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Multidomain vulnerability burden and incident cardiovascular disease among middle-aged and older adults: evidence from three longitudinal ageing cohorts

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Abstract

Functional and psychological vulnerabilities commonly coexist in ageing populations, but their cumulative association with cardiovascular disease is uncertain. We analysed 31,535 adults aged 50 years or older without baseline heart disease or stroke in the China Health and Retirement Longitudinal Study, Health and Retirement Study, and English Longitudinal Study of Ageing. Multidomain vulnerability burden was a non-weighted count of activities of daily living/instrumental activities of daily living limitation, mobility limitation, and elevated depressive symptoms. During follow-up, 8,950 participants developed cardiovascular disease. Each additional vulnerability domain was associated with incident cardiovascular disease in CHARLS (hazard ratio [HR] 1.238, 95% confidence interval [CI] 1.177–1.302), HRS (HR 1.172, 95% CI 1.133–1.213), and ELSA (HR 1.242, 95% CI 1.166–1.324). The pooled HR was 1.210 (95% CI 1.113–1.316; 95% prediction interval 1.051–1.393). Associations were graded across 0, 1, and ≥ 2 domains and persisted when each domain was removed in turn. Greater multidomain vulnerability burden was consistently associated with incident cardiovascular disease, although the count should be regarded as an analytic measure rather than a validated clinical risk instrument.

Introduction

Cardiovascular assessment in later life often occurs alongside functional limitation and psychological vulnerability. Frailty and depressive symptoms have each been associated with cardiovascular morbidity [1–3], yet conventional biomedical risk factors do not describe daily functioning, mobility or depressive symptoms. We therefore considered activities of daily living/instrumental activities of daily living (ADL/IADL) limitation, mobility limitation and elevated depressive symptoms jointly as a transparent summary of accumulated functional and psychological vulnerability, without labelling the construct as biological frailty.

Recent studies have examined multidomain ageing constructs and cardiovascular outcomes across international cohorts [4–10], including analyses using the same three cohorts [4, 10]. Less clear is whether a parsimonious fixed-baseline count focused on limitations in daily activities, mobility and depressive symptoms shows a cumulative association with cardiovascular disease across cohorts, and whether such an association depends on any single component. This count is a distinct analytic operationalisation rather than a validated frailty or cardiovascular risk instrument.

We therefore examined the association between a fixed-baseline count of ADL/IADL limitation, mobility limitation and elevated depressive symptoms and incident cardiovascular disease in the China Health and Retirement Longitudinal Study, the US Health and Retirement Study and the English Longitudinal Study of Ageing. Participants were aged 50 years or older and free of heart disease and stroke at baseline. We evaluated the burden per one additional vulnerability domain and in categories of 0, 1 and ≥ 2 domains. We also examined incident stroke and age-specific associations and, in exploratory leave-one-domain-out analyses, whether the cumulative association persisted after removing each domain in turn.

Results

Study population and baseline characteristics

The primary analysis included 31,535 participants: 10,652 from CHARLS, 13,091 from HRS and 7,792 from ELSA. During follow-up, 8,950 participants developed incident cardiovascular disease: 2,571 in CHARLS, 4,856 in HRS and 1,523 in ELSA (Fig. 1 and Table 1). Mean age, follow-up and baseline characteristics varied across cohorts (Table 1).

Table 1
Baseline characteristics of participants across CHARLS, HRS, and ELSA.

Characteristic	CHARLS	HRS	ELSA
Participants	10,652	13,091	7,792
Age, years	61.7 ± 8.3	65.7 ± 9.4	64.2 ± 9.0
Male sex	5,391 (50.6)	5,142 (39.3)	3,445 (44.2)
Hypertension	2,510 (23.7)	5,302 (40.5)	2,820 (36.2)
Diabetes	548 (5.2)	1,491 (11.4)	621 (8.0)
Current smoking	3,251 (31.6)	2,048 (15.6)	1,061 (13.8)
BMI, kg/m²	23.1 ± 3.9	27.2 ± 5.2	28.3 ± 5.3
ADL/IADL limitation	2,899 (27.5)	2,076 (15.9)	1,731 (22.2)
Mobility limitation	160 (1.6)	2,738 (21.3)	643 (8.3)
Elevated depressive symptoms	3,568 (36.2)	1,604 (13.3)	970 (12.8)
0 vulnerability domains	4,977	8,155	5,303
1 vulnerability domain	2,911	2,206	1,471
≥ 2 vulnerability domains	1,297	1,538	787
Incomplete vulnerability-domain data	1,467	1,192	231
Follow-up duration, years	6.9 ± 2.7	11.3 ± 6.5	7.5 ± 3.1
Incident CVD events	2,571 (24.1)	4,856 (37.1)	1,523 (19.5)
Incident stroke events	732 (6.9)	1,741 (13.3)	310 (4.0)

Notes: Percentages were calculated among participants with nonmissing data for the corresponding variable unless otherwise specified. Vulnerability burden categories are based only on participants with complete observed data for all three vulnerability domains. The difference between the analysis sample and the category counts is shown as incomplete vulnerability-domain data. No between-cohort P-values are reported.

