA) modelled as a natural spline with three knots positioned at the 25th, 50th, and 75th percentiles of NOPA, measured in MET-hour/week. Reference = 0 MET-h/week. Evidence of non-linearity was assessed using a likelihood ratio test comparing the spline model with a linear model (p=0.95 in EPIC and p=0.032 in UKB).
The models were stratified by age (5-year categories), sex, and recruitment centre, and adjusted for education, BMI, height, smoking status, alcohol consumption, diet quality, occupational PA/employment, menopause status, and menopausal hormone use.
Abbreviations: BMI, body mass index; CI, confidence interval; EPIC, European Prospective Investigation into Cancer and Nutrition; MET-h/week, metabolic equivalent task hours per week; UKB, UK Biobank.

**Supplementary Figure 6: The association between non-occupational physical activity and risk of all cancers in the fully adjusted model of EPIC (a) and UKB (b) by cardiometabolic disease status.**

a) b)

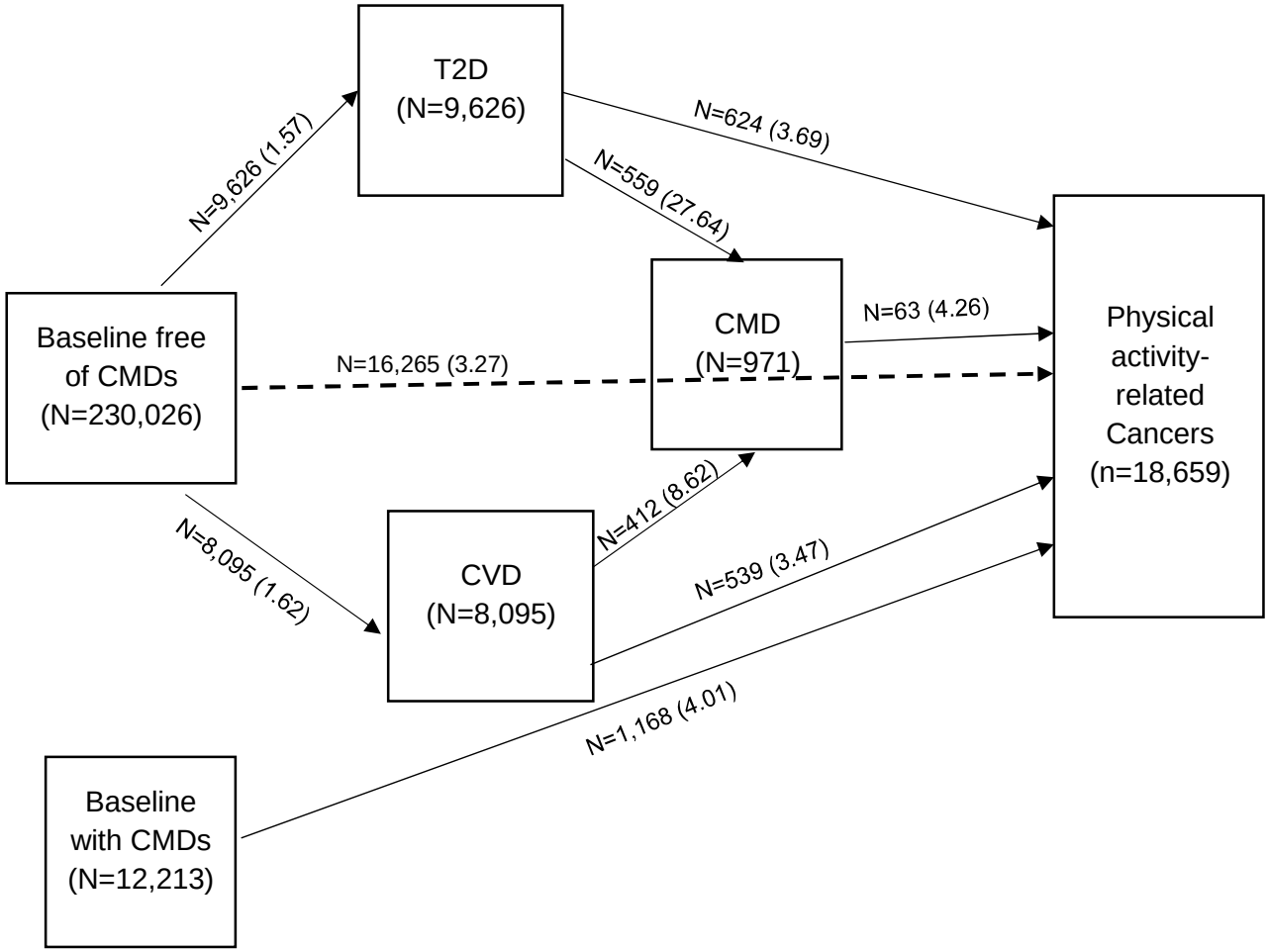



a) EPIC study; b) UK Biobank. The solid blue line represents the adjusted HRs for participants without cardiometabolic disease, while the red lines represent those with cardiometabolic disease, and the broken lines indicate the 95% CIs from the Cox regression with non-occupational physical activity (NOPA) modelled as a natural spline with three knots positioned at the 25$^{th}$, 50$^{th}$, and 75$^{th}$ percentiles of NOPA, measured in MET-hour/week. Reference = 0 MET-h/week.

The models were stratified by age (5-year categories), sex, and recruitment centre, and adjusted for education, BMI, height, smoking status, alcohol consumption, diet quality, occupational PA/employment, menopause status, and menopausal hormone use.

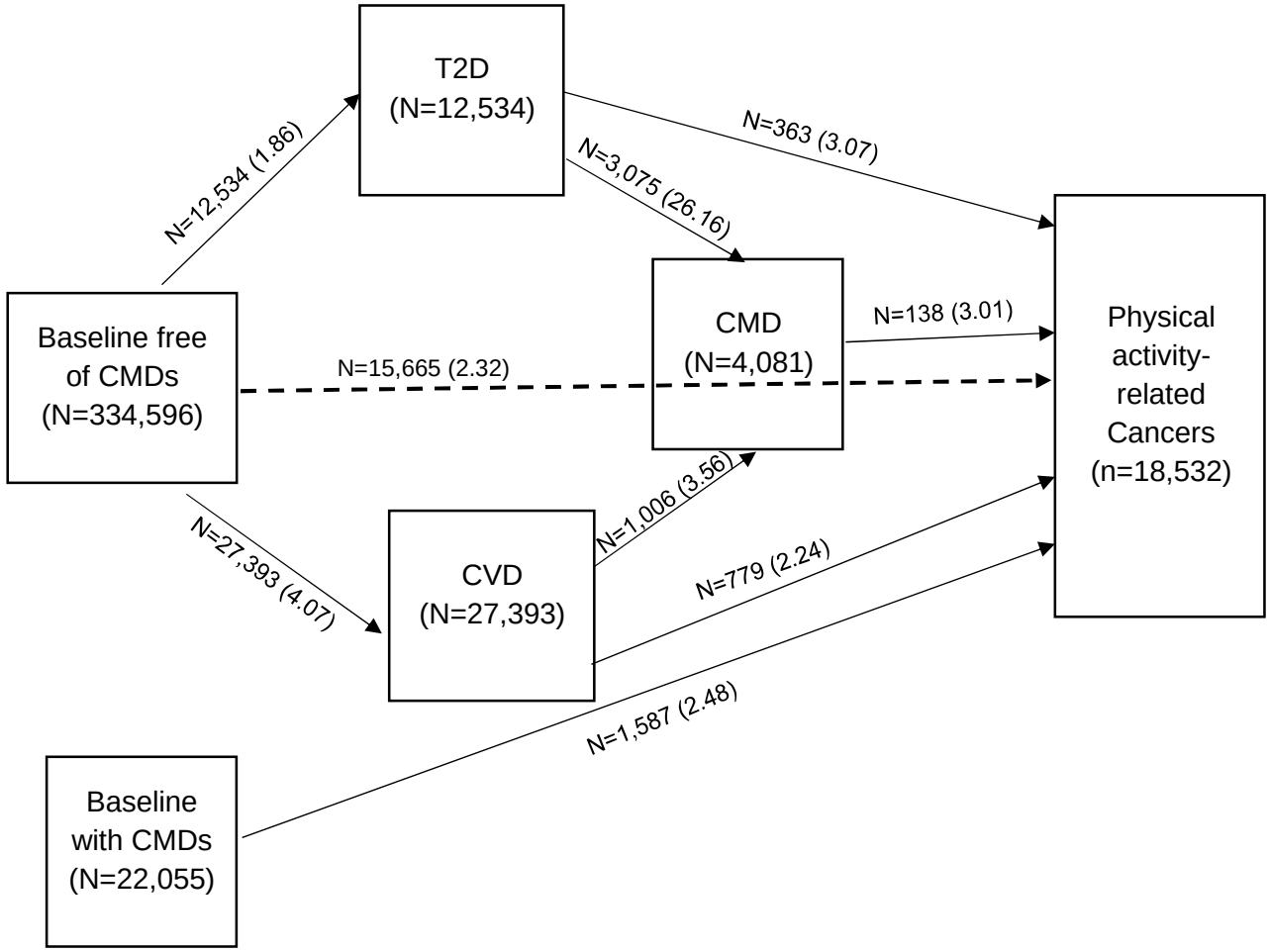
Abbreviations: BMI, body mass index; CI, confidence interval; CMD: T2D and/or CVD; CVD, cardiovascular disease; EPIC, European Prospective Investigation into Cancer and Nutrition; MET-h/week, metabolic equivalent task hours per week; T2D, type 2 diabetes; UKB, UK Biobank.

**Supplementary Figure 7: Transitions from baseline to physical activity-related cancers, CVD, T2D, and subsequent transition from T2D, and CVD to cancer in EPIC.**




Transitions from baseline to physical activity-related cancers, type 2 diabetes (T2D), and cardiovascular disease (CVD).
Physical activity-related cancers refer to a composite outcome of breast, adenocarcinoma of the oesophagus, endometrial, colon, kidney, gastric cardia, bladder, gallbladder, liver, lung, small intestine, multiple myeloma, myeloid leukaemia, rectal, and head and neck cancer.
The state-specific number of events is reported in boxes, and the transition-specific number of events and age-standardized incidence rates per 1000 person-years (within brackets) are reported on the arrows. Baseline CMDs refer to having CVD, T2D, or both before recruitment, with counts of 4615, 7007, and 591, respectively. ASIRs used the WHO 2000-2025 standard (9) via direct age-standardization (0–<40, 40–<45, 45–<50, 50–<55, 55–<60, 60–<65, 65–<70, ≥70 years) with Lexis expansion. Incident T2D/CVD is defined only if it occurs before cancer diagnosis.
Abbreviations: CMD; cardiometabolic disease (T2D and/or CVD); CVD, cardiovascular disease; EPIC, European Prospective Investigation into Cancer and Nutrition; T2D, type 2 diabetes.

**Supplementary Figure 8: Transitions from baseline to physical activity-related cancers, CVD, T2D, and subsequent transition from T2D, and CVD to cancer in UKB.**




Transitions from baseline to physical activity (PA) related cancers, T2D, and CVD.
PA-related cancer refers to breast, adenocarcinoma of the oesophagus, endometrial, colon, kidney, gastric cardia, bladder, gallbladder, liver, lung, small intestine, multiple myeloma, myeloid leukaemia, rectal, and head and neck cancer. Deaths were censored and not modelled as a separate outcome.
The state-specific number of events is reported in boxes, and the transition-specific number of events and age-standardized incidence rates (ASIRs) per 1000 person-years (within brackets) are reported in arrows. Baseline CMDs refer to having CVD, T2D, or both before recruitment, with counts of 16270, 3689, and 2096, respectively. ASIRs used the WHO 2000-2025 standard (9) via direct age-standardization (0–<40, 40–<45, 45–<50, 50–<55, 55–<60, 60–<65, 65–<70, ≥70 years) with Lexis expansion. Incident T2D/CVD is defined only if it occurs before cancer diagnosis.
Abbreviations: CMD, cardiometabolic disease (i.e., T2D and/or CVD); CVD, cardiovascular disease; T2D, type 2 diabetes; UKB, UK Biobank.

**Supplementary Table 8: Associations between non-occupational physical activity (per 1 SD increase in MET-h/week[a]) and the risk of all cancers combined by cardiometabolic disease status.**

| Models | EPIC | | | | | | | UKB | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | N | Cases | HR | 95% CI | p1 | p2 | p3 | N | Cases | HR | 95% CI | p1 | p2 | p3 |
| Overall [4] | 242239 | 30194 | 0.972 | 0.959, 0.986 | <0.001 | | | 356651 | 35392 | 0.972 | 0.961, 0.984 | <0.001 | | |
| Overall Adj T2D and CVD[5] | 242239 | 30194 | 0.973 | 0.960, 0.986 | <0.001 | | | 356651 | 35392 | 0.973 | 0.962, 0.984 | <0.001 | | |
| Without T2D[6] | 224172 | 27860 | 0.973 | 0.959, 0.987 | <0.001 | | | 335470 | 33548 | 0.971 | 0.96, 0.982 | <0.001 | | |
| With T2D[6] | 18067 | 2334 | 0.972 | 0.931, 1.015 | 0.192 | 0.952 | 0.952 | 21181 | 1844 | 1.008 | 0.965, 1.053 | 0.72 | 0.099 | 0.101 |
| Without CVD[6] | 227735 | 28230 | 0.973 | 0.96, 0.987 | <0.001 | | | 306864 | 30872 | 0.975 | 0.963, 0.987 | <0.001 | | |
| With CVD[6] | 14504 | 1964 | 0.968 | 0.923, 1.015 | 0.180 | 0.827 | 0.827 | 49787 | 4520 | 0.963 | 0.937, 0.99 | 0.007 | 0.435 | 0.435 |
| Without CMD[6] | 212326 | 26236 | 0.972 | 0.958, 0.987 | <0.001 | | | 294705 | 29768 | 0.974 | 0.962, 0.986 | <0.001 | | |
| With CMD[6] | 29913 | 3958 | 0.976 | 0.944, 1.009 | 0.159 | 0.820 | 0.820 | 61946 | 5624 | 0.967 | 0.943, 0.991 | 0.007 | 0.568 | 0.568 |

[a] One SD = 51.4 MET-h/week and 34.0 MET-h/week in EPIC and in UK Biobank, respectively.

