

Social isolation, loneliness and functional transitions among middle-aged and older adults with cardiometabolic multimorbidity: a multistate Markov analysis of CHARLS

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Article

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Abstract

Background

Isolated or lonely older adults are more likely to become disabled; whether these exposures shape the *direction* of functional change — deterioration versus recovery — in cardiometabolic multimorbidity (CMM) is unknown. We examined how the two exposures relate to functional-state transitions and death in middle-aged and older adults with CMM.

Methods

We studied 1,731 adults aged ≥ 45 with CMM (≥ 2 of hypertension, dyslipidaemia, diabetes, heart disease or stroke) from waves 1–5 (2011–2020) of the China Health and Retirement Longitudinal Study. Isolation was a four-item index (unpartnered, living alone, no weekly child contact, no social activity); loneliness came from the Center for Epidemiologic Studies Depression Scale (CES-D) item. Crossed, they defined four groups (G1 low isolation/no loneliness, G2 loneliness only, G3 isolation only, G4 both). Multistate Markov models estimated associations with nine transitions among independence, instrumental activities of daily living (IADL) limitation, activities of daily living (ADL) limitation and death.

Results

Over 9 years, 286 participants (16.5%) died. Loneliness was linked to deterioration onset (G2 vs G1: independence→IADL limitation hazard ratio [HR] 2.83, 95% confidence interval [CI] 1.09–7.31; independence→ADL limitation 2.01, 1.28–3.15). Dual exposure carried a distinct signature: faster early deterioration (1→2 HR 2.66, 1.62–4.37), 66% lower recovery from ADL limitation (3→1 0.34, 0.17–0.70) and higher post-disability mortality (3→4 1.57, 1.04–2.39). Expected years independent between ages 60–90 were 4.83 (G1) versus 0.65 (G4): a 4.18-year gap.

Conclusions

In CMM, loneliness acted mainly at deterioration onset; dual exposure was marked by lost recovery and excess post-disability mortality. Social connection may be a modifiable target for preserving function across CMM trajectories.

Background

Cardiometabolic multimorbidity (CMM) — hypertension, dyslipidaemia, diabetes, heart disease and stroke occurring together — becomes increasingly common as populations age, and its risks exceed the sum of its components, accelerated functional decline among them [1–4]. For older adults with CMM, losing the ability to manage daily activities is where disease burden turns into lost independence, care

dependency and death [5–7]. Functional trajectories are not one-way, though: people deteriorate, but they also recover, and death can follow any functional state. Whether the drivers of deterioration differ from the drivers of recovery matters directly for intervention – preventing disability and reversing it are not the same task.

Social isolation – a structural deficit in social contacts – and loneliness, its subjective counterpart, are common among older adults with chronic disease, and both have been linked to mortality, incident cardiovascular disease and cognitive decline [8–13]. Evidence connecting these social exposures to functional disability has begun to accumulate: a recent whole-population analysis of Chinese older adults reported associations of isolation and loneliness with functional decline [14–16]. What the literature leaves open is where, exactly, the harm acts. Disability is usually treated as a single static endpoint, so it remains unclear whether social exposures hasten deterioration onset, block recovery, or shorten survival once disability is present – distinctions that imply different interventions. Adults with CMM, who carry the highest disability risk and the greatest care burden, have rarely been studied as a population in their own right, although the cardiovascular–psychoneurological literature suggests their vulnerability to social stressors may be amplified [17–19]. And life-expectancy summaries that integrate deterioration, recovery and death – arguably the quantities most legible to clinicians and patients – are largely absent.

Here we fitted multistate Markov models to five waves of the China Health and Retirement Longitudinal Study (CHARLS) [20], asking how social isolation and loneliness, alone and in combination, relate to transitions among functional independence, limitation in instrumental activities of daily living (IADL), limitation in activities of daily living (ADL) and death in adults with CMM. We summarised the models as state occupancy – the expected years spent in each state between ages 60 and 90 – and tested whether the associations differed from those in adults without CMM.

Methods

Study population

CHARLS is a nationally representative longitudinal survey of Chinese adults aged ≥ 45 years that has re-interviewed participants every 2–4 years since 2011 (waves 2011, 2013, 2015, 2018, 2020); response and follow-up rates are reported elsewhere [20]. All participants gave written informed consent, and the study was approved by the Biomedical Ethics Review Committee of Peking University (IRB00001052-11015). Our secondary analysis used de-identified public data.

