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Association of physical activity trajectories across a cardiovascular disease diagnosis with death and non-fatal cardiovascular events: three prospective cohorts

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Article

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Abstract

Physical activity is recommended after a diagnosis of cardiovascular disease (CVD), but whether changes in activity across diagnosis affect prognosis is unclear; evidence comes largely from single countries, coronary heart disease and mortality endpoints. In three prospective cohorts of adults aged 50 years and older — the US Health and Retirement Study (HRS; 3,042 participants, 1,385 events), the English Longitudinal Study of Ageing (ELSA; 539, 102) and the China Health and Retirement Longitudinal Study (CHARLS; 769, 87) — activity before and after incident CVD was cross-classified into four trajectories (maintained, stopped, started, remained inactive) and, from a one-year landmark, related to a composite of non-fatal myocardial infarction, stroke and all-cause death. Remaining inactive was associated with higher risk than maintaining activity in HRS (hazard ratio 1.85, 95% confidence interval 1.62–2.11) and ELSA (2.58, 1.55–4.31), but not in CHARLS (1.10, 0.59–2.02). Pooled, remaining inactive raised risk 81% (1.81, 1.28–2.55) and stopping 53% (1.53, 1.26–1.86); starting showed a smaller increase (1.28, 0.99–1.64). Risk fell steeply with frequency, with half the maximal benefit at one to three sessions per month, and conclusions were consistent across three trajectory definitions.

Introduction

Most patients now survive the acute phase of myocardial infarction and stroke, and the number of people living with cardiovascular disease has nearly doubled since 1990.[1] Physical activity is central to secondary prevention and is recommended by international guidelines.[2, 3] What the guidelines cannot say is how activity changes as patients pass through a diagnosis, and what such changes mean for subsequent risk. Most evidence comes from a single measurement taken after diagnosis, which cannot separate people who were never active from those who stopped because of their illness.

Several studies have therefore treated physical activity as a trajectory rather than a fixed exposure. In a meta-analysis of nine prospective cohorts of patients with coronary heart disease (33,576 patients), those who maintained or increased activity had about half the all-cause mortality of those who remained inactive, and those who became inactive retained part of the benefit.[4] Cohort studies have since extended the question: a Swedish registry of 47,153 survivors of myocardial infarction found that patients who remained active had a lower risk of recurrent non-fatal cardiovascular events than those who remained inactive;[5] Australian patients with coronary heart disease showed a similar gradient across threshold-defined trajectories;[6] and in Italian older people, activity modelled as a time-varying exposure was associated with incident cardiovascular disease.[7] A recent study charted activity before and after an event in young American patients but did not relate trajectories to subsequent events.[8] The design has also been carried into oncology, where activity change across a cancer diagnosis was associated with subsequent cardiovascular events in 269,943 cancer survivors.[9] Two features of this literature stand out: the endpoints are either mortality alone or non-fatal events in a single country, and the diagnoses studied are almost always coronary heart disease or myocardial infarction.

Three gaps follow. First, whether trajectories spanning a diagnosis are associated with a composite of non-fatal myocardial infarction, non-fatal stroke and all-cause death remains unclear: the meta-analysis covered mortality alone,[4] and the one large registry study covered non-fatal events without deaths, in Swedish survivors of myocardial infarction.[5] A composite of this kind captures the total risk patients face after a diagnosis rather than survival alone. Second, evidence comes almost entirely from high-income countries and coronary heart disease; the one analysis from a middle-income setting examined primary prevention, so whether the associations extend to patients after a cardiovascular diagnosis in such settings is unknown.[10] Third, each study used a single way of defining trajectories — prespecified categories, group-based models, or data-driven sex-specific thresholds[4, 6, 10] — so it is unknown whether conclusions depend on that choice.

We therefore examined physical activity trajectories before and after a cardiovascular diagnosis in three prospective cohorts of older adults: the Health and Retirement Study in the United States, the English Longitudinal Study of Ageing, and the China Health and Retirement Longitudinal Study. Activity was cross-classified across the diagnosis into four trajectories (maintained activity, stopped, started activity after diagnosis, remained inactive) and related to the composite endpoint above. The design adds a composite endpoint rather than mortality alone, diagnoses beyond coronary heart disease, a middle-income setting, a dose–response analysis across the full range of post-diagnosis activity, and a test of whether conclusions depend on how trajectories are defined, using prespecified categories, group-based trajectory models and data-driven sex-specific thresholds. We also examined whether inflammatory markers and depressive symptoms lie on the pathway, and whether estimated cardiorespiratory fitness explains the associations.

Results

Cohorts and participants

Of 23,130 HRS participants with eCRF data, 3,875 developed incident cardiovascular disease (CVD); 3,199 had physical activity (PA) assessed both before and after diagnosis and 3,042 entered the 1-year landmark analysis (1,385 events). In ELSA, 1,282 incident cases had paired PA assessments; because mortality linkage ended in 2012, the primary analysis was restricted to the 776 cases diagnosed by wave 5 (2010), for whom outcome ascertainment was complete within the window (154 events); 539 had complete covariate data and entered the eCRF-adjusted primary model (102 events); non-fatal events ascertained to 2018 were used in a sensitivity analysis (Supplementary Table S13). In CHARLS, 769 of 772 incident cases entered the primary analysis (87 events); the eCRF-adjusted model retained 707 participants (76 events). Figure 1 shows the participant flow for all three cohorts. Surveys were biennial (triennial in CHARLS), so the first post-diagnosis assessment always postdated the start of follow-up (median 2.0 years after diagnosis in HRS and ELSA, 3.0 in CHARLS; Supplementary Table S12). In an HRS analysis placing time zero one year after this assessment, estimates were similar (remained inactive, HR 1.77, 95% CI 1.52–2.07; Supplementary Table S6).

Physical activity trajectories and baseline characteristics

The four trajectories comprised 1,421 participants (46.7%) who maintained activity in HRS, 478 (15.7%) who stopped, 356 (11.7%) who started, and 787 (25.9%) who remained inactive; the corresponding ELSA proportions were 45.7%, 14.8%, 9.9% and 29.5%, and CHARLS 36.9%, 24.3%, 15.5% and 23.3%. Baseline eCRF declined from maintained activity to remained inactive in all three cohorts (HRS 8.3 vs 7.1 METs; ELSA 8.5 vs 7.2; CHARLS 9.5 vs 8.8), as did employment (HRS 31.0% vs 12.2%; ELSA 29.6% vs 6.6%; CHARLS 73.1% vs 32.2%), education and marital status (Table 1). Depressive symptoms were lowest in those who maintained activity and highest in those who remained inactive in HRS (1.6 vs 2.6 points) and ELSA (1.5 vs 3.0), but not in CHARLS (9.2 vs 10.1; SMD 0.03). Participants who started activity differed from those active throughout: in HRS they had the highest BMI (30.0 kg/m²) and the lowest share with tertiary education (14.1%) of the four groups.

Table 1
Baseline characteristics of participants by physical activity trajectory before and after cardiovascular disease diagnosis

Characteristic	Maintained activity	Stopped	Started activity after diagnosis	Remained inactive	All	SMD†
HRS (United States)						
Participants, n	1,421	478	356	787	3,042	
Age at enrolment, years, mean (SD)	69.1 (11.3)	71.4 (11.1)	68.6 (11.6)	72.3 (12.1)	70.3 (11.6)	-0.18
Men, n (%)	777 (54.7)	232 (48.5)	164 (46.1)	301 (38.2)	1,474 (48.5)	0.24
Body mass index, kg/m², mean (SD)	28.6 (5.6)	29.5 (6.2)	30.0 (6.2)	29.5 (6.5)	29.1 (6.0)	-0.17
Resting heart rate, beats/min, mean (SD)	67.7 (11.5)	68.1 (11.2)	69.6 (12.5)	68.8 (10.0)	68.2 (11.3)	-0.10
Education: below high school, n (%)	234 (16.5)	101 (21.1)	89 (25.1)	179 (22.7)	603 (19.8)	-0.16
Education: high school, n (%)	883 (62.1)	289 (60.5)	216 (60.8)	524 (66.6)	1,912 (62.9)	-0.03
Education: college or above, n (%)	304 (21.4)	88 (18.4)	50 (14.1)	84 (10.7)	526 (17.3)	0.20
Married or cohabiting, n (%)	821 (57.9)	271 (56.7)	190 (53.4)	386 (49.0)	1,668 (54.9)	0.11
Employed, n (%)	440 (31.0)	101 (21.4)	87 (24.6)	96 (12.2)	724 (23.9)	0.32
Current smoker, n (%)	201 (14.2)	80 (16.8)	69 (19.4)	171 (21.9)	521 (17.2)	-0.15
Former smoker, n (%)	863 (61.0)	312 (65.4)	219 (61.7)	493 (63.2)	1,887 (62.4)	-0.05
Alcohol use, n (%)	813 (57.2)	220 (46.0)	156 (43.8)	297 (37.7)	1,486 (48.8)	0.32
Hypertension, n (%)	1,018 (71.6)	357 (74.7)	288 (80.9)	664 (84.4)	2,327 (76.5)	-0.22
Diabetes, n (%)	395 (27.8)	156 (32.6)	127 (35.7)	290 (36.8)	968 (31.8)	-0.16
Depressive symptoms score, mean (SD)‡	1.6 (2.1)	1.8 (2.0)	2.4 (2.5)	2.6 (2.5)	2.0 (2.3)	-0.33

