Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Loneliness and objective social isolation in observed depressive symptom transitions across six ageing cohorts

Lin Guo
Shandong Second Medical University
Jianing Yue
Shandong Second Medical University
Shanna Li
841551922@qq.com

Shandong Second Medical University
Ying Liu
Zhejiang Chinese Medical University

Research Article

Keywords: loneliness, social isolation, depressive symptoms, observed transitions, ageing cohorts, longitudinal analysis

Posted Date: November 3rd, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11280260/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Abstract

Background

Loneliness and objective social isolation may have different associations with changes in depressive symptoms. We examined transitions into and out of elevated symptom states across six ageing cohorts.

Methods

Adults aged 50–110 years in CHARLS, ELSA, HRS, KLoSA, MHAS and SHARE contributed 276,045 intervals between consecutive eligible observations. Cohort models related starting loneliness and a three component isolation index to subsequent symptom state using a complementary log-log link, nominal interval offset and participant clustered standard errors. Exponentiated coefficients were pooled using random effects meta-analysis and interpreted as cloglog association ratios (CARs), not observed recovery speeds.

Results

Per one cohort standard deviation higher loneliness, pooled CARs were 1.43 (1.27–1.61) for onset and 0.82 (0.78–0.85) for recovery. Corresponding isolation estimates were 1.03 (0.98–1.08) and 0.98 (0.93–1.02) per component. After correcting an overlapping-item score and adjusting for baseline symptom severity in four cohorts, the loneliness recovery CAR was 0.87 (0.83–0.91), with substantial heterogeneity and a prediction interval crossing 1 (0.69–1.10). Restricted-wave analyses were directionally similar.

Contributions to the literature

Loneliness predicts both the onset of depressive symptoms and reduced recovery in later life across six ageing cohorts.

Most depression studies focus only on onset; this study shows that loneliness also matters after symptoms emerge.

Screening for loneliness in older adults may be relevant not only for prevention but also during follow-up care.

Structural isolation measures alone may not capture the social experiences most relevant to mental health across different countries.

1 Background

Population ageing is increasing the number of people who must navigate later life while managing losses in health, roles, mobility, and social networks. Depressive symptoms remain common in later life, while loneliness and social isolation are now recognized as consequential dimensions of social health (Christl et al., 2025; World Health Organization, 2025, 2026). The social-connection literature, however, has long warned against treating objective network structure and subjective isolation as interchangeable. Social isolation describes a structural condition of sparse relationships or infrequent contact, whereas loneliness describes the distressing perception that one's relationships do not meet desired levels of connection (Berkman et al., 2000; Hughes et al., 2004; Cornwell and Waite, 2009; National Academies of Sciences, Engineering, and Medicine, 2020). Both have been studied in relation to mortality (Steptoe et al., 2013b; Holt-Lunstad et al., 2015), and loneliness has also been associated with functional decline (Perissinotto et al., 2012), but their implications for affective illness may differ because depressive states are shaped not only by the availability of social ties but also by how those ties are perceived and appraised.

Loneliness has repeatedly been linked to depressive symptoms. Longitudinal work identified loneliness as a prospective correlate of later depressive symptoms (Cacioppo et al., 2006), and a systematic review supports a longitudinal association (Van As et al., 2022), while a quantitative synthesis reports reciprocal associations over time (Chen et al., 2023). Recent work has broadened this question to cross-national ageing cohorts: social isolation has been associated with incident depression in England and Japan (Noguchi et al., 2021), observational social-isolation associations have been examined alongside genetic analyses of a combined loneliness/social-isolation phenotype (Zhu et al., 2024), and a five-cohort study across 24 countries found that loneliness and social inactivity contributed to socioeconomic differences in incident depressive symptoms (Wang et al., 2024). Yet three gaps remain. First, many studies isolate incident depression by excluding participants who are already symptomatic, which makes the determinants of recovery invisible. Second, loneliness and objective isolation are often considered separately or combined into broad social-risk scores, limiting direct comparison of their independent associations. Third, between-country heterogeneity is frequently treated as a nuisance rather than a substantive feature of social-health effects.

Recovery is particularly relevant in later life because depressive symptoms are dynamic rather than a one-way event. Clinical and population studies show marked heterogeneity in persistence, remission, relapse, and long-term trajectories (Holvast et al., 2015; Johnco et al., 2024; Qiu and Zhu, 2026; Harber-Aschan et al., 2026). Holvast et al. reported that loneliness predicted a poorer prognosis among older adults with depression, suggesting that loneliness may matter not only before depression emerges but also after a depressive state is established. This distinction is conceptually important: factors associated with entering a symptomatic state need not be identical to factors associated with leaving it. A transition framework can therefore reveal whether social disconnection primarily operates as a marker of vulnerability to onset, persistence after onset, or both.

We compared loneliness and a common objective-isolation index in six ageing cohorts spanning China, England, the United States, South Korea, Mexico and multiple European countries. We examined two

conditional outcomes: being above the symptom threshold at the next eligible observation among those initially below it, and being below the threshold among those initially above it. These observed transitions, termed onset and recovery, are not first lifetime episodes or clinical remission. Cohort-specific analyses and random-effects synthesis allowed us to examine the consistency of associations without assuming identical measurement or populations. We also assessed the consequences of skipped waves, baseline symptom severity, overlapping loneliness items, alternative links and uncertainty from pooling few cohorts.

