**Incident cardiovascular events and imaging phenotypes in UK Biobank participants with past cancer**

Zahra Raisi-Estabragh (MBChB, PhD)1, 2, Jackie Cooper (MSc)1, Celeste McCracken (MSc)3, Emma J. Crosbie (MBBS, PhD)4, 5, Fiona M. Walter (MBBS, PhD)6, 7, Charlotte H. Manisty (MBBS, PhD)2,8, John Robson (MBBS, MD)6, Mamas A. Mamas (MBBS, DPhil)9, 10, Nicholas C. Harvey (MBBS, PhD)11, 12, Stefan Neubauer (MBBS, PhD, FMedSci)3, Steffen E. Petersen (MBBS, DPhil)1, 2, 13, 14

1. William Harvey Research Institute, NIHR Barts Biomedical Research Centre, Queen Mary University of London, Charterhouse Square, London, EC1M 6BQ, UK
2. Barts Heart Centre, St Bartholomew’s Hospital, Barts Health NHS Trust, West Smithfield, EC1A 7BE, London, UK
3. Division of Cardiovascular Medicine, Radcliffe Department of Medicine, University of Oxford, National Institute for Health Research Oxford Biomedical Research Centre, Oxford University Hospitals NHS Foundation Trust, Oxford, OX3 9DU, UK
4. Division of Cancer Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Oxford Road, Manchester, M13 9WL, UK.
5. Department of Obstetrics and Gynaecology, St Mary’s Hospital, Manchester University NHS Foundation Trust, Manchester Academic Health Science Centre, Oxford Road, Manchester, M13 9WL, UK
6. Wolfson Institute of Population Health, Queen Mary University of London, Charterhouse Square, London, EC1M 6BQ, UK
7. Department of Public Health and Primary Care, University of Cambridge, UK
8. Institute of Cardiovascular Science, University College London, London, UK
9. Institute of Population Health, University of Manchester, UK
10. Keele Cardiovascular Research Group, Keele University, Keele, UK
11. MRC Lifecourse Epidemiology Centre, University of Southampton, Southampton, SO16 6YD, UK
12. NIHR Southampton Biomedical Research Centre, University of Southampton and University Hospital Southampton NHS Foundation Trust, Southampton, UK
13. Health Data Research UK, London, UK
14. Alan Turing Institute, London, UK

**Corresponding author:** Dr Zahra Raisi-Estabragh. William Harvey Research Institute, NIHR Barts Biomedical Research Centre, Queen Mary University of London, Charterhouse Square, London, EC1M 6BQ. E-mail: [zahraraisi@doctors.org.uk](mailto:zahraraisi@doctors.org.uk), Tel: +44 (20) 37658766

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**Abstract**

**Objectives:** To evaluate incident cardiovascular outcomes and imaging phenotypes in UK Biobank participants with previous cancer.

**Methods:** Cancer and cardiovascular disease (CVD) diagnoses were ascertained using health record linkage.Participants with cancer history (breast, lung, prostate, colorectal, uterus, haematological) were propensity matched on vascular risk factors to non-cancer controls.Competing risk regression was used to calculate sub-distribution hazard ratios (SHRs) for associations of cancer history with incident CVD [ischemic heart disease (IHD), non-ischemic cardiomyopathy (NICM), heart failure (HF), atrial fibrillation/flutter, stroke, pericarditis, venous thromboembolism (VTE)] and mortality outcomes (any CVD, IHD, HF/NICM, stroke, hypertensive disease) over 11.8±1.7years of prospective follow-up. Linear regression was used to assess associations of cancer history with left ventricular (LV) and left atrial (LA) metrics.

**Results**: We studied 18,714 participants (67% women, age:62 [interquartile range:57-66] years, 97% White ethnicities) with cancer history, including 1,354 individuals with cardiovascular magnetic resonance. Participants with cancer had high burden of vascular risk factors and prevalent CVD. Haematological cancer was associated with increased risk of all incident CVDs (SHRs:1.92-3.56), larger chamber volumes, lower ejection fractions, and poorer LV strain. Breast cancer was associated with increased risk of selected CVDs (NICM, HF, pericarditis, VTE; SHRs:1.34-2.03), HF/NICM death, hypertensive disease death, lower LV ejection fraction, and lower LV global function index. Lung cancer was associated with increased risk of pericarditis, HF, and CVD death. Prostate cancer was linked to increased VTE risk.

**Conclusions:** Cancer history is linked to increased risk of incident CVDs and adverse cardiac remodelling independent of shared vascular risk factors.

**Keywords:** Cardio-oncology; Cardiometabolic disease; Cardiovascular mortality; Cardiovascular magnetic resonance; Epidemiology.

**Key Messages**

**What is already known on this topic?**

Few studies have reported associations of past cancer with incident cardiovascular outcomes in large population-based cohorts, and none have included cardiovascular imaging.

**What this study adds?**

We studied 18,714 UK Biobank participants with history of six common cancers and an equal number of non-cancer comparators propensity matched on vascular risk factors. Our results demonstrate association of cancer history with increased risk of a wide range of incident cardiovascular disease and mortality outcomes over 12 years of prospective follow-up. In participants with cardiovascular magnetic resonance (n=1,354), cancer history was linked to adverse cardiac remodelling. The greatest range and magnitude of risk was observed in those with past breast and haematological cancers.

**How this study might affect research, practice or policy?**

People with past cancer have heightened cardiovascular risk, which appears independent of vascular risk factors and persists several years after initial cancer diagnosis. This study highlights the specific cardiovascular care needs of cancer patients and supports consideration of cancer-specific exposures in cardiovascular risk stratification.

**Abbreviations list**

AF: atrial fibrillation

BAME: Black, Asian, and Minority ethnic

BMI: body mass index

CI: confidence intervals

CMR: cardiovascular magnetic resonance

CVD: cardiovascular disease

DBP: diastolic blood pressure

DVT: deep vein thrombosis

GLS: global longitudinal strain

Haem: haematological

HbA1c: glycated haemoglobin

HES: hospital episode statistics

HDL: high density lipoprotein

HF: heart failure

IHD: ischemic heart disease

LA: left atrial

LAEF: left atrial ejection fraction

LAV: left atrial maximum volume

LDL: low density lipoprotein

LV: left ventricular

LVEDV: left ventricular end-diastolic volume

LVEF: left ventricular ejection fraction

LVGFI: left ventricular global function index

NICM: non-ischemic cardiomyopathies

PE: pulmonary embolus

SBP: systolic blood pressure

SHR: sub-distribution hazard ratios

VTE: venous thromboembolism

**Introduction**

Patients with cancer history represent a growing cohort at heightened cardiovascular risk, attributed to shared vascular risk factors, cardiotoxicities of cancer therapies, and biologic processes related to the cancer itself[1,2]. There is differential propensity to cardiovascular disease (CVD) across cancer sites, reflecting variation in these risk exposures[3,4].

Existing work indicates highest risk of cardiovascular complications to be in the first year after cancer diagnosis[5]. Few researchers have examined longer-term cancer-specific cardiovascular risk in population samples. Such analyses are important for informing cardiovascular risk stratification, surveillance, and treatment of patients with past cancer.

Cardiovascular imaging has a key role in detecting subclinical cardiotoxicity. However, associations of cancer with cardiovascular remodelling in population cohorts have not been previously reported.

We evaluated cardiovascular health in 18,714 UK Biobank participants with previous cancer, characterising disease and risk factor burden, incident disease and mortality outcomes, and cardiovascular remodelling patterns.

**Methods**

**Setting and study population**

The UK Biobank includes over 500,000 participants aged 40-69 years, characterised in detail at baseline recruitment (2006-2010)[6]. Incident health events are prospectively tracked through extensive health record linkages (Hospital Episode Statistics [HES], cancer register, death register). The UK Biobank Imaging Study is underway and aims to scan 100,000 of the original participants.

**Ascertainment of cancer history**

Cancer history was ascertained from cancer registry and HES records (**Supplementary Table 1**). We created six categories (lung, breast, prostate, haematological, uterus, colorectal) to capture the most common cancer sites[7]. The primary cancer site was defined from the first code for cancer in any of the linked databases.

**Ascertainment of incident cardiovascular outcomes**

We defined incident CVD [ischemic heart disease (IHD), stroke, atrial fibrillation (AF)/flutter, heart failure (HF), non-ischemic cardiomyopathies (NICM), venous thromboembolism [VTE: deep vein thrombosis (DVT), pulmonary embolus (PE)], pericarditis] and mortality outcomes (IHD, stroke, hypertensive diseases, HF or NICMs) using HES and death registration records (**Supplementary Table 2**).

**CMR acquisition and analysis**

CMR scans were performed according to pre-defined protocols and analysed using automated pipelines[8–10]. These are research scans without any clinical indication. The following metrics were included: left ventricular (LV) end-diastolic volume (LVEDV), LV ejection fraction (LVEF), LV global function index (LVGFI), LV global longitudinal strain (GLS), left atrial (LA) maximum volume (LAV), LA ejection fraction (LAEF).

**Statistical analysis**

Statistical analysis was performed using R studio version 4.1.0 [[https://www.R-project.org/](https://www.r-project.org/)] and Stata version 17[11]. Baseline characteristics are presented as number (percentage) for categorical variables, mean (standard deviation, SD) for normally distributed continuous variables, and median [interquartile range] for non-normally distributed continuous variables. A propensity matched non-cancer comparator cohort was created with a priori selection of covariates (**Supplementary Figure 1, Supplementary Tables 3 and 4**). Comparators were participants without record of cancer at baseline. Each cancer exposed participant was matched to one non-exposed participant using nearest neighbour propensity score matching on 20 pre-defined baseline covariates. Pairs were discarded if no matching participant had logit propensity score within 0.2 SDs of the case[12]. Balance of covariates was assessed in the unmatched and matched samples using the standardized mean difference between exposed and non-exposed groups (**Supplementary Figure 2**). Missing data values were imputed using Single Centre Imputation from the Multiple Chained Equation algorithm.

Competing risks regression was used to calculate sub-distribution hazard ratios (SHR) and 95% confidence intervals (CIs) for the association of cancer history at baseline with incident disease and mortality outcomes. Participants with the outcome of interest at baseline were excluded from analyses for that outcome (but included in analyses of other outcomes). Incident events were first occurrence of the outcome after baseline. Prevalent events were conditions present at baseline. The censor date was 26th March 2021, providing mean prospective follow-up of 11.8 ± 1.7 years. We performed sensitivity analyses using cause-specific Cox regression, limiting to cases with complete data (no imputation), and to cancers diagnosed within five-years prior to baseline. Given possible heterogeneities within the haematological cancer category, we examined associations with incident outcomes within its subcategories (lymphoma, leukaemia, myeloma). We tested for interaction of cancer exposure with time by defining time from cancer diagnosis to baseline for cases and assigning the same time to their matched controls.

Linear regression was used to estimate association of cancer exposure with each CMR metric, reporting standardized beta coefficients, 95% CIs, and p-values. For this analysis, cancer status was ascertained at imaging (any cancer diagnosis had been established prior to imaging). The samples all matched well on overall propensity score, individual covariates which were less well matched were included as covariates in final models, as per Nguyen et al. (**Supplementary Figure 3**)[13]. We repeated the analysis excluding individuals with CVD at time of imaging. A two-sided significance level of 0.05 was used for all comparisons.

**Results**

**Baseline characteristics**

We analysed 18,714 participants with past cancer (**Supplementary Figure 4**). Smoking was most common in those with lung (82.9%), colorectal (54.4%), and prostate (53.0%) cancer (**Table 1)**. Diabetes was most common in lung (9.9%), uterine (9.5%), and colorectal (8.8%) cancer. The highest rates of hypertension were in prostate (45.6%), colorectal (39.5%), and uterine (38.4%) cancer. Individuals with uterine cancer had the highest average body mass index. Among those with cancer, 17.6% had pre-existing CVD (**Table 2**).

**Incident events**

Almost one-third of participants with cancer, developed one of the incident CVDs (**Table 2**). The highest rates of incident CVD were in participants with lung (49.4%), haematological (48.4%), and prostate (40.6%) cancer. Incident IHD, AF/flutter, and HF were the top three incident CVDs across all cancers. Over the study period, 18.8% of participants with cancer died compared to 8.5% of controls. In those with cancer, 8.2% (287/3514) of deaths were primary cardiovascular deaths.

**Breast cancer**

Amongst participants with breast cancer, 22.3% (2130/9531) developed one of the incident CVDs considered and 15.3% (1454/9531) died. The most common incident CVDs were IHD (5.9%), AF/flutter (5.8%), HF (3.5%), VTE (3.2%), and stroke (2.2%). NICMs occurred in 0.9% and pericarditis in 0.8% of participants with breast cancer. A total of 5.1% (74/1454) of all deaths were primary cardiovascular deaths. The most common causes of CVD death were stroke and IHD.

Compared to matched non-cancer controls, those with past breast cancer had over 2-fold greater risk of incident pericarditis [SHR 2.03 (1.36, 3.00); p=0.0004], 80% greater risk of incident NICM [SHR 1.80 (1.27, 2.56), p=0.0008], and 45% greater risk of incident VTE [SHR 1.45 (1.21, 1.73); p=6.61x10-5] (**Table 3, Figure 1**). Breast cancer history was associated with 8.5-fold greater risk of death from HF or NICM [SHR 8.50 (1.95, 36.97); p=0.004] and 8-fold greater risk of death from hypertensive diseases [SHR 8.00 (1.00, 64.07); p=0.05].