Of the 17,596 wave-1 participants, 16,831 were aged ≥ 45 years at baseline, and 2,177 met the CMM definition (≥ 2 of five self-reported, physician-diagnosed cardiometabolic diseases: hypertension, dyslipidaemia, diabetes, heart disease and stroke). Excluding an incomplete isolation index ($n = 414$) or a missing loneliness item ($n = 32$) left an analytic sample of 1,731 (Table S1 and Figure S1), contributing 7,319 person-wave observations; 7,210 (98.5%) with complete covariates entered model fitting.

Functional states and death

At each wave we defined functional status from six ADL (dressing, bathing, eating, getting in or out of bed, toileting, continence) and five IADL (household chores, cooking, shopping, managing money, taking medications), each scored for difficulty [21, 22]. Four states follow: State 1, functionally independent (no ADL or IADL limitation); State 2, IADL disability (any IADL limitation without ADL limitation); State 3, ADL disability (any ADL limitation); and State 4, death, the absorbing state. Nine transitions between consecutive waves were possible: deterioration and recovery between the three living states ($1 \leftrightarrow 2$, $1 \leftrightarrow 3$, $2 \leftrightarrow 3$), and death from any of them ($1 \rightarrow 4$, $2 \rightarrow 4$, $3 \rightarrow 4$). Vital status and date of death came from exit interviews; for the 231 of 286 decedents (80.8%) whose death fell between waves, we imputed the death date at the interval midpoint, the standard handling of interval-censored mortality [23, 24].

Social isolation and loneliness

Following an established approach [25], we measured social isolation at baseline with a four-item index: (i) unpartnered (never married, divorced or widowed); (ii) living alone; (iii) contact with any child less than weekly, in person or by phone (from the child-contact module); and (iv) no participation in social activities. Each item scored 1, giving a 0–4 sum. Because the sample median was 0, we defined high isolation as a score of ≥ 1 ; the stricter ≥ 2 cut-point, examined in sensitivity analyses, yielded too few participants for stable transition estimation. Loneliness came from the 10-item Center for Epidemiologic Studies Depression Scale (CES-D-10) item “I felt lonely” (dc017); participants answering “some of the time (3–4 days)” or more were classed as lonely [14, 26–28]. Crossing isolation (low/high) with loneliness (no/yes) gave four groups: G1 (low isolation, no loneliness; $n = 584$), G2 (loneliness only; $n = 220$), G3 (isolation only; $n = 599$) and G4 (dual exposure; $n = 328$).

Covariates

Baseline covariates were sex, education (low: primary or below; middle; high: senior secondary or above), urban/rural residence, a non-cardiometabolic comorbidity count (0/1/ ≥ 2 of nine self-reported conditions: cancer, chronic lung disease, liver disease, kidney disease, digestive disease, psychiatric or emotional problems, memory-related disease, arthritis, asthma), smoking (never/former/current) and alcohol use (never/former/current). We deliberately did not adjust for depressive symptoms in the main model: the loneliness item is itself a CES-D-10 component, and adjusting for a score that contains the exposure would induce overadjustment. A sensitivity analysis instead adjusted for the CES-D-9 score with the loneliness item removed. Age was modelled as the time scale rather than a covariate because of quasi-complete separation (zero $2 \rightarrow 4$ events among participants aged 45–54 at baseline); residual age confounding was assessed in age-stratified sensitivity analyses (< 65 vs ≥ 65 years).

Statistical analysis

We fitted continuous-time multistate Markov models with constant (homogeneous) transition intensities on the exact-age time scale, using the *msm* package (version 1.8.2) [24] in R 4.5.1. All nine transitions were allowed in both the deterioration and recovery directions. Covariate effects are expressed as transition-specific hazard ratios (HRs) with 95% Wald confidence intervals (CIs) from model Hessian-based standard errors; coefficients that could not be estimated (sparse transitions) are reported as not estimable (NE). From each fitted model we obtained 2- and 5-year transition probabilities from State 1 for a reference covariate profile (female, low education, rural residence, no other comorbidity, never-smoker, never-drinker), together with the expected years spent in each state between ages 60 and 90 starting from independence. The overall exposure effect was tested by a likelihood ratio test (LRT) against a model without the four-group exposure.

Nine transitions $\times$ three exposure contrasts yielded 27 hazard ratios. We made no adjustment for multiple comparisons, so the results should be read as exploratory; the omnibus LRT serves as the global test, controlling the type I error for the global null hypothesis of no exposure effect.

