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Average cardiometabolic burden across waves and subsequent difficulties in basic activities of daily living among middle-aged and older adults in China: a longitudinal cohort study

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Abstract

Background

We assessed associations of cardiometabolic burden measured across several survey waves with subsequently confirmed difficulties in basic activities of daily living (ADL), quantified standardized 5-year risks accounting for competing mortality, and explored associations among participants without self-reported heart disease or stroke and after adjustment for current components.

Methods

We included 9587 adults aged ≥45 years from the China Health and Retirement Longitudinal Study (CHARLS) who had no ADL difficulties in 2015. Burden comprised hypertension, diabetes, central obesity, heart disease, and stroke, averaged across at least two valid waves in 2011–2015; scores were prorated when at least four components were assessable. Participants were followed through 2020. Event-specific discrete-time complementary log-log models incorporated inverse probability of censoring weighting, community-clustered inference, and multiple imputation of specific missing values. Joint multinomial models estimated standardized cumulative incidence. Exploratory analyses examined risk-factor burden among participants with negative heart disease and stroke histories at all three waves, and historical burden conditional on the five current components. Two principal supplementary ADL tests underwent Holm adjustment.

Results

There were 2167 ADL events and 492 preceding deaths. Per standard deviation (0.89 component units), the complementary log-log-scale ratio (CSR) for ADL difficulties was 1.24 (95% confidence interval [CI] 1.19–1.30). Among participants without self-reported heart disease or stroke at all three waves, the CSR per risk-factor component unit was 1.18 (95% CI 1.10–1.27). In participants with complete components at all three waves, the CSR per historical burden unit, adjusted for all five 2015 components, was 1.18 (95% CI 1.06–1.31). Standardized 5-year ADL risks at burden values of 3 and 0 were 35.0% and 19.5%, respectively: a difference of 15.5 percentage points (95% CI 12.1–18.9).

Conclusions

Higher repeatedly measured cardiometabolic burden was associated with subsequent ADL difficulties. Historical burden retained a conditional association after adjustment for current components. These findings support attention to self-care function during cardiometabolic follow-up, including among people without self-reported heart disease or stroke.

Keywords: cardiovascular prevention; cardiometabolic burden; activities of daily living; functional decline; competing risks; older adults

Background

Cardiovascular disease is a leading cause of death worldwide [1]. Risk assessment in preventive cardiology has traditionally focused on myocardial infarction, stroke, and mortality, whereas basic activities of daily living (ADL) reflect self-care functions such as dressing, bathing, eating, and toileting [2]. A 2025 European Association of Preventive Cardiology (EAPC) consensus statement recommends standardized assessment of functional dependence in cardiovascular risk-factor management for older adults [3]. Examining associations of cardiovascular risk factors and related diseases with subsequent ADL difficulties can add a functional perspective to the assessment of cardiovascular health in middle-aged and older adults.

Cardiometabolic burden in this study comprised hypertension, diabetes, central obesity, heart disease, and stroke. These conditions may affect mobility and self-care through pathways involving cerebral small-vessel disease, diabetic peripheral neuropathy, skeletal muscle dysfunction, and obesity-related inflammation [4–7]. Previous studies of disease co-occurrence and clustered risk factors have linked cardiometabolic health to functional limitations. Baseline cardiometabolic multimorbidity defined by diabetes, heart disease, and stroke has been associated with trajectories of ADL and instrumental ADL difficulties [8, 9]. Beyond baseline

status, repeated measurements and historical risk-factor information have also attracted attention. Disease-pattern trajectories and previous changes in systolic blood pressure have been associated with changes in ADL and other functional outcomes [10, 11]. These findings suggest that historical health records may contain information on functional risk that is not fully captured by a single assessment. Although an average component count across waves summarizes mean co-occurrence during the exposure window, it is not a strictly defined time-weighted cumulative exposure dose. Death may occur before ADL difficulties are observed; relative associations alone therefore do not describe the absolute probability of developing functional difficulties during follow-up. Estimates of cumulative incidence must account for competing mortality [12]. Further evidence is needed on the association of average burden combining repeatedly recorded risk factors with heart disease and stroke histories with subsequent basic ADL difficulties, and on whether historical burden retains an association after adjustment for currently measured components.

Using the nationally sampled CHARLS cohort, we averaged scores for hypertension, diabetes, central obesity, heart disease, and stroke across valid waves in 2011–2015 among eligible participants with no difficulties in any of six basic ADL in 2015. We examined the association of this average component burden with the first confirmed ADL difficulties after the fixed 2015 baseline through 2020 and quantified standardized cumulative incidence and risk differences accounting for competing mortality. We also distinguished risk-factor burden from pre-existing heart disease and stroke burden in a mutually adjusted model, examined the risk-factor association among participants with explicitly negative heart disease and stroke histories at all three exposure waves, and assessed the incremental association of historical 2011–2013 burden after adjustment for the five current 2015 components. These analyses aimed to clarify the relationship between cardiometabolic history and subsequent self-care function.

Methods

Study design and participants

This secondary longitudinal cohort analysis used data from the China Health and Retirement Longitudinal Study (CHARLS), with the 2015 survey as a fixed baseline and 2011–2015 as the historical exposure window. CHARLS uses multistage probability-proportional-to-size sampling. Its baseline survey was conducted in 2011–2012, enrolling adults aged ≥45 years and their spouses and collecting information on health, disease history, health behaviors, and physical measurements [13]. We used the waves conventionally labeled 2011, 2013, 2015, 2018, and 2020 and harmonized the corresponding exit and mortality data. Eligible participants had to be identifiable in the 2011 health interview, aged ≥45 years in 2011, and have complete sex information. They also had to complete the 2015 health interview, have no difficulty in any of six ADL as confirmed by direct responses or validated questionnaire skip logic, and have an assessable cardiometabolic component burden in at least two waves during 2011–2015. All 9587 participants meeting these criteria were included in the main analysis. Figure 1 presents the sequential selection process.

Average cardiometabolic component burden across waves

Average cardiometabolic component burden summarized the co-occurrence of five equally weighted conditions: hypertension, diabetes, central obesity, heart disease, and stroke. Hypertension was defined by a self-reported diagnosis, antihypertensive medication use, mean systolic blood pressure ≥140 mmHg (18.7 kPa), or mean diastolic blood pressure ≥90 mmHg (12.0 kPa) [14]. Blood pressure classification used the average of at least two valid paired readings. Diabetes was defined by a self-reported physician diagnosis or glucose-lowering

medication use. Heart disease was based on the questionnaire's self-reported physician-diagnosed conditions, including myocardial infarction, coronary heart disease, angina, and heart failure. Stroke was based on a self-reported physician diagnosis. Central obesity was defined using the waist-circumference thresholds in the 2018 Chinese hypertension guidelines: ≥90 cm for men and ≥85 cm for women [14].

We harmonized and reconstructed diabetes, heart disease, and stroke histories across waves. Previously reported diagnoses were carried forward by default. If a participant explicitly denied a preloaded diagnosis at a subsequent interview and there was no evidence of a new diagnosis or relevant medication use, the condition was coded as absent at that wave. Hypertension and central obesity were classified using the measurements or reports at each wave.