**Table 1. Baseline participant characteristics**

|  | **Cases** | **Controls** | **Breast** | **Lung** | **Prostate** | **Colorectal** | **Uterus** | **Haem** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| N | 18714 | 18714 | 9531\* | 313 | 3291 | 2412 | 937 | 2230 |
| Age | 62 [57-66] | 62 [57-66] | 61 [56-65] | 62 [58-66] | 65 [62-67] | 63 [59-66] | 63 [59-66] | 60 [53-65] |
| Men | 6095 (32.6) | 6095 (32.6) | 0 (0) | 170 (54.3) | 3291 (100) | 1383 (57.3) | 0 (0) | 1251 (56.1) |
| Women | 12619 (67.4) | 12619 (67.4) | 9531 (100) | 143 (45.7) | 0 (0) | 1029 (42.7) | 937 (100) | 979 (43.9) |
| White ethnicity | 18002 (96.7) | 18025 (96.7) | 9201 (96.9) | 301 (96.2) | 3143 (96.1) | 2324 (96.6) | 910 (97.5) | 2146 (96.7) |
| BAME | 617 (3.3) | 611 (3.3) | 299 (3.2) | 12 (3.8) | 129 (3.9) | 81 (3.4) | 23 (2.5) | 73 (3.3) |
| Townsend score | -2.3 [-3.7, 0.3] | -2.3 [-3.7, 0.3] | -2.3 [-3.7, 0.2] | -0.7 [-3.3, 2.5] | -2.4 [-3.8, -0.1] | -2.2 [-3.7, 0.4] | -2.2 [-3.6, 0.0] | -2.2 [-3.6, 0.5] |
| Degree or professional qualification | 8329 (45.5) | 8300 (45.4) | 4259 (45.5) | 96 (32.1) | 1513 (47.1) | 1022 (43.3) | 382 (42.0) | 1057 (48.5) |
| SBP (mmHg) | 140.2 ± 19.2 | 140.1 ± 19.1 | 138.5 ± 19.4 | 137.7 ± 19.3 | 145.0 ± 17.8 | 142.6 ± 19.2 | 141.2 ± 18.7 | 137.5 ± 18.9 |
| DBP (mmHg) | 82.0 ± 10.1 | 82.0 ± 10.0 | 81.4 ± 9.9 | 81.5 ±11.2 | 84.0 ± 9.9 | 82.6 ± 10.1 | 82.1 ± 9.6 | 81.1 ± 10.6 |
| HR (bpm) | 70.5 [63.5-78.5] | 70 [63-78] | 71.5 [65-79] | 75 [67-83.5] | 67.5 [60.5-75.5] | 69.5 [62.5-77.5] | 71 [64-78] | 70.5 [63-80] |
| BMI (kg/m2) | 26.8 [24.2-30.0] | 26.7 [24.1-29.9] | 26.4 [23.7-29.7] | 26.7 [24.3-30.1] | 27.4 [25.1-30.0] | 27.2 [24.7-30.2] | 28.4 [24.7-33.7] | 26.8 [24.2-30.0] |
| Physical activity (METS/week) | 1695 [754-3426] | 1742 [782-3471] | 1695 [777-3336] | 1175 [375-2799] | 1874 [817-3848] | 1626 [704-3412] | 1624 [710-3506] | 1578 [693-3279] |
| Ever Smoked | 8909 (48.0) | 9141 (49.2) | 4225 (44.6) | 257 (82.9) | 1725 (53.0) | 1304 (54.4) | 342 (36.8) | 1056 (47.6) |
| HbA1c (mmol/mol) | 36 [33.5-38.7] | 35.9 [33.4-38.5] | 36 [33.7-38.5] | 37 [34.1-39.7] | 36 [33.4-38.6] | 36 [33.4-39.1] | 36.4 [34.1-39.2] | 35.5 [32.8-38.4] |
| Random glucose (mmol/L) | 5.0 [4.7-5.4] | 5.0 [4.6-5.4] | 5.0 [4.7-5.4] | 4.9 [4.6-5.4] | 5.0 [4.7-5.5] | 5.1 [4.7- 5.5] | 5.0 [4.7- 5.5] | 5.0 [4.6-5.4] |
| Total cholesterol (mmol/L) | 5.8 ±1.2 | 5.8 ±1.2 | 6.0 ± 1.2 | 5.6 ± 1.3 | 5.4 ± 1.1 | 5.6 ± 1.2 | 5.9 ± 1.2 | 5.6 ±1.2 |
| HDL (mmol/L) | 1.4 [1.2-1.7] | 1.4 [1.2-1.7] | 1.6 [1.3-1.8] | 1.3 [1.1-1.6] | 1.3 [1.1-1.5] | 1.4 [1.1-1.7] | 1.5 [1.3-1.7] | 1.3 [1.1-1.6] |
| LDL (mmol/L) | 3.5 [2.9-4.2] | 3.6 [2.9-4.2] | 3.6 [3.0-4.3] | 3.4 [2.8-4.1] | 3.4 [2.8-4.0] | 3.4 [2.8-4.1] | 3.6 [3.0-4.3] | 3.5 [2.9-4.1] |
| Triglyceride level (mmol/L) | 1.6 [1.1-2.2] | 1.5 [1.1-2.2] | 1.5 [1.1-2.1] | 1.7 [1.2-2.3] | 1.7 [1.2-2.4 | 1.7 [1.2-2.4] | 1.6 [1.2-2.2] | 1.6 [1.1-2.4] |
| Diabetes | 1222 (6.5) | 1238 (6.6) | 463 (4.9) | 31 (9.9) | 264 (8.0) | 211 (8.8) | 89 (9.5) | 164 (7.4) |
| Hypertension | 6421 (34.3) | 6443 (34.4) | 2761 (29.0) | 108 (34.5) | 1499 (45.6) | 953 (39.5) | 360 (38.4) | 740 (33.2) |
| High cholesterol | 5659 (30.2) | 5627 (30.1) | 2272 (23.8) | 115 (36.7) | 1431 (43.5) | 882 (36.6) | 304 (32.4) | 655 (29.4) |

**Table 1 footnote.** \*39 males excluded. Continuous variables are shown as mean ±standard deviation, or median [IQR] if skewed. Count variables are shown as N (%). BAME: Black, Asian, and Minority ethnic; BMI: body mass index; HbA1c: glycated haemoglobin, HDL: high density lipoprotein, LDL: low density lipoprotein; DBP: diastolic blood pressure; Haem: haematological; SBP: systolic blood pressure.

**Table 2. Prevalent and incident cardiovascular diseases and mortality**

|  | **Cases** | **Controls** | **Breast** | **Lung** | **Prostate** | **Colorectal** | **Uterus** | **Haem** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| N (Total) | 18714 | 18714 | 9531 | 313 | 3291 | 2412 | 937 | 2230 |
| Prevalent CVDs (N, %) | 3289 (17.6) | 2856 (15.3) | 1119 (11.7) | 116 (37.1) | 805 (24.5) | 554 (23.0) | 121 (12.9) | 574 (25.7) |
| IHD | 1238 (6.6) | 1286 (6.9) | 348 (3.7) | 45 (14.4) | 375 (11.4) | 222 (9.2) | 45 (4.8) | 203 (9.1) |
| NICM | 52 (0.3) | 33 (0.2) | 21 (0.2) | 1 (0.3) | 11 (0.3) | 7 (0.3) | 2 (0.2) | 10 (0.4) |
| HF | 152 (0.8) | 97 (0.5) | 44 (0.5) | 7 (2.2) | 38 (1.2) | 21 (0.9) | 4 (0.4) | 38 (1.7) |
| AF/flutter | 431 (2.3) | 394 (2.1) | 111 (1.2) | 23 (7.3) | 138 (4.2) | 71 (2.9) | 14 (1.5) | 74 (3.3) |
| Stroke | 426 (2.3) | 448 (2.4) | 160 (1.7) | 18 (5.8) | 100 (3.0) | 63 (2.6) | 15 (1.6) | 70 (3.1) |
| Pericarditis | 35 (0.2) | 22 (0.1) | 17 (0.2) | 1 (0.3) | 7 (0.2) | 4 (0.2) | 0 | 6 (0.3) |
| VTE (DVT/PE) | 955 (5.1) | 576 (3.1) | 418 (4.4) | 21 (6.7) | 136 (4.1) | 166 (6.9) | 41 (4.4) | 173 (7.8) |
| Incident CVDs (N, %)  [rate per 1000 person-years] | 5753 (30.7)  [21.5] | 4594 (24.5)  [16.3] | 2130 (22.3)  [14.7] | 155 (49.5)  [32.3] | 1335 (40.6)  [27.6] | 803 (33.3)  [22.8] | 250 (26.7)  [15.9] | 1080 (48.4)  [30.7] |
| IHD | 1584 (8.5)  [7.8] | 1425 (7.6)  [7.0] | 560 (5.9)  [5.5] | 40 (12.8)  [19.4] | 385 (11.7)  [12.3] | 245 (10.2)  [20.8] | 68 (7.3)  [6.9] | 286 (12.8)  [14.1] |
| NICM | 225 (1.2)  [1.0] | 134 (0.7)  [0.6] | 90 (0.9)  [0.8] | 2 (0.6)  [0.7] | 38 (1.2)  [1.1] | 31 (1.3)  [1.2] | 7 (0.7)  [0.6] | 57 (2.6)  [2.5] |
| HF | 950 (5.1)  [4.3] | 705 (3.8)  [3.2] | 337 (3.5)  [3.2] | 32 (10.2)  [12.5] | 205 (6.2)  [5.8] | 107 (4.4)  [4.2] | 42 (4.5)  [3.9] | 227 (10.1)  [10.0] |
| AF/flutter | 1539 (8.2)  [7.2] | 1317 (7.0)  [6.1] | 555 (5.8)  [5.4] | 38 (12.1)  [15.4] | 382 (11.6)  [11.6] | 236 (9.8)  [9.7] | 69 (7.4)  [6.3] | 259 (11.6)  [11.8] |
| Stroke | 590 (3.2)  [2.7] | 477 (2.5)  [2.2] | 211 (2.2)  [2.0] | 16 (5.1)  [6.6] | 148 (4.5)  [4.4] | 83 (3.4)  [3.3] | 30 (3.2)  [2.8] | 102 (4.6)  [4.6] |
| Pericarditis | 188 (1.0)  [0.8] | 94 (0.5)  [0.4] | 75 (0.8)  [0.7] | 12 (3.8)  [4.8] | 28 (0.9)  [0.8] | 19 (0.8)  [0.7] | 7 (0.7)  [0.6] | 47 (2.1)  [2.0] |
| VTE (DVT/PE) | 677 (3.6)  [3.4] | 442 (2.4)  [2.1] | 302 (3.2)  [2.9] | 15 (4.8)  [5.8] | 149 (4.5)  [4.3] | 82 (3.4)  [3.4] | 27 (2.9)  [2.7] | 102 (4.6)  [4.7] |
| Mortality outcomes (N, %)  [rate per 1000 person-years] | 3514 (18.8)  [17.0] | 1582 (8.5)  [7.2] | 1454 (15.3)  [13.5] | 160 (51.1)  [59.0] | 683 (20.8)  [18.9] | 499 (20.7)  [19.1] | 113 (12.1)  [10.4] | 605 (27.1)  [25.7] |
| Any CVD | 287 (1.5)  [1.4] | 265 (1.4)  [1.2] | 74 (0.8)  [0.7] | 17 (5.4)  [6.3] | 83 (2.5)  [2.3] | 54 (2.2)  [2.1] | 12 (1.3)  [1.1] | 47 (2.1)  [2.0] |
| IHD | 154 (0.8)  [0.7] | 160 (0.9)  [0.7] | 24 (0.3)  [0.2] | 14 (4.5)  [5.2] | 53 (1.6)  [1.5] | 34 (1.4)  [1.3] | 3 (0.3)  [0.3] | 26 (1.2)  [1.1] |
| HF/NICM | 37 (0.2)  [0.2] | 17 (0.1)  [0.1] | 17 (0.2)  [0.2] | 0 | 7 (0.2)  [0.2] | 5 (0.2)  [0.2] | 3 (0.3)  [0.3] | 5 (0.2)  [0.2] |
| Stroke | 65 (0.3)  [0.3] | 60 (0.3)  [0.3] | 21 (0.2)  [0.2] | 2 (0.6)  [0.7] | 16 (0.5)  [0.4] | 11 (0.5)  [0.4] | 5 (0.5)  [0.5] | 10 (0.4)  [0.4] |
| Hypertensive diseases | 21 (0.1)  [0.1] | 9 (0.1)  [0.04] | 8 (0.1)  [0.1] | 0 | 5 (0.2)  [0.1] | 3 (0.1)  [0.1] | 2 (0.2)  [0.2] | 3 (0.1)  [0.1] |

**Table 2 footnote.** Figures are numbers of participant with each condition/outcome. Percentages are shown in brackets with denominator taken as the total number of participants in each category (“total” row). Prevalent CVDs were present at baseline recruitment. Incident CVDs represent first occurrence of the condition after baseline. AF: atrial fibrillation; CVD: cardiovascular disease; DVT: deep vein thrombosis; Haem: haematological; HF: heart failure; IHD: ischaemic heart disease; NICM: non-ischaemic cardiomyopathies; PE: pulmonary embolism; VTE: venous thromboembolism.