Sensitivity analyses (Supplementary Materials) covered an isolation cut-point of ≥ 2 (S1); follow-up truncated at 2018 (S2); adjustment for CES-D-9 excluding the loneliness item (S3); a cardiovascular disease (CVD)-inclusive CMM definition (heart disease or stroke plus ≥ 2 diseases, $n = 1,089$; S4); ADL disability defined as ≥ 2 limitations (S5); baseline age strata (S6, < 65 $n = 1,190$; ≥ 65 $n = 541$); and exclusion of psychiatric and memory-related diseases from the comorbidity count as potential mediators (S7). Effect modification by CMM status was tested on the full CHARLS sample ($n = 13,143$) through LRTs of exposure $\times$ CMM interaction terms. Model selection records — piecewise-constant and age-covariate specifications that failed numerical or identifiability criteria — are documented in the Supplementary Materials.

Analyses used complete cases; covariate missingness was $< 2\%$. Reporting followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist [29].

Results

Sample characteristics

The 1,731 participants had a mean baseline age of 60.8 years, and 53.0% were women (Table 1). Baseline function already differed markedly across the groups: 72.1% of G1 were functionally independent, compared with 52.3% (G2), 61.8% (G3) and 44.5% (G4), and ADL disability at baseline ranged from 17.8% (G1) to 41.8% (G4) ($\chi^2=87.7$, $P < 0.001$). Depressive symptoms (CES-D-10 ≥ 10) were most prevalent in the lonely groups (G2 75.5%, G4 83.5% vs G1 22.4%).

Over a maximum of 9 years of follow-up, 286 participants (16.5%) died. Between consecutive waves we observed 299 independence $\rightarrow$ IADL and 564 independence $\rightarrow$ ADL deteriorations, alongside 653 recoveries (Fig. 1, Figures S2 and S3).

Transition-specific associations

The four-group exposure was strongly associated with transition intensities: the exposure model was clearly favoured over the no-exposure model by the likelihood ratio test ($\chi^2=97.56$, 27 df, $P = 6.5 \times 10^{-10}$) and by the Akaike information criterion (AIC; $\Delta\text{AIC} = -43.6$, Table S2). Table 2 and Fig. 2 give the transition-specific HRs.

Loneliness was associated with the onset of deterioration. Among participants with low isolation, loneliness (G2 vs G1) more than doubled the rates of both independence→IADL limitation (1→2 HR 2.83, 95% CI 1.09–7.31) and independence→ADL limitation (1→3 HR 2.01, 1.28–3.15). Isolation without loneliness (G3) was associated with the 1→3 transition (HR 1.85, 1.32–2.62) but not with 1→2 (1.25, 0.85–1.84).

Dual exposure (G4) showed a distinct signature: faster early deterioration (1→2 HR 2.66, 1.62–4.37), a two-thirds reduction in recovery from ADL limitation to independence (3→1 HR 0.34, 0.17–0.70) and higher mortality once ADL-limited (3→4 HR 1.57, 1.04–2.39). Direct 1→3 progression was not elevated (1.11, 0.59–2.09) despite a twofold higher crude rate in G4 (103/435 vs 160/1,312 person-wave observations in State 1): over half of G4 (55.5%) were already disabled at baseline, leaving a smaller, positively selected at-risk set, and covariate adjustment absorbed the crude excess (Supplementary Materials). Death transitions from independence and IADL limitation were sparse and non-estimable for G2 and G4. Female sex was associated with lower 3→4 mortality (HR 0.50, 0.25–0.97) and urban residence with higher (1.43, 1.02–2.00); a non-cardiometabolic comorbidity count of ≥ 2 was associated with higher 1→3 (1.90, 1.34–2.69) and, among ADL-disabled participants, lower 3→4 (0.61, 0.41–0.90) (Table S3).

Transition probabilities and state occupancy

For the reference profile starting independent, model-based 5-year probabilities of death were 5.0% (G1), 7.5% (G2), 5.7% (G3) and 8.6% (G4); the probabilities of remaining independent were 60.8%, 46.2%, 50.8% and 40.1% respectively (Table S4, Figure S4).

Figure 3 shows the expected years in each state between ages 60 and 90 (Table S5). Expected years independent were 4.83 (G1), 2.04 (G2), 3.89 (G3) and 0.65 (G4) – a G4 – G1 difference of –4.18 years, an 87% reduction – while expected years dead by age 90 were 21.5, 25.4, 22.0 and 28.1. Of the expected surviving years, the proportion spent independent was 56.9% (G1) versus 33.8% (G4).