Characteristic	Maintained activity	Stopped	Started activity after diagnosis	Remained inactive	All	SMD†
HRS (United States)						
eCRF, METs, mean (SD)§	8.3 (1.9)	7.6 (1.8)	7.7 (2.0)	7.1 (1.9)	7.8 (2.0)	0.49
Year of diagnosis, median [IQR]	2010 [2010–2014]	2011 [2010–2014]	2010 [2010–2014]	2012 [2010–2016]	2010 [2010–2014]	-0.07
Diagnosis type: angina, n (%)	216 (15.2)	54 (11.3)	43 (12.1)	102 (13.0)	415 (13.6)	0.09
Diagnosis type: heart failure, n (%)	183 (12.9)	84 (17.6)	52 (14.6)	112 (14.2)	431 (14.2)	-0.07
Diagnosis type: myocardial infarction, n (%)	558 (39.3)	186 (38.9)	136 (38.2)	288 (36.6)	1,168 (38.4)	0.03
Diagnosis type: stroke, n (%)	464 (32.7)	154 (32.2)	125 (35.1)	285 (36.2)	1,028 (33.8)	-0.05
Follow-up, years, mean (SD)	7.1 (3.6)	6.0 (3.6)	6.7 (3.8)	5.6 (3.6)	6.5 (3.7)	0.31
Composite endpoint, n (%)	523 (36.8)	253 (52.9)	163 (45.8)	446 (56.7)	1,385 (45.5)	-0.33
Death, n (%)	443 (31.2)	227 (47.5)	141 (39.6)	407 (51.7)	1,218 (40.0)	-0.35
ELSA (England)						
Participants, n	355	115	77	229	776	
Age at enrolment, years, mean (SD)	67.2 (9.0)	71.1 (11.1)	71.8 (10.4)	72.4 (11.2)	69.8 (10.4)	-0.47
Men, n (%)	218 (61.4)	57 (49.6)	45 (58.4)	104 (45.4)	424 (54.6)	0.25
Body mass index, kg/m², mean (SD)	28.2 (4.5)	29.8 (5.1)	29.7 (5.8)	28.8 (5.6)	28.7 (5.1)	-0.22
Education: below high school, n (%)	114 (35.6)	46 (44.2)	36 (52.2)	141 (66.5)	337 (43.4)	-0.43
Education: high school, n (%)	172 (53.8)	50 (48.1)	27 (39.1)	59 (27.8)	308 (39.7)	0.33
Education: college or above, n (%)	34 (10.6)	8 (7.7)	6 (8.7)	12 (5.7)	60 (7.7)	0.13

Characteristic	Maintained activity	Stopped	Started activity after diagnosis	Remained inactive	All	SMD†
HRS (United States)						
Married or cohabiting, n (%)	261 (73.5)	72 (62.6)	44 (57.1)	126 (55.0)	503 (64.8)	0.34
Employed, n (%)	105 (29.6)	19 (16.5)	10 (13.0)	15 (6.6)	149 (19.2)	0.49
Current smoker, n (%)	48 (13.7)	18 (15.8)	8 (10.8)	45 (20.2)	119 (15.6)	-0.10
Former smoker, n (%)	239 (68.1)	83 (72.8)	48 (64.9)	147 (65.3)	517 (67.7)	0.02
Alcohol use, n (%)	278 (90.8)	71 (74.7)	50 (80.6)	100 (64.5)	499 (80.7)	0.53
Hypertension, n (%)	210 (59.2)	73 (63.5)	51 (66.2)	141 (61.6)	475 (61.2)	-0.08
Diabetes, n (%)	44 (12.4)	26 (22.6)	13 (16.9)	43 (18.8)	126 (16.2)	-0.19
Depressive symptoms score, mean (SD)‡	1.5 (1.8)	2.2 (2.2)	2.4 (2.2)	3.0 (2.3)	2.1 (2.2)	-0.58
eCRF, METs, mean (SD)§	8.5 (1.8)	7.3 (1.7)	7.7 (2.0)	7.2 (2.0)	7.9 (1.9)	0.65
Year of diagnosis, median [IQR]	2008 [2006–2008]	2008 [2006–2008]	2008 [2006–2008]	2008 [2004–2008]	2008 [2006–2008]	-0.04
Diagnosis type: angina, n (%)	120 (33.8)	27 (23.5)	27 (35.1)	52 (22.7)	226 (29.1)	0.19
Diagnosis type: heart failure, n (%)	5 (1.4)	8 (7.0)	4 (5.2)	9 (3.9)	26 (3.4)	-0.21
Diagnosis type: myocardial infarction, n (%)	134 (37.7)	36 (31.3)	21 (27.3)	62 (27.1)	253 (32.6)	0.20
Diagnosis type: stroke, n (%)	96 (27.0)	44 (38.3)	25 (32.5)	106 (46.3)	271 (34.9)	-0.31
Follow-up, years, mean (SD)	3.8 (2.3)	3.8 (2.2)	3.5 (2.1)	3.2 (2.0)	3.6 (2.2)	0.16
Composite endpoint, n (%)	46 (13.0)	29 (25.2)	11 (14.3)	68 (29.7)	154 (19.8)	-0.33

Characteristic	Maintained activity	Stopped	Started activity after diagnosis	Remained inactive	All	SMD†
HRS (United States)						
Death, n (%)	13 (3.7)	18 (15.7)	6 (7.8)	52 (22.7)	89 (11.5)	-0.48
CHARLS (China)						
Participants, n	284	187	119	179	769	
Age at enrolment, years, mean (SD)	60.0 (8.6)	64.8 (9.1)	61.5 (8.2)	67.2 (10.0)	63.1 (9.5)	-0.53
Men, n (%)	115 (40.5)	88 (47.1)	40 (33.6)	83 (46.4)	326 (42.4)	-0.06
Body mass index, kg/m², mean (SD)	24.8 (3.6)	24.6 (4.8)	25.4 (4.3)	24.5 (4.1)	24.8 (4.1)	0.01
Education: below high school, n (%)	244 (85.9)	161 (86.1)	103 (86.6)	161 (89.9)	669 (87.0)	-0.05
Education: high school, n (%)	33 (11.6)	25 (13.4)	13 (10.9)	13 (7.3)	84 (10.9)	0.04
Education: college or above, n (%)	7 (2.5)	1 (0.5)	3 (2.5)	5 (2.8)	16 (2.1)	0.04
Married or cohabiting, n (%)	254 (89.4)	153 (81.8)	103 (86.6)	137 (76.5)	647 (84.1)	0.24
Employed, n (%)	207 (73.1)	111 (60.0)	54 (46.2)	56 (32.2)	428 (56.4)	0.57
Current smoker, n (%)	56 (20.9)	44 (24.2)	21 (18.8)	30 (17.8)	151 (20.7)	0.01
Former smoker, n (%)	115 (40.5)	80 (42.8)	37 (31.1)	84 (46.9)	316 (41.1)	-0.02
Alcohol use, n (%)	111 (39.1)	60 (32.1)	29 (24.4)	53 (29.6)	253 (32.9)	0.21
Hypertension, n (%)	116 (41.4)	78 (42.4)	57 (48.7)	97 (54.8)	348 (45.9)	-0.14
Diabetes, n (%)	34 (12.3)	19 (10.5)	19 (16.1)	33 (18.6)	105 (13.9)	-0.08
Depressive symptoms score, mean (SD)‡	9.2 (6.6)	8.7 (6.1)	9.7 (6.2)	10.1 (6.8)	9.4 (6.5)	-0.03
eCRF, METs, mean (SD)§	9.5 (1.8)	9.3 (2.1)	9.1 (1.7)	8.8 (2.2)	9.2 (2.0)	0.24