[1] p-values for the association (from Wald tests in Cox proportional hazards models).

[2] p-values for local interaction tests (from the full models including interaction terms).

[3] p-value for the global interaction test (from the likelihood ratio test comparing models with and without interaction).

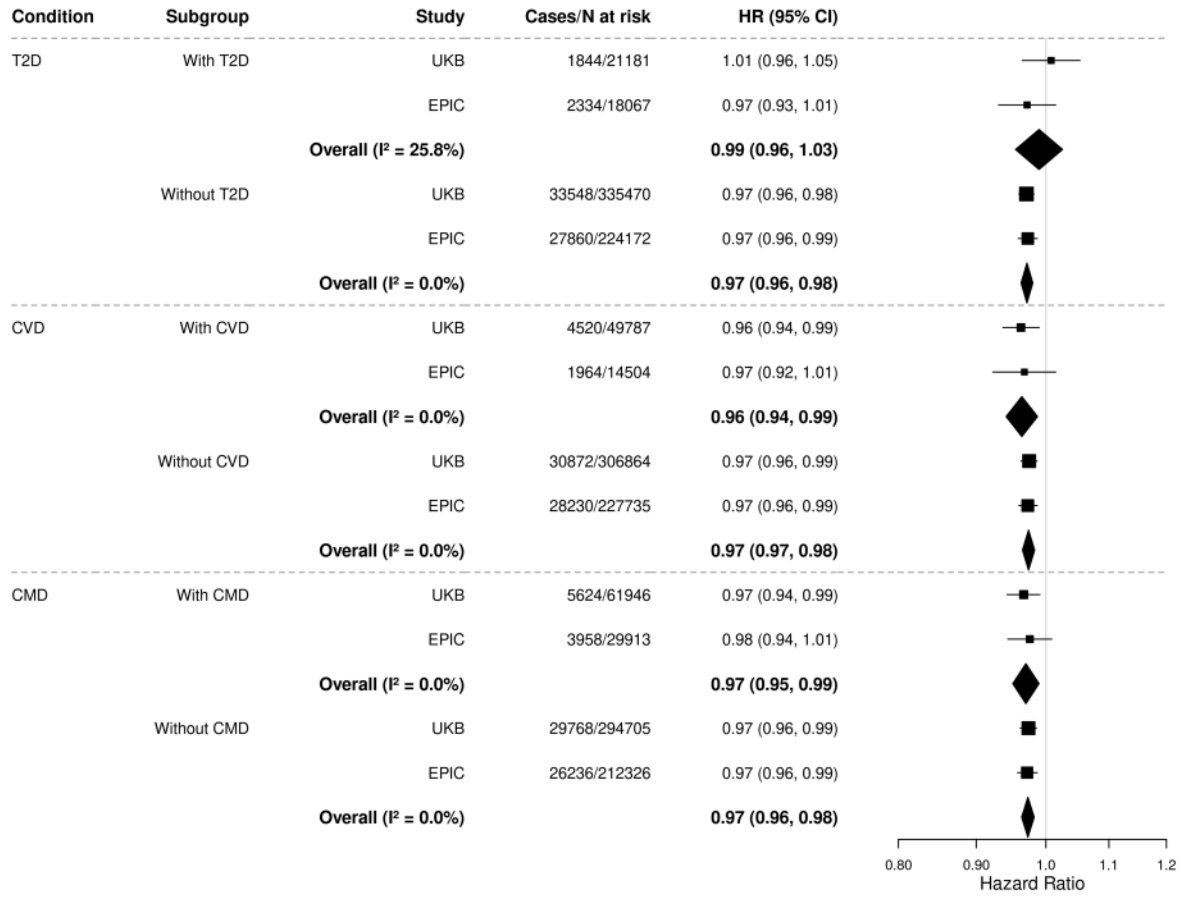
[4] Model 1: adjusted for education, BMI, height, smoking status, alcohol consumption, diet quality, occupational PA/employment, menopause status, menopausal hormone use, and stratified by age (5-year categories), sex, and recruitment centre.

[5] Model 2: further adjusted for T2D and CVD, and the duration of these comorbidities.

[6] Model 3: further including interaction terms between NOPA and T2D, CVD, and CMD (adjusted multiplicative interaction computed from the full model with interaction). All statistical tests were two-sided. p-values smaller than 0.001 are shown as '<0.001' for readability.

Abbreviations: BMI, body mass index, CI, confidence interval; CMD, cardiometabolic disease (T2D and/or CVD); CVD, cardiovascular disease; EPIC, European Prospective Investigation into Cancer and Nutrition; HR, hazard ratio; MET-h/week, metabolic equivalent task hours per week; NOPA, non-occupational physical activity, SD, standard deviation; T2D, type 2 diabetes; UKB, UK Biobank.

**Supplementary Figure 9: Association between non-occupational physical activity (per 1 SD increase in MET-h/week) and the risk of all cancers by cardiometabolic disease status.**



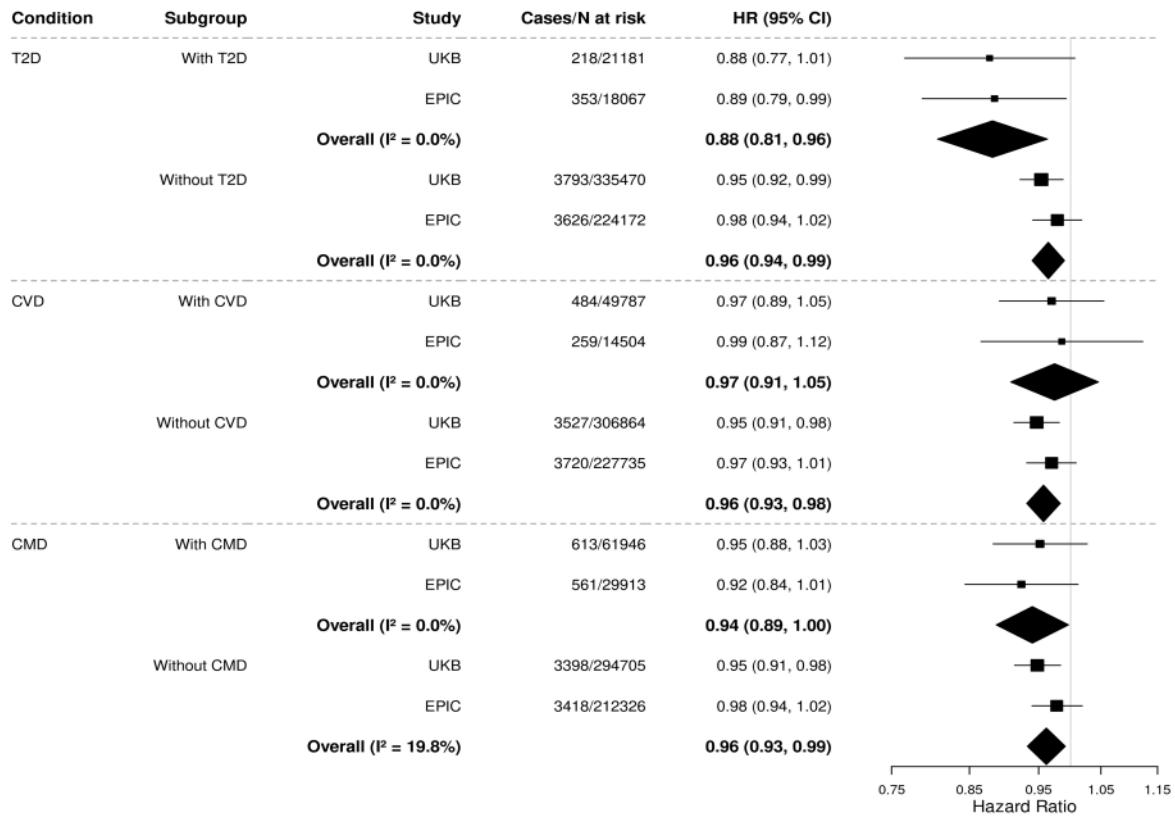

One SD = 51.4 MET-h/week and 34.0 MET-h/week in EPIC and UKB, respectively.
$I^2$: The proportion of total variability due to between-study heterogeneity from random effects meta-analysis.
The models were stratified by age (5-year categories), sex, and recruitment centre, and adjusted for education, BMI, height, smoking status, alcohol consumption, diet quality, occupational PA/employment, menopause status, menopausal hormone use, CVD and T2D (modelled as binary time-varying variables) and time since diagnosis of CVD and T2D, and interaction term between physical activity and each condition (T2D, CVD, and combined) in each model. Hazard ratios for each cohort were estimated using multivariable Cox proportional hazards models. The overall estimates (in bold) were obtained using a random-effects meta-analysis. All statistical tests were two-sided. The measure of centre of the diamonds or the squares represents the point estimates of hazard ratios, and the error bars represent 95% confidence intervals.
Abbreviations: BMI, body mass index; CI, confidence interval; CMD, cardiometabolic disease (T2D and/or CVD); CVD, cardiovascular disease; EPIC, European Prospective Investigation into Cancer and Nutrition; HR, hazard ratio; MET-h/week, metabolic equivalent task hours per week; SD, standard deviation; T2D, type 2 diabetes; UKB, UK Biobank.

**Supplementary Table 9: Associations between non-occupational physical activity (per 1 SD increase in MET-h/week[a]) and the risk of colorectal and breast cancer by cardiometabolic disease status.**

| Outcomes | Models | EPIC | | | | | | | UKB | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | N | Cases | HR | 95% CI | p1 | p2 | p3 | N | Cases | HR | 95% CI | p1 | p2 | p3 |
| Colorectal cancer | Overall [4a] | 242239 | 3979 | 0.970 | 0.934, 1.008 | 0.121 | | | 356651 | 4011 | 0.950 | 0.919, 0.983 | 0.003 | | |
| | Overall, Adj T2D and CVD[5] | 242239 | 3979 | 0.971 | 0.934, 1.009 | 0.128 | | | 356651 | 4011 | 0.950 | 0.918, 0.983 | 0.003 | | |
| | Without T2D6 | 224172 | 3626 | 0.979 | 0.941, 1.018 | 0.292 | | | 335470 | 3793 | 0.954 | 0.922, 0.988 | 0.008 | | |
| | With T2D6 | 18067 | 353 | 0.885 | 0.788, 0.993 | 0.036 | 0.092 | 0.089 | 21181 | 218 | 0.878 | 0.766, 1.007 | 0.062 | 0.242 | 0.235 |
| | Without CVD[6] | 227735 | 3720 | 0.970 | 0.932, 1.009 | 0.124 | | | 306864 | 3527 | 0.947 | 0.913, 0.982 | 0.003 | | |
| | With CVD[6] | 14504 | 259 | 0.986 | 0.866, 1.123 | 0.834 | 0.727 | 0.726 | 49787 | 484 | 0.970 | 0.892, 1.055 | 0.477 | 0.588 | 0.589 |
| | Without CMD[6] | 212326 | 3418 | 0.978 | 0.94, 1.019 | 0.291 | | | 294705 | 3398 | 0.948 | 0.914, 0.984 | 0.004 | | |
| | With CMD[6] | 29913 | 561 | 0.924 | 0.844, 1.012 | 0.089 | 0.242 | 0.239 | 61946 | 613 | 0.952 | 0.883, 1.027 | 0.205 | 0.919 | 0.919 |
| Breast cancer | Overall [4b] | 149049 | 6747 | 0.975 | 0.948, 1.004 | 0.086 | | | 172019 | 5921 | 0.952 | 0.924, 0.982 | 0.002 | | |
| | Overall Adj T2D and CVD[5] | 149049 | 6747 | 0.975 | 0.948, 1.004 | 0.086 | | | 172019 | 5921 | 0.953 | 0.924, 0.982 | 0.002 | | |
| | Without T2D[6] | 140189 | 6449 | 0.973 | 0.945, 1.002 | 0.069 | | | 164831 | 5758 | 0.95 | 0.921, 0.979 | 0.0009 | | |
| | With T2D[6] | 8860 | 298 | 1.026 | 0.916, 1.150 | 0.657 | 0.368 | 0.370 | 7188 | 163 | 1.057 | 0.915, 1.221 | 0.453 | 0.151 | 0.159 |
| | Without CVD[6] | 143132 | 6555 | 0.976 | 0.948, 1.005 | 0.098 | | | 156304 | 5590 | 0.958 | 0.928, 0.988 | 0.006 | | |
| | With CVD[6] | 5917 | 192 | 0.956 | 0.829, 1.103 | 0.540 | 0.782 | 0.782 | 15715 | 331 | 0.889 | 0.798, 0.989 | 0.031 | 0.182 | 0.177 |
| | Without CMD[6] | 135224 | 6272 | 0.974 | 0.946, 1.002 | 0.072 | | | 151474 | 5469 | 0.956 | 0.927, 0.987 | 0.005 | | |
| | With CMD[6] | 13825 | 475 | 1.003 | 0.916, 1.098 | 0.950 | 0.530 | 0.531 | 20545 | 452 | 0.916 | 0.836, 1.003 | 0.058 | 0.360 | 0.360 |