Sensitivity analyses and effect modification

The findings replicated in the two sensitivity analyses with full estimator precision: with the CVD-inclusive CMM definition (S4), the G4 1→2 HR was 1.95 (1.00–3.79) and the 3→1 HR was 0.40 (0.19–0.84); in participants aged < 65 (S6), the G4 1→2 HR was 3.10 (1.57–6.15) and the 3→1 HR was 0.04 (0.00–0.71). Adjusting for CES-D-9 without the loneliness item (S3) left the associations materially unchanged (G4 1→2 1.82, 3→1 0.39), as did excluding psychiatric and memory-related diseases from

the comorbidity count (S7: G4 1→2 2.67, 1.64–4.35; 3→1 0.34, 0.17–0.68), although G4 3→4 became borderline (1.48, 0.96–2.28). The other analyses (S1, S2, S5, age ≥ 65 stratum) were directionally consistent but yielded point estimates only, because sparse transition cells precluded variance estimation (Table S6, Figure S5).

On the full sample (n = 13,143), the exposure×CMM interaction was not significant (LRT $\chi^2=27.61$, 27 df, P = 0.43): associations were directionally consistent in adults without CMM (e.g., G4 1→2 HR 1.86) but with smaller point estimates than in the CMM stratum. We therefore found no evidence that the associations are CMM-specific, which supports generalisability (Table S7).

Discussion

Principal findings. In this multistate analysis of Chinese middle-aged and older adults with CMM, the two social exposures had dissociable signatures on functional dynamics. Loneliness — largely independent of structural isolation — was associated with the onset of deterioration, doubling the rates of both independence→IADL and independence→ADL transitions; structural isolation without loneliness shared the 1→3 association. The most distinctive profile belonged to dual exposure, and it was not simply an amplified version of either exposure alone: G4 was marked by faster early deterioration, a two-thirds lower recovery rate from ADL limitation, and excess mortality once ADL-disabled. Integrated over ages 60–90, these dynamics compounded into a 4.2-year shortfall in expected independent years.

Comparison with previous work. Most of the literature has modelled disability as a static or monotone endpoint; separating deterioration from recovery extends it. The recovery finding (3→1 HR 0.34) is, to our knowledge, among the first demonstrations that social disconnection is associated not only with becoming disabled but with failing to regain independence — a pathway invisible to standard incident-disability analyses. The post-disability mortality association (3→4 HR 1.57) accords with meta-analytic evidence linking isolation and loneliness to mortality [8–10], and with reports of amplified social-risk effects in cardiovascular populations [30]. The recent whole-population CHARLS analysis reported associations of isolation and loneliness with functional decline [14–16]; our CMM-restricted analysis adds transition-level resolution, recovery pathways, life-expectancy summaries and effect-modification testing.

The non-monotonic pattern for direct independence→ADL progression — elevated in G2 and G3 but not G4 — deserves comment. G4's susceptibility to severe limitation was already expressed at baseline (41.8% ADL-disabled vs 17.8% in G1), leaving a positively selected at-risk set, and the crude twofold excess in 1→3 rates was absorbed by measured covariates. That the pattern held across sensitivity analyses suggests a genuine absence of association rather than noise, and it cautions against interpreting group HRs for a transition without examining the baseline state distribution.

Mechanisms and implications. Several pathways could link social disconnection to these transitions: reduced health-protective behaviours and adherence [31], blunted rehabilitation engagement, chronic hypothalamic–pituitary–adrenal and inflammatory activation [32, 33], and accelerated cardiometabolic

and cognitive deterioration. Two implications follow for clinicians managing CMM. Because loneliness was associated with deterioration even at low structural isolation, asking about loneliness — not merely about living arrangements — may surface risk that structural measures miss. The recovery deficit, in turn, suggests that social support belongs in cardiac and geriatric rehabilitation: interventions that pair functional rehabilitation with social components [30, 31, 34], such as group-based or community-linked programmes, could plausibly modify recovery, although this requires trial evidence. At the population level, a 4.2-year difference in expected independent years between G1 and G4 is of an order that would materially affect care needs in ageing societies with rising CMM prevalence.