Abbreviations: ADL, activities of daily living; BMI, body mass index; CHARLS, China Health and Retirement Longitudinal Study; CVD, cardiovascular disease; ELSA, English Longitudinal Study of Ageing; HRS, Health and Retirement Study; IADL, instrumental activities of daily living.

Multidomain vulnerability burden and incident cardiovascular disease

Each additional vulnerability domain was associated with a higher hazard of incident cardiovascular disease in all three cohorts. The cohort-specific HRs per one additional vulnerability domain were 1.238

(95% CI 1.177–1.302) in CHARLS, 1.172 (95% CI 1.133–1.213) in HRS, and 1.242 (95% CI 1.166–1.324) in ELSA; all cohort-specific P-values were < 0.001. The pooled HR was 1.210 (95% CI 1.113–1.316), with I^2 = 53.3%, τ^2 = 0.0007, Q-test P = 0.115, and a 95% prediction interval of 1.051–1.393 (Fig. 2 and Table 2).

Table 2. Associations of multidomain vulnerability burden with incident cardiovascular disease.

Panel A. Per one additional vulnerability domain

Cohort	Analysis n	Events	Adjusted HR	95% CI	P-value
CHARLS	10,652	2,571	1.238	1.177–1.302	<0.001
HRS	13,091	4,856	1.172	1.133–1.213	<0.001
ELSA	7,792	1,523	1.242	1.166–1.324	<0.001
Pooled estimate	31,535	8,950	1.210	1.113–1.316	

Heterogeneity: I^2=53.3%; τ^2=0.0007; Q-test P=0.115; 95% prediction interval 1.051–1.393.

Panel B. Categorical vulnerability burden

Cohort	Vulnerability burden	Observed participants, n	Observed events	Adjusted HR	95% CI	P-value
CHARLS	0	4,977	1,047	1.000	Reference	
CHARLS	1	2,911	770	1.295	1.181–1.421	<0.001
CHARLS	≥2	1,297	398	1.564	1.404–1.742	<0.001
HRS	0	8,155	2,894	1.000	Reference	
HRS	1	2,206	880	1.215	1.128–1.309	<0.001
HRS	≥2	1,538	669	1.434	1.318–1.560	<0.001
ELSA	0	5,303	912	1.000	Reference	
ELSA	1	1,471	354	1.303	1.149–1.477	<0.001
ELSA	≥2	787	217	1.621	1.389–1.892	<0.001

Notes: Hazard ratios are from the prespecified adjusted analyses. Adjusted models included age, sex, hypertension, diabetes, current smoking, and body mass index. Descriptive category counts are based on participants with complete observed data for all three domains; adjusted categorical estimates were obtained from multiply imputed analyses.

Abbreviations: BMI, body mass index; CHARLS, China Health and Retirement Longitudinal Study; CI, confidence interval; CVD, cardiovascular disease; ELSA, English Longitudinal Study of Ageing; HR, hazard ratio; HRS, Health and Retirement Study.

A graded pattern was observed: compared with 0 vulnerability domains, hazards were higher for 1 and ≥ 2 domains in every cohort (Fig. 3 and Table 2).

Secondary and sensitivity analyses

For the prespecified secondary stroke outcome, 31,532 participants contributed 2,783 events. Cohort-specific HRs per one additional vulnerability domain were 1.230 (95% CI 1.119–1.351) in CHARLS, 1.164 (95% CI 1.100–1.231) in HRS, and 1.315 (95% CI 1.151–1.503) in ELSA. The pooled HR was 1.210 (95% CI 1.051–1.394), with I^2 = 38.4%, τ^2 = 0.0013 and Q-test P = 0.199; the 95% prediction interval included 1 (0.981–1.493) (Supplementary Fig. S1 and Supplementary Table S10).