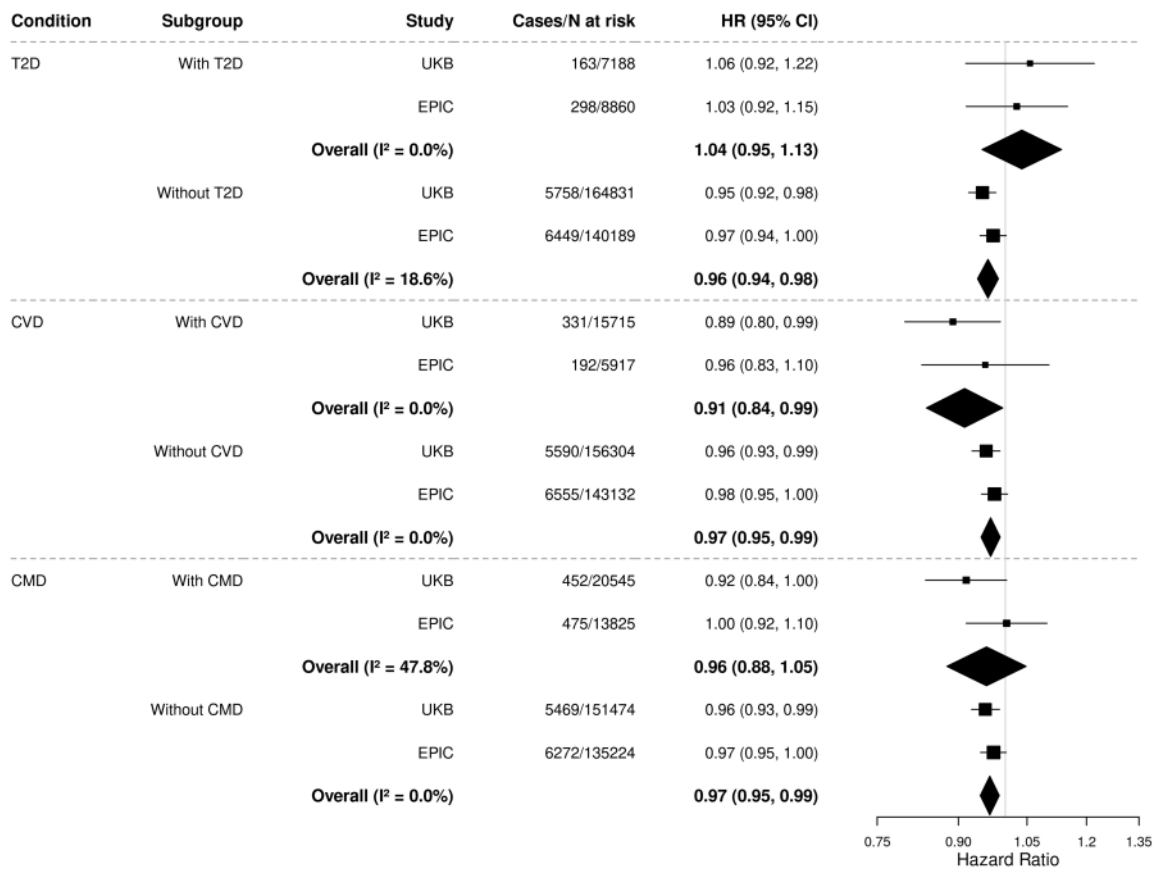
[a] One SD = 51.4 MET-h/week and 34.0 MET-h/week in EPIC and in UK Biobank, respectively.
[1] p-values for the association (from Wald tests in Cox proportional hazards models).
[2] p-values for local interaction tests (from the full models including interaction terms).
[3] p-value for the global interaction test (from the likelihood ratio test comparing models with and without interaction).
[4a] Model 1: adjusted for education, BMI, height, smoking status, alcohol consumption, diet quality, occupational PA/employment, menopause status, menopausal hormone use, and stratified by age (5-year categories), sex, and recruitment centre.
[4b] Model 1: adjusted for education, BMI, height, smoking status, alcohol consumption, diet quality, occupational PA/employment, menopause status, menopausal hormone use, age at menarche, age at first birth, parity, family history of breast cancer, and stratified by age (5-year categories) and recruitment centre.
[5] Model 2: further adjusted for T2D and CVD, and the duration of these comorbidities.
[6] Model 3: further including interaction terms between NOPA and T2D, CVD, and CMD (adjusted multiplicative interaction computed from the full model with interaction). All statistical tests were two-sided.
Abbreviations: BMI, body mass index; CI, confidence interval; CMD, cardiometabolic disease (T2D and/or CVD); CVD, cardiovascular disease; EPIC, European Prospective Investigation into Cancer and Nutrition; HR, hazard ratio; MET-h/week, metabolic equivalent task hours per week; NOPA, Non-occupational physical activity; SD, standard deviation; T2D, type 2 diabetes; UKB, UK Biobank.

**Supplementary Figure 10: Association between non-occupational physical activity (per 1 SD increase in MET-h/week) and the risk of colorectal cancer by cardiometabolic disease status in EPIC and UKB cohorts**




One SD = 51.4 MET-h/week and 34.0 MET-h/week in EPIC and UKB, respectively.
$I^2$: The proportion of total variability due to between-study heterogeneity from random effects meta-analysis.
The models were stratified by age (5-year categories), sex, and recruitment centre, and adjusted for education, BMI, height, smoking status, alcohol consumption, diet quality, occupational PA/employment, menopause status, menopausal hormone use, CVD and T2D (modelled as binary time-varying variables) and time since diagnosis of CVD and T2D, and interaction term between physical activity and each condition (T2D, CVD, and combined) in each model. Hazard ratios for each cohort were estimated using multivariable Cox proportional hazards models. The overall estimates (in bold) were obtained using a random-effects meta-analysis. All statistical tests were two-sided. The measure of centre of the diamonds or the squares represents the point estimates of hazard ratios, and the error bars represent 95% confidence intervals.
Abbreviations: BMI, body mass index; CI, confidence interval; CMD, cardiometabolic disease (T2D and/or CVD); CVD, cardiovascular disease; EPIC, European Prospective Investigation into Cancer and Nutrition; HR, hazard ratio; MET-h/week, metabolic equivalent task hours per week; SD, standard deviation; T2D, type 2 diabetes; UKB, UK Biobank.

**Supplementary Figure 11: Association between non-occupational physical activity (per 1 SD increase in MET-h/week) and the risk of breast cancer by cardiometabolic disease status in EPIC and UKB cohorts**




One SD = 51.4 MET-h/week and 34.0 MET-h/week in EPIC and UKB, respectively.
$I^2$: The proportion of total variability due to between-study heterogeneity from random effects meta-analysis.
The models were stratified by age (5-year categories) and recruitment centre, and adjusted for education, BMI, height, smoking status, alcohol consumption, diet quality, occupational PA/employment, menopause status, menopausal hormone use, age at menarche, age at first birth, parity, family history of breast cancer, CVD and T2D (modelled as binary time-varying variables) and time since diagnosis of CVD and T2D, and interaction term between physical activity and each condition (T2D, CVD, and combined) in each model. Hazard ratios for each cohort were estimated using multivariable Cox proportional hazards models. The overall estimates (in bold) were obtained using a random-effects meta-analysis. All statistical tests were two-sided. The measure of centre of the diamonds or the squares represents the point estimates of hazard ratios, and the error bars represent 95% confidence intervals.
Abbreviations: BMI, body mass index; CI, confidence interval; CMD, cardiometabolic disease (T2D and/or CVD); CVD, cardiovascular disease; EPIC, European Prospective Investigation into Cancer and Nutrition; HR, hazard ratio; MET-h/week, metabolic equivalent task hours per week; SD, standard deviation; T2D, type 2 diabetes; UKB, UK Biobank.

**Supplementary Table 10: Subgroup analysis of associations between non-occupational physical activity ([a]per 1 SD increase in MET-h/week) and the risk of physical activity-related cancers by cardiometabolic disease status.**

| Subgroups | CMD status | EPIC | | | | | UKB | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | N | Cases | HR (95% CI) | p1 | p2 | N | Cases | HR (95% CI) | p1 | p2 |
| Ever smokers | No | 127075 | 9851 | 0.957 (0.934, 0.98) | <0.001 | | 148045 | 8172 | 0.946 (0.924, 0.969) | < 0.001 | |
| | Yes | 18816 | 1682 | 0.929 (0.881, 0.98) | 0.007 | 0.30 | 33914 | 1966 | 0.943 (0.904, 0.984) | 0.007 | 0.89 |
| Never smokers | No | 104215 | 6418 | 0.968 (0.941, 0.996) | 0.027 | | 189164 | 7500 | 0.940 (0.916, 0.965) | < 0.001 | |
| | Yes | 11097 | 699 | 0.97 (0.900, 1.046) | 0.434 | 0.95 | 28032 | 894 | 0.880 (0.825, 0.940) | < 0.001 | 0.062 |
| Employed | No | 154660 | 10023 | 0.985 (0.961, 1.01) | 0.23 | | 209372 | 8015 | 0.928 (0.896, 0.961) | < 0.001 | |
| | Yes | 16997 | 1231 | 0.984 (0.92, 1.053) | 0.64 | 0.98 | 26175 | 855 | 0.854 (0.763, 0.956) | 0.006 | 0.16 |
| Unemployed | No | 76630 | 6246 | 0.95 (0.924, 0.977) | <0.001 | | 127837 | 7657 | 0.952 (0.933, 0.972) | < 0.001 | |
| | Yes | 12916 | 1150 | 0.923 (0.871, 0.98) | 0.008 | 0.37 | 35771 | 2005 | 0.932 (0.896, 0.97) | 0.001 | 0.35 |
| BMI <25kg/m$^2$ | No | 99026 | 6991 | 0.982 (0.955, 1.01) | 0.21 | | 113419 | 5107 | 0.949 (0.921, 0.978) | 0.001 | |
| | Yes | 6702 | 529 | 0.913 (0.83, 1.005) | 0.062 | 0.14 | 11897 | 440 | 0.866 (0.792, 0.947) | 0.002 | 0.051 |
| BMI ≥25kg/m$^2$ | No | 132264 | 9278 | 0.955 (0.932, 0.978) | <0.001 | | 223790 | 10565 | 0.943 (0.923, 0.964) | < 0.001 | |
| | Yes | 23211 | 1852 | 0.949 (0.905, 0.996) | 0.034 | 0.81 | 50049 | 2420 | 0.942 (0.906, 0.979) | 0.003 | 0.95 |
| Male | No | 87138 | 4917 | 0.971 (0.937, 1.007) | 0.11 | | 161034 | 5492 | .937 (0.912, 0.964) | < 0.001 | |
| | Yes | 16088 | 1251 | 0.975 (0.913, 1.041) | 0.45 | 0.92 | 40455 | 1718 | 0.913 (0.872, 0.956) | < 0.001 | 0.32 |
| Female | No | 144152 | 11352 | 0.963 (0.942, 0.984) | 0.001 | | 176175 | 10180 | 0.951 (0.930, 0.973) | < 0.001 | |
| | Yes | 13825 | 1130 | 0.948 (0.893, 1.006) | 0.077 | 0.61 | 21491 | 1142 | 0.944 (0.893, 0.999) | 0.045 | 0.81 |
| Using medication | No | | | | | | 43134 | 1930 | 0.950 (0.908, 0.995) | 0.029 | |
| | Yes | | | | | | 25565 | 1315 | 0.942 (0.893, 0.993) | 0.026 | 0.78 |
| No medication | No | | | | | | 117874 | 3560 | 0.933 (0.900, 0.966) | < 0.001 | |
| | Yes | | | | | | 14882 | 403 | 0.841 (0.764, 0.926) | < 0.001 | 0.043 |
| Self-rated good/excellent health | No | | | | | | 266521 | 12229 | 0.949 (0.930, 0.968) | < 0.001 | |
| | Yes | | | | | | 35664 | 1354 | 0.927 (0.882, 0.975) | 0.003 | 0.38 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Self-rated fair/bad health | No | | | | | | 70688 | 3443 | 0.953 (0.918, 0.989) | 0.011 | |
| | Yes | | | | | | 26282 | 1506 | 0.947 (0.900, 0.997) | 0.039 | 0.85 |
| Low deprivation | No | | | | | | 169570 | 7797 | 0.952 (0.929, 0.976) | < 0.001 | |
| | Yes | | | | | | 28627 | 1192 | 0.932 (0.882, 0.985) | 0.012 | 0.47 |
| High deprivation | No | | | | | | 167639 | 7875 | 0.939 (0.916, 0.963) | < 0.001 | |
| | Yes | | | | | | 33319 | 1668 | 0.923 (0.881, 0.967) | 0.001 | 0.50 |
| Low income | No | | | | | | 151693 | 8364 | 0.947 (0.927, 0.968) | < 0.001 | |
| | Yes | | | | | | 37881 | 2058 | 0.932 (0.895, 0.970) | 0.001 | 0.47 |
| High income | No | | | | | | 185516 | 7308 | 0.944 (0.917, 0.972) | < 0.001 | |
| | Yes | | | | | | 24065 | 802 | 0.905 (0.838, 0.977) | 0.010 | 0.29 |
| Low sedentary | No | | | | | | 187549 | 8615 | 0.947 (0.925, 0.970) | < 0.001 | |
| | Yes | | | | | | 27661 | 1167 | 0.924 (0.875, 0.976) | 0.005 | 0.40 |
| High sedentary | No | | | | | | 149660 | 7057 | 0.947 (0.923, 0.972) | < 0.001 | |
| | Yes | | | | | | 34285 | 1693 | 0.932 (0.890, 0.977) | 0.003 | 0.55 |

[a] One SD = 51.4 MET-h/week and 34.0 MET-h/week in EPIC and UKB, respectively. Empty cells: data not available.
[1] p-values for the association (from Wald tests in Cox proportional hazards models).
[2] p-values for local interaction tests (p-values in the full model with interaction between NOPA and CMD within each model).
Employment status: “employed” refers to those who had sitting/standing/manual occupational physical activity in EPIC, while in UKB, to those in paid employment or self-employed, doing unpaid or voluntary work, full or part-time students.
Medication status: “using medication” refers to those reporting use of blood pressure medication, cholesterol-lowering medication, or insulin; while no medication refers to those who do not know, none of the above, or prefer not to answer.
Deprivation: “low” refers to <= the median (-2.2419) while “high " refers to> the median (-2.2419).
Income: “low income” refers to household income <= 30,999 GBP; “high income” if > 31,000 GBP.
Sedentary: “low sedentary" refers to sedentary < 5 hours/day; “high sedentary" refers to sedentary >= 5 hours/day (10).
All models were adjusted for the duration of T2D and CVD, smoking, BMI, alcohol consumption, diet quality, occupational PA, education, height, menopause status, and menopausal hormone use. All statistical tests were two-sided. p-values smaller than 0.001 are shown as “<0.001” for readability. No adjustments were made for multiple comparisons.
Abbreviations: BMI, body mass index; CI, confidence interval; CMD, cardiometabolic disease (T2D and/or CVD); CVD, cardiovascular disease; EPIC, European Prospective Investigation into Cancer and Nutrition; HR, hazard ratio; MET-h/week, metabolic equivalent task hours per week; NOPA, non-occupational physical activity; SD, standard deviation; T2D, type 2 diabetes; UKB, UK Biobank.