Characteristic	Maintained activity	Stopped	Started activity after diagnosis	Remained inactive	All	SMD†
HRS (United States)						
Year of diagnosis, median [IQR]	2015 [2013–2015]	2015 [2013–2015]	2015 [2013–2015]	2015 [2013–2015]	2015 [2013–2015]	0.00
Diagnosis type: heart disease, n (%)	248 (87.3)	165 (88.2)	110 (92.4)	143 (79.9)	666 (86.6)	0.03
Diagnosis type: stroke, n (%)	36 (12.7)	22 (11.8)	9 (7.6)	36 (20.1)	103 (13.4)	-0.03
Follow-up, years, mean (SD)	2.5 (0.9)	2.4 (0.9)	2.5 (0.9)	2.5 (0.9)	2.5 (0.9)	0.00
Composite endpoint, n (%)	27 (9.5)	19 (10.2)	12 (10.1)	29 (16.2)	87 (11.3)	-0.09
Death, n (%)	0 (0.0)	2 (1.1)	0 (0.0)	1 (0.6)	3 (0.4)	-0.11

Values are n (%) or mean (SD) unless stated otherwise. Activity was defined as vigorous or moderate physical activity at least once per week. The composite endpoint was non-fatal myocardial infarction, non-fatal stroke or all-cause death. †SMD = standardised mean difference comparing participants who stopped, started activity after diagnosis or remained inactive (combined) with those who maintained activity; absolute values above 0.1 indicate imbalance. ‡Depressive symptoms were measured with the CES-D (range 0–8) in HRS and ELSA and with the CES-D-10 (range 0–30) in CHARLS. §eCRF = non-exercise-estimated cardiorespiratory fitness.

Physical activity trajectories and risk of the composite endpoint

Rates of the composite endpoint increased across the four groups in all three cohorts, from 5.21 to 10.18 events per 100 person-years in HRS (maintained activity to remained inactive), 3.40 to 9.14 in ELSA, and 3.83 to 6.47 in CHARLS (Table 2; Supplementary Fig. 2, top panels). After adjustment for age, sex, baseline eCRF and diagnosis type, stopping and remaining inactive were associated with higher risk than maintaining activity in HRS (stopped, HR 1.59, 95% CI 1.36–1.85, $P = 2.7\times10^{-9}$; remained inactive, HR 1.85, 95% CI 1.62–2.11, $P = 4.6\times10^{-20}$; started activity, HR 1.39, 95% CI 1.16–1.66, $P = 3.2\times10^{-4}$). In ELSA, participants who remained inactive had more than twice the risk of those who maintained activity (HR 2.58, 95% CI 1.55–4.31, $P = 2.7\times10^{-4}$), whereas those who stopped (HR 1.69, 95% CI 0.95–3.03) or started activity after diagnosis (HR 0.75, 95% CI 0.31–1.81) did not differ significantly. In CHARLS, no contrast was significant in the eCRF-adjusted primary model (707 participants, 76 events; inactive, HR 1.10, 95% CI 0.59–2.02), and dropping eCRF to retain all 769 gave similar null estimates (inactive, HR 1.37, 95% CI 0.78–2.41). In a random-effects meta-analysis, remaining inactive was associated with an

81% higher risk (pooled HR 1.81, 95% CI 1.28–2.55, P = 7.8×10^{-4}; I^2=55%), stopping with a 53% higher risk (pooled HR 1.53, 95% CI 1.26–1.86, P = 1.6×10^{-5}; I^2=10%), and starting activity after diagnosis with a 28% higher risk that did not reach significance (pooled HR 1.28, 95% CI 0.99–1.64, P = 0.059; I^2=13%).

Table 2
Rates of and hazard ratios for the composite endpoint by physical activity trajectory

Trajectory	Participants, n	Events, n	Crude rate per 100 person-years‡	Hazard ratio (95% CI)†	P value
HRS (United States)					
Maintained activity	1,421	523	5.21	1 (Reference)	—
Stopped	478	253	8.78	1.59 (1.36–1.85)	< 0.001
Started activity after diagnosis	356	163	6.82	1.39 (1.16–1.66)	< 0.001
Remained inactive	787	446	10.18	1.85 (1.62–2.11)	< 0.001
ELSA (England)					
Maintained activity	355	46	3.40	1 (Reference)	—
Stopped	115	29	6.61	1.69 (0.95–3.03)	0.076
Started activity after diagnosis	77	11	4.07	0.75 (0.31–1.81)	0.52
Remained inactive	229	68	9.14	2.58 (1.55–4.31)	< 0.001
CHARLS (China)					
Maintained activity	284	27	3.83	1 (Reference)	—
Stopped	187	19	4.19	0.98 (0.52–1.84)	0.94
Started activity after diagnosis	119	12	3.97	1.04 (0.52–2.09)	0.91
Remained inactive	179	29	6.47	1.10 (0.59–2.02)	0.77
Pooled (random effects)§					
Stopped			—	1.53 (1.26–1.86)	< 0.001
Started activity after diagnosis			—	1.28 (0.99–1.64)	0.059
Remained inactive			—	1.81 (1.28–2.55)	< 0.001

† Hazard ratios were adjusted for age, sex, baseline eCRF and diagnosis type. The HRS model includes 3,042 participants (1,385 events); the ELSA model includes 539 cases with complete covariate data (102 events); the CHARLS model includes 707 participants with complete physical measurements (76 events).

‡ Crude rates were calculated in the full trajectory frames, which include participants without complete covariate data (ELSA: 776 cases diagnosed by wave 5 with follow-up censored in 2012, 154 events; CHARLS: 769 cases, 87 events).

§ Pooled estimates are from a random-effects meta-analysis (DerSimonian–Laird) of the three cohort estimates (4,288 participants, 1,563 events). Between-cohort heterogeneity: I^2 = 10% (stopped), 13% (started activity after diagnosis) and 55% (remained inactive); tau^2 = 0.006, 0.013 and 0.053 respectively. Leave-one-cohort-out pooled estimates for remained inactive ranged from 1.56 (omitting ELSA) to 1.99 (omitting CHARLS).

In a binary comparison, participants who were active after diagnosis had a 37% lower risk of the composite endpoint than those who were inactive (HRS HR 0.63, 95% CI 0.56–0.70, P = 2.3×10^{-17}).

Because all-cause death was a component, we also examined the outcome without it. In HRS, deaths accounted for 1,050 of 1,385 events (76%). When the outcome was restricted to non-fatal events (318 events), the inactive contrast was attenuated (cause-specific HR 1.31, 95% CI 0.99–1.73; Fine–Gray subdistribution HR 1.16, 95% CI 0.88–1.52; Supplementary Table S3), although all HRS estimates remained above 1.0 and 5-year cumulative incidence of non-fatal events remained higher in the inactive group (10.7% vs 7.5%; Supplementary Fig. 2). In ELSA (30 non-fatal events) and CHARLS (74 events, with only two deaths ascertained), none of the non-fatal contrasts was significant. Non-fatal events were few, and the present data cannot determine whether PA trajectories influence non-fatal events.

Dose–response

We modelled pre-to-post diagnosis MVPA frequency as a continuous exposure using restricted cubic splines (n = 3,023; 1,379 events; 19 participants whose post-diagnosis frequency response was missing or otherwise not quantifiable were excluded). Each additional weekly session was associated with a 9% lower risk of the composite endpoint (HR 0.91, 95% CI 0.88–0.93), and the association was non-linear (P for non-linearity 2.4×10^{-8}): risk fell steeply from no activity to about two sessions per week and levelled off, with about half the maximal benefit already reached at one to three sessions per month (Fig. 2).

Time-varying and cumulative activity

With post-diagnosis PA modelled as a time-varying exposure across 11,032 person-intervals, participants who were currently active had a 46% lower risk than those who were inactive (HR 0.54, 95%

CI 0.48–0.60, P = 2.7×10^{-28}), and each 0.25 increment in the cumulative average activity probability was associated with a 15% lower risk (HR 0.85, 95% CI 0.82–0.87).