Associations remained directionally consistent in complete-case analyses, after excluding cardiovascular events within the first 2 years, when event time was assigned to the first positive survey, and when the strict single-item mobility definition was used (Supplementary Tables S5–S8). Associations remained positive during both the first 5 years and the period after 5 years of follow-up (Supplementary Table S9). Exposure-specific Schoenfeld tests did not indicate violation of the proportional hazards assumption. Covariate-level tests suggested departures for hypertension in CHARLS, diabetes in HRS and body mass index in ELSA, although the global test was significant only in HRS and ELSA (Supplementary Table S9).

Additional analyses

In age-stratified analyses, pooled HRs were 1.234 (95% CI 1.213–1.255) for participants aged 50–64 years and 1.224 (95% CI 1.145–1.308) for those aged 65–74 years. Among participants aged ≥ 75 years, the pooled estimate remained above 1 but was imprecise and heterogeneous (HR 1.175, 95% CI 0.825–1.673; I^2 = 81.3%). Evidence of effect modification by age was observed in HRS, where the global interaction P-value was < 0.001 and the association was attenuated among participants aged ≥ 75 years (ratio of HRs 0.825, 95% CI 0.759–0.897; P < 0.001) (Supplementary Tables S11 and S12).

Exploratory construct-decomposition analyses suggested that associations for individual domains varied across cohorts; for example, CHARLS mobility was not associated with incident cardiovascular disease in the mutually adjusted domain model (HR 0.956, 95% CI 0.710–1.287; P = 0.766) (Supplementary Table S13). The cumulative association was retained when each domain was removed in turn: excluding ADL/IADL, mobility, and depressive symptoms yielded pooled HRs of 1.265 (95% CI 1.143–1.400), 1.240 (95% CI 1.154–1.333), and 1.255 (95% CI 1.144–1.377), respectively (Supplementary Table S14). Similar associations were observed for incident heart disease, an additional component-outcome analysis (pooled HR 1.206, 95% CI 1.138–1.277; 95% prediction interval 1.130–

1.286) (Supplementary Table S15). Allowing the identified covariate effects to vary with log follow-up time changed the exposure estimates by less than 0.1% in each cohort (Supplementary Table S16).

Discussion

In this analysis of three longitudinal ageing cohorts, greater accumulation of functional and psychological vulnerability domains was associated with a higher hazard of incident cardiovascular disease. The association was graded across burden categories and remained directionally consistent in complete-case, early-event exclusion, event-time and mobility-definition sensitivity analyses. Leave-one-domain-out analyses and the additional heart disease analysis suggested that the association was not dependent entirely on any single domain or on one component of the composite outcome. Age-stratified results were more nuanced: positive pooled estimates were observed among adults aged 50–64 and 65–74 years, whereas the pooled estimate among those aged ≥ 75 years was imprecise and heterogeneous. The prespecified stroke analysis showed a positive pooled association, but its prediction interval included 1.

Previous studies have linked frailty, depressive symptoms and impaired intrinsic capacity with cardiovascular outcomes. Meta-analytic and cohort evidence has associated frailty and pre-frailty with cardiovascular morbidity and mortality, and multicohort work has related changes in frailty, and the joint presence of frailty and depressive symptoms, to incident cardiovascular disease [1, 2, 23, 24]. Recent studies have examined baseline status, transitions and trajectories of five-domain intrinsic capacity in relation to incident cardiovascular disease across individual and multinational ageing cohorts [4–7, 25, 26]. One 2026 study used CHARLS, HRS and ELSA, the same three ageing cohorts as the present analysis, to examine baseline intrinsic capacity, four-year change patterns and trajectories in relation to incident cardiovascular disease [4]. Other multicohort studies evaluated changes in intrinsic capacity, its joint association with physical activity, or incident stroke [5, 6, 8]. The present study differs by using a fixed-baseline count focused specifically on ADL/IADL limitation, mobility limitation and depressive symptoms, together with multiple imputation and leave-one-domain-out analyses to evaluate whether the association depended on a single component.

The cumulative pattern may reflect the clustering of reduced functional reserve, lower physical activity, depressive symptoms and broader cardiometabolic vulnerability [3, 27–32]. These pathways were not tested directly. The construct-decomposition analyses help clarify this interpretation. The leave-one-domain-out results suggest that the cumulative association was not attributable exclusively to one component. However, the varying mutually adjusted associations across cohorts, including the weak mutually adjusted mobility association in CHARLS, indicate that the three domains should not be interpreted as having identical or universally independent contributions. Consistent with such domain-level variability, a recent analysis of HRS, ELSA and CHARLS found muscle function to be the intrinsic-capacity domain most consistently associated with incident cardiovascular disease, with the association varying by metabolic and inflammatory burden [10]. That domain-specific analysis is not directly equivalent to the present mobility measure or cumulative three-domain count.