**Supplementary Table 11: Subgroup analysis of associations between non-occupational physical activity ([a]per 1 SD increase in MET-h/week) and the risk of all cancers by cardiometabolic disease status.**

| Subgroups | CMD status | EPIC | | | | | UKB | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | N | Cases | HR (95% CI) | p1 | p2 | N | Cases | HR (95% CI) | p1 | p2 |
| Ever smokers | No | 127075 | 15949 | 0.965 (0.946, 0.983) | < 0.001 | | 148045 | 14903 | 0.972 (0.956, 0.989) | 0.001 | |
| | Yes | 18816 | 2789 | 0.950 (0.911, 0.991) | 0.016 | 0.50 | 33914 | 3588 | 0.959 (0.930, 0.990) | 0.009 | 0.44 |
| Never smokers | No | 104215 | 10287 | 0.980 (0.957, 1.003) | 0.081 | | 189164 | 14865 | 0.974 (0.957, 0.992) | 0.004 | |
| | Yes | 11097 | 1169 | 1.019 (0.962, 1.080) | 0.52 | 0.19 | 28032 | 2036 | 0.972 (0.933, 1.013) | 0.178 | 0.93 |
| Employed | No | 154660 | 16675 | 0.981 (0.961, 1.000) | 0.052 | | 209372 | 15233 | 0.979 (0.957, 1.003) | 0.084 | |
| | Yes | 16997 | 2139 | 1.005 (0.954, 1.059) | 0.84 | 0.37 | 26175 | 1766 | 0.945 (0.881, 1.015) | 0.119 | 0.35 |
| Unemployed | No | 76630 | 9561 | 0.966 (0.945, 0.988) | 0.003 | | 127837 | 14535 | 0.973 (0.959, 0.988) | <0.001 | |
| | Yes | 12916 | 1819 | 0.952 (0.908, 0.997) | 0.038 | 0.55 | 35771 | 3858 | 0.964 (0.937, 0.991) | 0.011 | 0.54 |
| BMI <25kg/m$^2$ | No | 99026 | 10789 | 0.982 (0.959, 1.005) | 0.12 | | 113419 | 9178 | 0.971 (0.949, 0.993) | 0.009 | |
| | Yes | 6702 | 887 | 0.951 (0.884, 1.023) | 0.18 | 0.41 | 11897 | 946 | 0.967 (0.912, 1.025) | 0.26 | 0.89 |
| BMI ≥25kg/m$^2$ | No | 132264 | 15447 | 0.967 (0.949, 0.985) | < 0.001 | | 223790 | 20590 | 0.977 (0.962, 0.991) | 0.002 | |
| | Yes | 23211 | 3071 | 0.976 (0.939, 1.013) | 0.12 | 0.65 | 50049 | 4678 | 0.967 (0.940, 0.994) | 0.016 | 0.51 |
| Male | No | 87138 | 10990 | 0.986 (0.963, 1.010) | 0.26 | | 161034 | 15901 | 0.981 (0.965, 0.997) | 0.020 | |
| | Yes | 16088 | 2462 | 0.984 (0.939, 1.031) | 0.50 | 0.93 | 40455 | 4101 | 0.964 (0.936, 0.993) | 0.014 | 0.29 |
| Female | No | 144152 | 15246 | 0.966 (0.948, 0.984) | < 0.001 | | 176175 | 13867 | 0.965 (0.947, 0.984) | <0.001 | |
| | Yes | 13825 | 1496 | 0.959 (0.911, 1.010) | 0.11 | 0.79 | 21491 | 1523 | 0.967 (0.922, 1.014) | 0.17 | 0.94 |
| Using medication | No | | | | | | 43134 | 5199 | 0.972 (0.946, 1.000) | 0.046 | |
| | Yes | | | | | | 25565 | 3127 | 0.981 (0.948, 1.014) | 0.25 | 0.68 |
| No medication | No | | | | | | 117874 | 10699 | 0.989 (0.969, 1.009) | 0.26 | |
| | Yes | | | | | | 14882 | 974 | 0.915 (0.862, 0.972) | 0.004 | 0.015 |
| Self-rated good/excellent health | No | | | | | | 266521 | 23606 | 0.979 (0.965, 0.993) | 0.003 | |
| | Yes | | | | | | 35664 | 2856 | 0.974 (0.941, 1.007) | 0.12 | 0.78 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Self-rated fair/bad health | No | | | | | | 70688 | 6162 | 0.969 (0.943, 0.996) | 0.026 | |
| | Yes | | | | | | 26282 | 2768 | 0.972 (0.936, 1.009) | 0.13 | 0.89 |
| Low deprivation | No | | | | | | 169570 | 15390 | 0.975 (0.958, 0.992) | 0.004 | |
| | Yes | | | | | | 28627 | 2609 | 0.981 (0.946, 1.017) | 0.29 | 0.76 |
| High deprivation | No | | | | | | 167639 | 14378 | 0.974 (0.956, 0.991) | 0.003 | |
| | Yes | | | | | | 33319 | 3015 | 0.952 (0.92, 0.986) | 0.005 | 0.24 |
| Low income | No | | | | | | 151693 | 15260 | 0.97 (0.955, 0.985) | <0.001 | |
| | Yes | | | | | | 37881 | 3835 | 0.972 (0.944, 1.001) | 0.054 | 0.90 |
| High income | No | | | | | | 185516 | 14508 | 0.982 (0.962, 1.001) | 0.069 | |
| | Yes | | | | | | 24065 | 1789 | 0.948 (0.902, 0.996) | 0.035 | 0.19 |
| Low sedentary | No | | | | | | 187549 | 15739 | 0.973 (0.956, 0.990) | 0.002 | |
| | Yes | | | | | | 27661 | 2321 | 0.966 (0.930, 1.004) | 0.079 | 0.74 |
| High sedentary | No | | | | | | 149660 | 14029 | 0.979 (0.962, 0.997) | 0.021 | |
| | Yes | | | | | | 34285 | 3303 | 0.968 (0.936, 1.000) | 0.051 | 0.51 |

[a] One SD = 51.4 MET-h/week and 34.0 MET-h/week in EPIC and UKB, respectively. Empty cells: data not available.

[1] p-values for the association (from Wald tests in Cox proportional hazards models).

[2] p-values for local interaction tests (p-values in the full model with interaction between NOPA and CMD within each model).

Employment status: “employed” refers to those who had a sitting/standing/manual occupational PA in EPIC, while in UKB, to those in paid employment or self-employed, doing unpaid or voluntary work, full or part-time students.

Medication status: “using medication” refers to those reporting use of blood pressure medication, cholesterol-lowering medication, or insulin; while no medication refers to those who do not know, none of the above, or prefer not to answer.

Deprivation: “low” refers to <= the median (-2.2419) while “high " refers to> the median (-2.2419).

Income: “low income” refers to household income <= 30,999 GBP; “high income” if > 31,000 GBP.

Sedentary: “low sedentary" refers to sedentary < 5 hours/day; “high sedentary" refers to sedentary >= 5 hours/day (10).

All models were adjusted for the duration of T2D and CVD, smoking, BMI, alcohol consumption, diet quality, occupational PA, education, height, menopause status, and menopausal hormone use. All statistical tests were two-sided. p-values smaller than 0.001 are shown as “<0.001” for readability. No adjustments were made for multiple comparisons.

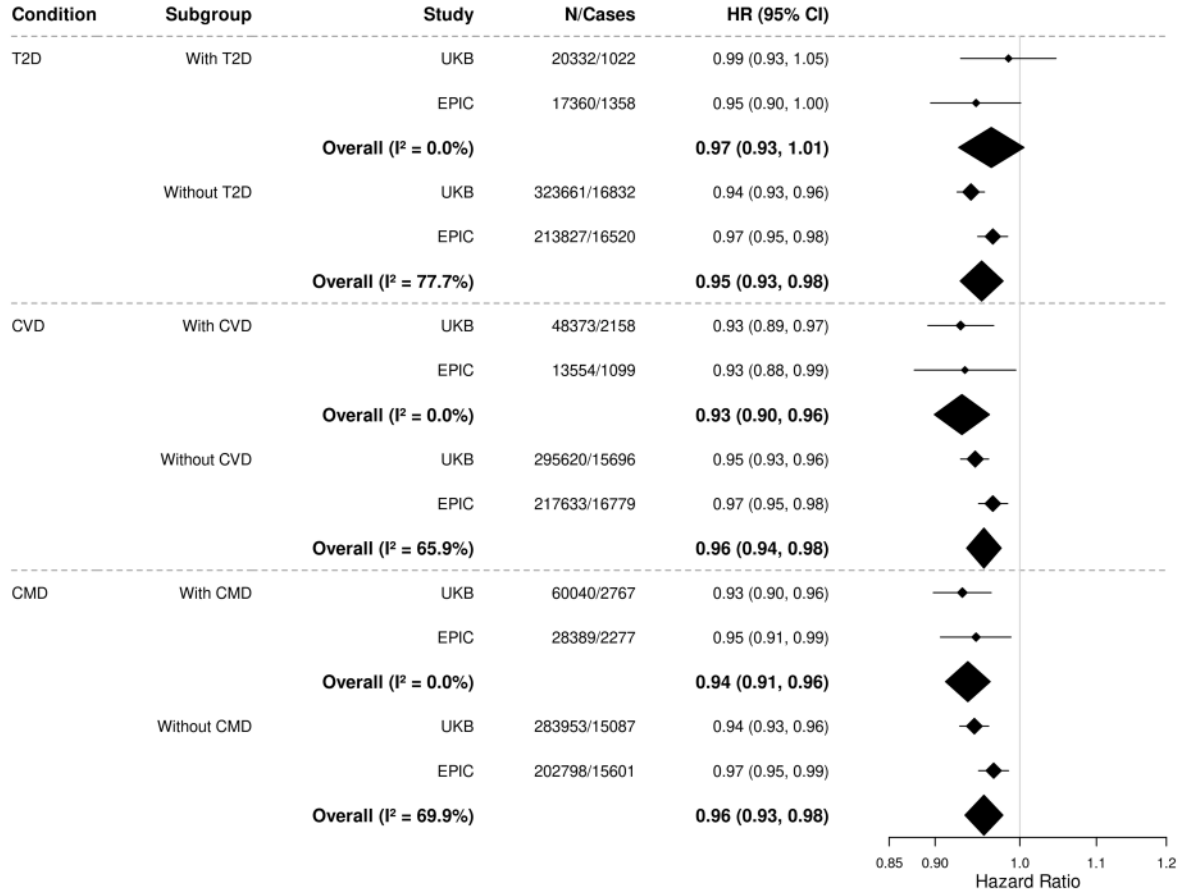
Abbreviations: BMI, body mass index; CI, confidence interval; CMD, cardiometabolic disease (T2D and/or CVD); CVD, cardiovascular disease; EPIC, European Prospective Investigation into Cancer and Nutrition; HR, hazard ratio; MET-h/week, metabolic equivalent task hours per week; NOPA, non-occupational physical activity; SD, standard deviation; T2D, type 2 diabetes; UKB, UK Biobank.