When at least four components were assessable at a wave, the score was prorated as 5 × the number of known present components / the number of components with known status. Each participant required at least two valid waves. Average burden was the arithmetic mean of all valid wave-specific scores. Data-cleaning rules and disease-history harmonization algorithms are provided in Additional file 1 (Supplementary Methods SM1.1 and Table S1A and Table S1B).

ADL outcomes and competing mortality

The primary outcome was the first confirmed difficulty after the fixed 2015 baseline in any basic ADL: dressing, bathing, eating, getting into or out of bed or transferring, toileting, or continence. Outcomes were assessed at the 2018 and 2020 visits, with events assigned to the corresponding follow-up interval. A difficulty reported for any valid ADL item defined a positive outcome. Participants were classified as negative only when all six items were confirmed as having no difficulty through direct responses or validated questionnaire skip logic; all other outcomes were coded as unknown. Structurally skipped responses were inferred to be negative only when

preceding screening information was complete, explicitly supported the absence of functional limitations, and conformed to the skip logic for that wave. Skip-path provenance and the original blank values were retained. Wave-specific item identifiers, skip rules, and the composition of eligible samples by inclusion criterion are detailed in Supplementary Methods SM1.2, Table S1F, and Table S2B.

Death before the first recorded ADL difficulty was treated as a competing event. Mortality information was compiled from exit interviews, death-related interviews, and sample records. Deaths were assigned to follow-up intervals using the available evidence, without midpoint imputation. Participants with unknown outcomes were censored at their last visit with confirmed event-free status and subsequently removed from the risk set. Supportive outcomes were multiple ADL difficulties or need for assistance (at least two difficulties, or at least one item requiring help or impossible to perform) and difficulties reported at both the 2018 and 2020 visits. Definitions and estimation details are provided in Supplementary Methods SM1.2 and SM3.4 and Table S7.

Covariates

Core covariates were measured in 2011 and included age, sex, education, and the official urban–rural classification to control for potential demographic and socioeconomic confounding. Age was modeled using a natural cubic spline. Figure S1 presents covariate measurement times, hypothesized relationships assembled after the analyses, and the processes governing study inclusion and follow-up observation.

The extended model additionally adjusted for 2011 smoking, alcohol consumption, marital status, and tertiles of per-capita household consumption. Core and extended models were compared in the same 8050 complete cases, using identical risk records and observation weights.

Education categories, household consumption definitions, and spline parameters are provided in Supplementary Methods SM2.1; missing covariate data are summarized in Table S1C.

Missing data and adjustment for selection

Missing exposure components were handled by prorating the wave-specific scores as described above. Participants with unknown follow-up outcomes were censored at their last confirmed event-free visit, and observation weights accounted for outcome availability. Missing education information for six participants was imputed in a participant-level, wide-format dataset using a multilevel latent-normal model for categorical data with community random intercepts [15]. We generated 20 imputed datasets and combined estimates using Rubin's rules [16]. The imputation model included age, sex, urban–rural classification, average burden, and follow-up interval status. Specifications and diagnostics for the three chains are provided in Supplementary Methods SM2.1 and Table S3C and Table S3D.

We used stabilized inverse probability of censoring weighting (IPCW) to account for differences in follow-up outcome observability. The censoring model included follow-up interval, cardiometabolic burden, age, sex, education, urban–rural classification, and historical and lagged health indicators. Deaths reliably assigned to an interval were treated as observed outcomes. IPCW depends on conditional ignorability, positivity, and adequate specification of the observation model [17]. Observation models and diagnostics are detailed in Supplementary Methods SM2.2, Table S1D and Table S1E, and Table S3A. Among participants who survived, completed the interview, and had no difficulty in any of six ADL in 2015, inverse probability weights for exposure-data availability were used to assess the impact of requiring at least two valid exposure waves. Target populations, weights, and balance diagnostics are provided in Supplementary Methods SM3.3, Table S3B, and Figure S2B. Figure S2A compares participants included at the fixed baseline with other individuals meeting the age and sex criteria.

Statistical analysis

We expanded the data into person–interval records and fitted separate discrete-time event-specific binomial models with a complementary log-log (cloglog) link for the first confirmed ADL difficulties and death before ADL difficulties [18]. Models included follow-up interval fixed effects, continuous average burden, and the core covariates. When modeling either event, the competing event was coded as absence of the target event in that interval, and the participant was removed from subsequent risk sets.

Sequential models were demographically unadjusted, adjusted for age and sex, and additionally adjusted for education and urban–rural classification in the core model. Average burden entered the main model on its original component scale. We multiplied its regression coefficient by the fixed standard deviation of the main sample (SD = 0.89) and exponentiated the result to obtain a complementary log-log-scale ratio (CSR) per 1-SD increase. If q denotes the interval event probability conditional on the risk set and covariates, the CSR is the ratio of $-\log(1-q)$ between the two compared conditions.

Standard errors were clustered by 446 official communities. Uncertainty in weights and their estimation was propagated using influence functions from stacked estimating equations [19]. Multiply imputed estimates were combined using Rubin's rules, with degrees of freedom determined by the Barnard–Rubin method [20]. Because observations were sparse in the upper tail, supportive analyses categorized burden as 0, >0–1, >1–2, and >2. We also assessed nonlinearity using a natural cubic spline with fixed knots and tested the interaction between burden and follow-up interval. Estimands, variance estimation, and spline specifications are detailed in Supplementary Methods SM2.3–SM2.4.

To estimate absolute risk accounting for competing mortality, we fitted a joint multinomial logit model in the same risk set. This model estimated probabilities for three mutually exclusive states in each interval: event-free, ADL difficulties, and death, summing to 1. Holding each participant's other covariates at their observed values, we set burden successively to 0, 1, 2, and 3 component units, recursively calculated cumulative incidence functions (CIFs) at the nominal 3- and 5-year time points [12], and averaged these estimates over the 9587 participants in the main analysis.

The CSR describes interval-specific conditional associations among participants who have experienced neither event. CIFs and risk differences quantify marginal absolute risk accounting for competing mortality. We assessed local data support for fixed burden values within strata defined by age, sex, urban–rural classification, and education. Data support, probability recursion, and standardization procedures are provided in Supplementary Methods SM2.4 and Table S4C.

Supplementary analyses examined burden composition and historical information. Component analyses were restricted to participants with complete data on all five components in at least two common waves. Using these common waves, we constructed a risk-factor score (hypertension, diabetes, and central obesity) and a pre-existing disease score (heart disease and stroke), including both in the same model. Disease-history restrictions required explicitly negative histories of the relevant conditions at all three exposure waves. Historical analyses were restricted to participants with complete data on all five components at all three waves and estimated the conditional association of historical burden after adjustment for the current 2015 components. Comparisons in the same samples and detailed specifications are provided in Supplementary Methods SM3.1–SM3.2 and Table S6A, Table S6B, and Table S6C.