The age-stratified findings indicate that the association may vary across later life. The pooled estimate among adults aged ≥ 75 years remained above 1 but had a wide confidence interval (HR 1.175, 95% CI 0.825–1.673) and substantial heterogeneity (I^2 = 81.3%). The attenuation observed among the oldest participants in HRS and the cohort-specific evidence of effect modification argue against assuming uniform associations across later life. Possible explanations include survival selection, competing morbidity, higher background disability and multimorbidity, cohort-specific composition, outcome reporting differences and selective attrition. These explanations are cautious inferences rather than directly tested mechanisms.

The component-outcome and stroke findings also require caution. A recent four-cohort study reported an inverse association between five-domain intrinsic capacity and incident stroke, with stronger estimates among adults aged ≥ 80 years [8]. A CHARLS analysis similarly associated higher baseline intrinsic capacity with lower incident stroke risk [9]. In contrast, the pooled cardiovascular disease estimate among participants aged ≥ 75 years in the present study was imprecise and heterogeneous, and the stroke prediction interval included the null (0.981–1.493). These differences may reflect variation in the exposure construct, age thresholds, cohort composition, outcome definition, missing data handling and statistical integration. The broadly similar direction of association for heart disease and stroke provided some reassurance that the overall cardiovascular disease association was not confined to a single component outcome, but the stroke finding should remain secondary.

The findings support attention to functional and psychological vulnerability alongside conventional cardiovascular risk factors in ageing adults. ADL/IADL limitation, mobility difficulty and depressive symptoms are common in ageing studies and may contextualise conventional risk factors. The study adds a transparent three-domain operationalisation to the literature on frailty, intrinsic capacity and cardiovascular outcomes. However, the count was an analytic measure, not a clinical screening or prediction instrument, and should not guide treatment or formal risk stratification without further research.

Strengths include three large longitudinal ageing cohorts, fixed baseline waves, transparent domain definitions, multiple imputation, cohort-specific modelling followed by random-effects meta-analysis, sensitivity analyses and construct-decomposition analyses. Limitations should also be recognised. The observational design leaves potential for residual confounding by socioeconomic, behavioural, healthcare and multimorbidity factors. Cardiovascular outcomes were based on self-reported physician diagnoses and may be affected by reporting error, under-ascertainment and cross-cohort differences. The component items were not identical across cohorts, mobility prevalence varied, ADL/IADL and mobility domains overlap conceptually, and the equal-weighted count is an analytic operational definition rather than a clinical scale. Vulnerability was measured at baseline only, so changes over time could not be assessed. Event timing was approximated because cardiovascular status was measured intermittently at survey waves. A harmonised competing-risk analysis could not be undertaken because cardiovascular outcomes were ascertained intermittently at survey waves and death timing could not be reliably ordered relative to interval-based cardiovascular event times across all three cohorts. Finally,

inclusion required at least one valid follow-up, and meta-analysis across only three cohorts makes τ^2, I^2 and prediction intervals, especially in age-stratified analyses, inherently imprecise.

Greater accumulation of functional and psychological vulnerability domains was associated with incident cardiovascular disease across three longitudinal ageing cohorts. The association persisted when individual domains were removed in turn, although estimates among adults aged 75 years or older varied across cohorts. These findings support further evaluation of multidomain vulnerability within cardiovascular prevention research, but the three-domain measure should not be interpreted as a clinical screening or prediction instrument.

Methods

Study design and data sources

We analysed three population-based longitudinal ageing cohorts with repeated follow-up: the China Health and Retirement Longitudinal Study (CHARLS), the Health and Retirement Study (HRS) and the English Longitudinal Study of Ageing (ELSA) [11–13]. Fixed baselines were CHARLS wave 1 (2011), HRS wave 5 (2000) and ELSA wave 4 (2008). We used harmonised participant-wave variables, analysed each cohort separately and then combined cohort-specific estimates; participant records were not pooled.

Study population

Eligible participants were aged ≥ 50 years, had explicit baseline values of 0 for heart disease and stroke, no earlier report of either outcome where pre-baseline data were available, and at least one informative post-baseline cardiovascular disease assessment. Those with missing baseline cardiovascular disease status or no informative follow-up were excluded. The cardiovascular disease analysis included 10,652 CHARLS, 13,091 HRS and 7,792 ELSA participants (31,535 total; Fig. 1; Supplementary Table S4).