**Supplementary Table 12: Association between non-occupational physical activity ([a]per 1 SD increase in MET-h/week) and the risk of physical activity-related cancers and all cancers by cardiometabolic disease status in EPIC and UKB (complete case analysis).**

| Outcomes | Models | EPIC | | | | | | | UK Biobank | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | N | Cases | HR | 95% CI | p1 | p2 | p3 | N | Cases | HR | 95% CI | p1 | p2 | p3 |
| Physical activity-related cancer | Overall [4] | 231187 | 17878 | 0.964 | 0.947, 0.981 | <0.001 | | | 343993 | 17854 | 0.941 | 0.925, 0.956 | <0.001 | | |
| | Overall, Adj T2D and CVD[5] | 231187 | 17878 | 0.965 | 0.948, 0.983 | <0.001 | | | 343993 | 17854 | 0.943 | 0.928, 0.959 | <0.001 | | |
| | Without T2D[6] | 213827 | 16520 | 0.967 | 0.949, 0.985 | <0.001 | | | 323661 | 16832 | 0.941 | 0.925, 0.957 | <0.001 | | |
| | With T2D[6] | 17360 | 1358 | 0.947 | 0.895, 1.001 | 0.055 | 0.47 | 0.47 | 20332 | 1022 | 0.986 | 0.929, 1.046 | 0.633 | 0.13 | 0.13 |
| | Without CVD[6] | 217633 | 16779 | 0.967 | 0.95, 0.985 | <0.001 | | | 295620 | 15696 | 0.946 | 0.929, 0.962 | <0.001 | | |
| | With CVD[6] | 13554 | 1099 | 0.934 | 0.877, 0.995 | 0.0345 | 0.28 | 0.28 | 48373 | 2158 | 0.929 | 0.892, 0.968 | <0.001 | 0.41 | 0.41 |
| | Without CMD[6] | 202798 | 15601 | 0.968 | 0.95, 0.986 | <0.001 | | | 283953 | 15087 | 0.945 | 0.928, 0.962 | <0.001 | | |
| | With CMD[6] | 28389 | 2277 | 0.947 | 0.906, 0.989 | 0.014 | 0.34 | 0.34 | 60040 | 2767 | 0.931 | 0.898, 0.965 | <0.001 | 0.44 | 0.44 |
| All cancers | Overall [4] | 231187 | 28741 | 0.973 | 0.959, 0.987 | <0.001 | | | 343993 | 34352 | 0.972 | 0.961, 0.984 | <0.001 | | |
| | Overall, Adj T2D and CVD[5] | 231187 | 28741 | 0.974 | 0.960, 0.988 | <0.001 | | | 343993 | 34352 | 0.973 | 0.962, 0.984 | <0.001 | | |
| | Without T2D[6] | 213827 | 26508 | 0.974 | 0.960, 0.988 | <0.001 | | | 323661 | 32569 | 0.971 | 0.959, 0.983 | <0.001 | | |
| | With T2D[6] | 17360 | 2233 | 0.975 | 0.933, 1.019 | 0.27 | 0.94 | 0.94 | 20332 | 1783 | 1.007 | 0.964, 1.053 | 0.74 | 0.11 | 0.11 |
| | Without CVD[6] | 217633 | 26898 | 0.974 | 0.960, 0.989 | <0.001 | | | 295620 | 29957 | 0.974 | 0.962, 0.986 | <0.001 | | |
| | With CVD[6] | 13554 | 1843 | 0.968 | 0.921, 1.016 | 0.19 | 0.79 | 0.79 | 48373 | 4395 | 0.968 | 0.942, 0.996 | 0.023 | 0.71 | 0.71 |
| | Without CMD[6] | 202798 | 24989 | 0.973 | 0.959, 0.988 | <0.001 | | | 283953 | 28892 | 0.973 | 0.961, 0.986 | <0.001 | | |
| | With CMD[6] | 28389 | 3752 | 0.978 | 0.945, 1.013 | 0.213 | 0.76 | 0.76 | 60040 | 5460 | 0.970 | 0.946, 0.994 | 0.016 | 0.79 | 0.79 |

[a] One SD = 51.4 MET-h/week and 34.0 MET-h/week in EPIC and in UK Biobank, respectively.
[1] p-values for the association (from Wald tests in Cox proportional hazards models).
[2] p-values for local interaction tests (p-values in the full model with interaction).
[3] p-value for the global interaction test (likelihood ratio test).
[4] Model 1: adjusted for education, BMI, height, smoking status, alcohol consumption, diet quality, occupational PA/employment, menopause status, menopausal hormone use, and stratified by age (5-year categories), sex, and recruitment centre.
[5] Model 2: further adjusted for T2D and CVD, and the duration of these comorbidities.
[6] Model 3: further including interaction terms between NOPA and T2D, CVD, and CMD (adjusted multiplicative interaction computed from the full model with interaction). All statistical tests were two-sided. p-values smaller than 0.001 are shown as "<0.001" for readability.
Abbreviations: BMI, body mass index, CI, confidence interval; CMD, cardiometabolic disease (T2D and/or CVD); CVD, cardiovascular disease; EPIC, European Prospective Investigation into Cancer and Nutrition; HR, hazard ratio; MET-h/week, metabolic equivalent task hours per week; NOPA, non-occupational physical activity; SD, standard deviation; T2D, type 2 diabetes; UKB, UK Biobank.

**Supplementary Figure 12: Association between non-occupational physical activity (per 1 SD increase in MET-h/week) and the risk of physical activity-related cancers by cardiometabolic disease status in EPIC and UKB cohorts (complete case analysis).**




One SD = 51.4 MET-h/week and 34.0 MET-h/week in EPIC and UKB, respectively.
$I^2$: The proportion of total variability due to between-study heterogeneity from random effects meta-analysis.
The models were stratified by age (5-year categories), sex, and recruitment centre, and adjusted for education, BMI, height, smoking status, alcohol consumption, diet quality, occupational PA/employment, menopause status, menopausal hormone use, CVD and T2D (modelled as binary time-varying variables) and time since diagnosis of CVD and T2D, and interaction term between physical activity and each condition (T2D, CVD, and combined) in each model. Hazard ratios for each cohort were estimated using multivariable Cox proportional hazards models, and all statistical tests were two-sided. The overall estimate (in bold) was obtained using a random-effects meta-analysis with two-sided tests. The measure of centre of the diamonds or the squares represents the point estimates of hazard ratios, and the error bars represent 95% confidence intervals.
Abbreviations: BMI, body mass index; CI, confidence interval; CMD, cardiometabolic disease (T2D and/or CVD); CVD, cardiovascular disease; EPIC, European Prospective Investigation into Cancer and Nutrition; HR, hazard ratio; MET-h/week, metabolic equivalent task hours per week; SD, standard deviation; T2D, type 2 diabetes; UKB, UK Biobank.

**Supplementary Table 13: Joint association of non-occupational physical activity and cardiometabolic diseases with the risk of all cancers.**

| Joint exposures | Study | N | Cases | HR (95% CI) | p-value |
|---|---|---|---|---|---|
| High NOPA, without T2D | UKB | 139854 | 14573 | Ref. | |
| | EPIC | 95443 | 10243 | Ref. | |
| High NOPA, with T2D | UKB | 7754 | 739 | 1.105 (0.948, 1.288) | 0.201 |
| | EPIC | 6588 | 752 | 1.077 (0.923, 1.257) | 0.347 |
| | **Overall (I2 = 0.0%)** | | | **1.091 (0.979, 1.216)** | |
| Moderate NOPA, without T2D | UKB | 142444 | 12893 | 1.052 (1.026, 1.079) | <0.001 |
| | EPIC | 94495 | 11572 | 1.037 (1.008, 1.068) | 0.014 |
| | **Overall (I2 = 0.0%)** | | | **1.046 (1.026, 1.066)** | |
| Moderate NOPA, with T2D | UKB | 7820 | 646 | 1.061 (0.908, 1.241) | 0.453 |
| | EPIC | 6931 | 946 | 1.136 (0.978, 1.320) | 0.094 |
| | **Overall (I2 = 0.0%)** | | | **1.099 (0.987, 1.225)** | |
| Low NOPA, without T2D | UKB | 69525 | 6082 | 1.100 (1.064, 1.137) | <0.001 |
| | EPIC | 45915 | 6045 | 1.065 (1.027, 1.104) | <0.001 |
| | **Overall (I2 = 40.0%)** | | | **1.083 (1.05, 1.118)** | |
| Low NOPA, with T2D | UKB | 5607 | 459 | 1.150 (0.975, 1.355) | 0.096 |
| | EPIC | 4548 | 636 | 1.119 (0.956, 1.309) | 0.161 |
| | **Overall (I2 = 0.0%)** | | | **1.134 (1.012, 1.27)** | |
| High NOPA, without CVD | UKB | 134238 | 13261 | Ref. | |
| | EPIC | 96331 | 10368 | Ref. | |
| High NOPA, with CVD | UKB | 22346 | 2051 | 1.046 (0.946, 1.155) | 0.381 |
| | EPIC | 5088 | 627 | 0.986 (0.838, 1.160) | 0.867 |
| | **Overall (I2 = 0.0%)** | | | **1.029 (0.945, 1.121)** | |
| Moderate NOPA, without CVD | UKB | 138383 | 11914 | 1.039 (1.012, 1.067) | 0.005 |
| | EPIC | 94661 | 11702 | 1.039 (1.010, 1.070) | 0.009 |
| | **Overall (I2 = 0.0%)** | | | **1.039 (1.019, 1.059)** | |
| Moderate NOPA, with CVD | UKB | 18074 | 1625 | 1.155 (1.043, 1.279) | 0.006 |
| | EPIC | 5884 | 816 | 1.012 (0.864, 1.186) | 0.880 |
| | **Overall (I2 = 50.0%)** | | | **1.097 (0.967, 1.245)** | |
| Low NOPA, without CVD | UKB | 67654 | 5697 | 1.089 (1.052, 1.127) | <0.001 |
| | EPIC | 46169 | 6160 | 1.062 (1.024, 1.101) | 0.001 |
| | **Overall (I2 = 0.0%)** | | | **1.076 (1.050, 1.103)** | |
| Low NOPA, with CVD | UKB | 9367 | 844 | 1.193 (1.065, 1.337) | 0.002 |
| | EPIC | 3532 | 521 | 1.060 (0.897, 1.253) | 0.495 |
| | **Overall (I2 = 20.0%)** | | | **1.143 (1.023, 1.278)** | |
| High NOPA, without CMD | UKB | 133075 | 12811 | Ref. | |
| | EPIC | 93821 | 9702 | Ref. | |
| High NOPA, with CMD | UKB | 26655 | 2501 | 1.056 (0.968, 1.153) | 0.221 |
| | EPIC | 10861 | 1293 | 1.049 (0.934, 1.178) | 0.419 |
| | **Overall (I2 = 0.0%)** | | | **1.053 (0.982, 1.130)** | |
| Moderate NOPA, without CMD | UKB | 137294 | 11527 | 1.042 (1.014, 1.07) | 0.003 |
| | EPIC | 92608 | 10896 | 1.039 (1.008, 1.07) | 0.012 |
| | **Overall (I2 = 0.0%)** | | | **1.041 (1.02, 1.062)** | |
| Moderate NOPA, with CMD | UKB | 22646 | 2012 | 1.138 (1.04, 1.245) | 0.005 |
| | EPIC | 11759 | 1622 | 1.088 (0.971, 1.218) | 0.145 |
| | **Overall (I2 = 0.0%)** | | | **1.118 (1.042, 1.200)** | |
| Low NOPA, without CMD | UKB | 66840 | 5430 | 1.090 (1.053, 1.129) | <0.001 |
| | EPIC | 44861 | 5638 | 1.067 (1.028, 1.107) | <0.001 |
| | **Overall (I2 = 0.0%)** | | | **1.079 (1.052, 1.107)** | |
| Low NOPA, with CMD | UKB | 12645 | 1111 | 1.194 (1.081, 1.318) | <0.001 |
| | EPIC | 7293 | 1043 | 1.090 (0.967, 1.229) | 0.156 |
| | **Pooled** | | | **1.148 (1.051, 1.254)** | |

Reference category (not shown): High NOPA (>=60th percentile of the MET-h/week) without cardiometabolic disease.
Low NOPA was defined as less than the 20th percentile, and moderate NOPA was defined as the 20th-60th percentile of MET-h/week in NOPA.
In EPIC, the 20th and 60th percentiles were 42 MET-h/week and 94.54 MET-h/week, respectively. In UKB, the 20th and 60th percentiles were 4.8 MET-h/week and 22.3 MET-h/week, respectively.

$I^2$: The proportion of total variability due to between-study heterogeneity from random effects meta-analysis.
The models were stratified by age (5-year categories), sex, and recruitment centre, and adjusted for education, BMI, height, smoking status, alcohol consumption, diet quality, occupational PA/employment, menopause status, menopausal hormone use, CVD and T2D (modelled as binary time-varying variables) and time since diagnosis of CVD and T2D, and joint categories of physical activity and each condition (T2D, CVD, and combined) in each model. Hazard ratios for each cohort were estimated using multivariable Cox proportional hazards models. The overall estimates were obtained using a random-effects meta-analysis. All statistical tests were two-sided. p-values smaller than 0.001 are shown as "<0.001" for readability.
Relative excess risk due to interactions (RERI) for those who had low NOPA with T2D, CVD, and CMD was -0.04 (95% CI: -0.29, 0.21), 0.04 (95% CI: -0.26, 0.35), and 0.02 (95% CI: -0.48, 0.52), respectively.
Abbreviations: CI, confidence interval; CMD, having incident T2D and/or CVD; CVD, cardiovascular disease; EPIC, European Prospective Investigation into Cancer and Nutrition; HR, hazard ratio; MET-h/week, metabolic equivalent task hours per week; NOPA, non-occupational physical activity; T2D, type 2 diabetes; UKB, UK Biobank.