Complete-case sensitivity analyses separately restricted the sample to participants with confirmed absence of difficulty in all six ADL in 2011, 2013, and 2015, and to participants directly reporting no difficulty in all six ADL in 2015. Among participants with complete data on all five components in at least two common waves, we compared the original score with an average calculated only from complete waves using the same participants and risk records. We also applied an alternative disease-history rule under which diabetes, heart disease, and stroke remained positive once reported. Observation weights were re-estimated within restricted samples, and effect estimates were scaled using the fixed SD of the main sample (Supplementary Methods SM3.5 and Table S5).

Component and historical burden analyses were conducted as exploratory supplementary analyses; their model specifications and complete results are provided in Supplementary Methods SM3.1–SM3.2 and Table S6A, Table S6B, and Table S6C. For the two supplementary ADL tests of risk factor burden and historical burden, P values were corrected using the Holm method [21]. Sample restrictions based on functional history, comparisons with extended covariate adjustment within the same sample, and paired exposure score comparisons were used to assess the robustness of the results; sensitivity analyses and secondary ADL outcome analyses are detailed in Supplementary Methods SM3.4–SM3.5, Table S5 and Table S7. Cognitive effect modification analyses and longitudinal cognitive analyses were both conducted as exploratory analyses, as detailed in Supplementary Methods SM3.4 and Table S8A and Table S8B. All tests were two-sided, and effect estimates were reported with 95% confidence intervals (CIs). Analyses were performed using R 4.4.1 [22], and software and package versions are listed in Supplementary Methods SM4.

Results

Participant characteristics and follow-up outcomes

Of 17596 participants who completed a health interview in 2011, 9587 met the inclusion criteria at the fixed 2015 baseline (Figure 1). In the main sample, mean age in 2011 was 58.1 years (SD 8.8), and mean average burden was 1.10 (SD 0.89). Participants in higher burden categories were older, more frequently urban residents, and less frequently current smokers (Table 1). Approximately 65% had primary-school education or less.

The burden categories 0, >0–1, >1–2, and >2 included 1972, 3442, 3001, and 1172 participants, respectively. There were 6739 participants with three valid exposure waves and 2848 with two. Wave-specific component coverage is provided in Table S1B. The two nominal follow-up intervals, 2015–2018 and 2018–2020, generated 17031 person–interval risk records, of which 16072 had observed outcomes. Outcome observability was 93.5% and 95.4% in the two intervals, respectively. Interval-specific risk sets and outcome counts are reported in Table S2A.

After the fixed baseline, we recorded 2167 first confirmed ADL events, 492 deaths preceding ADL difficulties, and 959 unknown outcomes; 5969 participants remained event-free through 2020. Unknown outcomes comprised 951 participants without a health interview and eight with indeterminate ADL status, with 620 and 339 unknown outcomes in the two intervals, respectively. In the main sample, 914 participants reported ADL difficulties in 2011, representing 9.7% of the 9456 participants with ascertainable ADL status at that wave. ADL status in 2011 is reported in Table 1, functional history in 2011–2013 and subsequent outcomes in Table S2C, and samples defined by the inclusion criteria for each analysis in Table S2B.

Associations of average burden with ADL difficulties

Average cardiometabolic burden across waves showed a graded positive association with the first confirmed ADL difficulties. Per 1-SD increase (0.89 component units), the CSR was 1.24 (95% CI 1.19–1.30; P < 0.001) for ADL difficulties and 1.12 (95% CI 1.02–1.22; P = 0.013) for competing mortality (Table 2). The demographically unadjusted CSR for ADL difficulties was 1.28, decreased to 1.19 after adjustment for age and sex, and increased to 1.24 after further adjustment for education and urban–rural classification. Relative to burden 0, the CSRs for ADL difficulties at burden >0–1, >1–2, and >2 were 1.10 (95% CI 0.97–1.26), 1.36 (1.19–1.55), and 2.00 (1.72–2.33), respectively. Full categorical estimates are reported in Table 2.

There was no statistical evidence of nonlinearity in the association of continuous burden with ADL difficulties (P = 0.251; Figure 2) or of an interaction between burden and follow-up interval (P = 0.569). Above burden 2.75, the spline extended linearly on the log-CSR scale with wider confidence intervals (Figure 2A); the exposure distribution is shown in Figure 2B. Categorical mortality estimates were not monotonic: CSRs in the three nonzero burden categories were 1.16, 1.45, and 1.32, respectively. Their confidence intervals are reported in Table 2.

Standardized absolute risks

To quantify the population-level absolute risk associated with different cardiometabolic burden levels, we estimated standardized cumulative incidence accounting for competing mortality. With burden set to 0, 1, 2, and 3 component units, the 3-year CIFs were 10.2%, 12.8%, 15.9%, and 19.6%, and the 5-year CIFs were 19.5%, 24.0%, 29.2%, and 35.0%, respectively (Figure 3 and Table S4A). The standardized 5-year risk difference comparing burden 3 with 0 was 15.5 percentage points (95% CI 12.1–18.9), equivalent to 155 events per 1000 people; the difference comparing burden 2 with 0 was 9.7 percentage points (7.7–11.7). Risk differences and

confidence intervals are reported in Table S4A. Supportive categorical-model estimates and data support for fixed burden values are provided in Table S4B and Table S4C, respectively. Descriptive first-event probabilities and the joint model's in-sample observed and fitted proportions are reported in Table S4D and Table S4E.

Component-specific and historical burden analyses

To distinguish associations of risk-factor components from those of self-reported pre-existing heart disease and stroke, we included both component groups in the same model. Among 8786 participants with complete data on all five components in at least two common waves, there were 1985 ADL events and 447 competing deaths. After mutual adjustment, risk-factor burden and pre-existing disease burden both remained associated with ADL difficulties: their CSRs per component unit were 1.19 (95% CI 1.12–1.26) and 1.51 (95% CI 1.34–1.71), respectively (Table 3 and Table S6A).

The positive association of risk-factor burden was present both among participants with explicitly negative stroke histories at all three waves (N = 8206) and among those with explicitly negative heart disease and stroke histories at all three waves (N = 6736). In the latter restricted sample, the CSR per component-unit increase in average risk-factor burden was 1.18 (95% CI 1.10–1.27). Results for disease-history exclusions are reported in Table S6A.

To assess whether historical burden remained associated with ADL difficulties after accounting for contemporaneous cardiometabolic status, we additionally adjusted for the individual 2015 components. Among 5084 participants with complete data on all five components at all three waves, there were 1188 ADL events and 249 competing deaths. Historical burden was the average of the 2011 and 2013 burden scores. After adjustment for all five current 2015

components, the CSR per component-unit increase in historical burden was 1.18 (95% CI 1.06–1.31) for ADL difficulties and 1.16 (95% CI 0.95–1.42) for death (Table 3 and Table S6B).

The two principal supplementary ADL tests, for risk-factor burden and historical burden, remained statistically significant after Holm adjustment. Four saturated component-pattern models failed to produce finite unpenalized maximum-likelihood estimates because events were sparse and were recorded as non-estimable. Full model results and conditional-variation diagnostics are provided in Table S6B and Table S6C.