Strengths and limitations. Strengths include a nationally representative cohort with five waves, bidirectional transition modelling, an exact-age time scale, and life-expectancy summaries that integrate deterioration, recovery and death. Several limitations qualify the findings. Exposure was measured once at baseline; within-person changes are unmodelled, and associations may partly reflect reverse causation (subclinical decline causing withdrawal), although the recovery-specific associations are hard to explain by prodromal disability alone. Functional status and diseases were self-reported. Death dates were imputed for 80.8% of decedents; mid-point imputation is standard in cohort studies with interval-censored mortality, but the resulting transition times may be subject to non-differential misclassification. Homogeneous intensities over the exact-age scale, though conventional, are an approximation, and piecewise-constant alternatives were numerically unstable at this sample size. Baseline age could not enter as a covariate (quasi-complete separation) and was instead handled through the time scale and age-stratified sensitivity analyses. The 2020 wave coincided with the COVID-19 pandemic, which may have affected functional assessments and mortality ascertainment; because exposure was measured in 2011, any misclassification is likely non-differential. Finally, with 27 exploratory HRs, individual findings should be interpreted against the omnibus test.

Conclusions

Among middle-aged and older adults with cardiometabolic multimorbidity, loneliness is associated with the onset of functional deterioration, while dual isolation–loneliness exposure is marked by lost recovery and excess post-disability mortality — dynamics that compound into substantially fewer expected years of independence. Social connection is a potentially modifiable target across the functional trajectory of CMM, not only to prevent deterioration but to support recovery.

Declarations

Ethics approval and consent to participate

The China Health and Retirement Longitudinal Study (CHARLS) was approved by the Biomedical Ethics Review Committee of Peking University (IRB00001052-11015), and all participants provided written informed consent. The present secondary analysis used de-identified, publicly available CHARLS data and did not require separate ethical approval.

Consent for publication

Not applicable. No individual person's data appear in any form in this manuscript.

Competing interests

The authors declare that they have no competing interests.

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Author Contribution

J.S. contributed to data curation, formal analysis, visualisation, and writing of the original draft. Z.X. contributed to data curation, validation, and critical revision of the manuscript. A.C. contributed to conceptualisation, methodology, supervision, project administration, and critical revision of the manuscript. All authors read and approved the final manuscript.

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Data Availability

The CHARLS data are publicly available to registered researchers from the official CHARLS website (<http://charls.pku.edu.cn/>).

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Tables

Table 1

Baseline characteristics of 1,731 adults with cardiometabolic multimorbidity, by social isolation and loneliness group (CHARLS 2011)

Characteristic	G1 (n = 584)	G2 (n = 220)	G3 (n = 599)	G4 (n = 328)
Age, years, mean (SD)	60.0 (9.0)	60.6 (8.0)	60.9 (8.9)	62.1 (8.5)
Female	281 (48.1)	132 (60.0)	303 (50.6)	201 (61.3)
Education low ($\leq$ primary)	454 (77.7)	194 (88.2)	519 (86.6)	292 (89.0)
Urban residence	360 (61.6)	104 (47.3)	324 (54.1)	138 (42.1)
No. of cardiometabolic diseases	2.4 (0.6)	2.4 (0.6)	2.3 (0.6)	2.4 (0.6)
Non-CM comorbidity ≥ 1	324 (55.5)	151 (68.6)	363 (60.6)	225 (68.6)
Current smoker	131 (22.4)	56 (25.5)	133 (22.2)	68 (20.7)
Current drinker	172 (29.5)	58 (26.4)	148 (24.7)	61 (18.6)
Depressive symptoms (CES-D-10 ≥ 10)	131 (22.4)	166 (75.5)	198 (33.1)	274 (83.5)
Baseline functional state				
Independent	421 (72.1)	115 (52.3)	370 (61.8)	146 (44.5)
IADL-limited	59 (10.1)	30 (13.6)	89 (14.9)	45 (13.7)
ADL-limited	104 (17.8)	75 (34.1)	140 (23.4)	137 (41.8)

Values are n (%) unless stated otherwise. G1 = low isolation, no loneliness (reference); G2 = loneliness only; G3 = isolation only; G4 = dual exposure. CMM = ≥ 2 of hypertension, dyslipidaemia, diabetes, heart

disease and stroke. Depressive symptoms are shown for description only and were not model covariates. Baseline state distribution differed across groups ($\chi^2 = 87.7$, 6 df, $P < 0.001$). Overall, 286 participants (16.5%) died during follow-up.