**Supplementary Table 14: Joint and additive interactive effects of non-occupational physical activity and cardiometabolic diseases on colorectal cancer risk in EPIC and UKB**

| Joint exposures | Study | N | Cases | 95% CI | p-value |
|---|---|---|---|---|---|
| High NOPA, without T2D | UKB | 139854 | 1658 | Ref. | |
| | EPIC | 95443 | 1288 | Ref. | |
| High NOPA, with T2D | UKB | 7754 | 76 | 0.815 (0.503, 1.319) | 0.405 |
| | EPIC | 6588 | 101 | 1.044 (0.702, 1.552) | 0.832 |
| | **Overall (I2 = 0.0%)** | | | **0.945 (0.695, 1.283)** | |
| Moderate NOPA, without T2D | UKB | 142444 | 1465 | 1.089 (1.011, 1.174) | 0.025 |
| | EPIC | 94495 | 1513 | 1.041 (0.961, 1.129) | 0.324 |
| | **Overall (I2 = 0.0%)** | | | **1.067 (1.010, 1.127)** | |
| Moderate NOPA, with T2D | UKB | 7820 | 78 | 0.941 (0.582, 1.523) | 0.806 |
| | EPIC | 6931 | 146 | 1.275 (0.874, 1.860) | 0.208 |
| | **Overall (I2 =0.0 %)** | | | **1.136 (0.844, 1.528)** | |
| Low NOPA, without T2D | UKB | 69525 | 670 | 1.138 (1.030, 1.257) | 0.011 |
| | EPIC | 45915 | 825 | 1.068 (0.967, 1.179) | 0.194 |
| | **Overall (I2 = 0.0%)** | | | **1.102 (1.028, 1.182)** | |
| Low NOPA, with T2D | UKB | 5607 | 64 | 1.216 (0.741, 1.994) | 0.439 |
| | EPIC | 4548 | 106 | 1.327 (0.895, 1.967) | 0.159 |
| | **Overall (I2 = 0.0%)** | | | **1.283 (0.943, 1.746)** | |
| High NOPA, without CVD | UKB | 134238 | 1515 | Ref. | |
| | EPIC | 96331 | 1305 | Ref. | |
| High NOPA, with CVD | UKB | 22346 | 219 | 1.144 (0.855, 1.530) | 0.366 |
| | EPIC | 5088 | 84 | 0.907 (0.578, 1.426) | 0.673 |
| | **Overall (I2 = 0.0%)** | | | **1.069 (0.837, 1.365)** | |
| Moderate NOPA, without CVD | UKB | 138383 | 1369 | 1.087 (1.006, 1.175) | 0.036 |
| | EPIC | 94661 | 1550 | 1.055 (0.974, 1.144) | 0.188 |
| | **Overall (I2 =0.0 %)** | | | **1.071 (1.013, 1.133)** | |
| Moderate NOPA, with CVD | UKB | 18074 | 174 | 1.293 (0.959, 1.744) | 0.092 |
| | EPIC | 5884 | 109 | 0.943 (0.607, 1.466) | 0.795 |
| | **Overall (I2 = 30.0%)** | | | **1.153 (0.856, 1.553)** | |
| Low NOPA, without CVD | UKB | 67654 | 643 | 1.152 (1.040, 1.276) | 0.007 |
| | EPIC | 46169 | 865 | 1.088 (0.986, 1.201) | 0.093 |
| | **Overall (I2 = 0.0%)** | | | **1.118 (1.042, 1.201)** | |
| Low NOPA, with CVD | UKB | 9367 | 91 | 1.388 (0.993, 1.940) | 0.055 |
| | EPIC | 3532 | 66 | 0.940 (0.589, 1.499) | 0.794 |
| | **Overall (I2 = 40.0%)** | | | **1.183 (0.813, 1.723)** | |
| High NOPA, without CMD | UKB | 133075 | 1465 | Ref. | |
| | EPIC | 93821 | 1219 | Ref. | |
| High NOPA, with CMD | UKB | 26655 | 269 | 1.038 (0.798, 1.351) | |
| | EPIC | 10861 | 170 | 0.967 (0.704, 1.327) | 0.780 |
| | **Overall (I2 =0.0 %)** | | | **1.008 (0.824, 1.235)** | 0.834 |
| Moderate NOPA, without CMD | UKB | 137294 | 1325 | 1.091 (1.008, 1.180) | |
| | EPIC | 92608 | 1427 | 1.043 (0.960, 1.133) | 0.031 |
| | **Overall (I2 = 0.0%)** | | | **1.068 (1.009, 1.131)** | 0.319 |
| Moderate NOPA, with CMD | UKB | 22646 | 218 | 1.149 (0.878, 1.504) | |
| | EPIC | 11759 | 232 | 1.093 (0.804, 1.486) | 0.310 |
| | **Overall (I2 = 0.0%)** | | | **1.124 (0.918, 1.377)** | 0.569 |
| Low NOPA, without CMD | UKB | 66840 | 608 | 1.145 (1.031, 1.271) | |
| | EPIC | 44861 | 772 | 1.067 (0.964, 1.182) | 0.011 |
| | **Overall (I2 = 0.0%)** | | | **1.104 (1.027, 1.188)** | 0.213 |
| Low NOPA, with CMD | UKB | 12645 | 126 | 1.305 (0.972, 1.753) | |
| | EPIC | 7293 | 159 | 1.152 (0.835, 1.589) | 0.076 |
| | **Overall (I2 = 0.0%)** | | | **1.233 (0.992, 1.532)** | 0.388 |

Reference category: High NOPA without cardiometabolic disease.
Physical activity categories based on total non-occupational MET-hours/week: Low (<20th percentile), Moderate (20th-60th percentile), High (≥60th percentile).

In EPIC, the 20th and 60th percentiles were 42 MET-h/week and 94.54 MET-h/week, respectively. In UKB, the 20th and 60th percentiles were 4.8 MET-h/week and 22.3 MET-h/week, respectively.
Joint NOPA-disease exposure: Six mutually exclusive categories combining baseline NOPA level with baseline disease status. The models were stratified by age (5-year categories), sex, and recruitment centre, and adjusted for education, BMI, height, smoking status, alcohol consumption, diet quality, occupational PA/employment, menopause status, menopausal hormone use, CVD and T2D (modelled as binary time-varying variables) and time since diagnosis of CVD and T2D, and Joint PA-disease exposure for each condition (T2D, CVD, and combined) in each model. Hazard ratios for each cohort were estimated using multivariable Cox proportional hazards models. The overall estimates were obtained using a random-effects meta-analysis. All statistical tests were two-sided. Relative excess risk due to interactions (RERI) for those who had low NOPA with T2D, CVD, and CMD was 0.23 (95% CI: -0.08, 0.55), 0.02 (95% CI: -0.93, 0.97), and 0.12 (95% CI: -0.38, 0.61), respectively.
Abbreviations: CI, confidence interval; CMD, having incident T2D and/or CVD; CVD, cardiovascular disease; EPIC, European Prospective Investigation into Cancer and Nutrition; HR, hazard ratio; MET-h/week, metabolic equivalent task hours per week; NOPA, non-occupational physical activity; RERI, Relative excess risk due to interactions; T2D, type 2 diabetes; UKB, UK Biobank.

**Supplementary Table 15: Joint and additive interactive effects of non-occupational physical activity and cardiometabolic diseases on breast cancer risk in EPIC and UKB**

| Joint exposures | study | N | Cases | HR (95% CI) | p-value |
|---|---|---|---|---|---|
| High NOPA, without T2D | UKB | 65793 | 2117 | Ref | |
| | EPIC | 57570 | 2265 | Ref | |
| High NOPA, with T2D | UKB | 2722 | 69 | 1.690 (1.061, 2.694) | 0.890 |
| | EPIC | 3694 | 117 | 1.157 (0.778, 1.720) | 0.336 |
| | **Overall (I2 = 30.0%)** | | | **1.370 (0.947, 1.982)** | |
| Moderate NOPA, without T2D | UKB | 68948 | 2354 | 1.091 (1.024, 1.162) | 0.032 |
| | EPIC | 58642 | 2606 | 0.999 (0.941, 1.061) | 0.967 |
| | **Overall (I2 = 70.0%)** | | | **1.043 (0.957, 1.137)** | |
| Moderate NOPA, with T2D | UKB | 2582 | 45 | 1.179 (0.718, 1.934) | 0.485 |
| | EPIC | 3265 | 106 | 1.039 (0.700, 1.541) | 0.602 |
| | **Overall (I2 = 0.0%)** | | | **1.091 (0.801, 1.486)** | |
| Low NOPA, without T2D | UKB | 33945 | 1179 | 1.162 (1.073, 1.260) | 0.003 |
| | EPIC | 29034 | 1521 | 1.055 (0.979, 1.137) | 0.200 |
| | **Overall (I2 = 70.0%)** | | | **1.106 (1.006, 1.216)** | |
| Low NOPA, with T2D | UKB | 1884 | 49 | 1.832 (1.122, 2.993) | 0.018 |
| | EPIC | 1901 | 75 | 1.099 (0.727, 1.661) | 0.253 |
| | **Overall (I2 = 60.0%)** | | | **1.394 (0.846, 2.297)** | |
| High NOPA, without CVD | UKB | 66245 | 2168 | Ref | |
| | EPIC | 59058 | 2379 | Ref | |
| High NOPA, with CVD | UKB | 7287 | 126 | 0.756 (0.520, 1.098) | 0.142 |
| | EPIC | 2232 | 60 | 1.085 (0.677, 1.737) | 0.735 |
| | **Overall (I2 = 30.0%)** | | | **0.879 (0.620, 1.247)** | |
| Moderate NOPA, without CVD | UKB | 68056 | 2273 | 1.063 (0.997, 1.134) | 0.060 |
| | EPIC | 58979 | 2634 | 0.993 (0.935, 1.054) | 0.821 |
| | **Overall (I2 = 0.0%)** | | | **1.026 (0.960, 1.097)** | |
| Moderate NOPA, with CVD | UKB | 5559 | 126 | 1.018 (0.701, 1.478) | 0.926 |
| | EPIC | 2407 | 78 | 1.128 (0.713, 1.784) | 0.606 |
| | **Overall (I2 = 0.0%)** | | | **1.060 (0.794, 1.416)** | |
| Low NOPA, without CVD | UKB | 33547 | 1149 | 1.136 (1.047, 1.232) | 0.002 |
| | EPIC | 29136 | 1542 | 1.045 (0.970, 1.125) | 0.249 |
| | **Overall (I2 = 50.0%)** | | | **1.088 (1.002, 1.180)** | |
| Low NOPA, with CVD | UKB | 2869 | 79 | 1.220 (0.818, 1.820) | 0.329 |
| | EPIC | 1278 | 54 | 1.352 (0.833, 2.193) | 0.222 |
| | **Overall (I2 = 0.0%)** | | | **1.272 (0.935, 1.731)** | |
| High NOPA, without CMD | UKB | 65793 | 2117 | Ref | |
| | EPIC | 57570 | 2265 | Ref | |
| High NOPA, with CMD | UKB | 9061 | 177 | 0.979 (0.723, 1.324) | 0.027 |
| | EPIC | 5587 | 174 | 1.162 (0.855, 1.579) | 0.472 |
| | **Overall (I2 = 0.0%)** | | | **1.065 (0.859, 1.321)** | |
| Moderate NOPA, without CMD | UKB | 67689 | 2241 | 1.073 (1.006, 1.145) | 0.007 |
| | EPIC | 57928 | 2534 | 0.999 (0.94, 1.061) | 0.969 |
| | **Overall (I2 = 0.0%)** | | | **1.034 (0.964, 1.109)** | |
| Moderate NOPA, with CMD | UKB | 7332 | 158 | 1.115 (0.821, 1.514) | 0.515 |
| | EPIC | 5316 | 178 | 1.084 (0.800, 1.468) | 0.850 |
| | **Overall (I2 = 0.0%)** | | | **1.099 (0.886, 1.364)** | |
| Low NOPA, without CMD | UKB | 33252 | 1111 | 1.133 (1.044, 1.230) | <0.001 |
| | EPIC | 28654 | 1473 | 1.051 (0.974, 1.133) | 0.158 |
| | **Overall (I2 = 0.0%)** | | | **1.089 (1.012, 1.172)** | |
| Low NOPA, with CMD | UKB | 4152 | 117 | 1.474 (1.068, 2.032) | 0.016 |
| | EPIC | 2922 | 123 | 1.206 (0.875, 1.660) | 0.655 |
| | **Overall (I2 = 0.0%)** | | | **1.333 (1.062, 1.672)** | |

Reference category: High NOPA without cardiometabolic disease.

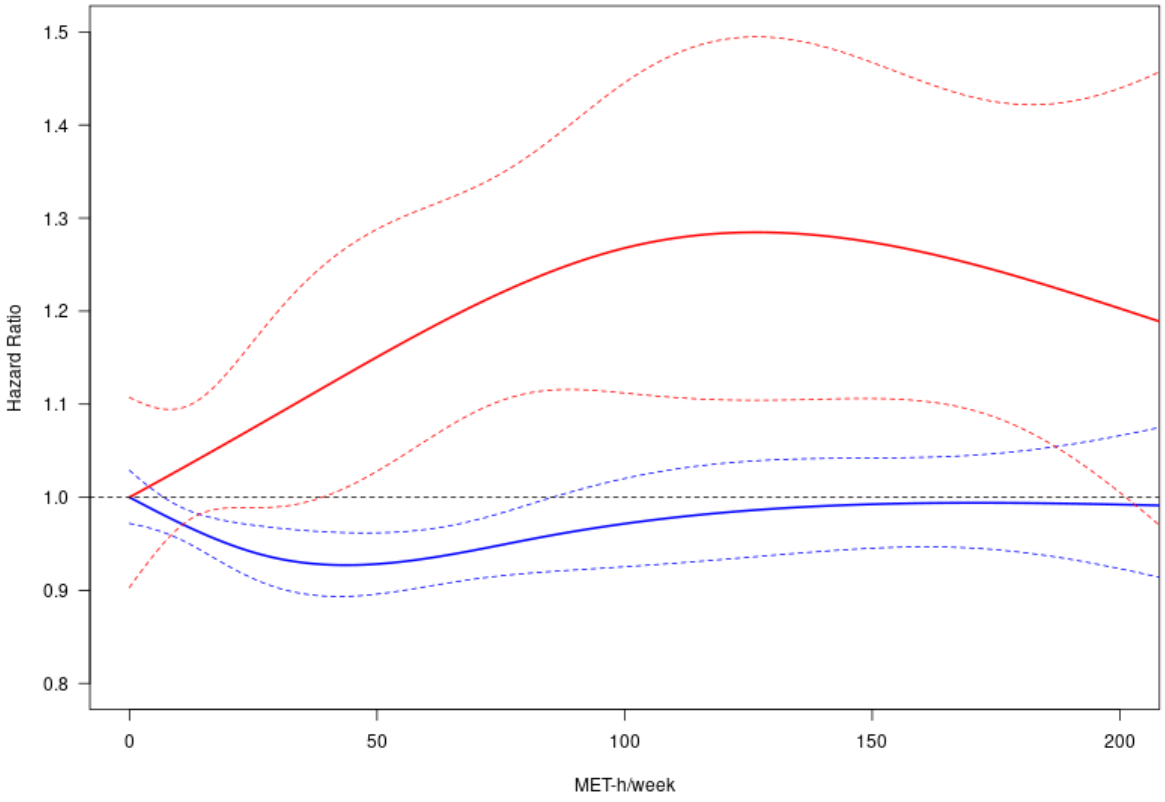
Physical activity categories based on total non-occupational MET-hours/week: Low NOPA (<20th percentile), Moderate NOPA (20th-60th percentile), High NOPA (≥60th percentile). In EPIC, the 20th and 60th percentiles were 55 MET-h/week

and 112.5 MET-h/week, respectively. In UKB, the 20th and 60th percentiles were 4.8 MET-h/week and 21.6 MET-h/week, respectively.