Robustness analyses and secondary outcomes

The direction of the association with ADL difficulties was consistent across the sensitivity and restriction analyses performed. Restriction to participants with confirmed absence of difficulty in all six ADL in 2011, 2013, and 2015 yielded 7454 complete cases and 1395 ADL events; the CSR per 1-SD increase in burden was 1.22 (95% CI 1.15–1.29; Table S5). Restriction to participants with directly confirmed absence of difficulty in all six ADL in 2015 yielded 6224 complete cases and 1823 ADL events; the CSR per 1-SD increase was 1.18 (95% CI 1.13–1.24; Table S5).

In the same 8050 complete cases, 1801 ADL events were recorded. The CSR per 1-SD increase in burden was 1.25 (95% CI 1.19–1.31) in the core model and 1.26 (1.20–1.32) in the extended model (Table S5). In the same complete-component subset of 8786 participants, the CSR was 1.24 (95% CI 1.18–1.30) for the original score and 1.23 (1.17–1.28) for the average calculated only from complete waves. Supportive analyses of persistent-positive disease-history coding, waist-circumference and blood-pressure cleaning rules, and death-interval handling are reported in Table S5. IPCW effective sample sizes were 8954 and 7080 in the two follow-up intervals, respectively, each retaining more than 99.6% of observed records. Main-analysis weights were

not truncated; the maximum was 1.41. The selection-weighted analysis of exposure-data availability included 9581 participants. The CSR was 1.24 both before and after weighting; the maximum standardized mean difference decreased from 0.066 to 0.005, and 99.0% of the effective sample size was retained. Diagnostics for observation and inclusion weights are provided in Table S3A and Table S3B, covariate balance in Figure S2, and association comparisons in Table S5.

There were 1141 events involving multiple ADL difficulties or need for assistance; in the model including 9581 participants, the CSR per 1-SD increase in burden was 1.28 (95% CI 1.21–1.36). Among 7980 participants observed at both the 2018 and 2020 visits with complete core covariates, 549 reported difficulties at both visits; the adjusted odds ratio was 1.39 (95% CI 1.26–1.52). Definitions and results for secondary outcomes are provided in Supplementary Methods SM3.4 and Table S7.

Discussion

Principal findings

Among community-dwelling middle-aged and older adults in China with confirmed absence of difficulty in all six basic ADL in 2015, average cardiometabolic component burden across the 2011–2015 waves showed a positive graded association with the first confirmed post-baseline ADL difficulties. There was no statistical evidence supporting nonlinearity. The CSR per 1-SD increase (0.89 component units) was 1.24 (95% CI 1.19–1.30). The risk-factor association was also present among participants with explicitly negative heart disease and stroke histories at all three waves. Historical average burden in 2011–2013 retained a conditional association with subsequent ADL difficulties after adjustment for the five current 2015 cardiometabolic components. Accounting for competing mortality, the standardized 5-year risk difference with

average burden fixed at 3 versus 0 component units was 15.5 percentage points (95% CI 12.1–18.9).

Comparison with previous studies

The positive association between cardiometabolic burden and subsequent ADL difficulties is consistent with previous longitudinal evidence on cardiometabolic multimorbidity. In CHARLS, He et al. found that participants with at least two of diabetes, heart disease, and stroke at baseline subsequently experienced faster increases in the number of ADL and instrumental ADL (IADL) difficulties [8]. Zhang et al.'s four-cohort study also linked baseline cardiometabolic multimorbidity to worsening basic ADL function [9]. These studies primarily relied on disease status at a single assessment. By combining repeated records of hypertension, diabetes, central obesity, and pre-existing heart disease and stroke in an average component burden, our study adds evidence on functional associations of the co-occurrence of risk factors and diseases. Exploratory analyses further showed that risk-factor burden was associated with subsequent ADL difficulties among participants with explicitly negative heart disease and stroke histories at all three waves, extending the evidence to people who did not report these diseases.

Previous research also supports attention to health records across waves. Shi et al. found that cardiometabolic and cardiometabolic/brain-disease trajectories were associated with ADL difficulties, although disease trajectories and functional outcomes were assessed during the same follow-up period [10]. Our study used a fixed 2015 baseline among participants without basic ADL difficulties, separating exposure assessment through baseline from subsequent outcome observation. Hajjar et al. found that remote and concurrent increases in systolic blood pressure were associated with functional decline, including Katz ADL, in older adults without a stroke history [11]. Building on this evidence, we examined historical states of multiple components and found that average burden in 2011–2013 retained a conditional association after adjustment

for the current 2015 components. Historical records may therefore contain association information not fully summarized by current component status. However, this exploratory finding does not establish incremental predictive value. The average count used here summarizes mean co-occurrence during the exposure window and is not equivalent to a disease trajectory or a time-weighted cumulative dose.

Zhang et al. excluded participants who died during follow-up and primarily described functional changes among survivors [9]. We treated death before the first recorded ADL difficulty as a competing event and estimated standardized 5-year cumulative incidence at different burden levels. This adds population-level absolute risk information on basic ADL difficulties during follow-up to the existing evidence on functional trajectories and relative associations. Together, these studies support a relationship between cardiometabolic health and functional deterioration. Differences in exposure composition, functional outcomes, and estimands mean that their effect estimates should not be compared directly.

Potential mechanisms and interpretation

The observed associations may involve several neurovascular and muscular processes. Hypertension-related cerebral small-vessel changes may affect motor control, and diabetic peripheral neuropathy may affect sensation, postural control, and balance [4, 5]. Obesity-related inflammation, muscle dysfunction, and mechanical loading of joints may also limit strength and activity [7, 23, 24]. These changes could increase the difficulty of self-care tasks such as transferring, dressing, and bathing. At the clinical disease level, the ASPREE study observed increased frailty burden after cardiovascular events, particularly after stroke and hospitalization for heart failure [25]; frailty, however, is not equivalent to basic ADL difficulties. We did not directly measure these intermediate processes, and the equally weighted score did not distinguish

different disease combinations. These pathways therefore offer possible explanations, but their relative contributions cannot be determined.

In exploratory analyses, risk-factor burden remained associated with ADL difficulties among participants with explicitly negative heart disease and stroke histories at all three waves. This result cannot distinguish subclinical vascular changes, neuromuscular processes, or other health factors. The conditional association of historical burden after adjustment for current components may mark previous health experiences or persistent changes relevant to function. Disease severity, treatment, or measurement error not fully captured by the five current binary components, as well as residual confounding, could also explain the result. The average count reflects mean co-occurrence during the exposure window and does not demonstrate cumulative injury or metabolic memory. Future studies should incorporate longitudinal neurological, muscular, and cardiac functional measurements and establish their temporal order relative to exposure and ADL outcomes to test these explanations.

Clinical and preventive implications

This study provides longitudinal evidence supporting attention to self-care function in cardiovascular risk-factor management. The 2025 EAPC consensus statement recommends standardized instruments such as the Katz basic ADL index to assess functional dependence in older adults [3]. Among community-dwelling middle-aged and older Chinese adults without basic ADL difficulties at the fixed baseline, higher average cardiometabolic burden across waves was associated with subsequent ADL difficulties. Exploratory analyses also identified an association of risk-factor burden among participants with explicitly negative heart disease and stroke histories at all three waves. These findings are consistent with comprehensive assessment and suggest that, in populations resembling this study sample, brief standardized questions about self-care function could be incorporated into existing risk-factor follow-up, with further

assessment of newly emerging difficulties. This could help cardiovascular health management address patients' ability to perform everyday activities.