Assessment of multidomain vulnerability burden

Multidomain vulnerability burden summed three binary domains: ADL/IADL limitation, mobility limitation and elevated depressive symptoms. For multi-item functional domains, a deficit was present if any observed item indicated difficulty, absent only when all prespecified items were observed and normal, and otherwise missing. Mobility items differed across cohorts but used this common domain rule. Elevated depressive symptoms were defined using the Center for Epidemiologic Studies Depression Scale (CES-D): CES-D-10 ≥ 10 in CHARLS, CES-D-8 ≥ 4 in HRS and CES-D-8 ≥ 4 in ELSA [14–16]. The 0–3 count was analysed per additional domain and as 0, 1 or ≥ 2 domains, with 0 as reference (Supplementary Table S1). It was a transparent analytic measure, not a validated clinical frailty or risk-prediction instrument.

Outcome ascertainment

The primary outcome was incident overall cardiovascular disease, defined as the first new post-baseline self-reported physician diagnosis of heart disease or stroke, based on harmonised cohort variables. An assessment was positive if either component was explicitly positive and negative only if both components were explicitly negative; assessments without a positive component but without confirmation that both components were negative were treated as uninformative. Incident stroke was defined as the first new post-baseline self-reported physician diagnosis of stroke and was the prespecified secondary outcome. Incident heart disease was defined as the first new post-baseline self-reported physician diagnosis of heart disease and was examined as an additional component outcome independently of stroke status. Because outcomes were recorded at intermittent survey waves, event time in the main analyses was approximated by the midpoint between the last explicitly negative wave and the first explicitly positive wave. Participants without an event were censored at their last informative negative assessment. The first positive survey date was used in a sensitivity analysis. Outcome-specific follow-up availability yielded a CHARLS stroke sample of 10,649; details are reported in Supplementary Table S10.

Covariates

Covariates measured at the fixed baseline were continuous age, sex, hypertension, diabetes, current smoking, and body mass index. Body mass index was modelled continuously; hypertension, diabetes, and current smoking were binary variables harmonised within the common analysis framework.

Missing data

Missing baseline exposure and covariate data were handled separately within each cohort using multiple imputation by chained equations [17]. Twenty imputed datasets were generated with 20 iterations. Binary variables were imputed by logistic regression and body mass index by predictive mean matching. The three vulnerability domains were imputed separately, after which multidomain vulnerability burden was calculated passively. Outcome indicators and Nelson–Aalen cumulative hazards were included as auxiliary variables; outcome status was not imputed, and neither follow-up time nor the passive burden count was used as an independent imputation predictor. Cox model estimates were combined across imputations using Rubin's rules [18]. Complete-case analyses were performed as sensitivity analyses. Further settings are provided in Supplementary Table S3.

Statistical analysis

Baseline characteristics were summarised by cohort as mean (standard deviation) or number (percentage), without between-cohort tests. Burden-category counts used participants with complete observed data for all three domains. Cohort-specific associations were estimated using Cox proportional hazards regression [19]. The primary exposure was modelled per one additional vulnerability domain; categorical models compared 1 and ≥ 2 domains with 0 domains. Models adjusted for age, sex, hypertension, diabetes, current smoking, and body mass index and reported hazard ratios with 95% confidence intervals. Cohort-specific log hazard ratios and standard errors were subsequently pooled using random-effects meta-analysis. Between-cohort variance was estimated by restricted maximum

likelihood, with Hartung–Knapp confidence intervals [20, 21]. Heterogeneity was assessed using Cochran's Q, I^2, and τ^2, and 95% prediction intervals were calculated. Proportional hazards were assessed using covariate-specific, exposure-specific and global Schoenfeld residual tests [22]. All tests were two-sided, with $P < 0.05$ indicating statistical significance. Analyses were conducted in R using packages for multiple imputation, survival analysis, and random-effects meta-analysis.

Additional and sensitivity analyses

Sensitivity analyses used complete cases, excluded cardiovascular events within the first 2 years, assigned event time to the first positive survey, applied the strict single-item mobility definition, and estimated 0–5-year and > 5-year associations. Extended Cox sensitivity models allowed hypertension × log(time) in CHARLS, diabetes × log(time) in HRS, and body mass index × log(time) in ELSA; age-stratified analyses used groups of 50–64, 65–74 and ≥ 75 years, retained covariates within strata, tested vulnerability burden × age group in full-sample models and meta-analysed stratum-specific estimates. Exploratory construct-decomposition analyses modelled domains separately, mutually adjusted all three domains and omitted each domain in turn. Incident heart disease used the same exposure, covariates, event-time rule, Cox framework and meta-analysis approach as the primary outcome.