Fully adjusted model

Further adjustment for education, smoking, alcohol use, marital status, employment, hypertension and diabetes, all measured before diagnosis, attenuated the HRS estimates by 5–12% without changing the pattern (stopped, HR 1.50, 95% CI 1.29–1.75; started, 1.29, 1.08–1.54; remained inactive, 1.63, 1.42–1.86; all P < 0.01; multiple imputation, n = 3,042). In ELSA, the inactive association remained significant (HR 2.20, 95% CI 1.26–3.83), CHARLS estimates remained close to 1 (all P > 0.5), and the ELSA participants excluded for missing physical measurements were younger, more often male, more often inactive and had higher crude event rates (6.2 vs 5.2 per 100 person-years; Supplementary Table S11).

Sensitivity analyses

The results did not depend on how activity trajectories were defined. A group-based trajectory model fitted to the continuous frequency data selected five classes in HRS and ELSA and two in CHARLS. In HRS, HRs for classes 2–5 versus the most active class were 1.66 (95% CI 1.43–1.93), 1.13 (0.90–1.41), 1.87 (1.60–2.19) and 2.35 (1.99–2.77): risk was highest in the least active class; the middle class, containing many who started activity, did not differ from the most active class. Class assignment agreed with the four-category classification (Cramér's V 0.54–0.73; Supplementary Table S1), and the two-class CHARLS solution reproduced the classification reported independently by Yao and colleagues.[10] Sex-specific thresholds derived from the data gave similar or larger estimates (HRS: started activity, 1.42; stopped, 1.65; inactive, 2.16; Supplementary Table S2). Multiple imputation of missing post-diagnosis PA or eCRF gave similar results (HRS inactive, HR 1.96, 95% CI 1.73–2.22; n = 3,247), as did weighting for cohort sampling probabilities and a second landmark (Supplementary Tables S4–S6). The inactive contrast remained significant in every HRS stratum of sex, age, diagnosis type and diabetes (hazard ratios 1.49–1.95; Fig. 3); stratified estimates for ELSA and CHARLS are shown in Supplementary Fig. 1, and none of the 24 interaction tests across the three cohorts was significant (all P > 0.11; Supplementary Table S7).

Alt text: Forest plot of hazard ratios for remaining inactive versus maintaining activity across HRS subgroups defined by demographic and clinical characteristics.

Supplementary Fig. 1 Hazard ratios for remaining inactive versus maintaining activity across subgroups in the three cohorts (HRS n = 3,042, 1,385 events; ELSA n = 539, 102 events; CHARLS n = 691, 74 events). Cox models with age as the time scale, adjusted for sex, baseline eCRF and diagnosis type (the matching covariate was dropped within its own strata); participants with missing diabetes status were excluded. Subgroups: sex; age at landmark entry (< 70 or ≥ 70 years); diagnosis type as defined in each cohort (angina, heart failure, myocardial infarction and stroke in HRS; angina, myocardial infarction and stroke in ELSA; heart disease and stroke in CHARLS); diabetes. Estimates

correspond to Supplementary Table S7. The dashed line marks a hazard ratio of 1.0; the horizontal axis is on the log scale.

Mediation

In HRS, inflammatory biomarkers were measured a median of 6.0 years after diagnosis at the 2016 examination[25] (Supplementary Table S8), among participants alive and free of the composite endpoint, with follow-up limited to five years. In these subsamples the total effect of remaining inactive was 10–12% for inflammatory mediators and 9.4% for depressive symptoms (Supplementary Table S10). For participants who remained inactive, inflammation mediated part of the excess risk: the proportion mediated was 26% (95% CI 10–70) for the composite inflammatory score, 29% (14–93) for soluble tumour necrosis factor receptor-1, 19% (6–56) for albumin and 14% (4–40) for interleukin-6, whereas the indirect effects through C-reactive protein, interleukin-1 receptor antagonist and white blood cell count included the null (Fig. 4); for participants who stopped, only soluble tumour necrosis factor receptor-1 reached significance (14%, 95% CI 1–40). Restricting HRS to biomarkers drawn within five years of diagnosis preserved the soluble tumour necrosis factor receptor-1 indirect effects (natural indirect effect 7.8 percentage points, 95% CI 0.1–16.9 for remaining inactive; 6.8, 1.4–14.3 for stopping) (Supplementary Table S9). For those who started activity, the total effect was close to zero and proportions mediated were unstable (Fig. 4). Mediation through post-diagnosis depressive symptoms was smaller (5.9%, 95% CI 1.0–15.7, for remaining inactive; 5.8%, 0.5–24.9, for stopping). In ELSA (246–263 participants, 41–42 events) and CHARLS (130 participants, 19 events, after excluding cases diagnosed in 2015 whose post-diagnosis activity postdated the blood sample), the intersecting samples were small and no indirect effect was significant (Supplementary Table S9); the median diagnosis-to-sampling interval in CHARLS was 2.0 years. Mediation in ELSA and CHARLS is therefore exploratory; full estimates are in Supplementary Table S10.

Alt text: Path diagram of the mediation framework from physical activity trajectory through inflammatory markers to the composite endpoint, and a forest plot of the proportion of the total effect mediated by each marker for remaining inactive versus maintaining activity in HRS; markers whose confidence intervals exclude zero are shown in blue.

Estimated cardiorespiratory fitness

To examine whether the trajectory associations reflected subclinical deterioration in fitness, we analysed eCRF trajectories around diagnosis. In all three cohorts, eCRF trajectories did not differ between cases and matched controls at diagnosis (HRS β=−0.033, P = 0.34; ELSA β=+0.058, P = 0.44; CHARLS β=+0.032, P = 0.34), and reconstructing eCRF without its physical activity component gave the same null result (HRS β=−0.002, P = 0.94). The associations are therefore unlikely to reflect measurable pre-diagnostic declines in fitness.

Discussion

In three prospective cohorts of adults aged 50 and over in the United States, England and China, patients who stopped or remained inactive after a cardiovascular diagnosis had a higher subsequent risk of the composite endpoint than those who maintained activity. The pooled hazard ratios were 1.53 for stopping and 1.81 for remaining inactive; starting activity was associated with a smaller increase that did not reach significance (1.28). Three findings qualify the main one. First, deaths accounted for 76% of composite events in the US cohort, and the non-fatal component alone could not be estimated precisely, so the results describe total post-diagnosis risk rather than non-fatal events separately. Second, risk fell steeply from no activity to about two sessions per week, with about half of the maximal benefit already present at one to three sessions per month. Third, findings were similar across trajectory definitions. The study thus extends this evidence from mortality endpoints and single countries to a composite endpoint that mostly reflects deaths.

Our results agree with the two largest previous studies. In a meta-analysis of nine cohorts with 33,576 patients with coronary heart disease, remaining active was associated with a 50% lower risk of death than remaining inactive, becoming active with a 45% lower risk, and becoming inactive with a 20% lower risk.[4] Our pooled contrast corresponds to about 45% lower risk for maintaining rather than remaining inactive (1/1.81), close to those estimates, but includes stroke, heart failure and angina, not only coronary heart disease. The ordering also matches the Swedish registry study of 47,153 patients after myocardial infarction (fully adjusted hazard ratios for recurrent non-fatal events versus remaining inactive: 0.67 remaining active, 0.78 increasing, 0.81 decreasing).[5]

Two recent studies examined activity around a cardiovascular event but asked different questions. In CARDIA, Gerber and colleagues described activity change around events in young and middle-aged adults, with low activity after the event, not a subsequent clinical event, as the outcome.[8] Activity was already declining more than a decade before the event, supporting the pre-to-post design and 1-year landmark used here. In CHARLS, Yao and colleagues modelled activity trajectories in people free of cardiovascular disease at baseline and found no association with self-reported disease at a single follow-up about two years later (94 events, odds ratio 0.72).[10] That analysis could not separate fatal from non-fatal disease or address competing death; ours is restricted to diagnosed patients and uses survival methods. No previous study, to our knowledge, has related such trajectories to a composite endpoint in more than one country.