**Table 3. Associations of cancer patients with incident cardiovascular events compared to propensity matched non-cancer controls**

|  | **Breast** | **Lung** | **Prostate** | **Colorectal** | **Uterus** | **Haematological** |
| --- | --- | --- | --- | --- | --- | --- |
| **Incident disease** |  |  |  |  |  |  |
| IHD | 1.05 (0.93, 1.19) | 1.03 (0.68, 1.57) | 0.92 (0.79, 1.07) | 1.14 (0.94, 1.38) | 1.03 (0.74, 1.42) | **1.92 (1.57, 2.34)** |
|  | 0.428 | 0.899 | 0.297 | 0.181 | 0.868 | 2.02 x 10-10 |
| NICM | **1.80 (1.27, 2.56)** | – | 1.16 (0.73, 1.86) | 1.25 (0.73, 2.14) | 3.49 (0.72, 16.78) | **2.51 (1.54, 4.10)** |
|  | 0.0008 | – | 0.543 | 0.416 | 0.121 | 0.002 |
| Heart failure | **1.34 (1.14, 1.57)** | **1.92 (1.07, 3.46)** | 1.04 (0.85, 1.26) | **0.77 (0.60, 0.99)** | 1.38 (0.86, 2.18) | **3.56 (2.69, 4.66)** |
|  | 0.0004 | 0.029 | 0.72 | 0.044 | 0.181 | 1.19 x 10-19 |
| AF/flutter | 1.11 (0.98, 1.25) | 1.39 (0.84, 2.32) | 1.00 (0.86, 1.15) | **1.26 (1.04, 1.52)** | 1.00 (0.71, 1.42) | **1.97 (1.60, 3.22)** |
|  | 0.114 | 0.206 | 0.969 | 0.02 | 0.996 | 4.43 x 10-6 |
| Stroke | 1.13 (0.91, 1.38) | 1.23 (0.58, 2.61) | 1.17 (0.92. 1.49) | 1.12 (0.82, 1.52) | 1.15 (0.68, 1.95) | **2.27 (1.60, 2.44)** |
|  | 0.259 | 0.575 | 0.194 | 0.48 | 0.59 | 2.62 x 10-10 |
| Pericarditis | **2.03 (1.36, 3.00)** | **12.18 (1.57, 94.63)** | 1.16 (0.68, 2.01) | 1.36 (0.68, 2.72) | 3.49 (0.73, 16.95) | **2.94 (1.67, 5.21)** |
|  | 0.0004 | 0.017 | 0.585 | 0.385 | 0.119 | 0.0002 |
| VTE | **1.45 (1.21, 1.73)** | 1.14 (0.53, 2.46) | **1.70 (1.30, 2.23)** | 1.21 (0.87, 1.67) | 1.70 (0.91, 3.19) | **2.69 (1.86, 3.94)** |
|  | 6.61 x 10-5 | 0.736 | 0.0001 | 0.2639 | 0.095 | 2.47 x 10-7 |
| **Mortality outcomes** |  |  |  |  |  |  |
| All-cause | **2.48 (2.25, 2.72)** | **5.00 (3.63, 6.89)** | **1.65 (1.46, 1.86)** | **2.08 (1.79, 2.41)** | **2.41 (1.73, 3.32)** | **4.14 (3.49, 4.90)** |
|  | 3.65 x10-80 | 7.25 x 10-21 | 2.40 x10-16 | 1.30 x10-21 | 3.06 x 10-7 | 3.10 x 10-59 |
| Any CVD | 0.97 (0.70, 1.34) | 2.46 (1.00, 5.99) | 0.87 (0.65, 1.17) | 1.20 (0.80, 1.79) | 1.20 (0.56, 2.59) | 1.48 (0.94, 2.32) |
|  | 0.871 | 0.05 | 0.371 | 0.374 | 0.64 | 0.087 |
| IHD | 0.63 (0.38, 1.05) | 1.99 (0.79, 5.05) | 0.87 (0.60, 1.26) | 1.06 (0.65, 1.72) | – | 1.73 (0.91, 3.29) |
|  | 0.079 | 0.14 | 0.461 | 0.820 | – | 0.090 |
| Heart failure or NICM | **8.50 (1.95, 36.97)** | – | 0.78 (0.29, 2.10) | 5.00 (0.58, 42.95) | – | 1.01 (0.29, 3.49) |
|  | 0.004 | – | 0.615 | 0.142 | – | 0.991 |
| Stroke | 0.88 (0.49, 1.57) | – | 0.94 (0.47, 1.86) | 1.22 (0.51, 2.94) | 5.00 (0.58, 42.95) | 1.12 (0.45, 2.77) |
|  | 0.656 | – | 0.853 | 0.652 | 0.142 | 0.806 |
| Hypertensive diseases | **8.00 (1.00, 64.07)** | – | 1.25 (0.34, 4.66) | – | **–** | – |
|  | 0.050 | **–** | 0.741 | – | **–** | – |

**Table 3 footnote.** Results are sub-distribution hazard ratio (95% confidence interval) and p-value associated with cancer exposure (vs no cancer). Blank cells indicate that no analysis was performed due to small number of outcomes (<5) in that category. Comparators are matched on age, sex, ethnicity, deprivation, education, blood pressure, heart rate, body mass index, glycated haemoglobin, random glucose, total cholesterol, high density lipoprotein, low density lipoprotein, triglyceride level, physical activity, smoking, diabetes, hypertension, and high cholesterol. AF: atrial fibrillation; CVD: cardiovascular disease; IHD: ischaemic heart disease; NICM: non-ischaemic cardiomyopathies; VTE: venous thromboembolism

**Lung cancer**

Amongst the cancer sites considered, participants with a history of lung cancer (n=313) had the highest rates of incident CVD (49.4%), all-cause death (51.1%), and CVD death (5.4%). The most common incident CVDs were IHD (12.8%), AF/flutter (12.1%), and HF (10.2%). Amongst participants with lung cancer who died, 10.1% (17/160) died of a primary cardiovascular cause.

Lung cancer was associated with over 12-fold greater risk of incident pericarditis [SHR 12.18 (1.57, 94.63); p=0.017], 88% greater risk of incident HF [SHR 1.88 (1.07, 3.29); p=0.029], and almost 2.5-fold greater risk of CVD death [SHR 2.46 (1.00, 5.99); p=0.05]. The risk of IHD death was increased in lung cancer patients, although with wide CIs [SHR 1.99 (0.79, 5.05); p=0.14].

**Prostate cancer**

Amongst 3,291 participants with prostate cancer, 40.6% developed incident CVD and 20.1% died. Primary cardiovascular deaths contributed 12.2% (83/683) of all deaths. The most common incident CVDs were IHD (11.7%), AF/flutter (11.6%), and HF (6.2%). Incident stroke and VTE each occurred in 4.5%, NICMs in 1.2%, and pericarditis in 0.9%.

Compared to matched non-cancer controls, participants with prostate cancer had increased risk of incident VTE [SHR 1.70 (1.30, 2.23); p=0.0001] and all-cause death [HR 1.65 (1.46, 1.86); p=2.40 x10-16]. Associations with all other outcomes were statistically non-significant.

**Colorectal cancer**

One-third (803/2,412) of participants with colorectal cancer developed incident CVD, 20.1% died, and 2.2% died of primary cardiovascular causes (10.8% of all deaths– 54/499). The most common incident CVDs were IHD (10.2%), AF/flutter (9.8%), and HF (4.4%).

Participants with colorectal cancer had 26% greater risk of incident AF/flutter [SHR 1.26 (1.04, 1.52); p=0.02] compared to matched non-cancer controls. Colorectal cancer was associated with higher risk of HF/NICM death, but with wide CIs [SHR 5.00 (0.58, 42.95); p=0.14]. Aside from all-cause death, there was no statistically significant difference in risk of any other outcome.

**Uterine cancer**

Amongst the 937 participants with uterine cancer, 26.7% developed incident CVD and 12.1% died. Primary cardiovascular deaths contributed 10.6% (12/113) of all deaths. The most common incident CVDs were AF/flutter (7.4%), IHD (7.3%), and HF (4.5%). Incident stroke occurred in 3.2%, VTE in 2.9%, and NICMs and pericarditis were each observed in 0.7% of individuals.

Compared to matched non-cancer controls, uterine cancer patients had increased (statistically non-significant) risk of incident NICM [SHR 3.49 (0.72, 16.78); p=0.12], pericarditis [SHR 3.49 (0.73, 16.95); p=0.12], and stroke death [SHR 5.00 (0.58, 42.95); p=0.14].

**Haematological cancer**

Amongst 2,230 participants with past haematological cancer, 48.5% (n=1080) developed incident CVD and 27.1% died. A total of 7.8% (47/605) of all deaths were attributed to a primary cardiovascular cause. The most common CVDs were IHD (12.8%), AF/flutter (11.6%), and HF (10.2%). Incident stroke and VTE each occurred in 4.6%, NICMs in 2.6%, and pericarditis in 2.1% of haematological cancer patients.

Participants with past haematological cancer had significantly greater risk of all incident CVDs (**Table 3**, **Figure 1**). The risk of incident HF was increased by over 3.5-fold [SHR 3.56 (2.69, 4.66); p=1.19x10-19], pericarditis by almost 3-fold [SHR 2.94 (1.67, 5.21); p=0.0002], and there was over 2.5-fold greater risk of both incident VTE [SHR 2.69 (1.86, 3.94); p=2.47x10-7] and NICM [SHR 2.51 (1.54, 4.10); p=0.002]. There was almost 2-fold increased risk of incident AF/flutter [SHR 1.97 (1.60, 2.44); p=2.62x10-10] and IHD [SHR 1.92 (1.57, 2.34); p=2.02x10-10]. Associations with CVD mortality outcomes were statistically non-significant; however, participants with a history of haematological cancer appeared at higher risk of CVD [SHR 1.48 (0.94, 2.32); p=0.087] and IHD [SHR 1.73 (0.91, 3.29); p=0.090] death.

Associations with incident events were broadly similar across myeloma, leukaemia, and lymphomas (**Supplementary Table 5 and 6**).

**Sensitivity analyses**

In analyses limiting to cases with complete data, associations remained similar across all outcomes (**Supplementary Table 7 and 8**). The results were consistent in cause-specific Cox regression models (**Supplementary Table 9**) and when restricting to participants diagnosed with cancer within 5-years of baseline (**Supplementary Table 10 and 11**). The interaction of cancer exposure with time from diagnosis was non-significant for all models, except for the association of lung cancer with incident stroke, where risk was higher in the earlier years after cancer incidence.

**Associations with CMR metrics**

We investigated associations of past cancer with cardiovascular phenotypes in 1,354 participants who had CMR data available (**Supplementary Table 12**). Compared to matched non-cancer controls, participants with past haematological cancer had larger LVEDV, poorer LV function by both LVEF and LV GLS, larger LAV, and lower LAEF (**Table 4, Figure 2**). Breast cancer was associated with significantly poorer LV function by LVEF and LVGFI. These relationships were similar in individuals without CVD at imaging (**Supplementary Table 13**).

**Table 4. Association of cancer with CMR metrics**

|  | Breast | Lung | Prostate | Colorectal† | Uterus† | Haem† |
| --- | --- | --- | --- | --- | --- | --- |
| LVM (g) | 0.07 (-0.05, 0.18) | -0.41 (-1.27, 0.46) | -0.01 (-0.14, 0.12) | -0.23 (-0.78, 0.32) | 0.14 (-0.23, 0.51) | 0.11 (-0.11, 0.33) |
|  | 0.27 | 0.33 | 0.84 | 0.40 | 0.45 | 0.33 |
| LVEDV (ml) | 0.10 (-0.01, 0.22) | -0.56 (-1.48, 0.35) | 0.05 (-0.08, 0.18) | -0.32 (-0.85, 0.22) | -0.01 (-0.37, 0.35) | **0.22 (-0.00, 0.44)** |
|  | 0.07 | 0.21 | 0.44 | 0.24 | 0.94 | 0.05 |
| LVEF (%) | **-0.18 (-0.30, -0.06)** | 0.62 (-0.26, 1.50) | 0.02 (-0.10, 0.15) | -0.12 (-0.60, 0.36) | 0.03 (-0.34, 0.41) | **-0.28 (-0.49, -0.06)** |
|  | 0.003 | 0.15 | 0.73 | 0.61 | 0.87 | 0.01 |
| LVGFI (%) | **-0.14 (-0.26, -0.02)** | 0.25 (-0.68, 1.18) | 0.05 (-0.07, 0.18) | -0.13 (-0.59, 0.34) | -0.06 (-0.45, 0.33) | -0.18 (-0.39, 0.04) |
|  | 0.02 | 0.56 | 0.41 | 0.58 | 0.76 | 0.10 |
| LV GLS (%) | -0.02 (-0.13, 0.10) | -0.87 (-1.71, -0.04) | -0.03 (-0.17, 0.11) | 0.38 (-0.26, 1.02) | 0.33 (-0.14, 0.80) | **0.25 (0.03, 0.47)** |
|  | 0.78 | 0.05 | 0.65 | 0.24 | 0.17 | 0.02 |
| LAV max (ml) | 0.08 (-0.04, 0.20) | -0.82 (-1.69, 0.05) | 0.02 (-0.11, 0.16) | -0.35 (-0.76, 0.05) | -0.01 (-0.39, 0.37) | **0.30 (0.06, 0.53)** |
|  | 0.18 | 0.06 | 0.75 | 0.09 | 0.96 | 0.01 |
| LAEF (%) | -0.12 (-0.24, 0.00) | 0.42 (-0.11, 0.94) | -0.02 (-0.15, 0.11) | 0.15 (-0.24, 0.54) | -0.07 (-0.41, 0.27) | **-0.33 (-0.56, -0.11)** |
|  | 0.06 | 0.11 | 0.74 | 0.45 | 0.68 | 0.004 |

**Table 4 footnote.** The results are standardised beta-coefficients and 95% confidence intervals, thus representing standard deviation change in CMR metrics with change in cancer exposure status from non-cancer to cancer; for standard deviation of each metric please refer to Supplementary Table 5. The bold and yellow shaded cells represent statistically significant associations. †doubly robust model.LA: left atrium; LV: left ventricle; LV end-diastolic volume (LVEDV), LV mass (LVM), LV ejection fraction (LVEF), LV global function index (LVGFI), LV global longitudinal strain (GLS), LA maximum volume (LAV), LA ejection fraction (LAEF).

**Discussion**

**Summary of findings**

In this large population-based study, covering an average of 12-years prospective follow-up, past cancer was linked to increased risk of a wide range of incident cardiovascular outcomes and adverse remodelling, independent of shared vascular risk factors. Previous haematological cancer was linked to increased incidence of all CVDs considered, poorer LV function (by LVEF and GLS), larger LV and LA size, and poorer LA function (lower LAEF). Past breast cancer was linked to increased incidence of NICM, HF, pericarditis, VTE, HF/NICM mortality, hypertensive disease death, and poorer LV function (by LVEF and LVGFI). Lung cancer was associated with increased risk of incident HF, pericarditis, and CVD death. Colorectal cancer was associated with increased risk of incident AF/flutter. Prostate cancer was linked to increased VTE risk.

**Comparison with previous work**

The most common incident CVDs in our cancer exposed cohort were IHD, AF/flutter, and HF. This distribution reflects both the risk factor profile of individuals with cancer and general population trends[14]. Consistent with previous reports, we found high burden of vascular risk factors in participants with cancer[15,16]. The observed CVD patterns are similar to studies from China and the USA[15,17]. In our cancer cohort, 8.2% of deaths were attributed to primary cardiovascular causes. Similarly, an analysis of the UK Clinical Primary Records Datalink, identified CVD as the primary cause of death in 9.7% of men and 7.7% of women with cancer[18].