The models were stratified by age (5-year categories) and recruitment centre, and adjusted for education, BMI, height, smoking status, alcohol consumption, diet quality, occupational PA/employment, menopause status, menopausal hormone use, age at menarche, age at first birth, parity, family history of breast cancer, CVD and T2D (modelled as binary time-varying variables) and time since diagnosis of CVD and T2D, and Joint NOPA-disease exposure for each condition (T2D, CVD, and combined) in each model. Hazard ratios for each cohort were estimated using multivariable Cox proportional hazards models. The overall estimates were obtained using a random-effects meta-analysis. All statistical tests were two-sided. p-values smaller than 0.001 are shown as "<0.001" for readability. Relative excess risk due to interactions (RERI) for those with low NOPA and T2D, CVD, and CMD was -0.09 (95% CI: -0.57, 0.39), 0.30 (95% CI: -0.36, 0.95), and 0.16 (95% CI: -2.18, 2.51), respectively.

Abbreviations: CI, confidence interval; CMD, having incident T2D and/or CVD; CVD, cardiovascular disease; EPIC, European Prospective Investigation into Cancer and Nutrition; HR, hazard ratio; MET-h/week, metabolic equivalent task hours per week; NOPA, non-occupational physical activity; RERI, Relative excess risk due to interactions; T2D, type 2 diabetes; UKB, UK Biobank.

**Supplementary Figure 13: The association between occupational physical activity and risk of physical activity-related cancers in the fully adjusted model of UKB by cardiometabolic disease status.**




The solid blue line represents the adjusted HRs for participants without cardiometabolic disease, while the red lines represent those with cardiometabolic disease, and the broken lines indicate the 95% CIs from the Cox regression with occupational physical activity (OPA) modelled as a natural spline with three knots positioned at the 25$^{th}$, 50$^{th}$, and 75$^{th}$ percentiles of OPA, measured in MET-hour/week, capped at 200. Reference = 0 MET-h/week.
The models were stratified by age (5-year categories), sex, and recruitment centre, and adjusted for non-occupational PA, education, BMI, height, smoking status, alcohol consumption, diet quality, menopause status, and menopausal hormone use.
Abbreviations: BMI, body mass index; CI, confidence interval; CMD, T2D and/or CVD; CVD, cardiovascular disease; MET-h/week, metabolic equivalent task hours per week; OPA, occupational physical activity; T2D, type 2 diabetes; UKB, UK Biobank.

**Supplementary Table 16: Associations between occupational physical activity (per 1 SD increase in MET-h/week) and the risk of physical activity-related cancer by cardiometabolic disease status in UKB.**

| **Models** | N | Cases | HR | 95% CI | p1 | p2 | p3 |
|---|---|---|---|---|---|---|---|
| Overall [4] | 215097 | 8840 | 1.008 | 0.984, 1.032 | 0.521 | | |
| Overall, Adj T2D and CVD[5] | 215097 | 8840 | 1.008 | 0.984, 1.032 | 0.536 | | |
| Without T2D[6] | 206228 | 8528 | 1.005 | 0.981, 1.03 | 0.670 | | |
| With T2D[6] | 8869 | 312 | 1.060 | 0.952, 1.179 | 0.287 | 0.35 | 0.35 |
| Without CVD[6] | 194878 | 8201 | 0.998 | 0.973, 1.023 | 0.858 | | |
| With CVD[6] | 20219 | 639 | 1.115 | 1.037, 1.199 | 0.003 | 0.005 | 0.005 |
| Without CMD[6] | 189049 | 7988 | 0.998 | 0.973, 1.023 | 0.871 | | |
| With CMD[6] | 26048 | 852 | 1.083 | 1.016, 1.155 | 0.015 | 0.019 | 0.019 |

[a] One SD = 64.0 MET-h/week.

[1] p-values for the association (from Wald tests in Cox proportional hazards models).

[2] p-values for local interaction tests (p-values in the full model with interaction).

[3] p-value for the global interaction test (likelihood ratio test).

[4] Model 1: adjusted for non-occupational PA, education, BMI, height, smoking status, alcohol consumption, diet quality, menopause status, menopausal hormone use, and stratified by age (5-year categories), sex, and recruitment centre.

[5] Model 2: further adjusted for T2D and CVD, and the duration of these comorbidities.

[6] Model 3: further including interaction terms between OPA and T2D, CVD, and CMD (adjusted multiplicative interaction computed from the full model with interaction). All statistical tests were two-sided.

Abbreviations: BMI, body mass index; CI, confidence interval; CMD, cardiometabolic disease (T2D and/or CVD); CVD, cardiovascular disease; HR, hazard ratio; MET-h/week, metabolic equivalent task hours per week; SD, standard deviation; OPA, occupational physical activity; T2D, type 2 diabetes; UKB, UK Biobank.

**Supplementary Table 17: Subgroup analysis of associations between occupational physical activity ([a]per 1 SD increase in MET-h/week) and the risk of PA-related cancers by cardiometabolic disease status in UKB.**

| Subgroups | CMD status | N | Cases | HR (95% CI) | p1 | p2 |
|---|---|---|---|---|---|---|
| Ever smokers | No | 86927 | 3905 | 1.036 (1.001, 1.072) | 0.041 | |
| | Yes | 13343 | 541 | 1.055 (0.974, 1.143) | 0.192 | 0.682 |
| Never smokers | No | 121654 | 4083 | 0.958 (0.923, 0.995) | 0.027 | |
| | Yes | 12705 | 311 | 1.135 (1.018, 1.265) | 0.022 | 0.004 |
| High non-occupational PA | No | 107628 | 3707 | 0.996 (0.959, 1.034) | 0.821 | |
| | Yes | 11904 | 324 | 1.106 (0.999, 1.226) | 0.053 | 0.055 |
| Low non-occupational PA | No | 100953 | 4281 | 0.993 (0.96–1.027) | 0.681 | |
| | Yes | 14144 | 528 | 1.059 (0.975–1.151) | 0.172 | 0.149 |
| BMI <25kg/m$^2$ | No | 71503 | 2723 | 0.971 (0.926, 1.017) | 0.209 | |
| | Yes | 4793 | 118 | 1.142 (0.96, 1.358) | 0.134 | 0.074 |
| BMI $\geq$25kg/m$^2$ | No | 137078 | 5265 | 1.010 (0.980, 1.040) | 0.534 | |
| | Yes | 21255 | 734 | 1.079 (1.007, 1.157) | 0.032 | 0.079 |
| Male | No | 104608 | 2657 | 1.019 (0.982, 1.058) | 0.314 | |
| | Yes | 18233 | 517 | 1.059 (0.979, 1.145) | 0.155 | 0.379 |
| Female | No | 103973 | 5331 | 0.953 (0.919, 0.987) | 0.007 | |
| | Yes | 7815 | 335 | 1.084 (0.962, 1.221) | 0.187 | 0.042 |
| Using medication | No | 20880 | 736 | 1.015 (0.944, 1.091) | 0.685 | |
| | Yes | 9719 | 356 | 1.032 (0.935, 1.140) | 0.531 | 0.78 |
| No medication | No | 83714 | 1920 | 1.018 (0.974, 1.063) | 0.435 | |
| | Yes | 8512 | 161 | 1.136 (0.996, 1.296) | 0.057 | 0.111 |
| Self-rated good/excellent health | No | 169524 | 6437 | 0.994 (0.966, 1.023) | 0.698 | |
| | Yes | 16414 | 469 | 1.107 (1.014, 1.207) | 0.023 | 0.021 |
| Self-rated fair/bad health | No | 39057 | 1551 | 1.010 (0.958, 1.064) | 0.71 | |
| | Yes | 9634 | 383 | 1.049 (0.953, 1.155) | 0.328 | 0.483 |
| Low deprivation | No | 102832 | 3976 | 0.993 (0.956, 1.031) | 0.718 | |
| | Yes | 12107 | 376 | 1.101 (0.995, 1.219) | 0.063 | 0.058 |
| High deprivation | No | 105749 | 4012 | 1.001 (0.967, 1.036) | 0.954 | |
| | Yes | 13941 | 476 | 1.067 (0.982, 1.16) | 0.127 | 0.156 |
| Low income | No | 62088 | 2730 | 0.993 (0.954, 1.033) | 0.718 | |
| | Yes | 9825 | 393 | 1.059 (0.967, 1.159) | 0.216 | 0.191 |
| High income | No | 146493 | 5258 | 0.993 (0.96, 1.027) | 0.68 | |
| | Yes | 16223 | 459 | 1.076 (0.979, 1.183) | 0.13 | 0.114 |
| Low sedentary | No | 121689 | 4772 | 0.962 (0.930, 0.996) | 0.028 | |
| | Yes | 12266 | 383 | 1.084 (0.985, 1.193) | 0.099 | 0.020 |
| High sedentary | No | 86892 | 3216 | 1.042 (1.003, 1.081) | 0.032 | |
| | Yes | 13782 | 469 | 1.084 (0.994, 1.183) | 0.069 | 0.397 |

[a] One SD = 64 MET-h/week

[1] p-values for the association (from Wald tests in Cox proportional hazards models).

[2] p-values for local interaction tests (p-values in the full model with interaction between OPA and CMD within each model).

High non-occupational PA: refers to those who had >= 10 MET-h/week of non-occupational PA. Low non-occupational PA refers to <10 MET-h/week (2). The threshold at 10 MET-h/week is equivalent to reaching the recommended guidelines (150 min per week) for moderate-intensity PA.

Medication status: “using medication” refers to those reporting use of blood pressure medication, cholesterol-lowering medication, or insulin; while no medication refers to those who do not know, none of the above, or prefer not to answer.

Deprivation: “low” refers to <= the median (-2.2686) while high if > the median (-2.2419).

Income: “low income” refers to household income <= 30,999 GBP; “high income” if > 31,000 GBP.

Sedentary: “low sedentary" refers to sedentary < 5 hours/day; “high sedentary" refers to sedentary >= 5 hours/day (10).

All models were adjusted for the duration of T2D and CVD, non-occupational PA, smoking, BMI, alcohol consumption, diet quality, education, height, menopause status, and menopausal hormone use. All statistical tests were two-sided. No adjustments were made for multiple comparisons.

Abbreviations: BMI, body mass index; CI, confidence interval; CMD, cardiometabolic disease (T2D and/or CVD); CVD, cardiovascular disease; HR, hazard ratio; MET-h/week, metabolic equivalent task hours per week; OPA, occupational physical activity; SD, standard deviation; T2D, type 2 diabetes; UKB, UK Biobank.

**Supplementary Table 18: Associations between occupational physical activity (per 1 SD increase in MET-h/week[a]) and the risk of colorectal and breast cancer by cardiometabolic disease status in UKB.**

| Outcomes | Models | N | Cases | HR | 95% CI | p1 | p2 | p3 |
|---|---|---|---|---|---|---|---|---|
| Colorectal cancer | Overall [4a] | 215097 | 1861 | 0.983 | 0.935, 1.033 | 0.499 | | |
| | Overall, Adj T2D and CVD[5] | 206228 | 1786 | 0.989 | 0.940, 1.040 | 0.659 | | |
| | Without T2D6 | 206228 | 1786 | 0.989 | 0.94, 1.040 | 0.659 | | |
| | With T2D6 | 8869 | 75 | 0.858 | 0.676, 1.089 | 0.208 | 0.24 | 0.24 |
| | Without CVD[6] | 194878 | 1708 | 0.982 | 0.933, 1.035 | 0.500 | | |
| | With CVD[6] | 20219 | 153 | 0.990 | 0.848, 1.155 | 0.894 | 0.93 | 0.93 |
| | Without CMD[6] | 189049 | 1657 | 0.984 | 0.934, 1.037 | 0.554 | | |
| | With CMD[6] | 26048 | 204 | 0.974 | 0.851, 1.115 | 0.701 | 0.88 | 0.88 |
| Breast cancer | Overall [4b] | 98890 | 3269 | 0.965 | 0.931, 1.002 | 0.061 | | |
| | Overall Adj T2D and CVD[5] | 96201 | 3219 | 0.964 | 0.928, 1.000 | 0.050 | | |
| | Without T2D[6] | 96201 | 3219 | 0.964 | 0.928, 1.000 | 0.050 | | |
| | With T2D[6] | 2689 | 50 | 1.071 | 0.828, 1.385 | 0.603 | 0.43 | 0.43 |
| | Without CVD[6] | 93548 | 3172 | 0.958 | 0.923, 0.995 | 0.026 | | |
| | With CVD[6] | 5342 | 97 | 1.181 | 0.987, 1.414 | 0.068 | 0.029 | 0.029 |
| | Without CMD[6] | 91510 | 3130 | 0.958 | 0.922, 0.995 | 0.025 | | |
| | With CMD[6] | 7380 | 139 | 1.119 | 0.960, 1.304 | 0.149 | 0.058 | 0.058 |

[a] One SD = 64 MET-h/week of OPA for the colorectal, and 46 MET-h/week for the breast cancer analysis.
[1] p-values for the association (from Wald tests in Cox proportional hazards models).
[2] p-values for local interaction tests (from the full models including interaction terms).
[3] p-value for the global interaction test (from the likelihood ratio test comparing models with and without interaction).
[4a] Model 1: adjusted for non-occupational PA, education, BMI, height, smoking status, alcohol consumption, diet quality, menopause status, menopausal hormone use, and stratified by age (5-year categories), sex, and recruitment centre.
[4b] Model 1: adjusted for non-occupational PA, education, BMI, height, smoking status, alcohol consumption, diet quality, menopause status, menopausal hormone use, age at menarche, age at first birth, parity, family history of breast cancer, and stratified by age (5-year categories) and recruitment centre.
[5] Model 2: further adjusted for T2D and CVD, and the duration of these comorbidities.
[6] Model 3: further including interaction terms between OPA and T2D, CVD, and CMD (adjusted multiplicative interaction computed from the full model with interaction). All statistical tests were two-sided.
Abbreviations: BMI, body mass index, CI, confidence interval; CMD, cardiometabolic disease (T2D and/or CVD); CVD, cardiovascular disease; EPIC, European Prospective Investigation into Cancer and Nutrition; HR, hazard ratio; MET-h/week, metabolic equivalent task hours per week; OPA, occupational physical activity; SD, standard deviation; T2D, type 2 diabetes; UKB, UK Biobank.