The pooled estimates leave room for a partial legacy of previous activity, consistent with the graded inverse relation between fitness change and mortality[26, 27]: patients who stopped had a lower risk than those who remained inactive (1.53 versus 1.81), and those who started after diagnosis did not return fully to the risk of those who had never stopped (1.28). Mediation was concentrated in patients who remained inactive, but the mediation samples comprised survivors free of the endpoint, with markers drawn a median of 6.0 years after diagnosis; these estimates are therefore hypothesis-generating, not established pathway contributions. Within those limits, in HRS the composite

inflammatory score accounted for about a quarter of the excess risk of remaining inactive (26%, 95% CI 10–70), with soluble TNF receptor-1, albumin and interleukin-6 contributing similar shares,[28] whereas C-reactive protein, a downstream acute-phase marker, did not mediate the association[29]; depressive symptoms accounted for about 6%. These proportions exceed the 1–11% reported for inflammatory and metabolic mediators in 77,324 UK Biobank patients with prior cardiovascular disease (mean 5.1 years after diagnosis),[30] although the intervals are wide. Depressive symptoms rise after a cardiovascular diagnosis in these cohorts,[31] and fitness declines precede depression,[32] so depression remains a plausible behavioural pathway. Finally, null eCRF trajectories around diagnosis, robust to re-estimation without the activity term,[33] argue against measurable subclinical declines in fitness.

Findings were similar across analytical choices, though the data-driven definitions cannot independently confirm the pre-specified ones. A group-based trajectory model produced classes whose risks bracketed the four-category estimates (hazard ratios 1.66 to 2.35) and agreed reasonably with them (Cramér's V 0.54–0.73); its two-class CHARLS solution reproduced the classification reported by Yao and colleagues.[10] Sex-specific thresholds selected from the data gave similar or larger estimates (1.42–2.16). Time-varying models gave a hazard ratio of 0.54 for currently active versus inactive participants. Full adjustment attenuated the HRS estimates by 5–12% without removing them; multiple imputation, survey weights and a second landmark gave similar results.

The 2026 ESC guidelines on cardiac rehabilitation recommend preserving or adopting an active lifestyle after a diagnosis of coronary artery disease to reduce cardiovascular and all-cause mortality.[2, 34] Our findings support it with prognostic data from routine surveys in three countries. The dose–response curve carries the practical message: about half of the maximal difference in risk was already present at one to three sessions per month, so patients who cannot reach recommended volumes still gain most of the benefit, and patients who are active have prognostic reason not to stop. This supports assessing activity change, not only activity level, at follow-up visits.[4] In China and other middle-income settings, where structured cardiac rehabilitation is scarce, the CHARLS null should not be read as absence of benefit: with 76 events precision was limited, and better ascertainment of deaths and activity in ageing cohorts from these settings is a research priority.

Heterogeneity qualifies the pooled estimates. For remained inactive, I^2 was 55% and leave-one-cohort-out pooled estimates ranged from 1.56 to 1.99, so the pooled value should not be read as a single reconciled effect. The cohorts also differed in outcome ascertainment: linked registers in HRS and mortality linkage in ELSA against interview status in CHARLS, which plausibly under-ascertains deaths after a cardiovascular diagnosis, leaving CHARLS events almost entirely self-reported and non-fatal. The pooled contrast is therefore carried mainly by the US and English cohorts, and the CHARLS contribution is best read as descriptive. The study has several limitations that bound its conclusions. First, the composite endpoint included all-cause rather than cardiovascular death, and deaths accounted for 76% of US composite events; non-fatal contrasts were attenuated and imprecise (cause-specific hazard ratio 1.31 and subdistribution hazard ratio 1.16 in HRS, with only 30 non-fatal events in ELSA and two deaths ascertained in CHARLS), so no conclusion can be drawn about non-fatal events alone. Second,

diagnoses were recorded as ever-flags, so recurrent events could not be identified and the endpoint counts first new events, understating total event burden. Third, physical activity was self-reported as frequency without intensity or duration, so exposure misclassification is likely and would tend to attenuate estimates[35]; sitting time was not available in all cohorts, and proxy-completed interviews could not be identified in the harmonised data. Fourth, the CHARLS analysis was uninformative rather than negative: patients who died after diagnosis had no post-diagnosis assessment and were excluded, activity was a binary item, and median follow-up was about two years. Fifth, although the 1-year landmark, time-varying models and eCRF analyses argue against reverse causation, subclinical deterioration not captured by these designs cannot be excluded. Sixth, mediators were measured a median of 6.0 years after diagnosis even in HRS, and the ELSA and CHARLS analyses are exploratory. Finally, the cohorts cover adults aged 50 and over in three countries; younger patients and other health systems may differ. Whether interventions that help patients maintain or resume activity after diagnosis reduce the composite risk we observed is a question for trials.

Methods

Study population

We analysed data from three prospective cohort studies of older adults: the US Health and Retirement Study (HRS)[11], the English Longitudinal Study of Ageing (ELSA)[12], and the China Health and Retirement Longitudinal Study (CHARLS)[13]. HRS is a biennial panel of adults aged 50 or older in the United States (waves 2006–2024); ELSA is a biennial panel of adults aged 50 or older in England (waves 1–9, 2002–2018); CHARLS is a nationally representative longitudinal survey of adults aged 45 years or older in China (2011, 2013, 2015 and 2018). Exposure, covariate and outcome definitions were harmonised across cohorts.

Within each cohort we identified participants who had the physical measurements required for the non-exercise-estimated cardiorespiratory fitness (eCRF) equations (23,130 in HRS). Participants entered the analysis if they received a first doctor-reported diagnosis of cardiovascular disease (myocardial infarction, stroke, heart failure or angina) at or after the second wave, and if activity was recorded before and after diagnosis (3,199 in HRS, 1,282 in ELSA, 769 in CHARLS). Because ELSA mortality linkage available to us ended in 2012, the primary ELSA analysis was restricted to cases diagnosed by wave 5 (2010) with complete outcome ascertainment; the eCRF-adjusted model included cases with complete covariate data. In CHARLS, 62 of 769 cases lacked the physical measurements needed for baseline eCRF and were excluded from the eCRF-adjusted primary model. Figure 1 shows the participant flow for all three cohorts.

Alt text: Flow diagram showing how participants from the Health and Retirement Study, the English Longitudinal Study of Ageing and the China Health and Retirement Longitudinal Study were selected and classified into four physical activity trajectory groups.

All three parent studies were approved by their institutional review boards, and participants gave informed consent. The present analysis is a secondary analysis of de-identified, publicly available data. We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines[14].

Physical activity assessment

At every wave, participants reported how often they took part in vigorous and in moderate physical activity or sports. Following previous work in these cohorts, participants were classified as active if they reported vigorous or moderate activity at least once a week, and inactive otherwise. Pre-diagnosis activity was taken from the most recent assessment at or before the diagnosis wave, and post-diagnosis activity from the first assessment after diagnosis; cross-classification yielded the four trajectories above. Time zero was the date of diagnosis. To limit reverse causation from the index event, follow-up began one year after diagnosis[15]: participants who died during the first year were excluded. In a sensitivity analysis, follow-up instead began one year after the first post-diagnosis activity assessment.

For the dose–response analysis in HRS, each frequency category was assigned its approximate weekly equivalent (hardly ever or never, 0; one to three times a month, 0.5; once a week, 1; more than once a week, 3; every day, 6) and vigorous and moderate activity were summed, giving weekly sessions of moderate-to-vigorous activity. CHARLS records activity as a binary item and did not contribute to these analyses.

Outcome

The primary endpoint was a composite of non-fatal myocardial infarction, non-fatal stroke and all-cause death (the composite endpoint). Non-fatal events were new doctor-diagnosed conditions first reported after the diagnosis wave; because the surveys record ever-diagnosed conditions, recurrences cannot be distinguished from the defining diagnosis, so the non-fatal component undercounts recurrences. Deaths were ascertained through national death index linkage with last-alive follow-up fields in HRS (deaths recorded to 2023), through life-status linkage in ELSA (available to 2012 in the data we accessed), and through interview status in CHARLS (to 2018). Event dates are recorded by wave year, so non-fatal event timing is precise to the survey interval. Secondary endpoints were all-cause death alone and a composite additionally including new-onset heart failure.