Our work extends previous reports by isolating cardiovascular risk associated with cancer independent of shared risk factors. A recent study from the UK used linked primary care and hospitalization records to examine risk of incident disease-specific CVDs in cancer patients independent of vascular risk factors[3]. Our findings validate these observations in an independent cohort and provide new insights by considering disease associations alongside CMR remodelling.

Participants with previous haematological cancer had significantly increased risk of all incident CVDs. They also had increased size and poorer function of both the LA and LV. Haematological cancer patients are exposed to many cardiotoxic cancer therapies such as tyrosine kinase inhibitors[19], cyclophosphamide[20], anthracyclines[21], and mediastinal radiotherapy[22]. The observed pattern of LV remodelling associated with haematological cancer may reflect subclinical cardiotoxicity, indicating a dilated LV with lower ejection fraction and poorer longitudinal function, and is consistent with our finding of increased risk of incident NICM and HF. The atrial remodelling patterns of a dilated and poorly functioning LA may reflect hemodynamic consequences of increased LV filling pressures which accompanies HF. There may also be direct effects on the atria via radiotherapy or other treatments. Regardless of underlying mechanism, atrial remodelling is both precipitated by and predisposes to AF, which we found to be significantly associated with haematological cancer history. We also found increased risk of stroke associated with past haematological cancer, which is likely driven by both ischaemic and haemorrhagic mechanisms, with the latter precipitated by coagulopathies related to the primary cancer and greater use of anticoagulants in these patients.

Increased risk of VTE was observed in participants with haematological, breast, and prostate cancer. Many factors promote a pro-thrombotic state in the setting of cancer, such as the systemic biologic processes of the cancer itself, tumour compression effects, chemotherapy, and long-term indwelling venous catheters. Previous studies have documented augmented risk of VTE in cancer patients[23]. In our study, the magnitude of increased VTE risk was highest amongst participants with past haematological cancer.

Radiation-induced heart disease has a range of possible manifestations[24]. Mediastinal radiotherapy has been linked to initiation and progression of atherosclerosis. Patients with lymphomas are often exposed to mediastinal radiotherapy, which may be a driver of the increased risk of IHD in participants with previous haematological cancer in our cohort. Our findings are consistent with a previous study by Van Nimwegen et al.[25] who also report increased risk of IHD in Hodgkin lymphoma survivors and attribute this, in part, to radiotherapy exposure.

Participants with previous lung, breast, or haematological cancer had increased risk of pericardial disease, with lung cancer patients having a markedly increased risk (over 12-fold). This may reflect metastatic disease presentations. Pericardial disease may also be an adverse consequence of mediastinal radiotherapy[24], which is common in all three cancers.

Participants with breast cancer had increased risk of incident HF, incident NICMs, and death from HF or NICM. Furthermore, breast cancer history was associated with poorer LV function by LVGFI and LVEF. These observations likely reflect cardiotoxicity linked to breast cancer therapies[21,26]. An interesting observation in our results was a markedly increased risk of death due to hypertensive disease (8-fold increase) in participants with previous breast cancer, which may reflect suboptimal control of hypertension in this cohort.

Participants with uterine cancer had the highest average body mass index of all cancers, high rates of hypertension and diabetes, and increased risk of stroke death. The clustering of cardiometabolic factors has been previously reported in uterine cancer[27,28]. In our analysis, uterine cancer was linked to increased stroke mortality, but with very wide CIs.

**Clinical implications**

Patients with cancer have a constellation of demographic and clinical risk factors that place them at higher cardiovascular risk. Our findings underscore the importance of controlling modifiable risk factors for all patients during and after their cancer treatment, as well as specific areas of risk where surveillance and/or preventive strategies should be focused. Importantly, we demonstrate that past cancer confers an increased risk of cardiovascular events, independent of traditional vascular risk factors and that this risk may extend several years beyond the initial cancer diagnosis. Thus, our results support consideration of cancer-specific exposures in cardiovascular risk stratification and lower thresholds for treatment of modifiable risk factors in this patient group. We demonstrate particular vulnerability of individuals with past breast and haematological cancer, who appeared at greatest risk, both with regards risk of incident clinical disease and adverse cardiac remodelling.

We found significant associations between breast and haematological cancer history and selected CMR metrics, even in the absence of prevalent CVD. The most consistent associations were observed with LVEF. We also demonstrate potential value of LVGFI, GLS, and LAEF as emerging novel imaging biomarkers of subclinical disease.

**Limitations**

Ascertainment of incident outcomes from health records may be subject to miscoding. We may be underpowered to detect associations in cancers with small sample sizes (e.g., lung, uterine). Our dataset does not permit characterisation by cancer histology or stage. Information about specific cancer therapies was not available and we cannot make inferences about treatment-specific effects. We are unable to consider ethnic disparities as our sample comprises a predominantly White cohort; future studies in more diverse cohorts are needed.

**Conclusions**

Individuals with past cancer have heightened cardiovascular risk, which appears independent of vascular risk factors and persists several years after initial cancer diagnosis. The pattern of CVDs varies by cancer site, likely reflecting specific characteristics of the cancer and its therapies. CMR measures of LV and LA structure and function provide pre-clinical indicators of cardiovascular health in this context.

**Figure 1. Associations of cancer exposure with incident cardiovascular disease and mortality outcomes**

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**Figure 1 footnote.** Results are association of cancer exposure with incident outcomes presented as subdistribution hazard ratios and 95% confidence intervals from competing risk regression; except for all-cause death where we report hazard ratio from Cox hazard proportional regression.

Hazard ratios and 95% confidence intervals are presented on a log10 scale. The comparators are propensity matched non-cancer controls. The dots represent the point estimate and the intervals are the confidence intervals. The greyed-out intervals indicate statistically non-significant associations. AF: atrial fibrillation; CVD: cardiovascular disease; NICM: non-ischaemic cardiomyopathies; Haem: haematological; HF: heart failure; HTN: hypertension; IHD: ischaemic heart disease.

**Figure 2. Association of breast and haematological cancer exposure with CMR metrics**

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**Figure 2 footnote.** Results are standardised beta-coefficients and 95% confidence intervals, thus representing standard deviation change in CMR metrics with change in cancer exposure status from non-cancer to cancer. CMR: cardiovascular magnetic resonance; LA: left atrium; LV: left ventricle; LV end-diastolic volume (LVEDV), LV mass (LVM), LV ejection fraction (LVEF), LV global function index (LVGFI), LV global longitudinal strain (GLS), LA maximum volume (LAV), LA ejection fraction (LAEF).

**Patient and Public Involvement**

There was no patient or public involvement in this study.

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**Data sharing statement**

This research was conducted using the UK Biobank resource under access application 2964. UK Biobank will make the data available to all bona fide researchers for all types of health-related research that is in the public interest, without preferential or exclusive access for any persons. All researchers will be subject to the same application process and approval criteria as specified by UK Biobank. For more details on the access procedure, see the UK Biobank website: <http://www.ukbiobank.ac.uk/register-apply>.

**Ethical approval**

This study complies with the Declaration of Helsinki; the work was covered by the ethical approval for UK Biobank studies from the NHS National Research Ethics Service on 17th June 2011 (Ref 11/NW/0382) and extended on 18th June 2021 (Ref 21/NW/0157) with written informed consent obtained from all participants.

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**Disclosures**

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**Supplementary Figure 1. Postulated causal pathways and potential and true confounders of the relationship between cancer and cardiovascular health**

Diagram

Description automatically generated

**Supplementary Figure 1 footnote.** Figure created using the dagitty package: Johannes Textor, Benito van der Zander, Mark K. Gilthorpe, Maciej Liskiewicz, George T.H. Ellison. [Robust causal inference using directed acyclic graphs: the R package 'dagitty'.](http://dx.doi.org/10.1093/ije/dyw341) *International Journal of Epidemiology* 45(6):1887-1894, 2016.

**Supplementary Figure 2. Balance plots for propensity score matching in the baseline set**

Diagram, schematic

Description automatically generated

**Supplementary Figure 2 footnote.** Vertical dashed lines show threshold of 0.1 standardised mean difference. There was good balance of overall propensity score and individual covariates for all cancer categories in the baseline set. BMI: body mass index; DBP: diastolic blood pressure; HbA1c: glycated haemoglobin, HDL: high density lipoprotein, IPAQ: international physical activity questionnaire; LDL: low density lipoprotein; METS: metabolic equivalent; SBP: systolic blood pressure.

**Supplementary Figure 3. Balance plots for propensity score matching in the imaging set**

Diagram, schematic

Description automatically generated

**Supplementary Figure 3 footnote.** Vertical dashed lines show threshold of 0.1 standardised mean difference. Dotted lines show caliper threshold of 0.2 standard deviations. We excluded 5 men with breast cancer. In the lung cancer category, age, sex, smoking, education, SBP, DBP, TG, IPAQ, heart rate and hba1c all have SMD >0.2. Townsend, BMI, HDL, LDL, hypertension and high cholesterol>0.1. For prostate cancer, 1 pair outside caliper was discarded. For colorectal cancer, 1 pair outside caliper discarded and age, ethnicity, Townsend, Education, SBP, DBP, hba1c,IPAQ, smoking all had SMD >0.1. For uterine cancer, 1 pair was unmatched and Townsend score SMD>0.2, whilst age, qualifications,DBP,LDL,IPAQ, smoking, diabetes, hypertension, high cholesterol all had SMD >0.1. For haematological cancer, Education had SMD>0.1. In conclusion, covariate balance is good for breast and prostate cancer. Overall propensity is balanced for the outcomes, but some individual covariates lack balance (SMD>0.1) and thus we used a doubly robust approach by including these as covariates in the final models as per Nguyen et al. (Nguyen TL, Collins GS, Spence J, Daurès JP, Devereaux PJ, Landais P, Le Manach Y. Double-adjustment in propensity score matching analysis: choosing a threshold for considering residual imbalance. BMC Med Res Methodol. 2017 Apr 28;17(1):78. doi: 10.1186/s12874-017-0338-0.). BMI: body mass index; DBP: diastolic blood pressure; HbA1c: glycated haemoglobin, HDL: high density lipoprotein, IPAQ: international physical activity questionnaire; LDL: low density lipoprotein; METS: metabolic equivalent; SBP: systolic blood pressure.

**Supplementary Figure 4. Flow of participants included in study**

Whole UK Biobank cohort – baseline sample

N=502415

Propensity-matched non-cancer controls

N=18714

Incident CVDs

Participants with past cancer and CMR N=1354

12 years follow up

Cancer history in the six sites of interest

N=18755

Excluded:

-Men with breast cancer (N=39)

-Participants without successful matched controls (N=2)