Ethics approval and informed consent

The original cohort studies received ethics approval as follows: CHARLS was approved by the Peking University Biomedical Ethics Review Committee (Institutional Review Board approval number IRB00001052-11015); HRS was approved by the University of Michigan Health Sciences and Behavioral Sciences Institutional Review Board (protocol HUM00061128); and ELSA received wave-specific approval from the National Hospital for Neurology and Neurosurgery & Institute of Neurology Joint Research Ethics Committee (wave 4, 07/H0716/48), the Berkshire Research Ethics Committee (wave 5, 09/H0505/124), the NRES Committee South Central - Berkshire (waves 6–7, 11/SC/0374 and 13/SC/0532), and the South Central - Berkshire Research Ethics Committee (waves 8–9, 15/SC/0526 and 17/SC/0588). All methods were carried out in accordance with relevant guidelines and regulations, and all participants provided informed consent. The present study was a secondary analysis of de-identified data and involved no direct participant contact or intervention. The Ethics Committee of the Second Affiliated Hospital of Nanjing Medical University determined that the present secondary analysis was exempt from additional ethical review. No reference number was issued for this determination.

Use of generative AI

During the preparation of this work, the authors used generative AI-assisted language support to improve wording, style, and readability. After using this support, the authors reviewed and edited the content as needed and take full responsibility for the content of the manuscript.

Declarations

Competing interests

The authors declare no competing interests.

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Author Contribution

RS contributed to conceptualisation, data curation, formal analysis, investigation, visualisation and writing of the original draft. LL contributed to methodology, validation, supervision and writing - review and editing. SZ contributed to conceptualisation, supervision, project administration, funding acquisition and writing - review and editing. All authors contributed to interpretation of the findings, critically reviewed the manuscript for important intellectual content, read and approved the final manuscript, and agree to be accountable for all aspects of the work.

Data Availability

The CHARLS, HRS and ELSA cohort data analysed during the current study are available to registered users through the respective study websites and data-use procedures. The authors do not have permission to redistribute participant-level data. Analytic code is available from the corresponding author on reasonable request, subject to the data-use requirements of the original cohorts.

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Figures

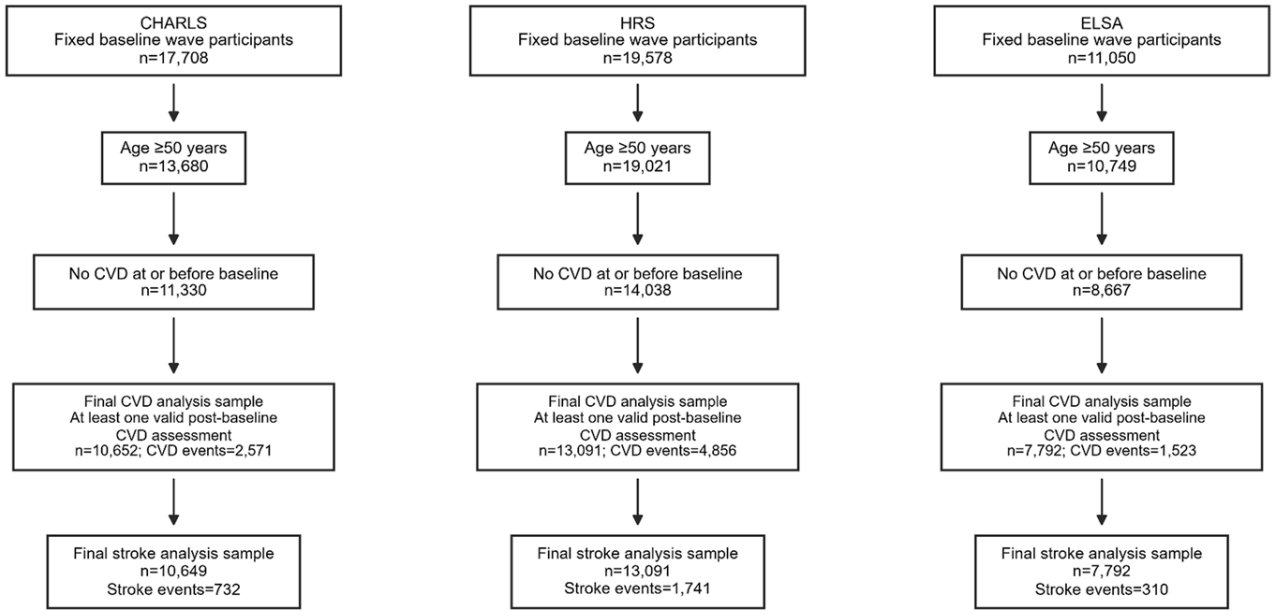

Figure 1

Participant selection in CHARLS, HRS, and ELSA.