Estimated cardiorespiratory fitness

eCRF was estimated in metabolic equivalents (METs) with sex-specific non-exercise equations[16] based on age, body mass index, waist circumference, resting heart rate, smoking and physical activity. In CHARLS the physical activity term was omitted (activity is a binary item), which removes a constant and does not affect within-person trajectories. Implausible input values were excluded by cohort-specific ranges (body mass index 15–50 kg/m², waist circumference 50–150 cm, resting heart rate 40–120 beats per minute), and estimates outside 4–20 METs were set to missing. eCRF entered models as a

covariate, was used to derive companion eCRF trajectories around diagnosis, and was re-estimated without its activity component in a reverse-causation sensitivity analysis.

Covariates

The primary model adjusted for sex, baseline eCRF and diagnosis type, with age as the time scale. A fully adjusted model added education, current smoking, alcohol use, marital status, employment, hypertension and diabetes, all measured at the wave preceding diagnosis. Depressive symptoms were not adjusted for in either model because they are analysed as mediators; body mass index was not adjusted for separately because it enters the eCRF algorithm.

Statistical analysis

Baseline characteristics were compared across the four trajectories with standardised mean differences.

The primary association was estimated with Cox proportional hazards models with age as the time scale, fitted separately in each cohort, with maintained activity as the reference; a binary contrast (active versus inactive after diagnosis) was also estimated. Proportional hazards were checked with Schoenfeld residuals. Cohort-specific estimates were combined in a random-effects meta-analysis (DerSimonian–Laird)[17], with heterogeneity quantified by I^2. Effect modification was examined in pre-specified subgroups (sex, age below or above 70 years, diagnosis type, diabetes) with interaction terms.

Because death competes with non-fatal events, we fitted cause-specific Cox models and Fine–Gray subdistribution hazard models[18] for non-fatal events, and estimated cumulative incidence functions by trajectory[19] (Supplementary Fig. 2).

Dose–response was modelled in HRS with restricted cubic splines[20] on weekly sessions of moderate-to-vigorous activity (four knots; Fig. 2), with no activity as reference and non-linearity tested against a linear model; models were adjusted for sex and baseline eCRF with age as the time scale, and a sensitivity model additionally for diagnosis type. In a complementary time-varying model, current activity (active versus inactive) was updated at each post-diagnosis wave in a counting-process formulation, and a cumulative average of the active indicator was constructed across waves.

Alt text: Dose–response curve of the composite endpoint against weekly moderate-to-vigorous activity sessions after diagnosis, showing risk falling steeply from no activity to about two sessions per week, with about half of the maximal benefit at one to three sessions monthly.

Missing data were addressed with multiple imputation by chained equations[21], and estimates are reported alongside their complete-case counterparts throughout: in the fully adjusted model (5 imputations) and, in sensitivity analyses of the primary model (20 imputations), for post-diagnosis activity missing because no visit occurred after diagnosis in HRS (205 of 3,247 landmark-eligible participants, 6.3%) and eCRF missing because of absent physical measurements in ELSA (237 of 776, 30.5%). Imputation models included the outcome and follow-up time, and estimates were combined with Rubin's rules[22]. CHARLS exclusions were structural and were not imputed.

Two further analyses tested whether the results depended on how trajectories were defined. First, group-based trajectory models[23] were fitted to the repeated frequency scores (ordinal 0–4 in HRS and ELSA; the binary item in CHARLS) within three years before to three years after diagnosis, requiring at least three observations spanning diagnosis; two- to five-class solutions were compared by Bayesian information criterion (minimum class 5%, mean posterior probability ≥ 0.7). Agreement with the four trajectories was assessed with Cramér's V, and class-specific hazard ratios were estimated in the primary Cox models. Second, sex-specific thresholds were selected by scanning candidate cut-points with score tests and re-fitting the four-trajectory model.

Mediation was analysed with the four trajectories as the exposure (maintained activity as reference), the same contrast as in the primary models. Mediators were inflammatory markers (C-reactive protein, interleukin-6, soluble tumour necrosis factor receptor-1, albumin, white blood cell count and interleukin-1 receptor antagonist, plus a composite inflammatory score in HRS; C-reactive protein, fibrinogen and white blood cell count in ELSA; C-reactive protein and white blood cell count in CHARLS) and post-diagnosis depressive symptoms (eight-item Center for Epidemiologic Studies Depression scale, adjusted for the pre-diagnosis score, in HRS). Effects were estimated on the risk scale with a probit closed-form approach[24], with mediators additionally categorised by quartiles, and percentile bootstrap confidence intervals (500 resamples). Participants with C-reactive protein above 10 mg/L were excluded. Biomarker timing differed by cohort with follow-up truncated accordingly; the diagnosis-to-measurement interval is reported per mediator (Supplementary Table S8); mediation in ELSA and CHARLS is reported as exploratory. Mediation samples are restricted to survivors free of the endpoint and are therefore selected on post-exposure survival; all mediation estimates are descriptive and hypothesis-generating. Because mediators measured long after diagnosis may reflect disease progression rather than mediation, the analysis was repeated with the sample restricted to biomarkers drawn within five years of diagnosis in HRS and within two years in ELSA (Supplementary Table S9).

Analyses were weighted by cohort sampling probabilities in sensitivity analyses, performed in R version 4.3.2 (packages survival, cmprsk, lcmm and mice) with Python 3.13 for data preparation. Analysis code is available from the authors on request.

Data availability

The data underlying this article are available through the Health and Retirement Study (https://hrs.isr.umich.edu), the English Longitudinal Study of Ageing (https://www.elsa-project.ac.uk) and the China Health and Retirement Longitudinal Study (https://charls.charlsdata.com), and can be accessed by approved researchers via registration and application on each study's website. No new data were generated in support of this research.

Abbreviations

CHARLS, China Health and Retirement Longitudinal Study; eCRF, estimated cardiorespiratory fitness; ELSA, English Longitudinal Study of Ageing; GBTM, group-based trajectory modelling; HF, heart failure; HRS, Health and Retirement Study; MVPA, moderate-to-vigorous physical activity; PA, physical activity.

Declarations

Competing interests

The authors declare no competing interests.

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Author Contribution

Xin Yang: Conceptualization, Methodology, Formal analysis, Data curation, Visualization, Writing – original draft. Guitao Xiao: Data curation, Validation, Investigation, Formal analysis, Software, Writing – review & editing. Lingfeng Yang: Data curation, Validation, Investigation, Writing – review & editing. Weiguo Li: Conceptualization, Supervision, Funding acquisition, Project administration, Writing – review & editing. All authors read and approved the final version of the manuscript.