Participants with past cancer

N=18714

Propensity-matched non-cancer controls with CMR N=1354

CMR associations

**Supplementary Figure 4 footnote.** CVD: cardiovascular disease.

**Supplementary Table 1. ICD-9 and ICD-10 codes used for ascertainment of cancer status**

| **Cancer site** | **ICD9/10 code** | **Description** |
| --- | --- | --- |
| Breast | 1740 | Malignant neoplasm of female breast - nipple and areola |
|  | 1743 | Malignant neoplasm of female breast - lower-inner quadrant |
|  | 1744 | Malignant neoplasm of female breast - upper-outer quadrant |
|  | 1745 | Malignant neoplasm of female breast - lower-outer quadrant |
|  | 1748 | Malignant neoplasm of female breast - other site |
|  | 1749 | Malignant neoplasm of female breast - unspecified site |
|  | 1740 | Malignant neoplasm of female breast - nipple and areola |
|  | 1743 | Malignant neoplasm of female breast - lower-inner quadrant |
|  | C50.0 | Nipple and areola |
|  | C50.1 | Central portion of breast |
|  | C50.2 | Upper-inner quadrant of breast |
|  | C50.3 | Lower-inner quadrant of breast |
|  | C50.4 | Upper-outer quadrant of breast |
|  | C50.5 | Lower-outer quadrant of breast |
|  | C50.6 | Axillary tail of breast |
|  | C50.8 | Overlapping lesion of breast |
|  | C50.9 | Breast, unspecified |
| Lung | 1623 | Malignant neoplasm of upper lobe, bronchus or lung |
|  | 1629 | Malignant neoplasm of bronchus and lung, unspecified |
|  | C34.0 | Main bronchus |
|  | C34.1 | Upper lobe, bronchus, or lung |
|  | C34.2 | Middle lobe, bronchus, or lung |
|  | C34.3 | Lower lobe, bronchus, or lung |
|  | C34.8 | Overlapping lesion of bronchus and lung |
|  | C34.9 | Bronchus or lung, unspecified |
| Prostate | 1859 | Malignant neoplasm of prostate |
|  | C61 | Malignant neoplasm of prostate |
| Colorectal | 1530 | Malignant neoplasm of colon, hepatic flexure |
|  | 1532 | Malignant neoplasm of descending colon |
|  | 1533 | Malignant neoplasm of sigmoid colon |
|  | 1534 | Malignant neoplasm of caecum |
|  | 1536 | Malignant neoplasm of ascending colon |
|  | 1537 | Malignant neoplasm of colon, splenic flexure |
|  | 1539 | Malignant neoplasm of colon, unspecified |
|  | C18.0 | Caecum |
|  | C18.1 | Appendix |
|  | C18.2 | Ascending colon |
|  | C18.3 | Hepatic flexure |
|  | C18.4 | Transverse colon |
|  | C18.5 | Splenic flexure |
|  | C18.6 | Descending colon |
|  | C18.7 | Sigmoid colon |
|  | C18.8 | Overlapping lesion of colon |
|  | C18.9 | Colon, unspecified |
|  | C19 | Malignant neoplasm of rectosigmoid junction |
|  | C20 | Malignant neoplasm of rectum |
| Uterus | 1820 | Malignant neoplasm of corpus uteri, except isthmus |
|  | C54.0 | Isthmus uteri |
|  | C54.1 | Endometrium |
|  | C54.2 | Myometrium |
|  | C54.3 | Fundus uteri |
|  | C54.8 | Overlapping lesion of corpus uteri |
|  | C54.9 | Corpus uteri, unspecified |
|  | C55 | Malignant neoplasm of uterus, part unspecified |
| Haematological | 2001 | Lymphosarcoma |
|  | 2015 | Hodgkin's disease, nodular sclerosis |
|  | 2016 | Hodgkin's disease, mixed cellularity |
|  | 2017 | Hodgkin's disease, lymphocytic depletion |
|  | 2019 | Hodgkin's disease, unspecified |
|  | 2020 | Nodular lymphoma |
|  | 2024 | Leukaemic reticuloendotheliosis |
|  | 2028 | Other lymphomas |
|  | 2029 | Other malig. neoplasm of lymphoid and histiocytic tissue |
|  | 2040 | Acute lymphoid leukaemia |
|  | 2050 | Acute myeloid leukaemia |
|  | 2051 | Chronic myeloid leukaemia |
|  | 2059 | Unspecified myeloid leukaemia |
|  | C81.0 | Lymphocytic predominance |
|  | C81.1 | Nodular sclerosis |
|  | C81.2 | Mixed cellularity |
|  | C81.3 | Lymphocytic depletion |
|  | C81.4 | Lymphocyte-rich classical Hodgkin lymphoma |
|  | C81.7 | Other Hodgkin's disease |
|  | C81.9 | Hodgkin's disease, unspecified |
|  | C82.0 | Small cleaved cell, follicular |
|  | C82.1 | Mixed small cleaved and large cell, follicular |
|  | C82.2 | Large cell, follicular |
|  | C82.3 | Follicular lymphoma grade IIIa |
|  | C82.4 | Follicular lymphoma grade IIIb |
|  | C82.5 | Diffuse follicle centre lymphoma |
|  | C82.6 | Cutaneous follicle centre lymphoma |
|  | C82.7 | Other types of follicular non-Hodgkin's lymphoma |
|  | C82.9 | Follicular non-Hodgkin's lymphoma, unspecified |
|  | C83.0 | Small cell (diffuse) |
|  | C83.1 | Small cleaved cell (diffuse) |
|  | C83.2 | Mixed small and large cell (diffuse) |
|  | C83.3 | Large cell (diffuse) |
|  | C83.4 | Immunoblastic (diffuse) |
|  | C83.5 | Lymphoblastic (diffuse) |
|  | C83.6 | Undifferentiated (diffuse) |
|  | C83.7 | Burkitt's tumour |
|  | C83.8 | Other types of diffuse non-Hodgkin's lymphoma |
|  | C83.9 | Diffuse non-Hodgkin's lymphoma, unspecified |
|  | C84.0 | Mycosis fungoides |
|  | C84.1 | Sezary's diease |
|  | C84.3 | Lymphoepithelioid lymphoma |
|  | C84.4 | Peripheral T-cell lymphoma |
|  | C84.5 | Other and unspecified T-cell lymphomas |
|  | C84.6 | Anaplastic large cell lymphoma, ALK-positive |
|  | C84.7 | Anaplastic large cell lymphoma, ALK-negative |
|  | C84.8 | Cutaneous T-cell lymphoma, unspecified |
|  | C84.9 | Mature T/NK-cell lymphoma, unspecified |
|  | C85.0 | Lymphosarcoma |
|  | C85.1 | B-cell lymphoma, unspecified |
|  | C85.2 | Mediastinal (thymic) large B-cell lymphoma |
|  | C85.7 | Other specified types of non-Hodgkin's lymphoma |
|  | C85.9 | Non-Hodgkin's lymphoma, unspecified type |
|  | C86.0 | Extranodal NK/T-cell lymphoma, nasal type |
|  | C86.2 | Enteropathy-type (intestinal) T-cell lymphoma |
|  | C86.3 | Subcutaneous panniculitis-like T-cell lymphoma |
|  | C86.4 | Blastic NK-cell lymphoma |
|  | C86.5 | Angioimmunoblastic T-cell lymphoma |
|  | C86.6 | Primary cutaneous CD30-positive T-cell proliferations |
|  | C88.0 | Waldenstrom's macroglobulinaemia |
|  | C88.2 | Gamma heavy chain disease |
|  | C88.3 | Immunoproliferative small intestinal disease |
|  | C88.4 | Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue [MALT-lymphoma] |
|  | C88.7 | Other malignant immunoproliferative diseases |
|  | C88.9 | Malignant immunoproliferative disease, unspecified |
|  | C90.0 | Multiple myeloma |
|  | C90.1 | Plasma cell leukaemia |
|  | C90.2 | Plasmacytoma, extramedullary |
|  | C90.3 | Solitary plasmacytoma |
|  | C91.0 | Acute lymphoblastic leukaemia |
|  | C91.1 | Chronic lymphocytic leukaemia |
|  | C91.2 | Subacute lymphocytic leukaemia |
|  | C91.3 | Prolymphocytic leukaemia |
|  | C91.4 | Hairy-cell leukaemia |
|  | C91.5 | Adult T-cell leukaemia |
|  | C91.6 | Prolymphocytic leukaemia of T-cell type |
|  | C91.7 | Other lymphoid leukaemia |
|  | C91.8 | Mature B-cell leukaemia Burkitt-type |
|  | C92.0 | Acute myeloid leukaemia |
|  | C92.1 | Chronic myeloid leukaemia |
|  | C92.2 | Subacute myeloid leukaemia |
|  | C92.3 | Myeloid sarcoma |
|  | C92.4 | Acute promyelocytic leukaemia |
|  | C92.5 | Acute myelomonocytic leukaemia |
|  | C92.6 | Acute myeloid leukaemia with 11q23-abnormality |
|  | C92.7 | Other myeloid leukaemia |
|  | C92.8 | Acute myeloid leukaemia with multilineage dysplasia |
|  | C93.0 | Acute monocytic leukaemia |
|  | C93.1 | Chronic monocytic leukaemia |
|  | C93.3 | Juvenile myelomonocytic leukaemia |
|  | C93.9 | Monocytic leukaemia, unspecified |
|  | C94.0 | Acute erythraemia and erythroleukaemia |
|  | C94.2 | Acute megakaryoblastic leukaemia |
|  | C94.4 | Acute panmyelosis |
|  | C94.5 | Acute myelofibrosis |
|  | C94.6 | Myelodysplastic and myeloproliferative disease, not elsewhere classified |
|  | C94.7 | Other specified leukaemias |
|  | C95.0 | Acute leukaemia of unspecified cell type |
|  | C95.1 | Chronic leukaemia of unspecified cell type |
|  | C95.9 | Leukaemia, unspecified |
|  | C96.1 | Malignant histiocytosis |
|  | C96.2 | Malignant mast cell tumour |
|  | C96.3 | True histiocytic lymphoma |
|  | C96.4 | Sarcoma of dendritic cells (accessory cells) |
|  | C96.5 | Multifocal and unisystemic Langerhans-cell histiocytosis |
|  | C96.6 | Unifocal Langerhans-cell histiocytosis |
|  | C96.7 | Other specified malignant neoplasms of lymphoid, haematopoietic and related tissue |
|  | C96.8 | Histiocytic sarcoma |
|  | C96.9 | Malignant neoplasms of lymphoid, haematopoietic and related tissue, unspecified |

**Supplementary Table 1 footnote.** ICD: international classification of disease

**Supplementary Table 2. Ascertainment of CVD outcomes, ICD and UK Biobank field codes**

| **Source** | **ICD code/UKB filed** | **Description** |
| --- | --- | --- |
| **Ischaemic heart disease (IHD)** | | |
| ICD9 | 4139 | Angina pectoris |
|  | 4140 | Coronary atherosclerosis |
|  | 4141 | Aneurysm of heart |
|  | 4148 | Other specified forms of chronic ischaemic heart disease |
|  | 4149 | Chronic ischaemic heart disease, unspecified |
|  | 4119 | Other acute and subacute forms of ischaemic heart disease |
| Self-report | 20002 | Angina |
| ICD10 | I20 | Angina pectoris |
|  | I24 | Other acute ischaemic heart diseases |
|  | I25 | Chronic ischaemic heart disease |
| First occurrences | 131296 | Angina pectoris |
|  | 131304 | Other acute ischaemic heart diseases |
|  | 131306 | Chronic ischaemic heart disease |
| Diagnosed by doctor | 3627 | Age angina diagnosed |
|  | 6150: 2 | Angina |
| **Ischaemic heart disease (Myocardial infarction)** | | |
| ICD9 | 4109 | Acute myocardial infarction |
|  | 4129 | Old myocardial infarction |
| Self-report | 20002 | Heart attack/myocardial infarction |
| ICD9 | 410 | Acute myocardial infarction |
|  | 411 | Other acute and subacute forms of ischaemic heart disease |
|  | 412 | Old myocardial infarction |
| ICD10 | I21 | Acute myocardial infarction |
|  | I22 | Subsequent myocardial infarction |
|  | I23 | Certain current complications following acute myocardial infarction |
| First occurrences | 131298 | Acute myocardial infarction |
|  | 131300 | Subsequent myocardial infarction |
|  | 131302 | Certain current complications following acute myocardial infarction |
| Diagnosed by doctor | 3894 | Age heart attack diagnosed |
|  | 6150: 1 | Heart attack |
| Algorithm | 42000 | Date of myocardial infarction |
| **Non-ischaemic cardiomyopathies** | | |
| ICD9 | 4254 | Other primary cardiomyopathies |
| Self-report | 20002 | Cardiomyopathy |
|  | 20002 | Hypertrophic cardiomyopathy (HCM / HOCM) |
| ICD10 | I42 | Cardiomyopathy |
|  | I43 | Cardiomyopathy in diseases classified elsewhere |
|  | I11 | Hypertensive heart disease |
|  | I13 | Hypertensive heart and renal disease |
| First occurrences | 131338 | Cardiomyopathy |
|  | 131340 | Cardiomyopathy in diseases classified elsewhere |
|  | 131288 | Hypertensive heart disease |
|  | 131292 | Hypertensive heart and renal disease |
| **Heart failure (unspecified aetiology)** | | |
| ICD9 | 4280 | Congestive heart failure |
|  | 4281 | Left heart failure |
| Self-report | 20002 | Heart failure/pulmonary oedema |
| ICD10 | I50.0 | Congestive heart failure |
|  | I50.1 | Left ventricular failure |
|  | I50.9 | Heart failure, unspecified |
| First occurrences | 131354 | Heart failure |
| **Cardiac arrhythmia (Atrial fibrillation)** | | |
| Self-report | 20002 | Atrial fibrillation |
| ICD9 | 4273 | Atrial fibrillation and flutter |
| ICD10 | I48.0 | Paroxysmal atrial fibrillation |
|  | I48.1 | Persistent atrial fibrillation |
|  | I48.2 | Chronic atrial fibrillation |
|  | I48.9 | Atrial fibrillation and atrial flutter, unspecified |
| **Stroke** | | |
| Self-report | 20002 | Stroke |
|  | 20002 | Ischaemic stroke |
|  | 20002 | Brain haemorrhage |
| ICD9 | 431 | Intracerebral haemorrhage |
|  | 4349 | Occlusion of cerebral arteries, unspecified |
| ICD10 | I64 | Stroke, not specified as haemorrhage or infarction |
|  | I63 | Cerebral infarction |
|  | I61 | Intracerebral haemorrhage |
|  | I62 | Other nontraumatic intracranial haemorrhage |
| First occurrences | 131368 | Date I64 first reported (stroke, not specified as haemorrhage or infarction) |
|  | 131366 | Cerebral infarction |
|  | 131362 | Intracerebral haemorrhage |
|  | 131364 | other nontraumatic intracranial haemorrhage |
| Diagnosed by doctor | 4056 | Age stroke diagnosed |
|  | 6150: 3 | Stroke |
| Algorithm | 42006 | Date of stroke |
|  | 42008 | Date of ischaemic stroke |
|  | 42010 | Date of intracerebral haemorrhage |
| **Pericarditis** | | |
| ICD10 | I30.0 | Acute nonspecific idiopathic pericarditis |
|  | I30.1 | Infective pericarditis |
|  | I30.8 | Other forms of acute pericarditis |
|  | I30.9 | Acute pericarditis, unspecified |
|  | I31.0 | Chronic adhesive pericarditis |
|  | I31.1 | Chronic constrictive pericarditis |
|  | I31.2 | Haemopericardium, not elsewhere classified |
|  | I31.3 | Pericardial effusion (noninflammatory) |
|  | I31.8 | Other specified diseases of pericardium |
|  | I31.9 | Disease of pericardium, unspecified |
|  | I32.0 | Pericarditis in bacterial diseases classified elsewhere |
|  | I32.1 | Pericarditis in other infectious and parasitic diseases classified elsewhere1 |
|  | I32.8 | Pericarditis in other diseases classified elsewhere |
| **Venous thromboembolism (DVT/PE)** | | |
| ICD9 | 4151 | Pulmonary embolism |
|  | 4538 | Embolism and thrombosis of other specified veins |
| ICD10 | I26.0 | Pulmonary embolism with mention of acute cor pulmonale |
|  | I26.9  I801  I802  I803 | Pulmonary embolism without mention of acute cor pulmonale  Phlebitis and thrombophlebitis of femoral vein  Phlebitis and thrombophlebitis of other deep vessels of lower extremities  Phlebitis and thrombophlebitis of lower extremities, unspecified |
|  | I82.8 | Embolism and thrombosis of other specified veins |
|  | I82.9 | Embolism and thrombosis of unspecified vein |
| Self report | 20002 | pulmonary embolism +/- DVT |
|  | 20002 | deep venous thrombosis (DVT) |
| **Hypertensive disease (for death certificate, main/underlying cause of death)** | | |
| ICD10 | I10 | Essential (primary) hypertension |
|  | I11.0 | Hypertensive heart disease with (congestive) heart failure |
|  | I11.9 | Hypertensive heart disease without (congestive) heart failure |
|  | I12.0 | Hypertensive renal disease with renal failure |
|  | I12.9 | Hypertensive renal disease without renal failure |
|  | I13.0 | Hypertensive heart and renal disease with (congestive) heart failure |
|  | I13.1 | Hypertensive heart and renal disease with renal failure |
|  | I13.2 | Hypertensive heart and renal disease with both (congestive) heart failure and renal failure |
|  | I13.9 | Hypertensive heart and renal disease, unspecified |
|  | I15.0 | Renovascular hypertension |
|  | I15.1 | Hypertension secondary to other renal disorders |
|  | I15.2 | Hypertension secondary to endocrine disorders |
|  | I15.8 | Other secondary hypertension |
| ICD9 | 4010 | Essential hypertension, specified as malignant |
|  | 4011 | Essential hypertension, specified as benign |
|  | 4019 | Essential hypertension, not specified as malignant or benign |
|  | 4039 | Hypertensive renal disease, not specified as malignant or benign |

**Supplementary Table 2 footnote.** CVD: cardiovascular disease; DVT: deep vein thrombosis; ICD: international classification of disease; PE: pulmonary embolism.