Alt text: Participant-flow diagram for CHARLS, HRS and ELSA showing progression from fixed-baseline participants aged 50 years or older through cardiovascular-disease eligibility exclusions to the final analytic samples for incident cardiovascular disease and stroke in each cohort.

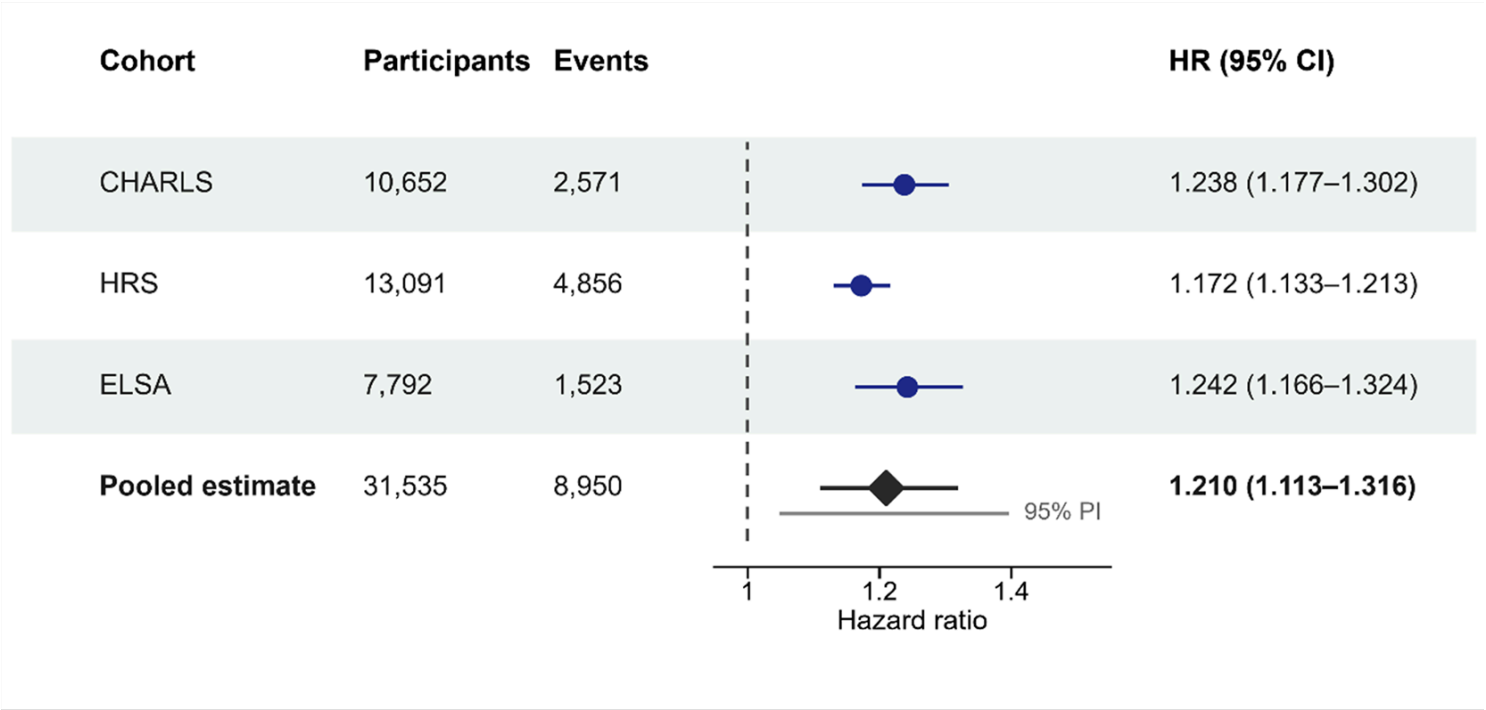

Figure 2

Association of multidomain vulnerability burden with incident cardiovascular disease. Cohort-specific hazard ratios were estimated using adjusted Cox models. The pooled estimate used random-effects meta-analysis with restricted maximum likelihood and Hartung–Knapp adjustment. The grey horizontal line indicates the 95% prediction interval.

Alt text: Forest plot showing cohort-specific and pooled hazard ratios for incident cardiovascular disease per one additional vulnerability domain. CHARLS, HRS and ELSA all show hazard ratios above 1, with confidence intervals and a pooled random-effects estimate accompanied by a 95% prediction interval.