Table 2

Adjusted hazard ratios (95% CI) for each functional transition, by exposure group versus G1 (multistate Markov model, $n = 1,731$)

Transition	G2 (loneliness only)	G3 (isolation only)	G4 (dual exposure)
1→2 Independent → IADL-limited	2.83 (1.09–7.31)*	1.25 (0.85–1.84)	2.66 (1.62–4.37)*
1→3 Independent → ADL-limited	2.01 (1.28–3.15)*	1.85 (1.32–2.62)*	1.11 (0.59–2.09)
1→4 Independent → Death	0.70 (0.07–6.82)	1.01 (0.20–5.20)	NE
2→1 IADL-limited → Independent	2.28 (0.84–6.17)	1.16 (0.74–1.80)	1.30 (0.75–2.28)
2→3 IADL-limited → ADL-limited	0.65 (0.26–1.60)	0.77 (0.44–1.36)	1.55 (0.91–2.64)
2→4 IADL-limited → Death	3.76 (0.50–28.23)	0.40 (0.04–3.89)	NE
3→1 ADL-limited → Independent	0.63 (0.29–1.36)	0.99 (0.65–1.51)	0.34 (0.17–0.70)*
3→2 ADL-limited → IADL-limited	1.40 (0.67–2.90)	1.28 (0.73–2.23)	1.32 (0.70–2.48)
3→4 ADL-limited → Death	1.25 (0.71–2.20)	0.88 (0.50–1.57)	1.57 (1.04–2.39)*

Hazard ratios (95% CI) versus G1 (low isolation, no loneliness), adjusted for sex, education, urban/rural residence, non-cardiometabolic comorbidity count, smoking and alcohol use; age is the model time scale. * $P < 0.05$ (Wald test). NE = not estimable (sparse transitions). Omnibus likelihood ratio test: $\chi^2 = 97.56$, 27 df, $P = 6.5 \times 10^{-10}$.

Figures

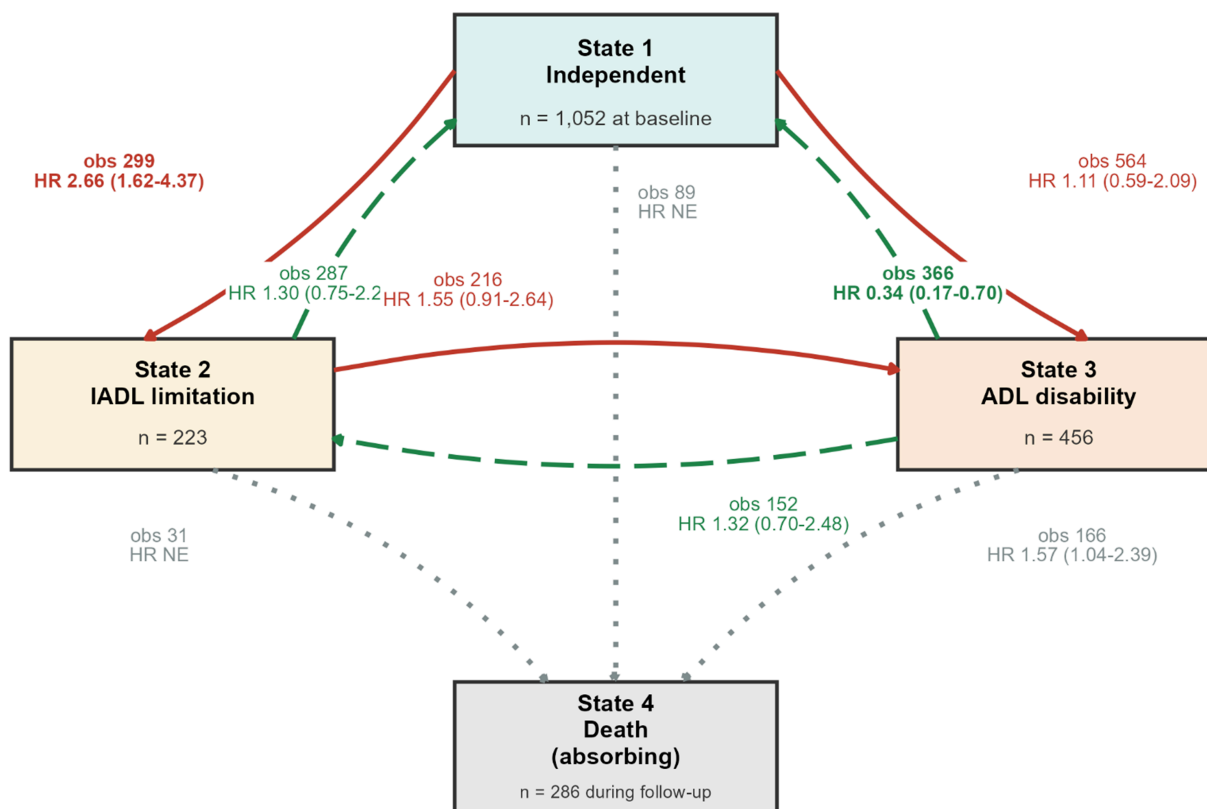


Figure 1

State space, observed transition counts and adjusted hazard ratios for G4 versus G1

Multistate model diagram with baseline state occupancy (2011) and observed transition counts between consecutive waves (n=1,731). Hazard ratios (95% CI) are for G4 (high isolation + loneliness) versus G1 (low isolation, no loneliness), adjusted for sex, education, residence, non-cardiometabolic comorbidity, smoking and alcohol use. Red arrows = deterioration transitions; green = recovery; grey = death. NE = not estimable (sparse transitions).