**Supplementary Table 3. Covariates included in the propensity score models**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Notes and UK Biobank data field** | **Baseline set** | **Imaging set** |
| **Socio-demographics** |  |  |  |
| Age (years) | 21003 | Instance 0 | Instance 2 |
| Sex | 31 |  |  |
| Ethnicity | 21000 |  |  |
| Townsend score | 189 |  |  |
| Education | 6138 | Instance 0 | Instance 2 |
| **Physical measurements** |  |  |  |
| Systolic blood pressure (mmHg) | Average of automated readings if available (4080), otherwise refer to manual reading (93) | Instance 0 | Instance 2 |
| Diastolic blood pressure (mmHg) | Average of automated readings if available (4079), otherwise refer to manual reading (94) | Instance 0 | Instance 2 |
| Heart rate (bpm) | Average of automated readings (102) if available, otherwise refer to manual reading (95) – reject heart rates below 40bpm | Instance 0 | Instance 2 |
| Body mass index (kg/m2) | Calculate from height (50) and weight (21002 -or 3160 if not available). | Instance 0 | Instance 2 |
| **Laboratory tests** |  |  |  |
| HbA1c (mmol/mol) | 30750 | Instance 0 | Instance 0 |
| Random glucose (mmol/L) | 30740 | Instance 0 | Instance 0 |
| Total cholesterol (mmol/L) | 30690 | Instance 0 | Instance 0 |
| HDL (mmol/L) | 30760 | Instance 0 | Instance 0 |
| LDL direct (mmol/L) | 30780 | Instance 0 | Instance 0 |
| Triglyceride level (mmol/L) | 30870 | Instance 0 | Instance 0 |
| **Vascular risk factors** |  |  |  |
| Physical activity (METS/week) | As per IPAQ |  |  |
| Smoking status | 20116 | Instance 0 | Instance 2 |
| Diabetes | As per Table 4 | ICD codes until instance 0 | ICD codes until instance 2 |
| Hypertension | As per Table 4 | ICD codes until instance 0 | ICD codes until instance 2 |
| High cholesterol | As per Table 4 | ICD codes until instance 0 | ICD codes until instance 2 |

**Supplementary Table 3 footnote.** Instance 0 indicates baseline visit, instance 2 indicates imaging visit. HbA1c: glycated haemoglobin, HDL: high density lipoprotein, IPAQ: international physical activity questionnaire; LDL: low density lipoprotein; METS: metabolic equivalent.

**Supplementary Table 4. ICD and UK Biobank field codes used to define clinical diagnosis of prevalent diabetes, hypertension, and high cholesterol**

|  |  |  |
| --- | --- | --- |
| **Diabetes** |  |  |
| Self-report | 20002 | Diabetes |
|  | 20002 | Type 1 diabetes |
|  | 20002 | Type 2 diabetes |
| Medications | 6177, 6153: 3 | Insulin |
| ICD9 | 250 | Diabetes mellitus |
| ICD10 | E10 | Type 1 diabetes mellitus |
|  | E11 | Type 2 diabetes mellitus |
|  | E13 | Other specified diabetes mellitus |
|  | E14 | Unspecified diabetes mellitus |
|  | G590 | Diabetic mononeuropathy |
|  | G632 | Diabetic polyneuropathy |
|  | H280 | Diabetic cataract |
|  | H360 | Diabetic retinopathy |
|  | M142 | Diabetic arthropathy |
|  | N083 | Glomerular disorders in diabetes mellitus |
|  | O240 | Diabetes mellitus in pregnancy: Pre-existing type 1 diabetes mellitus |
|  | O241 | Diabetes mellitus in pregnancy: Pre-existing type 2 diabetes mellitus |
|  | O243 | Diabetes mellitus in pregnancy: Pre-existing diabetes mellitus, unspecified |
|  | O244 | Diabetes mellitus arising in pregnancy |
|  | O249 | Diabetes mellitus in pregnancy, unspecified |
|  | Y423 | Insulin and oral hypoglycaemic [antidiabetic] drugs |
| First occurrences | 130706 | Date E10 first reported (insulin-dependent diabetes mellitus) |
|  | 130708 | Date E11 first reported (non-insulin-dependent diabetes mellitus) |
|  | 130712 | Date E13 first reported (other specified diabetes mellitus) |
|  | 130714 | Date E14 first reported (unspecified diabetes mellitus) |
| Diagnosed by doctor | 2443 | Diabetes diagnosed by doctor |
|  | 2976 | Age diabetes diagnosed by doctor |
| **High cholesterol** |  |  |
| Self-report | 20002 | High cholesterol |
| Medications | 6177, 6153: 1 | Cholesterol lowering medication |
| ICD9 | 272 | Disorders of lipoid metabolism |
| ICD10 | E780 | Pure hypercholesterolaemia |
|  | E782 | Mixed hyperlipidaemia |
|  | E783 | Hyperchylomicronaemia |
|  | E784 | Other hyperlipidaemia |
|  | E785 | Hyperlipidaemia, unspecified |
| First occurrences | 130814 | Date E78 first reported (disorders of lipoprotein metabolism and other lipidaemias) |
| **Hypertension** |  |  |
| Self-report | 20002 | Essential hypertension |
|  | 20002 | Hypertension |
| Medications | 6177, 6153: 2 | Blood pressure medication |
| First occurrences | 131286 | Date I10 first reported (essential (primary) hypertension) |
| Diagnosed by doctor | 2966 | Age high blood pressure diagnosed |
|  | 6150: 4 | High blood pressure |
| ICD10 | I10 | Essential (primary) hypertension |
|  | I11.0 | Hypertensive heart disease with (congestive) heart failure |
|  | I11.9 | Hypertensive heart disease without (congestive) heart failure |
|  | I12.0 | Hypertensive renal disease with renal failure |
|  | I12.9 | Hypertensive renal disease without renal failure |
|  | I13.0 | Hypertensive heart and renal disease with (congestive) heart failure |
|  | I13.1 | Hypertensive heart and renal disease with renal failure |
|  | I13.2 | Hypertensive heart and renal disease with both (congestive) heart failure and renal failure |
|  | I13.9 | Hypertensive heart and renal disease, unspecified |
|  | I15.0 | Renovascular hypertension |
|  | I15.1 | Hypertension secondary to other renal disorders |
|  | I15.2 | Hypertension secondary to endocrine disorders |
|  | I15.8 | Other secondary hypertension |
| ICD9 | 4010 | Essential hypertension, specified as malignant |
|  | 4011 | Essential hypertension, specified as benign |
|  | 4019 | Essential hypertension, not specified as malignant or benign |
|  | 4039 | Hypertensive renal disease, not specified as malignant or benign |

**Supplementary Table 4.** ICD: international classification of disease

**Supplementary Table 5. Number of incident events in the composite haematological cancer category and in subtypes of myeloma, lymphoma, and leukaemia.**

|  | All haem | Myeloma | Lymphoma | Leukaemia |
| --- | --- | --- | --- | --- |
| Incident CVDs (N, %) | 2032 | 198 | 1495 | 525 |
| IHD | 286 | 27 | 193 | 65 |
| NICM | 57 | 2 | 41 | 14 |
| HF | 227 | 21 | 157 | 47 |
| AF/flutter | 259 | 25 | 167 | 66 |
| Stroke | 102 | 11 | 59 | 30 |
| Pericarditis | 47 | 3 | 32 | 12 |
| VTE (DVT/PE) | 102 | 11 | 27 | 63 |
| Mortality outcomes (N, %) | 496 | 109 | 351 | 140 |
| Any CVD | 47 | 8 | 26 | 12 |
| IHD | 26 | 4 | 15 | 7 |
| HF/NICM | 5 | 1 | 4 | 0 |
| Stroke | 10 | 1 | 6 | 2 |
| Hypertensive diseases | 3 | 1 | 1 | 1 |

**Supplementary Table 5 footnote.** AF: atrial fibrillation; CVD: cardiovascular disease; IHD: ischaemic heart disease; NICM: non-ischaemic cardiomyopathies; VTE: venous thromboembolism

**Supplementary Table 6. Associations with events for those with any haematological cancer and in subtypes of myeloma, lymphoma, and leukaemia- compared to controls**

|  | All haem | Myeloma | Lymphoma | Leukaemia |
| --- | --- | --- | --- | --- |
| Incident disease |  |  |  |  |
| IHD | 1.96 (1.58-2.43) | 1.61 (0.87-2.97) | 1.95 (1.52-2.51) | 1.97 (1.31-3.00) |
|  | 6.0e-10 | 0.132 | 1.2e-7 | 0.001 |
| NICM | 2.53 (1.53-4.16) | 2.01 (0.18-22.31) | 2.29 (1.31-4.01) | 3.56 (1.15-10.91) |
|  | 0.0003 | 0.570 | 0.004 | 0.03 |
| Heart failure | 3.48 (2.61-4.62) | 4.44 (1.65-11.97) | 3.29 (2.39-4.53) | 4.44 (2.29-8.58) |
|  | 1.0e-17 | 0.003 | 3.1e-13 | 9.0e-6 |
| AF/flutter | 2.00 (1.60-2.50) | 1.73 (0.90-3.35) | 1.67 (1.30-2.16) | 4.10 (2.46-6.82) |
|  | 9.4e-10 | 0.102 | 0.0001 | 6.0e-8 |
| Stroke | 2.45 (1.68-3.58) | 1.39 (0.55-3.53) | 1.99 (1.27-3.10) | 3.90 (1.80-8.33) |
|  | 3.7e-6 | 0.488 | 0.002 | 0.0005 |
| Pericarditis | 2.95 (1.64-5.32) | 3.02 (0.31-29.24) | 2.66 (1.38-5.21) | 6.11 (1.36-27.39) |
|  | 0.0003 | 0.341 | 0.003 | 0.02 |
| VTE | 2.69 (1.80-4.00) | 2.83 (0.89-9.07) | 2.92 (1.77-4.76) | 2.23 (1.13-4.35) |
|  | 1.2e-6 | 0.079 | 0.00003 | 0.02 |
| Mortality outcomes |  |  |  |  |
| All-cause | 3.78 (3.17-4.52) | 7.74 (4.82-12.44) | 3.78 (3.06-4.66) | 3.67 (2.64-5.05) |
|  | 7.5e-49 | 2.9e-17 | 8.0e-35 | 7.8e-15 |
| Any CVD | 1.26 (0.79-2.01) | 8.10 (1.00-65.85) | 1.00 (0.58-1.73) | 2.46 (0.91-6.62) |
|  | 0.329 | 0.05 | 0.99 | 0.07 |
| IHD | 1.58 (0.80-3.09) | 4.01 (0.44-36.35) | 1.25 (0.58-2.67) | 3.53 (0.73-16.95) |
|  | 0.186 | 0.217 | 0.57 | 0.12 |
| Heart failure or NICM | 0.81 (0.22-3.01) | - | 0.80 (0.21-3.00) | - |
|  | 0.749 | - | 0.74 | - |
| Stroke | 1.01 (0.40-2.54) | - | 1.00 (0.32-3.11) | - |
|  | 0.988 | - | 0.999 | - |
| Hypertensive diseases | - | - | - | - |
|  | - | – | - | - |

**Supplementary Table 6 footnote.** AF: atrial fibrillation; CVD: cardiovascular disease; IHD: ischaemic heart disease; NICM: non-ischaemic cardiomyopathies; VTE: venous thromboembolism

**Supplementary Table 7. Incident events observed by cancer site (including all prevalent cancers, without covariate imputation – only those with complete data)**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Complete cases** | **Breast** | **Lung** | **Prostate** | **Colorectal** | **Uterus** | **Haem** | **Total** |
| **Incident disease** |  |  |  |  |  |  |  |
| IHD | 307 | 21 | 241 | 142 | 32 | 188 | 931 |
| NIC | 42 | 1 | 19 | 22 | 2 | 28 | 114 |
| HF | 156 | 14 | 121 | 71 | 17 | 138 | 517 |
| AF/flutter | 272 | 18 | 245 | 141 | 36 | 157 | 869 |
| Stroke | 101 | 8 | 90 | 44 | 11 | 62 | 316 |
| Pericarditis | 45 | 7 | 16 | 16 | 3 | 28 | 115 |
| VTE | 148 | 7 | 89 | 47 | 14 | 62 | 367 |
| **Mortality outcomes** |  |  |  |  |  |  |  |
| All-cause | 693 | 82 | 419 | 290 | 46 | 339 | 1869 |
| CVD (any) | 10 | 5 | 31 | 20 | 3 | 17 | 86 |
| IHD | 6 | 0 | 5 | 4 | 3 | 2 | 20 |
| HF/NIC | 11 | 1 | 12 | 2 | 0 | 9 | 35 |
| Stroke | 2 | 0 | 3 | 2 | 1 | 1 | 9 |
| Hypertensive diseases | 33 | 7 | 53 | 27 | 6 | 32 | 158 |

**Supplementary Table 7 footnote.** AF: atrial fibrillation; CVD: cardiovascular disease; DVT: deep vein thrombosis; HF: heart failure; IHD: ischaemic heart disease; NICM: non-ischaemic cardiomyopathies; PE: pulmonary embolism.