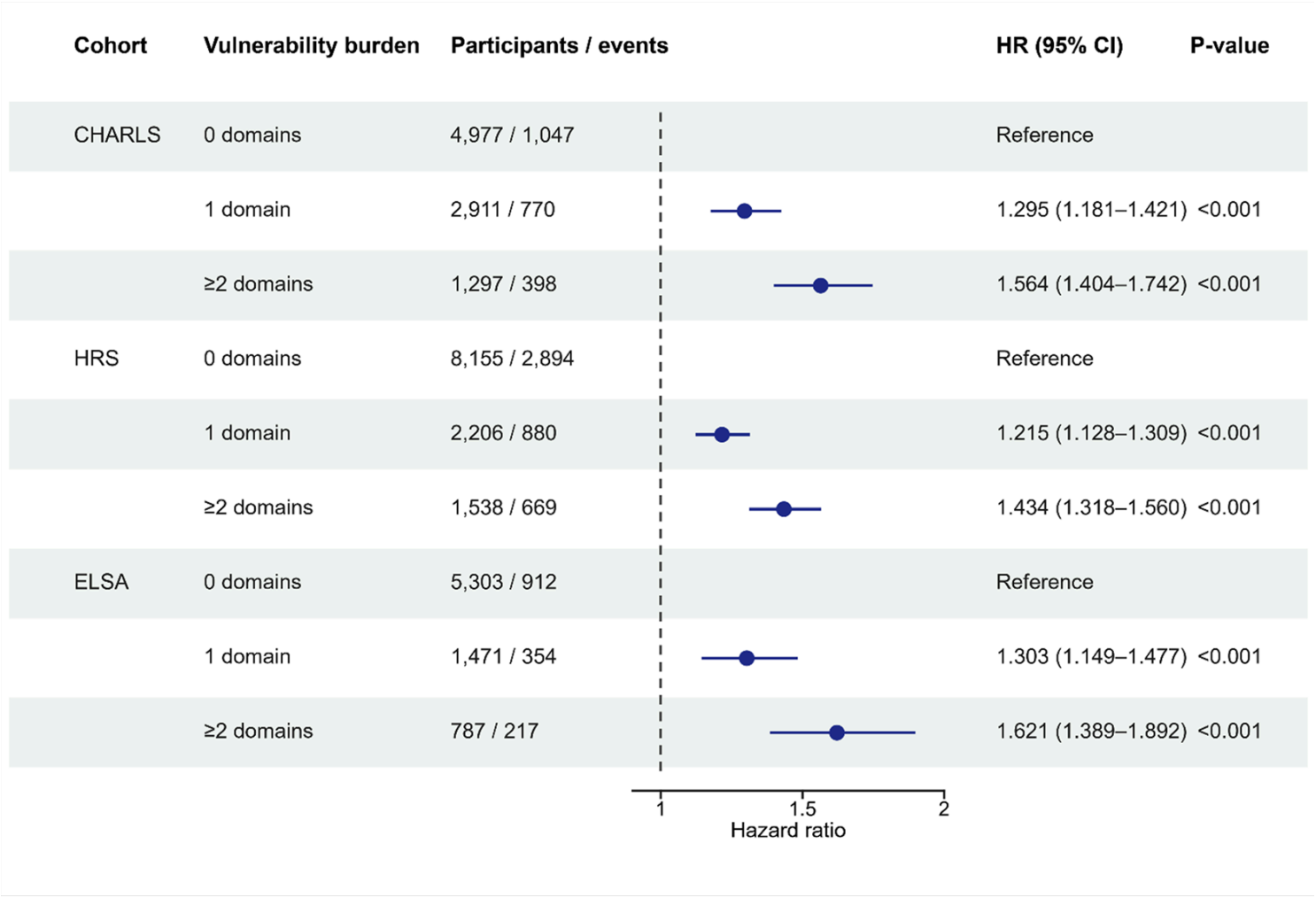

Figure 3

Categorical association of vulnerability burden categories with incident cardiovascular disease. Categories are 0, 1, and ≥2 vulnerability domains; 0 domains is the reference group. Hazard ratios were estimated from adjusted Cox models including age, sex, hypertension, diabetes, current smoking, and body mass index. Horizontal lines indicate 95% confidence intervals. Participant and event counts are descriptive values among participants with complete observed data for all three vulnerability domains; hazard ratios were estimated from multiply imputed analyses.

Alt text: Categorical forest plot comparing participants with 1 and ≥2 vulnerability domains against those with 0 domains across CHARLS, HRS and ELSA, showing a graded pattern of higher cardiovascular-disease hazard with greater vulnerability burden.

Supplementary Files

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

- SupplementaryInformation.pdf