**Supplementary Table 19: Joint and additive interactive effects of occupational physical activity and cardiometabolic diseases on physical activity-related cancer risk in UKB**

| Joint exposures | N | Cases | HR | 95% CI | p1 |
|---|---|---|---|---|---|
| High OPA, without T2D | 85219 | 3277 | Ref | Ref | |
| High OPA, with T2D | 4149 | 150 | 1.408 | 1.001, 1.982 | 0.050 |
| Moderate OPA, without T2D | 51081 | 2111 | 0.94 | 0.889, 0.994 | 0.030 |
| Moderate OPA with T2D | 2052 | 73 | 1.21 | 0.828, 1.768 | 0.326 |
| Low, without T2D | 77272 | 3140 | 1.021 | 0.970, 1.074 | 0.433 |
| Low, with T2D | 2668 | 89 | 1.222 | 0.846, 1.766 | 0.285 |
| **RERI** | | | **-0.21** | **-0.87, 0.45** | |
| High OPA, without CVD | 83466 | 3109 | Ref | Ref | |
| High OPA, with CVD | 9102 | 318 | 1.636 | 1.291, 2.072 | <0.001 |
| Moderate OPA, without CVD | 50129 | 2028 | 0.949 | 0.897, 1.005 | 0.075 |
| Moderate OPA with CVD | 4932 | 156 | 1.314 | 1.011, 1.709 | 0.041 |
| Low OPA, without CVD | 76105 | 3064 | 1.037 | 0.985, 1.093 | 0.165 |
| Low OPA, with CVD | 6185 | 165 | 1.228 | 0.947, 1.591 | 0.121 |
| **RERI** | | | **-0.44** | **-0.95, 0.06** | |
| High OPA, without CMD | 82977 | 3011 | Ref | Ref | |
| High OPA, with CMD | 11772 | 416 | 1.587 | 1.294, 1.947 | <0.001 |
| Moderate OPA, without CMD | 49825 | 1975 | 0.95 | 0.896, 1.007 | 0.082 |
| Moderate OPA with CMD | 6288 | 209 | 1.323 | 1.055, 1.659 | 0.015 |
| Low OPA, without CMD | 75779 | 3002 | 1.041 | 0.988, 1.097 | 0.132 |
| Low OPA, with CMD | 7988 | 227 | 1.250 | 1.000, 1.562 | 0.050 |
| **RERI** | | | **-0.38** | **-0.81, 0.05** | |

Reference category: High OPA without cardiometabolic disease.

Occupational Physical Activity (OPA) was categorized into three groups based on occupational physical activity (OPA) levels: Low (0 MET-hours/week, representing participants with no occupational physical activity),

Moderate OPA (>0 to 37.5 MET-hours/week) and High OPA (>37.5 MET-hours/week). The cutoff of 37.5 MET-hours/week corresponds to the 60th percentile of the OPA distribution. The models were stratified by age (5-year categories), sex, and recruitment centre, and adjusted for non-occupational PA, education, BMI, height, smoking status, alcohol consumption, diet quality, menopause status, menopausal hormone use, time since diagnosis of CVD and T2D, and Joint OPA-disease exposure for each condition (T2D, CVD, and combined) in each model. Hazard ratios for each cohort were estimated using multivariable Cox proportional hazards models. The overall estimates were obtained using a random-effects meta-analysis. All statistical tests were two-sided. All statistical tests were two-sided. p-values smaller than 0.001 are shown as '<0.001' for readability. Relative excess risk due to interactions (RERI) was computed for those who had low OPA with T2D, CVD, and CMD.

Abbreviations: CI, confidence interval; CMD, having incident T2D and/or CVD; CVD, cardiovascular disease; HR, hazard ratio; MET-h/week, metabolic equivalent task hours per week; OPA, occupational physical activity; RERI, Relative excess risk due to interactions; T2D, type 2 diabetes; UKB, UK Biobank.

**Supplementary Table 20: Joint and additive interactive effects of occupational physical activity and cardiometabolic diseases on colorectal cancer risk in UKB**

| Joint exposures | N | Cases | HR | 95% CI | p1 |
|---|---|---|---|---|---|
| High OPA, without T2D | 85219 | 747 | Ref | | Ref |
| High OPA, with T2D | 4149 | 32 | 0.764 | 0.340, 1.718 | 0.516 |
| Moderate OPA, without T2D | 51081 | 391 | 0.861 | 0.759, 0.977 | 0.020 |
| Moderate OPA, with T2D | 2052 | 15 | 0.706 | 0.290, 1.719 | 0.443 |
| Low OPA, without T2D | 77272 | 648 | 1.040 | 0.931, 1.162 | 0.487 |
| Low OPA, with T2D | 2668 | 28 | 1.088 | 0.477, 2.481 | 0.841 |
| **RERI** | | | **0.28** | **-0.81, 1.38** | |
| High OPA, without CVD | 83466 | 705 | Ref | | Ref |
| High OPA, With CVD | 9102 | 74 | 1.238 | 0.744, 2.058 | 0.411 |
| Moderate OPA, without CVD | 50129 | 370 | 0.866 | 0.761, 0.985 | 0.029 |
| Moderate OPA, with CVD | 4932 | 36 | 1.054 | 0.602, 1.845 | 0.854 |
| Low OPA, without CVD | 76105 | 633 | 1.068 | 0.954, 1.196 | 0.253 |
| Low OPA, with CVD | 6185 | 43 | 1.097 | 0.636, 1.893 | 0.740 |
| **RERI** | | | **-0.21** | **-1.09, 0.67** | |
| High OPA, without CMD | 82977 | 681 | Ref | | Ref |
| High OPA, with CMD | 11772 | 98 | 1.094 | 0.695, 1.720 | 0.698 |
| Moderate OPA, without CMD | 49825 | 363 | 0.874 | 0.767, 0.996 | 0.044 |
| Moderate OPA, with CMD | 6288 | 43 | 0.860 | 0.518, 1.425 | 0.557 |
| Low OPA, without CMD | 75779 | 613 | 1.062 | 0.947, 1.191 | 0.300 |
| Low OPA, CMD | 7988 | 63 | 1.073 | 0.665, 1.731 | 0.774 |
| **RERI** | | | **-0.08** | **-0.81, 0.64** | |

Reference category: High OPA without cardiometabolic disease.

Occupational Physical Activity (OPA) was categorized into three groups based on occupational physical activity (OPA) levels: Low (0 MET-hours/week, representing participants with no occupational physical activity),

Moderate OPA (>0 to 37.5 MET-hours/week) and High OPA (>37.5 MET-hours/week). The cutoff of 37.5 MET-hours/week corresponds to the 60th percentile of the OPA distribution. The models were stratified by age (5-year categories), sex, and recruitment centre, and adjusted for non-occupational PA, education, BMI, height, smoking status, alcohol consumption, diet quality, menopause status, menopausal hormone use, time since diagnosis of CVD and T2D, and Joint OPA-disease exposure for each condition (T2D, CVD, and combined) in each model. Relative excess risk due to interactions (RERI) was computed for those who had low OPA with T2D, CVD, and CMD. Hazard ratios for each cohort were estimated using multivariable Cox proportional hazards models. The overall estimates were obtained using a random-effects meta-analysis. All statistical tests were two-sided. All statistical tests were two-sided.

Abbreviations: CI, confidence interval; CMD, having incident T2D and/or CVD; CVD, cardiovascular disease; HR, hazard ratio; MET-h/week, metabolic equivalent task hours per week; OPA, occupational physical activity; RERI, Relative excess risk due to interactions; T2D, type 2 diabetes; UKB, UK Biobank.

**Supplementary Table 21: Joint and additive interactive effects of occupational physical activity and cardiometabolic diseases on breast cancer risk in UKB**

| Joint exposures | N | Cases | HR | 95% CI | p1 |
|---|---|---|---|---|---|
| High OPA, without T2D | 37194 | 1139 | Ref. | | Ref |
| High OPA, with T2D | 1162 | 24 | 1.749 | 0.813, 3.762 | 0.15 |
| Moderate OPA, without T2D | 23214 | 756 | 1.015 | 0.925, 1.113 | 0.76 |
| Moderate OPA, with T2D | 643 | 11 | 1.340 | 0.558, 3.220 | 0.51 |
| Low OPA, without T2D | 38042 | 1324 | 1.086 | 1.001, 1.177 | 0.046 |
| Low OPA, with T2D | 884 | 15 | 1.358 | 0.595, 3.098 | 0.47 |
| **RERI** | | | **-0.48** | **-2.23, 1.27** | |
| High OPA, without CVD | 36930 | 1115 | Ref. | | Ref |
| High OPA, With CVD | 2182 | 48 | 1.320 | 0.720, 2.421 | 0.37 |
| Moderate OPA, without CVD | 23011 | 748 | 1.029 | 0.937, 1.130 | 0.55 |
| Moderate OPA, with CVD | 1377 | 19 | 0.761 | 0.375, 1.543 | 0.45 |
| Low OPA, without CVD | 37818 | 1309 | 1.095 | 1.009, 1.188 | 0.029 |
| Low OPA, with CVD | 1783 | 30 | 0.945 | 0.495, 1.805 | 0.86 |
| **RERI** | | | **-0.47** | **-1.52, 0.58** | |
| High OPA, without CMD | 36775 | 1096 | Ref. | | Ref |
| High OPA, with CMD | 3064 | 67 | 1.519 | 0.939, 2.457 | 0.088 |
| Moderate OPA, without CMD | 22913 | 737 | 1.029 | 0.937, 1.131 | 0.55 |
| Moderate OPA, with CMD | 1855 | 30 | 1.044 | 0.601, 1.814 | 0.88 |
| Low OPA, without CMD | 37707 | 1297 | 1.099 | 1.012, 1.193 | 0.024 |
| Low OPA, CMD | 2461 | 42 | 1.131 | 0.675, 1.895 | 0.64 |
| **RERI** | | | **-0.49** | **-1.43, 0.45** | |

Reference category: High OPA without cardiometabolic disease.

Occupational Physical Activity (OPA) was categorized into three groups based on occupational physical activity (OPA) levels: Low (0 MET-hours/week, representing participants with no occupational physical activity),

Moderate OPA (>0 to 29.97 MET-hours/week) and High OPA (>29.97 MET-hours/week). The cutoff of 29.97 MET-hours/week corresponds to the 60th percentile of the OPA distribution. The models were stratified by age (5-year categories) and recruitment centre, and adjusted for non-occupational PA, education, BMI, height, smoking status, alcohol consumption, diet quality, menopause status, menopausal hormone use, age at menarche, age at first birth, parity, family history of breast cancer, time since diagnosis of CVD and T2D, and Joint OPA-disease exposure for each condition (T2D, CVD, and combined) in each model. Hazard ratios for each cohort were estimated using multivariable Cox proportional hazards models. The overall estimates were obtained using a random-effects meta-analysis. All statistical tests were two-sided. All statistical tests were two-sided. Relative excess risk due to interactions (RERI) computed for those who had low PA with T2D, CVD, and CMD.

Abbreviations: CI, confidence interval; CMD, having incident T2D and/or CVD; CVD, cardiovascular disease; HR, hazard ratio; MET-h/week, metabolic equivalent task hours per week; OPA, occupational physical activity; RERI, Relative excess risk due to interactions; T2D, type 2 diabetes; UKB, UK Biobank.

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**Supplementary Text 1: Ethical approval review board information for local EPIC centres**

| Center/Country | Ethical Review Board |
|---|---|
| Denmark | The National Committee on Health Research Ethics |
| Heidelberg, Germany | Ethics Committee of the Heidelberg University Medical School - Heidelberg, Germany |
| Potsdam, Germany | Ethikkommission der Landesärztekammer Brandenburg Cottbus - Potsdam, Germany |
| Milan, Italy | Comitato Etico Indipendente, Fondazione IRCCS Istituto nazionale dei Tumori – Milano-Italy |
| Turn, Italy | Human Genetics Foundation Torino: Ethics Committee - Turin, Italy |
| The Netherlands | The Medical Ethical Committee (METC = Medisch Ethische Toetsingscommissie) of the University Medical Center Utrecht (UMCU), Utrecht - the Netherlands |
| Spain | CEIC Comité de Ética de Investigación Clínica -Spain |
| Cambridge, UK | Norwich District Ethics Committee - Cambridge, UK |
| Oxford, UK | Scotland A Research Ethics Committee (Oxford); and the Imperial College Research Ethics Committee [ICREC] (UK). |