Historical burden retained a conditional association after adjustment for current components, suggesting that previous records of risk factors and diseases may add information for understanding subsequent functional risk; this does not establish improved risk prediction. Standardized risk estimates accounting for competing mortality quantified population-level probabilities of ADL difficulties at different burden levels. These estimates came from an observational analysis, and total burden included both risk factors and pre-existing diseases. The observed risk differences therefore cannot be interpreted as treatment benefits achievable through risk-factor control, and performance for individual risk assessment has not been validated. Associations and absolute risks should be evaluated in independent cohorts. Intervention studies should separately test the effects of risk-factor management on ADL outcomes and whether adding functional assessment and corresponding care improves function, while considering mortality, treatment burden, and adverse events.

Strengths

This study used the nationally sampled CHARLS community cohort to integrate risk-factor and disease-history records across 2011–2015, summarize their average co-occurrence, and examine the first recorded post-baseline ADL difficulties among participants without difficulty in any of six basic ADL in 2015. Exposure assessment was clearly separated from subsequent outcome observation. Using basic ADL difficulties, a functional event directly relevant to daily life, adds a functional-outcome perspective to cardiometabolic burden. Reporting relative associations alongside standardized 5-year cumulative incidence accounting for competing mortality provides a more complete population-risk description across burden levels. Exploratory supplementary analyses examined burden composition, risk-factor associations among participants with

negative heart disease and stroke histories at all three waves, and the conditional association of historical burden after adjustment for current components. Multiple sensitivity analyses of previous functional status, baseline ADL confirmation, measured covariates, exposure scoring, and observation selection yielded directionally consistent results, supporting robustness under the conditions examined.

Limitations

Several limitations require consideration. First, selection bias remains possible. The study was restricted to participants who survived to 2015, completed the health interview, and met the ADL-status and exposure-data requirements. Although censoring and exposure-inclusion weights can adjust for selection differences related to measured variables, they depend on conditional ignorability, positivity, and correct model specification. They cannot eliminate survivor bias before the fixed baseline or selection bias arising from unmeasured factors.

Second, exposure measurement was limited. The average burden of five equally weighted components reflects mean co-occurrence during the exposure window. It does not distinguish disease severity, exposure duration, burden trajectories, or specific component combinations and is not a time-weighted cumulative dose. Diabetes, heart disease, and stroke were mainly based on self-reported physician diagnoses, with medication information also used to identify diabetes; underreporting and misclassification are possible. An internal CHARLS validation study found low sensitivity of self-reported diabetes, with misclassification differing by education and urban–rural origin [26]. The direction and magnitude of the net bias from survivor selection and differential misclassification remain uncertain.

Third, outcome measurement was limited. Some participants reported ADL difficulties during the exposure window. Our outcome was the first confirmed event after the fixed 2015 baseline,

rather than an individual's first-ever ADL difficulty. Long intervals between visits also limited identification of exact onset times, recovery and recurrence between waves, and subclinical functional changes.

Fourth, residual confounding remains possible. Physical activity, cognitive function, depressive symptoms, social support, and other factors not included in the core adjustment model may have influenced associations. Adjustment for these variables requires consideration of temporal order and their roles as confounders or mediators to avoid overadjustment bias [27].

Fifth, results depend on model specification. Standardized absolute risks depend on the joint multinomial event-probability model, covariate functional forms, and assumptions about the observation process. Local data support was limited for some high burden values and covariate combinations. Relatively few deaths and events in some subgroups reduced precision for weak associations, nonlinear effects, and interactions. The results mainly apply to community-dwelling middle-aged and older adults with characteristics similar to those of our risk set. Independent replication is needed before extrapolation to other populations or direct use in individual clinical decisions. The source CHARLS data used in this study are accessible through the official data portal after registration and application, subject to CHARLS data-use requirements [28].

Conclusions

Higher repeatedly measured cardiometabolic burden was associated with subsequent ADL difficulties. Historical burden retained a conditional association after adjustment for current components. These findings support attention to self-care function during cardiometabolic follow-up, including among people without self-reported heart disease or stroke.

List of abbreviations

ADL: activities of daily living; CHARLS: China Health and Retirement Longitudinal Study; CI: confidence interval; CIF: cumulative incidence function; cloglog: complementary log-log; CSR: complementary log-log-scale ratio; EAPC: European Association of Preventive Cardiology; IADL: instrumental activities of daily living; IPCW: inverse probability of censoring weighting; SD: standard deviation.

Declarations

Ethics approval and consent to participate

The CHARLS survey was approved by the Biomedical Ethics Review Committee of Peking University (approval number: IRB00001052-11015), and all participants provided written informed consent at data collection. This study was a secondary analysis of deidentified CHARLS data and involved no additional participant recruitment or intervention. Therefore, no additional ethics approval was required. All methods were conducted in accordance with the Declaration of Helsinki.

Consent for publication

Not applicable. This manuscript contains no information, images, or case details that identify individual participants.

Availability of data and materials

The original CHARLS data used in this study are available through the official CHARLS data portal after registration and application, subject to CHARLS data-use requirements [28]. The study data and analysis code are available from the corresponding author on reasonable request, subject to the applicable CHARLS data-use conditions.

Competing interests

The authors declare that they have no competing interests.

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This study received no specific funding.

Authors' contributions

ZL conceived the study, curated the data, performed the statistical analysis, and drafted the manuscript. YW supervised the study. MZ curated the data. MS reviewed and revised the manuscript. YF and HS curated the data. LS supervised the study. All authors reviewed and approved the final manuscript and agreed to take responsibility for their contributions and the integrity of the work.

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Clinical trial number

not applicable

Additional files

Additional file 1 (.docx). Supplementary methods, tables and figures. Includes Supplementary Methods SM1–SM4, supplementary table groups S1 to S8 and their lettered component tables, whose titles are listed under Supplementary table captions at the end of this manuscript, Figures S1–S2, and supplementary references. The file documents variable harmonization, outcome ascertainment, missing-data and weighting methods, model specifications, diagnostics, and supplementary analyses.