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Figures

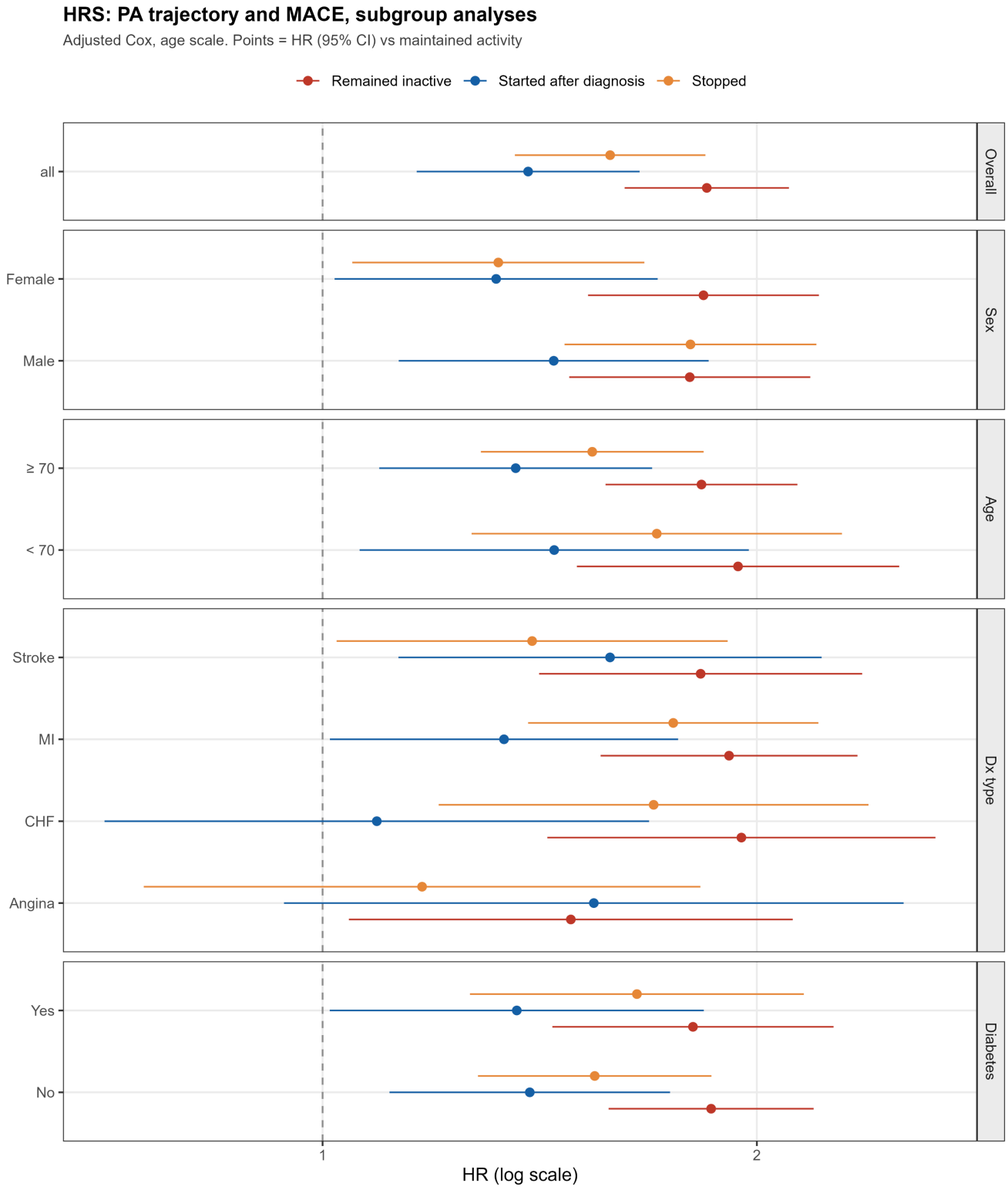


Figure 1

Figure 3. Subgroup analyses of the association between physical activity trajectories and the composite endpoint in HRS (n=3,042; 1,385 events). Hazard ratios with 95% confidence intervals for stopped, started activity after diagnosis and remained inactive versus maintained activity, from Cox models with age as the time scale, adjusted for sex, baseline eCRF and diagnosis type (the matching covariate was dropped within its own strata); the overall model is the primary eCRF-adjusted model. Subgroups: sex;

age at landmark entry (<70 or ≥70 years); diagnosis type (angina, heart failure, myocardial infarction or stroke); diabetes. The dashed line marks a hazard ratio of 1.0; the horizontal axis is on the log scale.

Alt text: Forest plot of hazard ratios for remaining inactive versus maintaining activity across HRS subgroups defined by demographic and clinical characteristics.

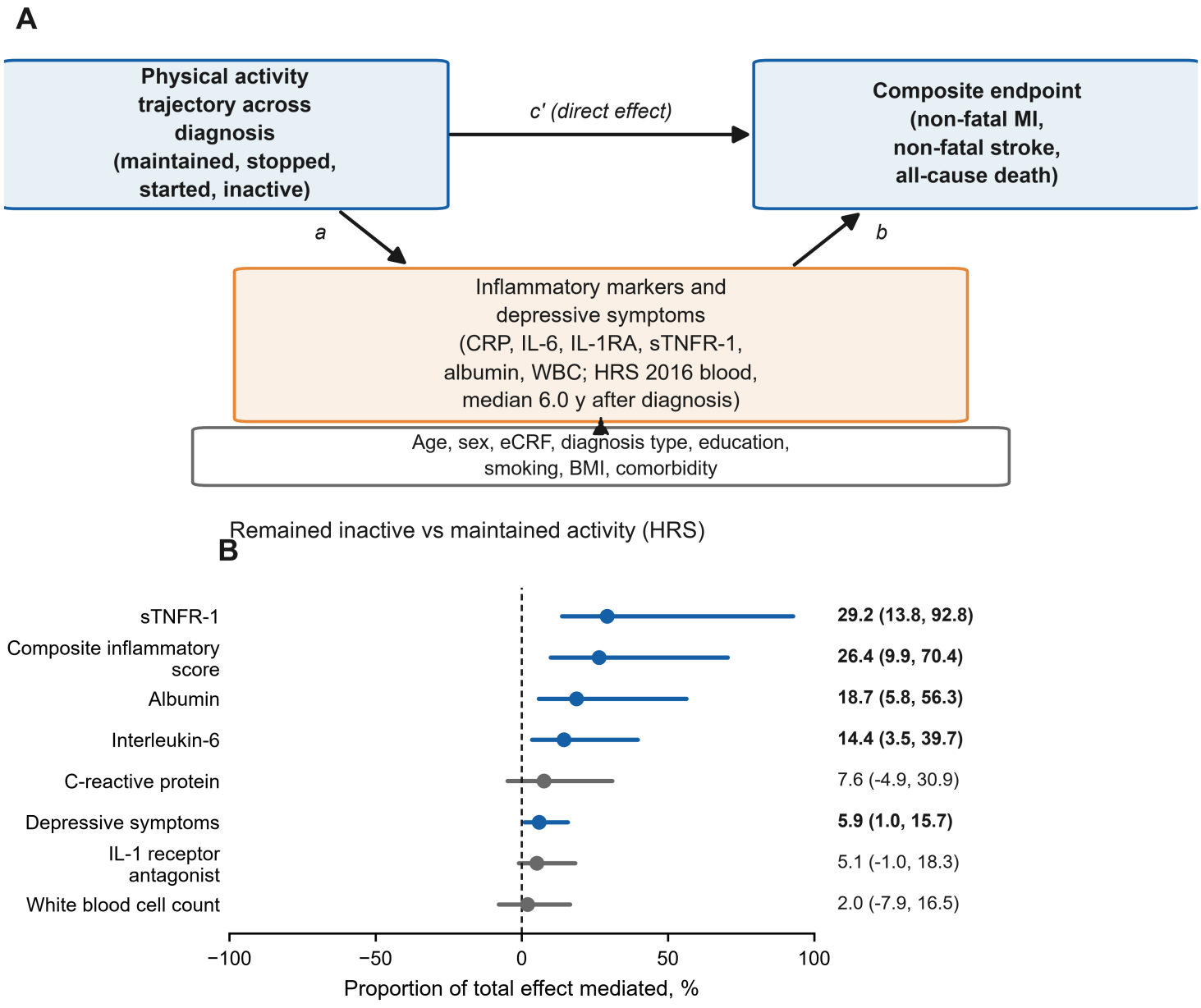


Figure 2

Figure 4. Mediation of the association between physical activity trajectory and the composite endpoint by inflammatory markers and depressive symptoms (HRS). (A) Counterfactual mediation framework: the natural indirect effect is the effect of the trajectory on the endpoint acting through each marker, and the proportion mediated expresses it as a percentage of the total effect. (B) Proportion mediated (95% CI) for remaining inactive versus maintaining activity; blue denotes confidence intervals

excluding zero. Estimates for started activity and for ELSA and CHARLS are shown in Supplementary Table S10.

Alt text: Path diagram of the mediation framework from physical activity trajectory through inflammatory markers to the composite endpoint, and a forest plot of the proportion of the total effect mediated by each marker for remaining inactive versus maintaining activity in HRS; markers whose confidence intervals exclude zero are shown in blue.