**Supplementary Table 8. Associations of cancer with incident events amongst all prevalent cancers with complete data (no imputation)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Breast** | **Lung** | **Prostate** | **Colorectal** | **Uterus** | **Haem** |
| **Incident disease** |  |  |  |  |  |  |
| IHD | 1.13 (0.96, 1.34) | 1.42 (0.70, 2.89) | 1.01 (0.84, 1.22) | 1.08 (0.85, 1.38) | 0.90 (0.54, 1.51) | 1.88 (1.48, 2.41) |
|  | 0.141 | 0.326 | 0.926 | 0.51 | 0.705 | 3.22 x 10-7 |
| NICM | 1.75 (1.06, 2.92) | – | 0.90 (0.49, 1.68) | 2.20 (1.07, 4.57) | **–** | 3.53 (1.60, 7.77) |
|  | 0.028 | – | 0.754 | 0.033 | **–** | 0.002 |
| HF | 1.31 (1.03, 1.67) | 2.05 (0.76, 5.58) | 0.94 (0.74, 1.21) | 1.21 (0.85, 1.70) | 1.62 (0.73, 3.60) | 2.18 (1.62, 2.94) |
|  | 0.028 | 0.159 | 0.653 | 0.285 | 0.244 | 2.75 x 10-7 |
| AF/flutter | 1.11 (0.93, 1.31) | 1.32 (0.62, 2.86) | 0.91 (0.76, 1.09) | 1.34 (1.04, 1.70) | 1.26 (0.78, 2.05) | 1.79 (1.38, 2.29) |
|  | 0.986 | 0.466 | 0.343 | 0.023 | 0.346 | 9.00 x 10-6 |
| Stroke | 1.00 (0.76, 1.31) | 1.15 (0.44, 3.00) | 0.83 (0.63, 1.11) | 0.79 (0.52, 1.19) | 0.92 (0.40, 2.12) | 2.89 (1.77, 4.76) |
|  | 0.986 | 0.783 | 0.206 | 0.248 | 0.844 | 2.67 x 10-5 |
| Pericarditis | 1.84 (1.12, 3.03) | 2.36 (0.61, 9.30) | 0.80 (0.41, 1.55) | 2.69 (1.04, 6.89) | – | 3.13 (1.48, 6.69) |
|  | 0.017 | 0.215 | 0.508 | 0.04 | – | 0.003 |
| VTE (DVT/PE) | 1.62 (1.23, 2.1) | 1.51 (0.41, 5.47) | 1.20 (0.89, 1.62) | 1.02 (0.67, 1.55) | 1.07 (0.53, 2.18) | 2.34 (1.49, 3.71) |
|  | 0.0005 | 0.537 | 0.243 | 0.927 | 0.841 | 0.0002 |
| **Mortality outcomes** |  |  |  |  |  |  |
| All-cause | 2.35 (2.01, 2.90) | 6.40 (0.79, 10.80) | 1.65 (1.41, 1.92) | 2.31 (1.88, 2.83) | 2.18 (1.31, 3.62) | 3.77 (3.01, 4.70) |
|  | 5.80 x 10-36 | 3.65 x 10-12 | 1.66 x 10-10 | 8.28 x 10-16 | 0.003 | 1.43 x 10-31 |
| Any CVD | 0.90 (0.56, 1.43) | 1.75 (0.50, 6.11) | 0.91 (0.63, 1.34) | 1.28 (0.73, 2.25) | 2.01 (0.50, 8.08) | 1.60 (0.92, 2.80) |
|  | 0.638 | 0.378 | 0.636 | 0.392 | 0.321 | 0.092 |
| IHD | 0.63 (0.28, 1.38) | 2.51 (0.48, 13.2) | 0.72 (0.45, 1.15) | 1.67 (0.81, 3.39) | **–** | 1.00 (0.51, 1.97) |
|  | 0.245 | 0.278 | 0.166 | 0.168 | **–** | 0.997 |
| HF/NIC | 2.01 (0.50, 8.00) | **–** | 1.67 (0.40, 6.96) | – | **–** | – |
|  | 0.323 | **–** | 0.484 | **–** | **–** | – |
| Stroke | 0.84 (0.38, 1.90) | **–** | 1.92 (0.662, 4.35) | **–** | **–** | 9.03 (1.14, 71.52) |
|  | 0.686 | **–** | 0.258 | **–** | **–** | 0.037 |
| Hypertensive diseases | – | **–** | – | **–** | **–** | – |
|  | – | **–** | – | **–** | **–** | – |

**Supplementary Table 8 footnote.** Results are sub-distribution hazard ratio (95% confidence interval) and p-value associated with cancer exposure (vs no cancer). Comparators are matched on age, sex, ethnicity, deprivation, education, blood pressure, heart rate, body mass index, glycated haemoglobin, random glucose, total cholesterol, high density lipoprotein, low density lipoprotein, triglyceride level, physical activity, smoking, diabetes, hypertension, and high cholesterol. AF: atrial fibrillation; CVD: cardiovascular disease; IHD: ischaemic heart disease; NICM: non-ischaemic cardiomyopathies; VTE: venous thromboembolism. AF: atrial fibrillation; CVD: cardiovascular disease; DVT: deep vein thrombosis; HF: heart failure; IHD: ischaemic heart disease; NIC: non-ischaemic cardiomyopathies; PE: pulmonary embolism.

**Supplementary Table 9. Associations of cancer with incident cardiovascular events compared to matched controls (cause specific hazard ratios)**

|  | **Breast** | **Lung** | **Prostate** | **Colorectal** | **Uterus** | **Haematological** |
| --- | --- | --- | --- | --- | --- | --- |
| **Incident disease** |  |  |  |  |  |  |
| IHD | 1.12 (0.99, 1.26) | 1.43 (0.95, 2.18) | 0.97 (0.84, 1.13) | **1.23 (1.02, 1.49)** | 1.06 (0.77, 1.48) | **2.14 (1.75, 2.61)** |
|  | 0.085 | 0.089 | 0.712 | **0.032** | 0.697 | 1.40 x 10-13 |
| NICM | **1.92 (1.36, 2.72)** | – | 1.22 (0.76, 1.97) | 1.36 (0.79, 2.34) | 3.63 (0.76, 17.64) | **2.89 (1.77, 4.71)** |
|  | 0.0002 | – | 0.399 | 0.257 | 0.107 | 0.00002 |
| Heart failure | **1.42 (1.21, 1.68)** | **2.59 (1.45, 4.66)** | 1.11 (0.90, 1.34) | 0.84 (0.66, 1.08) | 1.42 (0.90, 2.27) | **4.01 (3.03, 5.26)** |
|  | 0.00002 | 0.001 | 0.343 | 0.187 | 0.138 | 3.10 x 10-23 |
| AF/flutter | **1.17 (1.04, 1.32)** | **1.88 (1.14, 3.13)** | 1.06 (0.91, 1.22) | **1.36 (1.13, 1.65)** | 1.03 (0.73, 1.46) | **2.20 (1.79, 2.72)** |
|  | **0.011** | **0.014** | 0.451 | 0.002 | 0.846 | 1.4 x 10-13 |
| Stroke | 1.20 (0.97, 1.46) | 1.72 (0.83, 3.60) | 1.25 (0.98, 1.57) | 1.21 (0.89, 1.67) | 1.20 (0.71, 2.01) | **2.53 (1.80, 3.60)** |
|  | 0.087 | 0.150 | 0.078 | 0.219 | 0.498 | 1.6 x 10-7 |
| Pericarditis | **2.14 (1.45, 3.19)** | **16.78 (2.16, 131.63)** | 1.23 (0.71, 2.14) | 1.48 (0.74, 2.94) | 3.63 (0.75, 17.46) | **3.35 (1.90, 5.99)** |
|  | 0.0002 | 0.007 | 0.454 | 0.270 | 0.109 | 0.00003 |
| VTE | **1.52 (1.27, 1.82)** | 1.54 (0.73, 3.25) | **1.79 (1.36, 2.32)** | 1.30 (0.94, 1.80) | 1.75 (0.94, 3.29) | **3.03 (2.08, 4.39)** |
|  | 4.60 x 10-6 | 0.263 | 0.00003 | 0.114 | 0.076 | 7.9 x 10-9 |
| **Mortality outcomes** |  |  |  |  |  |  |
| All-cause | **2.48 (2.25, 2.72)** | **5.00 (3.63, 6.89)** | **1.65 (1.46, 1.86)** | **2.08 (1.79, 2.41)** | **2.41 (1.73, 3.32)** | **4.14 (3.49, 4.90)** |
|  | 3.65 x10-80 | 7.25 x 10-21 | 2.40 x10-16 | 1.30 x10-21 | 3.06 x 10-7 | 3.10 x 10-59 |
| Any CVD | 1.04 (0.76, 1.43) | **3.49 (1.43, 8.50)** | 0.93 (0.69, 1.26) | 1.31 (0.88, 1.95) | 1.26 (0.59, 2.69) | **1.70 (1.08, 2.66)** |
|  | 0.809 | **0.006** | 0.646 | 0.181 | 0.553 | **0.022** |
| IHD | 0.68 (0.40, 1.13) | **2.94 (1.16, 7.39)** | 0.93 (0.64, 1.35) | 1.16 (0.71, 1.88) | – | **1.99 (1.04, 3.78)** |
|  | 0.131 | **0.02** | 0.693 | 0.551 | – | 0.036 |
| Heart failure or NICM | **9.12 (2.10, 39.65)** | – | 0.83 (0.31, 2.23) | 5.42 (0.64, 45.50) | – | 1.17 (0.34, 4.10) |
|  | 0.003 | – | 0.708 | 0.121 | – | 0.797 |
| Stroke | 0.93 (0.52, 1.68) | – | 1.00 (0.51, 1.99) | 1.35 (0.56, 3.25) | 5.00 (0.58, 42.95) | 1.28 (0.52, 3.22) |
|  | 0.816 | – | 0.995 | 0.498 | 0.142 | 0.587 |
| Hypertensive diseases | **8.58 (1.07, 68.72)** | – | 1.34 (0.36, 5.00) | – | **–** | – |
|  | 0.043 | **–** | 0.668 | – | **–** | – |

**Supplementary Table 9 footnote.** Results are cause specific hazard ratio (95% confidence interval) and p-value associated with cancer history (vs no cancer). Comparators are matched on age, sex, ethnicity, deprivation, education, blood pressure, heart rate, body mass index, glycated haemoglobin, random glucose, total cholesterol, high density lipoprotein, low density lipoprotein, triglyceride level, physical activity, smoking, diabetes, hypertension, and high cholesterol. AF: atrial fibrillation; CVD: cardiovascular disease; IHD: ischaemic heart disease; NICM: non-ischaemic cardiomyopathies; VTE: venous thromboembolism.

**Supplementary Table 10. Incident events observed by cancer site (including cancers within preceding 5 years)**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **within 5 years** | **Breast** | **Lung** | **Prostate** | **Colorectal** | **Uterus** | **Haem** | **Total** |
| **Incident disease** |  |  |  |  |  |  |  |
| IHD | 197 | 17 | 273 | 136 | 29 | 99 | 751 |
| NIC | 33 | 0 | 22 | 15 | 4 | 21 | 95 |
| HF | 120 | 15 | 133 | 55 | 15 | 85 | 423 |
| AF/flutter | 178 | 22 | 261 | 120 | 25 | 120 | 726 |
| Stroke | 69 | 14 | 105 | 36 | 11 | 37 | 272 |
| Pericarditis | 27 | 6 | 20 | 10 | 3 | 17 | 83 |
| VTE (DVT/PE) | 129 | 14 | 108 | 43 | 10 | 47 | 351 |
| **Mortality outcomes** |  |  |  |  |  |  |  |
| All-cause | 594 | 124 | 502 | 321 | 56 | 309 | 1906 |
| CVD (any) | 30 | 9 | 58 | 25 | 7 | 20 | 149 |
| IHD | 15 | 7 | 38 | 19 | 2 | 14 | 95 |
| HF/NIC | 4 | 0 | 6 | 2 | 2 | 0 | 14 |
| Stroke | 7 | 1 | 10 | 3 | 2 | 6 | 29 |
| Hypertensive diseases | 2 | 0 | 4 | 2 | 2 | 0 | 10 |

**Supplementary Table 10 footnote.** AF: atrial fibrillation; CVD: cardiovascular disease; DVT: deep vein thrombosis; HF: heart failure; IHD: ischaemic heart disease; NIC: non-ischaemic cardiomyopathies; PE: pulmonary embolism.

**Supplementary Table 11. Associations of cancer with incident events amongst all prevalent cancers for cases diagnoses in the preceding 5 years**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Breast** | **Lung** | **Prostate** | **Colorectal** | **Uterus** | **Haem** |
| **Incident disease** |  |  |  |  |  |  |
| IHD | 1.15 (0.93, 1.40) | 0.93 (0.45, 1.92) | 0.94 (0.79, 1.13) | 1.12 (0.86, 1.45) | 0.76 (0.47, 1.21) | 1.16 (0.85, 1.57) |
|  | 0.195 | 0.843 | 0.518 | 0.399 | 0.245 | 0.347 |
| NICM | 1.84 (1.03, 3.29) | **–** | 0.70 (0.41, 1.22) | 1.07 (0.52, 2.25) | 4.01 (0.44, 36.23) | 2.64 (1.16, 5.99) |
|  | 0.038 | **–** | 0.213 | 0.847 | 0.215 | 0.02 |
| HF | 1.52 (1.14, 2.01) | 1.57 (0.66, 3.71) | 0.94 (0.79, 1.19) | 0.79 (0.55, 1.11) | 0.75 (0.39, 1.43) | 2.12 (1.48, 3.06) |
|  | 0.004 | 0.302 | 0.592 | 0.17 | 0.378 | 5.35 x 10-5 |
| AF/flutter | 0.98 (0.79, 1.21) | 1.65 (0.84, 3.25) | 0.94 (0.79, 1.12) | 1.02 (0.79, 1.32) | 0.76 (0.44, 1.27) | 1.68 (1.25, 2.27) |
|  | 0.859 | 0.153 | 0.485 | 0.864 | 0.29 | 0.001 |
| Stroke | 0.90 (0.65, 1.26) | 1.57 (0.66, 3.71) | 1.06 (0.80, 1.40) | 1.06 (0.66, 1.72) | 0.79 (0.35, 1.75) | 1.92 (1.11, 3.35) |
|  | 0.567 | 0.307 | 0.67 | 0.79 | 0.56 | 0.021 |
| Pericarditis | 3.03 (1.42, 6.42) | 6.05 (0.73, 50.91) | 1.54 (1.13, 2.10) | 0.59 (0.27, 1.30) | – | 2.44 (1.00, 5.87) |
|  | 0.004 | 0.096 | 0.006 | 0.186 | – | 0.049 |
| VTE (DVT/PE) | 1.90 (1.40, 2.53) | 2.89 (1.08, 7.69) | 1.54 (1.13, 2.10) | 1.19 (0.75, 1.86) | 0.71 (0.34, 1.51) | 2.14 (1.28, 3.53) |
|  | 2.14 x 10-5 | 0.034 | 0.006 | 0.47 | 0.375 | 0.004 |
| **Mortality outcomes** |  |  |  |  |  |  |
| All-cause | 3.40 (2.89, 4.01) | 6.12 (4.1, 9.14) | 1.69 (1.47, 1.95) | 3.20 (2.58, 3.96) | 1.55 (1.03, 2.34) | 4.48 (3.50, 5.72) |
|  | 1.56 x 10-48 | 6.69 x 10-19 | 2.14 x 10-13 | 1.13 x 10-26 | 0.037 | 3.55 x 10-33 |
| Any CVD | 0.97 (0.58, 1.60) | 1.12 (0.42, 2.97) | 1.12 (0.76, 1.63) | 1.26 (0.70, 2.27) | 1.19 (0.4, 3.53) | 1.43 (0.73, 2.77) |
|  | 0.898 | 0.824 | 0.56 | 0.449 | 0.761 | 0.298 |
| IHD | 1.00 (0.49, 2.03) | 1.39 (0.43, 4.48) | 1.16 (0.73, 1.86) | 1.27 (0.64, 2.51) | **–** | 1.39 (0.62, 3.16) |
|  | 0.997 | 0.578 | 0.541 | 0.491 | **–** | 0.424 |
| HF/NIC | – | **–** | 2.01 (0.50, 8.00) | **–** | **–** | – |
|  | – | **–** | 0.326 | **–** | **–** | – |
| Stroke | 0.70 (0.27, 1.84) | **–** | 0.83 (0.36, 1.92) | **–** | **–** | 3.00 (0.61, 14.88) |
|  | 0.472 | **–** | 0.83 | **–** | **–** | 0.179 |
| Hypertensive diseases | – | **–** | **–** | **–** | **–** | – |
|  | – | **–** | **–** | **–** | **–** | **–** |