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Tables

Table 1. Participant characteristics in 2011 by average cardiometabolic burden

Characteristic	Overall N = 9587	0 n = 1972	>0–1 n = 3442	>1–2 n = 3001	>2 n = 1172

Characteristic	Overall N = 9587	0 n = 1972	>0–1 n = 3442	>1–2 n = 3001	>2 n = 1172
Age in 2011 (years)	58.1 (8.8)	56.4 (8.0)	57.8 (8.8)	58.9 (9.1)	60.1 (8.7)
Female	4827 (50.3)	745 (37.8)	1711 (49.7)	1685 (56.1)	686 (58.5)
Urban residence	3546 (37.0)	539 (27.3)	1161 (33.7)	1205 (40.2)	641 (54.7)
Married and living with spouse	8083 (84.3)	1717 (87.1)	2906 (84.4)	2505 (83.5)	955 (81.5)
Prior ADL difficulty in 2011	914 (9.7)	157 (8.1)	259 (7.6)	323 (10.9)	175 (15.1)
Missing, n	131	31	48	37	15
Education: primary school or less	6275 (65.5)	1285 (65.2)	2290 (66.6)	1970 (65.7)	730 (62.3)
Education: middle school	2156 (22.5)	457 (23.2)	765 (22.2)	672 (22.4)	262 (22.4)
Education: high school / vocational or higher	1150 (12.0)	230 (11.7)	384 (11.2)	357 (11.9)	179 (15.3)
Missing, n	6	0	3	2	1
Hypertension	3681 (41.7)	1 (0.1)[a]	758 (23.9)	1926 (69.8)	996 (89.2)
Missing, n	754	183	275	240	56
Diabetes	501 (5.3)	0 (0.0)	42 (1.2)	126 (4.2)	333 (28.9)
Missing, n	80	20	19	23	18
Central obesity	3389 (40.8)	0 (0.0)	942 (30.3)	1667 (66.7)	780 (84.1)
Missing, n	1279	202	332	500	245
Heart disease	1009 (10.6)	2 (0.1)[a]	140 (4.1)	307 (10.3)	560 (48.0)
Missing, n	58	18	14	20	6
Stroke	133 (1.4)	2 (0.1)[a]	10 (0.3)	42 (1.4)	79 (6.8)
Missing, n	27	7	6	8	6
Current smoking	2970 (31.6)	828 (42.8)	1144 (33.6)	761 (26.0)	237 (20.7)

Characteristic	Overall N = 9587	0 n = 1972	>0–1 n = 3442	>1–2 n = 3001	>2 n = 1172
Missing, n	181	38	42	75	26
Current drinking	3357 (35.1)	815 (41.4)	1259 (36.6)	989 (33.0)	294 (25.2)
Missing, n	12	4	2	2	4
Annual per capita consumption (yuan)	4916 (2828–8568)	4632 (2740–7864)	4747 (2727–8170)	5077 (2910–8740)	5910 (3252–10776)
Missing, n	1393	266	505	440	182
Average burden, 2011–2015	1.1 (0.9)	0.0 (0.0)	0.7 (0.3)	1.6 (0.3)	2.7 (0.5)

Values are means (standard deviations), medians (interquartile ranges) for consumption, or n (percentage of nonmissing observations); counts are unweighted. All characteristics except average burden were measured in 2011. Groups were defined by average scores across valid waves in 2011–2015. The nonmissing denominator for prior ADL difficulty was 9456. The marital-status row corresponds to “married and living with spouse” in the original six-category variable; all six categories were retained in the extended model. a These participants had fewer than four assessable components in 2011; their average scores were based on the other valid waves. Definitions and coverage are provided in SM1.1 and Table S1A, Table S1B, and Table S1C. ADL, activities of daily living; SD, standard deviation.

Table 2. Associations of cardiometabolic burden with ADL difficulties and competing mortality

Outcome	Exposure contrast	N	Events	Demographically unadjusted CSR (95% CI)	Core-adjusted CSR (95% CI)

Outcome	Exposure contrast	N	Events	Demographically unadjusted CSR (95% CI)	Core-adjusted CSR (95% CI)
ADL	Per 1 SD (0.89 component units)	9587	2167	1.278 (1.225–1.333)	1.243 (1.189–1.300)
ADL	0 (reference)	1972	341	1.000 (reference)	1.000 (reference)
ADL	>0–1	3442	699	1.205 (1.060–1.368)	1.104 (0.970–1.256)
ADL	>1–2	3001	747	1.561 (1.369–1.780)	1.362 (1.193–1.555)
ADL	>2	1172	380	2.250 (1.937–2.614)	1.999 (1.718–2.328)
Death	Per 1 SD (0.89 component units)	9587	492	1.108 (1.019–1.204)	1.117 (1.024–1.218)
Death	0 (reference)	1972	80	1.000 (reference)	1.000 (reference)
Death	>0–1	3442	172	1.236 (0.951–1.605)	1.158 (0.890–1.506)
Death	>1–2	3001	178	1.507 (1.160–1.959)	1.447 (1.102–1.900)
Death	>2	1172	62	1.387 (0.990–1.943)	1.316 (0.932–1.857)

Continuous and categorical models were fitted separately, each including 9587 participants and 20 datasets with imputed education information. Category-specific sample sizes and event counts are shown. Both model types included the exposure, interval effects, and observation weights; core models additionally adjusted for the 2011 age spline, sex, education, and urban–rural classification. Conditional on the risk set and covariates, the CSR is the ratio of $-\log(1-q)$ between exposure values, where q is the conditional interval event probability. Community-level stacked variance estimation propagated uncertainty in weight estimation, and results were combined using Rubin's rules. Death denotes death before the first recorded ADL difficulty. Estimation and weighting/imputation diagnostics are provided in SM2.3 and Table S3A, Table

S3B, and Table S3C. ADL, activities of daily living; CSR, complementary log-log-scale ratio; CI, confidence interval; SD, standard deviation.

Table 3. Associations of component-specific and historical burden with subsequent outcomes

Exposure or model specification	N	ADL CSR (95% CI)	Death CSR (95% CI)	Holm P for ADL
Total complete-component burden	8786	1.256 (1.194–1.320)	1.140 (1.035–1.256)	—
Risk-factor block, separate model	8786	1.234 (1.163–1.310)	1.147 (1.024–1.284)	—
Risk-factor block, mutually adjusted	8786	1.187 (1.118–1.261)	1.131 (1.006–1.271)	<0.001
Pre-existing disease block, mutually adjusted	8786	1.515 (1.338–1.714)	1.171 (0.883–1.553)	—
Risk-factor block, disease-negative subset	6736	1.183 (1.099–1.273)	1.210 (1.053–1.391)	—
Historical burden conditional on current components	5084	1.177 (1.056–1.313)	1.159 (0.946–1.420)	0.003

Estimates are per component-unit increase. Total complete-component burden and risk-factor/disease models used the same 8786 participants (1985 ADL events and 447 competing deaths). The mutually adjusted model included risk-factor components (hypertension, diabetes, and central obesity) and pre-existing disease components (questionnaire-defined heart disease and stroke). The disease-negative subset required explicitly negative heart disease and stroke histories at all three exposure waves and included 6736 participants (1393 ADL events and 325 deaths). The historical analysis used 5084 participants with complete data at all three waves (1188 ADL events and 249 deaths), additionally adjusting for all five 2015 components; historical burden was the average total burden in 2011 and 2013. All models included core

covariates, with observation weights re-estimated within subsets and community-level stacked inference. Holm adjustment was applied to the two principal supplementary ADL tests; other entries are shown as "—". Specifications and complete results are provided in SM3.1–SM3.2 and Table S6A, Table S6B, and Table S6C. CSR, complementary log-log-scale ratio; CI, confidence interval; ADL, activities of daily living.