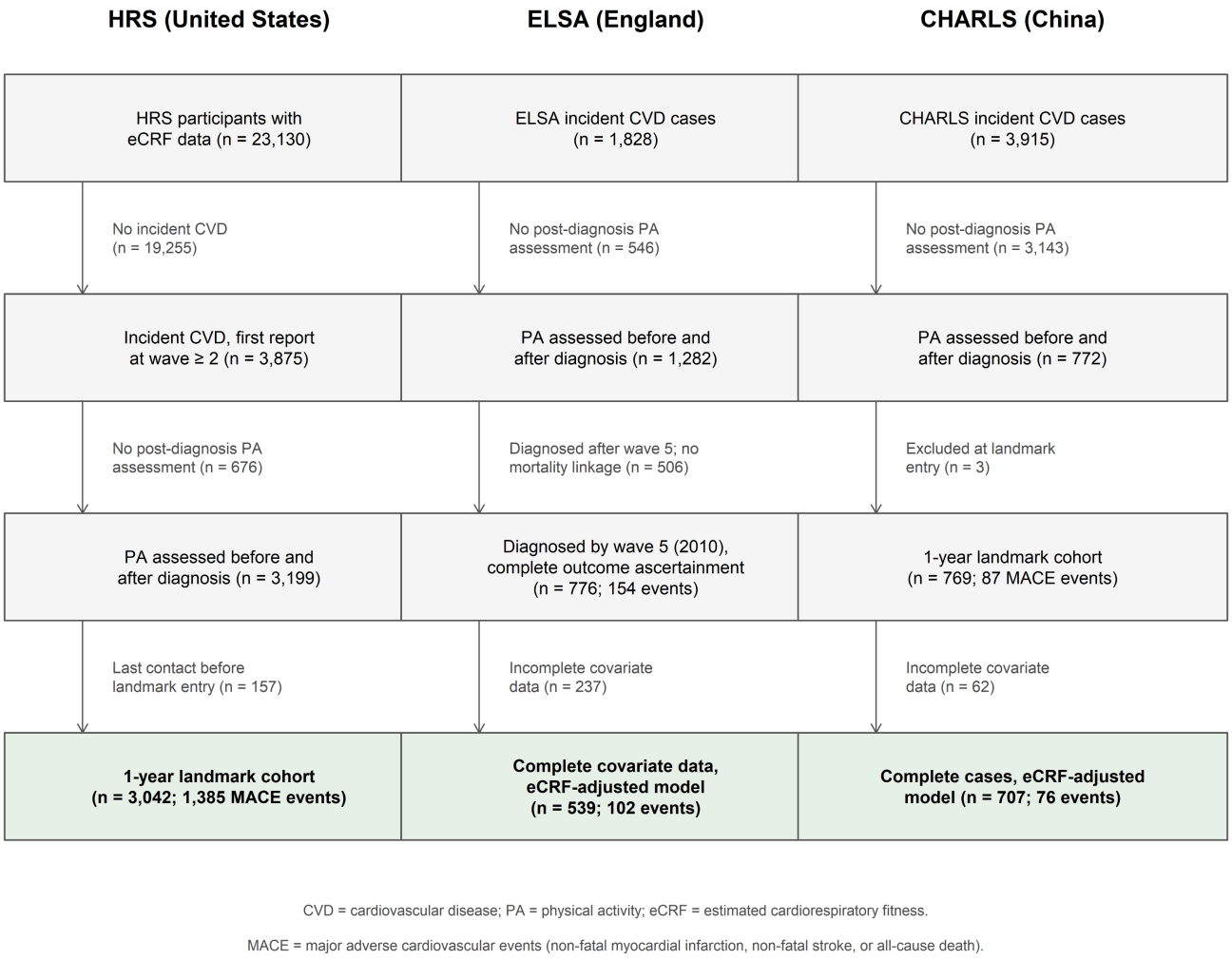


Figure 3

Figure 1. Selection of participants in the Health and Retirement Study (HRS), the English Longitudinal Study of Ageing (ELSA) and the China Health and Retirement Longitudinal Study (CHARLS). The composite endpoint was non-fatal myocardial infarction, non-fatal stroke or all-cause death. PA = physical activity; eCRF = non-exercise-estimated cardiorespiratory fitness. In ELSA, mortality linkage ended in 2012, so the primary analysis was restricted to cases diagnosed by wave 5 (2010), for whom outcome ascertainment was complete within the window; the final step retains cases with complete

covariate data for the eCRF-adjusted model. In HRS and CHARLS, follow-up began one year after diagnosis, and participants whose last contact preceded this landmark were excluded.

Alt text: Flow diagram showing how participants from the Health and Retirement Study, the English Longitudinal Study of Ageing and the China Health and Retirement Longitudinal Study were selected and classified into four physical activity trajectory groups.

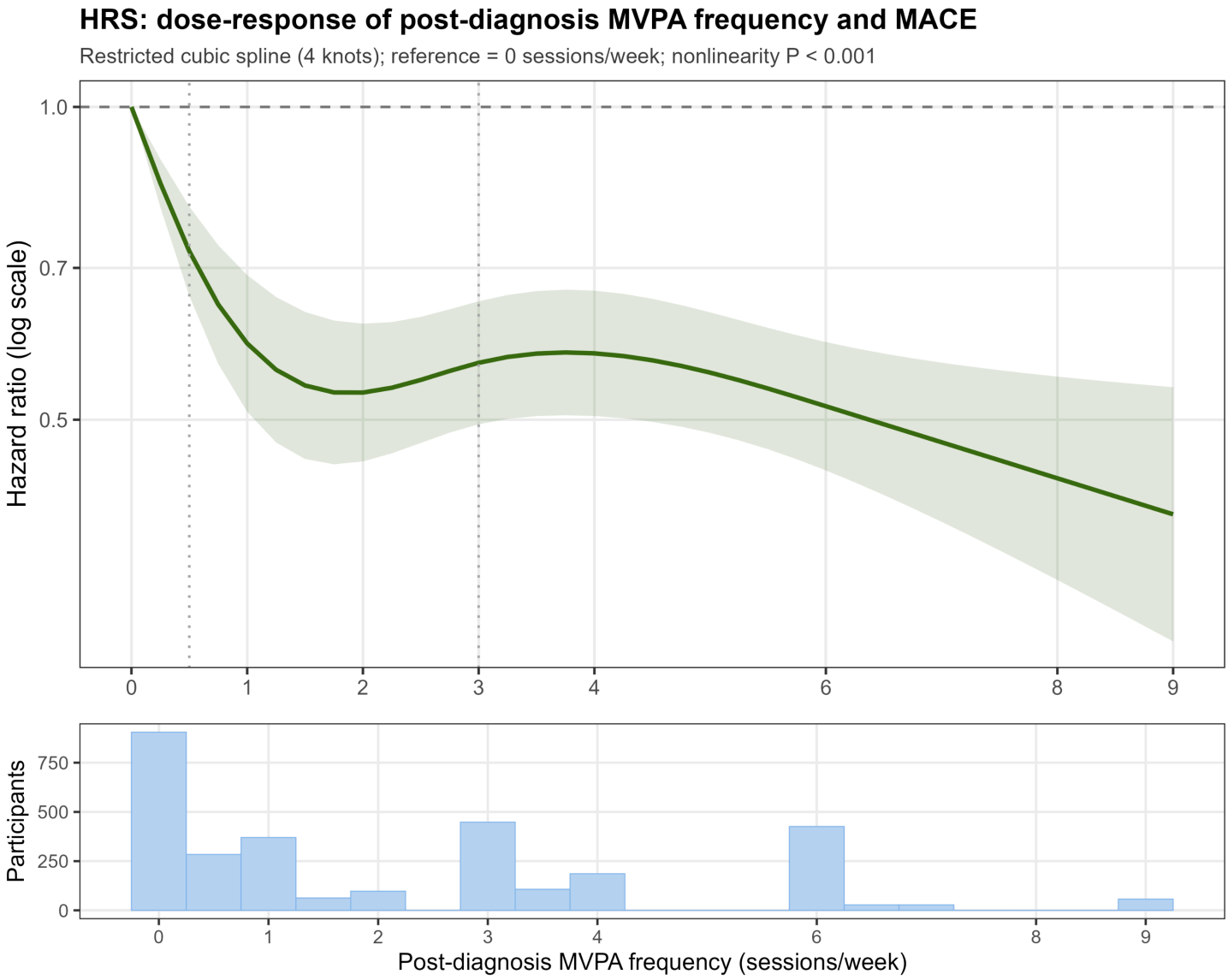


Figure 4

Figure 2. Dose–response association between post-diagnosis moderate-to-vigorous physical activity (MVPA) frequency and the composite endpoint in HRS. Restricted cubic splines with four knots at the 5th, 35th, 65th and 95th percentiles of weekly sessions; hazard ratios (solid line) with 95% confidence intervals (shaded band) relative to no activity (0 sessions/week), adjusted for sex and baseline eCRF with age as the time scale (n=3,023; 1,379 events; P for non-linearity 2.4×10^{-8}). The histogram shows the distribution of post-diagnosis weekly MVPA sessions among analysed participants.

Alt text: Dose–response curve of the composite endpoint against weekly moderate-to-vigorous activity sessions after diagnosis, showing risk falling steeply from no activity to about two sessions per week, with about half of the maximal benefit at one to three sessions monthly.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryTables.docx