**Supplementary Table 11 footnote.** Results are sub-distribution hazard ratio (95% confidence interval) and p-value associated with cancer exposure (vs propensity-matched non-cancer controls). AF: atrial fibrillation; CVD: cardiovascular disease; DVT: deep vein thrombosis; HF: heart failure; IHD: ischaemic heart disease; NIC: non-ischaemic cardiomyopathies; PE: pulmonary embolism.

**Supplementary Table 12. Characteristics of the imaging subset**

|  | **Cases** | **Controls** | **Breast** | **Lung** | **Prostate** | **Colorectal** | **Uterus** | **Haem** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| N | 1354 | 1354 | 586 | 13 | 473 | 47 | 76 | 159 |
| Age | 68 [62-72] | 68 [62-72] | 66 [59-70] | 68 [64-69] | 70 [66-73] | 67 [62-71] | 66 [59-70] | 67 [62-72] |
| Men | 603 (44.5) | 609 (45.0) | 0 (0) | 4 (30.8) | 473 (100) | 29 (61.7) | 0 (0) | 61.0 (97) |
| Women | 751 (55.5) | 745 (55.0) | 586 (100) | 9 (69.2) | 0 (0) | 18 (38.3) | 76 (100) | 62 (39.0) |
| White ethnicity | 1329 (98.2) | 1333 (98.6) | 576 (98.3) | 13 (100) | 466 (98.5) | 45 (95.7) | 74 (97.4) | 155 (98.1) |
| BAME | 24 (1.8) | 19 (1.4) | 10 (1.7) | 0 (0) | 7 (1.5) | 2 (4.3) | 2 (2.6) | 3 (1.9) |
| Townsend score | -2.8 [-4.0, -0.9] | -2.8 [-4.0, -0.7] | -2.8 [-3.9, -0.9] | -3.3 [-4.3, -2.7] | -3.0 [-4.1, -1.5] | -2.5 [-4.0, -0.8] | -2.6 [-3.6, -0.9] | -2.5 [-3.8, 0.0] |
| Degree or professional qualification | 882 (65.3) | 879 (65.0) | 377 (64.4) | 4 (30.8) | 316 (67.0) | 36 (76.6) | 49 (64.5) | 100 (63.3) |
| SBP (mmHg) | 138.9 ±17.9 | 139.2 ±18.8 | 135.3 ± 18.3 | 133.9 ± 13.1 | 142.7 ±16.1 | 142.2 ±18.8 | 137.8 ± 19.8 | 140.1 ±18.0 |
| DBP (mmHg) | 77.9 ±9.5 | 77.8 ± 9.8 | 77.1 ±9.4 | 79.9 ±7.5 | 78.4 ±9.3 | 80.2 ±9.1 | 78.6 ±9.5 | 78.2 ±10.4 |
| HR (bpm) | 70 [62.5-79.5] | 71 [63-79.5] | 72.5 [65-81.5] | 73.5 [62-86] | 67 [60-76] | 69.8 [61-81] | 70.5 [64.5-78] | 69.5 [62-79] |
| BMI (kg/m2) | 26.0 [23.4 – 29.0] | 25.9 [23.5-28.6] | 25.2 [22.7-28.6] | 26.7 [23.1- 29.3] | 26.5 [24.5- 28.9] | 27.1 [24.4- 31.8] | 27.7 [24.2- 31.3] | 25.5 [22.9- 28.6] |
| Physical activity (METS/week) | 2026 [1006- 3566] | 1939 [938-3492] | 2179 [1009-3546] | 1701 [1026- 3572] | 1983 [1045- 3594] | 1194 [718- 2549] | 1662 [974- 3512] | 2039 [1055 – 4086] |
| Ever Smoking | 508 (38.3) | 532 (40.0) | 210 (36.6) | 7 (53.9) | 195 (42.1) | 22 (46.8) | 19 (25.3) | 55 (35.3) |
| HbA1c (mmol/mol) | 35.1 [32.8- 37.4] | 35.2 [32.5- 37.5] | 35 [32.7- 37.1] | 34.2 [33.1- 37.7] | 35.4 [33.1- 37.5] | 35 [32.4- 38.3] | 36.0 [33.5- 38.7] | 34.8 [32.5-37.2] |
| Random glucose (mmol/L) | 4.9 [4.6- 5.3] | 4.9 [4.6- 5.3] | 4.9 [4.6- 5.3] | 5.0 [4.1- 5.6] | 4.9 [4.6- 5.3] | 5.0 [4.7- 5.5] | 4.9 [4.5- 5.2] | 4.9 [4.5- 5.2] |
| Total cholesterol (mmol/L) | 5.7 ±1.2 | 5.7 ±1.1 | 5.9 ±1.2 | 6.1 ±1.1 | 5.4 ±1.1 | 5.5 ±1.4 | 5.8 ±1.1 | 5.4 ±1.1 |
| HDL (mmol/L) | 1.4 [1.2- 1.7] | 1.4 [1.2- 1.7] | 1.6 [1.3- 1.8] | 1.5 [1.2- 1.6] | 1.2 [1.1- 1.5] | 1.3 [1.0- 1.5] | 1.4 [1.3- 1.8] | 1.3 [1.1- 1.6] |
| LDL direct (mmol/L) | 3.5 [3.0- 4.1] | 3.5 [2.9- 4.1] | 3.6 [3.0- 4.2] | 3.7 [3.2- 4.4] | 3.4 [2.9- 4.0] | 3.4 [2.8- 4.0] | 3.4 [3.0- 4.1] | 3.4 [2.9-4.0] |
| Triglyceride level (mmol/L) | 1.5 [1.1- 2.1] | 1.5 [1.0- 2.1] | 1.4 [1.0- 1.9] | 1.4 [1.4- 2.4] | 1.7 [1.2- 2.4] | 1.6 [1.3- 2.2] | 1.5 [0.9- 1.9] | 1.5 [1.0- 2.2] |
| Diabetes | 109 (8.1) | 121 (8.9) | 34 (5.8) | 1 (7.7) | 47 (9.9) | 8 (17.0) | 11 (14.5) | 8 (5.0) |
| Hypertension | 505 (37.3) | 485 (35.8) | 160 (27.3) | 4 (30.8) | 230 (48.6) | 24 (51.1) | 26 (34.2) | 61 (38.4) |
| High cholesterol | 618 (45.6) | 631 (46.6) | 206 (35.2) | 7 (53.9) | 280 (59.2) | 30 (63.8) | 30 (39.5) | 65 (40.9) |
| LVM (g) | - | - | 70.9 ± 12.8 | 80.4 ± 17.8 | 99.7 ± 17.4 | 92.4 ± 21.3 | 75.3 ± 18.0 | 91.1 ± 25.7 |
| LVEDV (ml) | - | - | 128.6 ± 22.1 | 131.7 ± 34.1 | 163.2 ± 32.1 | 150.0 ± 33.5 | 133.4 ±27.5 | 155.4 ± 42.2 |
| LVEF (%) | - | - | 60.5 ± 6.2 | 62.2 ± 3.3 | 57.8 ± 6.6 | 59.3 ± 4.5 | 61.8 ± 5.1 | 57.3 ± 6.7 |
| LVGFI (%) | - | - | 0.50 ± 0.07 | 0.49 ± 0.05 | 0.45 ± 0.07 | 0.46 ± 0.06 | 0.50 ± 0.06 | 0.45 ± 0.07 |
| LV GLS (%) | - | - | -19.1 ± 3.0 | -19.5 ± 2.2 | -17.7 ± 2.6 | -17.7 ± 2.5 | -19.4 ± 2.4 | -17.4 ± 2.7 |
| LAV max (ml) | - | - | 66.9 ± 19.4 | 62.8 ± 26.0 | 77.3 ± 29.7 | 72.3 ± 22.5 | 71.4 ± 22.7 | 77.4 ± 29.6 |
| LAEF (%) | - | - | 61.6 ± 9.1 | 62.5 ±14.3 | 59.1 ± 10.6 | 61.2 ± 8.5 | 61.4 ± 7.5 | 58.3 ± 10.8 |

**Supplementary Table 12 footnote.** Continuous variables are shown as mean ±standard deviation, or median [IQR] if skewed. Count variables are shown as N (%). BAME: Black, Asian, and Minority ethnic; HbA1c: glycated haemoglobin, HDL: high density lipoprotein, LDL: low density lipoproteinDBP: diastolic blood pressure; METS: metabolic equivalent of task; SBP: systolic blood pressure. LA: left atrium; LV: left ventricle; LA ejection fraction (LAEF); LA maximum volume (LAV); LV end-diastolic volume (LVEDV); LV mass (LVM); LV ejection fraction (LVEF); LV global function index (LVGFI); LV global longitudinal strain (GLS).

**Supplementary Table 13.** **Association of cancer with CMR metrics in participants without cardiovascular disease at time of imaging**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Breast | Lung | Prostate | Colorectal† | Uterus† | Haem† |
| LVM (g) | 0.05 (-0.08, 0.18) | -0.55 (-1.52, 0.41) | -0.12 (-0.29, 0.06) | -0.69 (-1.36, -0.02) | 0.16 (-0.22, 0.54) | 0.08 (-0.20, 0.37) |
|  | 0.44 | 0.22 | 0.19 | 0.04 | 0.40 | 0.56 |
| LVEDV (ml) | 0.07 (-0.05, 0.19) | -0.69 (-1.96, 0.58) | -0.07 (-0.23, 0.10) | -0.88 (-1.60, -0.15) | 0.14 (-0.25, 0.53) | 0.19 (-0.10, 0.47) |
|  | 0.26 | 0.24 | 0.42 | 0.02 | 0.47 | 0.20 |
| LVEF (%) | -0.17 (-0.30, -0.04) | 0.24 (-1.07, 1.55) | 0.12 (-0.04, 0.29) | 0.33 (-0.62, 1.29) | 0.15 (-0.23, 0.53) | -0.26 (-0.52, -0.00) |
|  | 0.01 | 0.68 | 0.14 | 0.47 | 0.42 | 0.05 |
| LVGFI (%) | -0.14 (-0.27, -0.01) | -0.08 (-1.72, 1.56) | 0.13 (-0.04, 0.3) | 0.22 (-0.74, 1.18) | 0.16 (-0.24, 0.56) | -0.17 (-0.42, 0.08) |
|  | 0.04 | 0.91 | 0.13 | 0.64 | 0.42 | 0.19 |
| LV GLS (%) | -0.02 (-0.15, 0.10) | -0.43 (-1.72, 0.86) | 0.03 (-0.14, 0.21) | -0.11 (-1.11, 0.89) | -0.00 (-0.37, 0.37) | 0.19 (-0.09, 0.47) |
|  | 0.74 | 0.45 | 0.71 | 0.82 | 0.99 | 0.18 |
| LAV max (ml) | 0.09 (-0.04, 0.21) | -1.10 (-2.28, 0.08) | -0.03 (-0.21, 0.15) | -0.92 (-1.80, 0.05) | 0.21 (-0.13, 0.55) | 0.21 (-0.07, 0.48) |
|  | 0.18 | 0.06 | 0.74 | 0.04 | 0.23 | 0.13 |
| LAEF (%) | -0.15 (-0.27, -0.02) | 0.59 (0.03, 1.15) | -0.01 (-0.18, 0.16) | 0.54 (-0.12, 1.21) | -0.07 (-0.38, 0.24) | -0.324(-0.60, -0.05) |
|  | 0.03 | 0.04 | 0.90 | 0.10 | 0.66 | 0.02 |

**Supplementary Table 13 footnote.** The results are standardised beta-coefficients and 95% confidence intervals, thus representing standard deviation change in CMR metrics with change in cancer exposure status from non-cancer to cancer; for standard deviation of each metric please refer to Supplementary Table 5. The bold and yellow shaded cells represent statistically significant associations. LA: left atrium; LV: left ventricle; LV end-diastolic volume (LVEDV), LV mass (LVM), LVM: LVEDV, LV stroke volume (LVSV), LV ejection fraction (LVEF), LV global function index (LVGFI), LV global longitudinal strain (GLS), LA maximum volume (LAV), LA ejection fraction (LAEF).