Figure legends

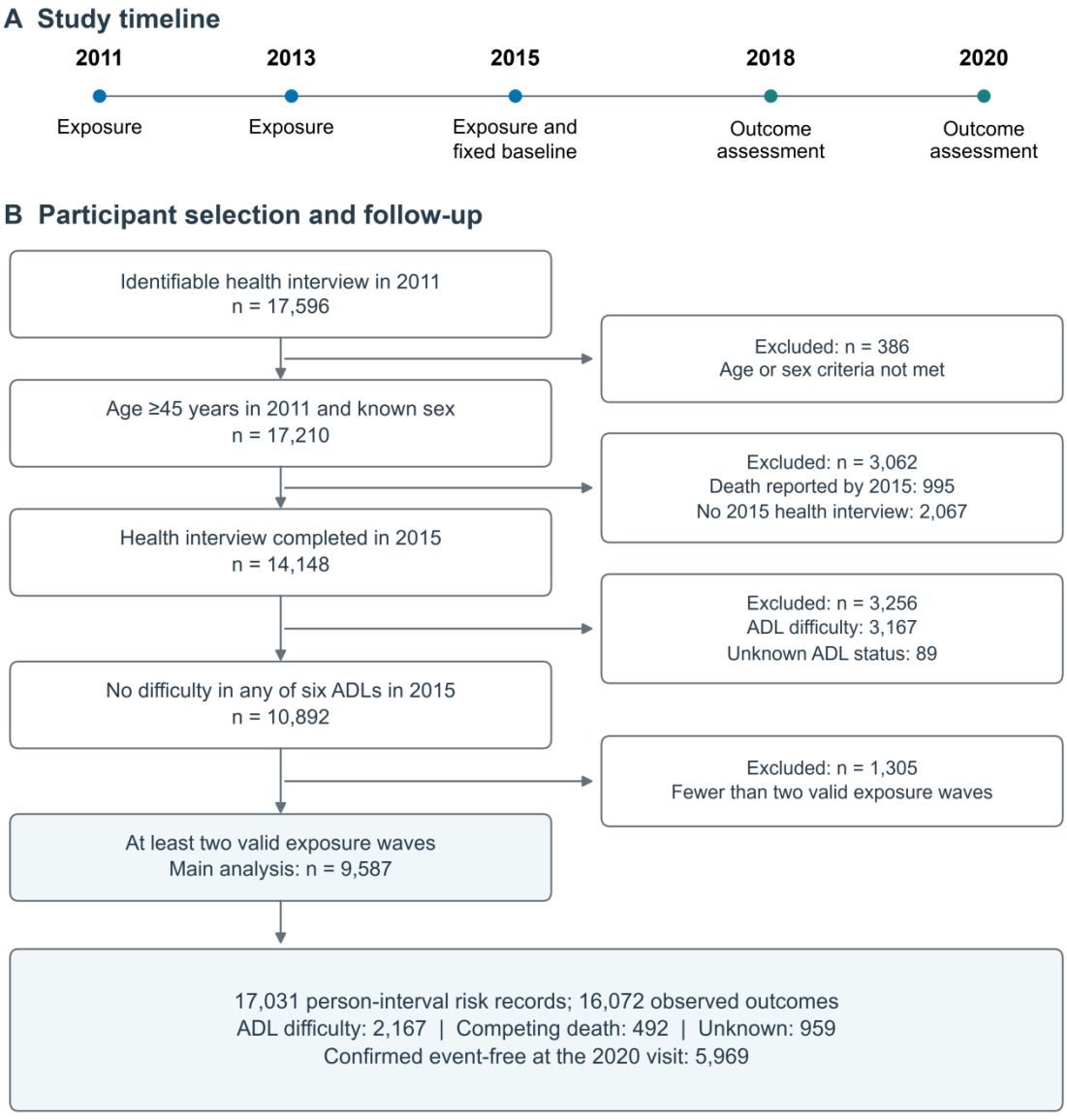
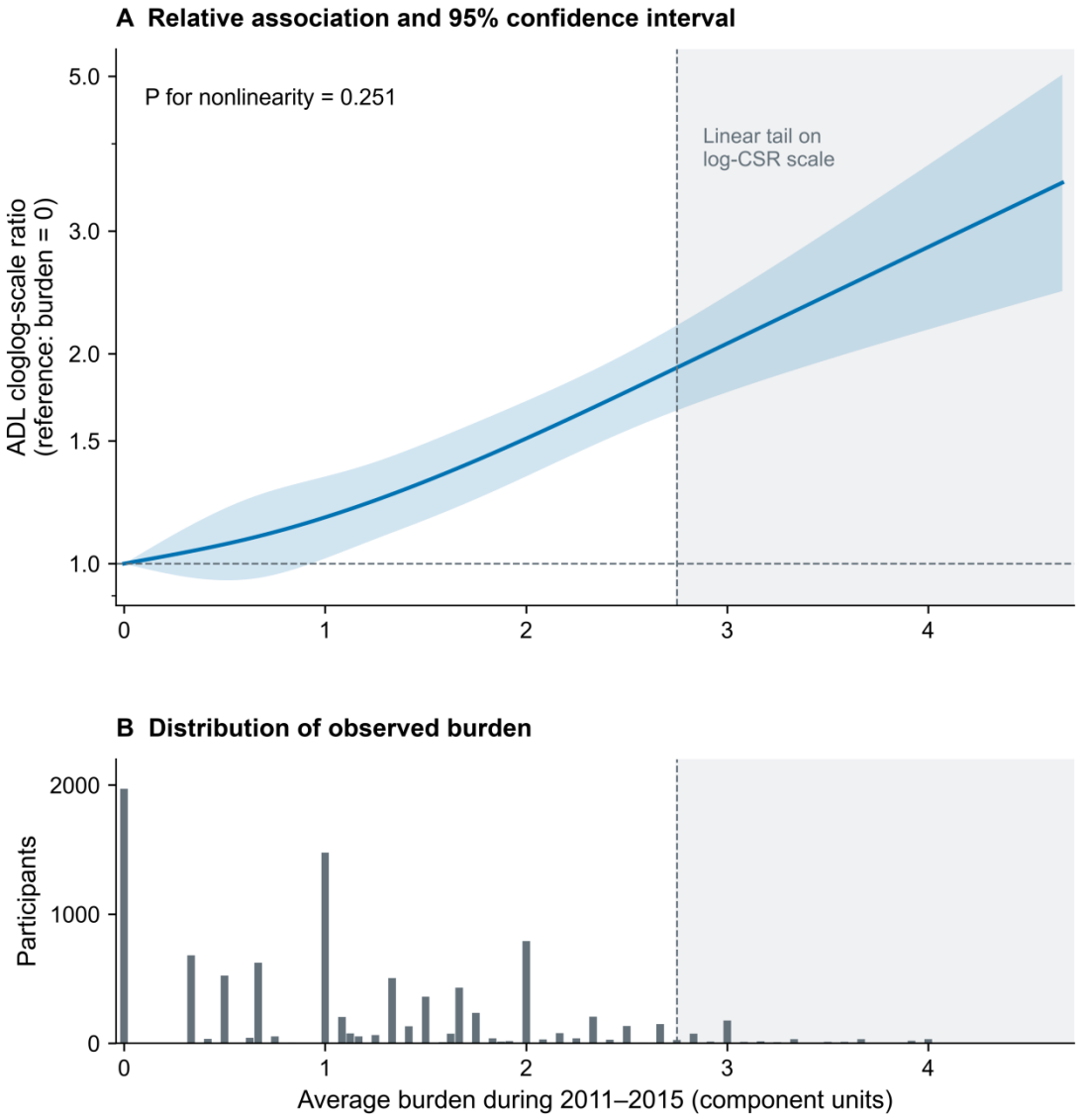


Figure 1. Study timeline and participant selection

A: Cardiometabolic burden was assessed in 2011, 2013, and 2015. Participants had no difficulty in any of six ADL in 2015; outcomes were assessed in 2018 and 2020. B: Exclusions were sequential and mutually exclusive. The starting denominator comprised identifiable 2011 health-
675 interview records. Deaths before the fixed baseline were determined from reports available at the 2015 wave. The main sample included 6228 participants classified as having no difficulties through direct responses and 3359 classified through validated questionnaire skip logic. Interval-specific counts, analysis samples, and ADL confirmation rules are provided in Table S2A, Table S2B, and Table S1F, respectively. ADL, activities of daily living.