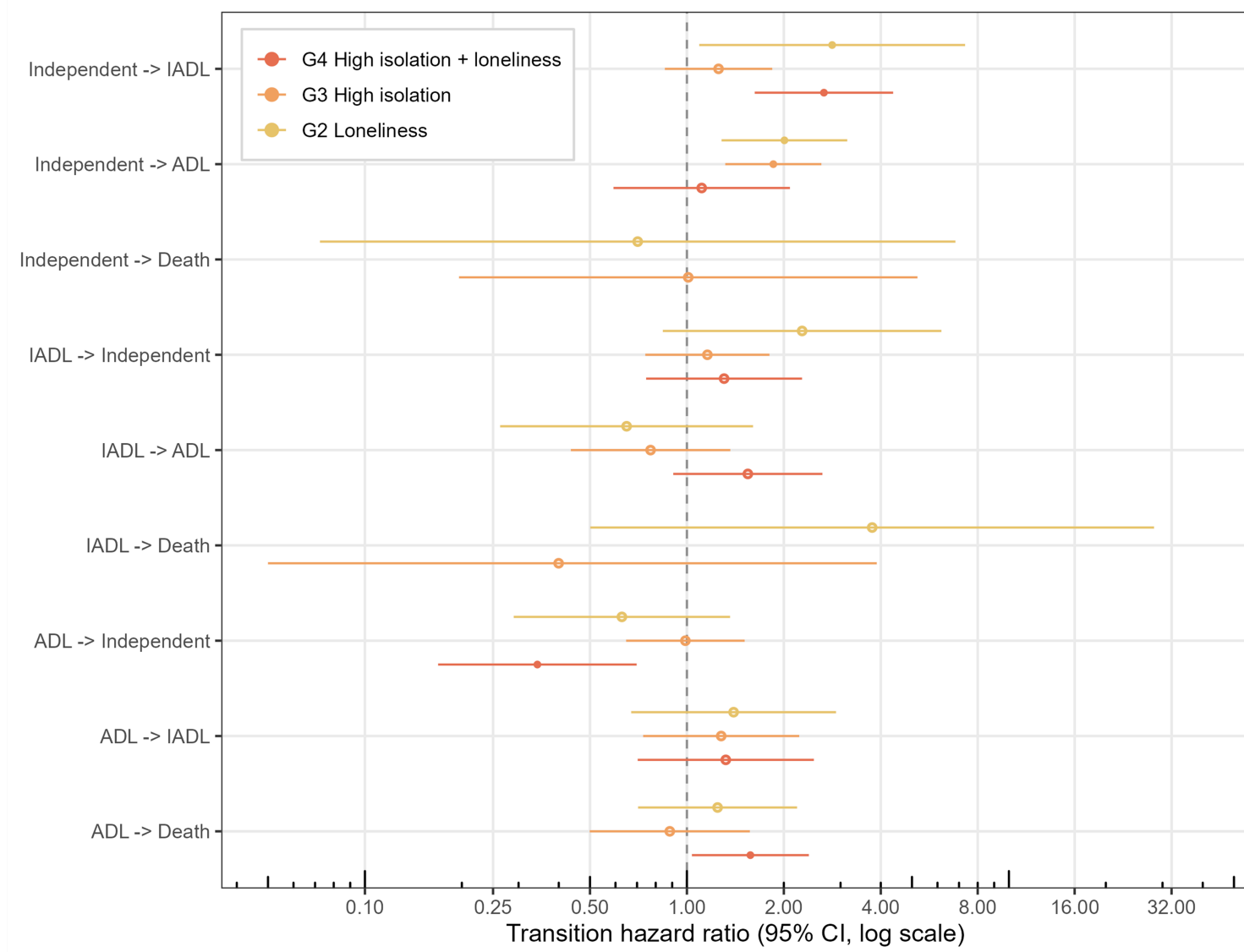


Figure 2

Transition-specific hazard ratios by exposure group

Adjusted hazard ratios (95% CI) for each functional transition by exposure group versus G1 (reference). Red = G4 (dual exposure); orange = G3 (isolation only); yellow = G2 (loneliness only). The vertical dashed line marks the null (HR=1). NE = not estimable (sparse transitions, not shown).

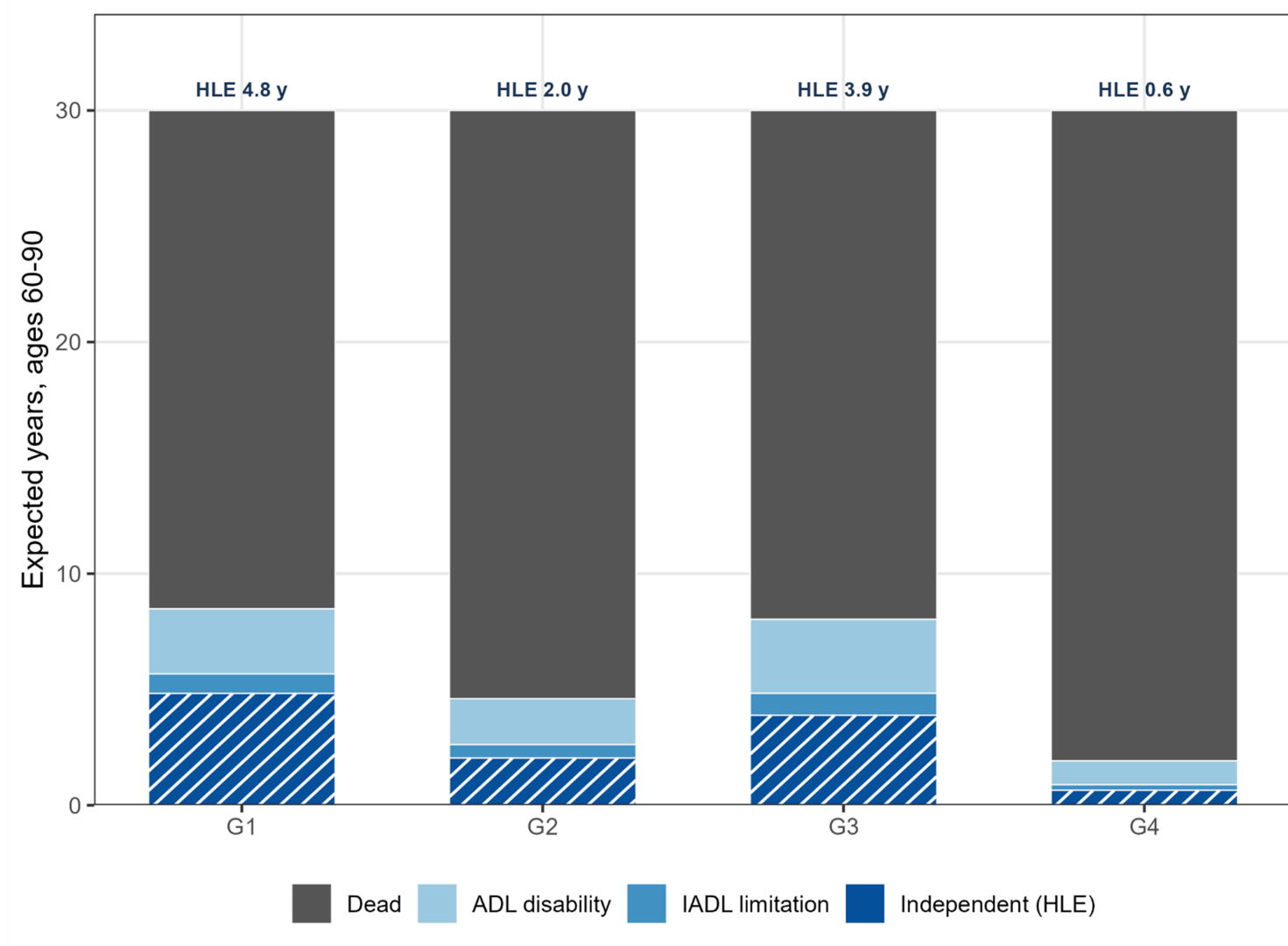


Figure 3

Expected years in each functional state between ages 60 and 90 by exposure group

Expected years spent in each state between ages 60 and 90 by exposure group, starting from independence (fixed-window occupancy, not life expectancy at birth). HLE = healthy life expectancy (years in state 1). The reference covariate profile is female, low education, rural residence, no non-cardiometabolic comorbidity, never-smoker, never-drinker.

Supplementary Files

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