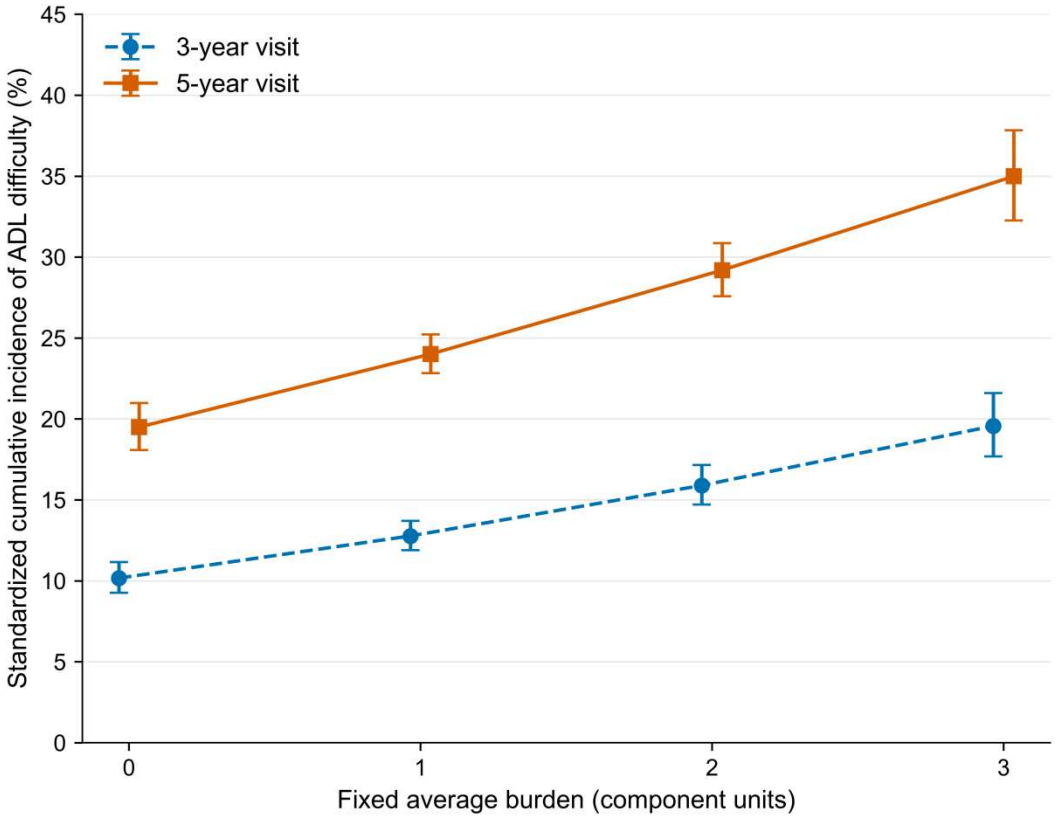


680

Figure 2. Association of average burden with ADL difficulties and exposure distribution

A: Natural cubic spline with burden 0 as the reference, using core adjustment, observation weighting, and 20 multiply imputed datasets. The blue band denotes pointwise 95% confidence intervals; the vertical axis uses a logarithmic scale. The vertical dashed line marks the upper
685 boundary knot at 2.75; shading identifies the tail that is linear on the log-CSR scale. P for nonlinearity = 0.251; knot specifications and testing are provided in SM2.4. B: Frequencies of observed burden values among 9587 participants; 468 had burden >2.75, and the maximum

observed value was 4.67. CSR, complementary log-log-scale ratio; ADL, activities of daily living.



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Figure 3. Standardized absolute risks of ADL difficulties accounting for competing mortality

Probabilities from the joint multinomial model were calculated recursively for each participant and standardized to the empirical covariate distribution of the 9587 participants, using core
695 adjustment, observation weighting, and 20 multiply imputed datasets. The horizontal axis shows average burden fixed at 0, 1, 2, or 3 component units. Circles with dashed lines and squares with solid lines denote risks at the nominal 3- and 5-year visits, respectively; error bars denote 95% confidence intervals. Model specifications, risks and risk differences, and marginal and

conditional data support are provided in SM2.4, Table S4A, and Table S4C, respectively. ADL, activities of daily living.

Supplementary table captions

All supplementary table data and detailed notes are provided in Additional file 1. Table groups S1 to S8 organize the existing tables; letter suffixes identify the component tables. The group descriptions and component-table titles are listed below.

Table S1. Variable definitions, measurement coverage, missing data, and ADL questionnaire routing

Table S1A. Definitions of exposure and outcome measures and core variables

Table S1B. Component measurement coverage

Table S1C. Missing baseline covariate data

Table S1D. Additional variables used in observation and selection models

Table S1E. Missing observation-model predictors and their coding across risk records

Table S1F. Wave-specific ADL item identifiers and questionnaire routing rules

Table S2. Risk sets, clinical entry criteria, and pre-baseline functional history

Table S2A. Interval-specific risk sets and outcome ascertainment

Table S2B. Clinical entry criteria and overlapping analytical samples

Table S2C. Pre-baseline functional history and follow-up outcomes

Table S3. Diagnostics for observation weighting, exposure selection, and imputation

Table S3A. Observation-weight diagnostics

Table S3B. Exposure-selection diagnostics and truncation cut points

Table S3C. Three-chain imputation diagnostics

Table S3D. Methods addressing missingness and selection

Table S4. Standardized absolute risks, data support, and model diagnostics

Table S4A. Standardized ADL risks and risk differences at fixed burden values

Table S4B. Standardized risks from the supporting categorical model

Table S4C. Marginal and conditional data support for fixed burden values

Table S4D. Descriptive discrete-time first-event probabilities

Table S4E. Within-sample observed and fitted proportions from the joint model

Table S5. Sensitivity analyses

Table S6. Component-specific and historical burden analyses

Table S6A. Component models

Table S6B. Historical burden and current-component models

Table S6C. Conditional-variation diagnostics for historical burden

Table S6B includes the continuation table in Additional file 1.

Table S7. Secondary ADL outcomes

Table S8. Exploratory cognition analyses

Table S8A. Exploratory effect modification by baseline cognition

Table S8B. Exploratory longitudinal cognition model

Supplementary Files

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