2 Methods

2.1 Study design and data sources

We conducted a harmonized longitudinal analysis of six ageing studies: the China Health and Retirement Longitudinal Study (CHARLS), English Longitudinal Study of Ageing (ELSA), U.S. Health and Retirement Study (HRS), Korean Longitudinal Study of Aging (KLoSA), Mexican Health and Aging Study (MHAS), and Survey of Health, Ageing and Retirement in Europe (SHARE). These studies were designed to collect repeated, multidisciplinary information on health, socioeconomic circumstances, family relationships, and functioning in middle-aged and older adults and have been described in published cohort descriptions (Zhao et al., 2014; Steptoe et al., 2013a; Sonnega et al., 2014; Lee, 2020; Wong et al., 2017; Börsch-Supan et al., 2013). We used waves in which depressive symptoms, loneliness, and the common components of objective social isolation overlapped: CHARLS 2011–2020, ELSA 2010–2018, HRS 2008–2020, KLoSA 2010–2020, MHAS 2012–2018, and SHARE 2011–2020. Measurement definitions and windows are summarized in Supplementary Table S1. Reporting was assessed against STROBE (von Elm et al., 2007).

The harmonized dataset contained 843,416 person-wave records. Records were eligible when they fell within the prespecified longitudinal age 50–110 windows and had observed depressive state, loneliness and objective isolation. This yielded 469,835 eligible records from 193,790 people; 127,408 people contributed 276,045 intervals between consecutive eligible observations with a positive nominal gap of at most 12 years (Fig. 1; Supplementary Table S2). The remaining 66,382 people contributed no eligible interval. Both endpoints had to satisfy exposure and outcome eligibility, although only interval-start exposures and covariates entered the models. This requirement can select a different sample from one requiring only follow-up outcome availability. Analyses therefore describe the eligible observed sample rather than nationally representative populations.

2.2 Depressive symptom states and observed transitions

Depressive symptoms were harmonized using established short-form scales appropriate to each cohort. CHARLS and KLoSA used 10-item CES-D scores with a primary threshold of 10 or higher; ELSA and HRS used 8-item CES-D scores with a threshold of 4 or higher; MHAS used the 9-item CES-D with a threshold of 5 or higher; and SHARE used the 12-item EURO-D with a threshold of 4 or higher. These instruments

and short forms have established use in older populations (Andresen et al., 1994; Turvey et al., 1999; Prince et al., 1999; Aguilar-Navarro et al., 2007), and comparable harmonization has been used in recent cross-national ageing research (Wang et al., 2024). We use the term 'depressed symptom state' rather than clinical major depressive disorder because scale thresholds do not establish a diagnostic interview diagnosis.

Within each participant, eligible records were ordered by nominal wave year. Consecutive eligible records could skip scheduled waves when intervening data were unavailable. We classified four endpoint combinations: below→below, below→elevated (onset), elevated→elevated and elevated→below (recovery). Separate models conditioned on the starting state; people could contribute multiple intervals and both types of transition. Repeated elevated endpoints do not establish uninterrupted symptoms, and repeated below-threshold endpoints do not establish freedom from intervening episodes. The exact timing, number and duration of episodes between interviews were not observed.

2.3 Loneliness and objective social isolation

ELSA, HRS and SHARE used three-item loneliness means on a 1–3 scale; CHARLS and KLoSA used a 1–4 loneliness item, and MHAS used a binary item. Short loneliness measures are designed for population surveys (Hughes et al., 2004), but response formats and administration modes differ. Within each cohort, loneliness was standardized as the raw score minus the cohort mean divided by the cohort sample standard deviation across all nonmissing records in the harmonized dataset, including records outside the primary age or wave restrictions. A one-SD estimate therefore refers to that cohort reference distribution rather than a common clinical unit. High loneliness was defined as raw score ≥ 3 in CHARLS/KLoSA, ≥ 2 in ELSA/HRS/SHARE, and 1 in MHAS (Supplementary Table S1).

The objective-isolation index summed being unpartnered, living alone and reporting no social participation (range 0–3); high isolation was defined as ≥ 2 components. The index captures a shared structural core rather than all relevant contact, support or relationship-quality dimensions (Cornwell and Waite, 2009; National Academies of Sciences, Engineering, and Medicine, 2020). Components were equally weighted, although living alone and partnership status may overlap. Joint phenotypes were neither, high loneliness only, high isolation only and both. Exposure units and measurement reliability differ, so coefficient magnitudes cannot rank the clinical importance of the two constructs.

2.4 Covariates and missing data

All covariates were measured at the interval start. The demographic model included age per 10 years, sex, three-category education and wave indicators. Primary models added current work, multimorbidity, ADL limitation and categorical self-rated health. Expanded models added wealth rank within cohort and wave, smoking, alcohol use and cognition standardized within cohort across available transition-start records. Loneliness and objective isolation entered these models simultaneously. Adjustment defines conditional associations; health and social variables need not be exclusively confounders and may also reflect mediating or reverse pathways.

Models used complete cases for their own covariate sets, without imputation or survey weighting. Model-specific participants, intervals and events and per-variable missingness are reported in Supplementary Tables S10 and S11. To distinguish added covariates from changing samples, expanded and baseline-severity analyses were compared with primary models fitted to the same records. Available survey weights were not used in the present analyses. Loss of observation and death were not jointly modelled, and cause-specific attrition could not be reconstructed from this harmonized dataset.

2.5 Statistical models and estimand

We fitted a binomial generalized linear model with a complementary log-log link separately by cohort and starting state, including log nominal interval duration as an offset and participant-clustered sandwich standard errors. This link has a grouped-event survival interpretation under appropriate assumptions (Prentice and Gloeckler, 1978; Singer and Willett, 1993). Here the outcome is a reversible state observed at interview endpoints, so an instantaneous event hazard is not identified from this regression. We report exponentiated coefficients as cloglog association ratios (CARs).

$$\log[-\log(1-p_{ijt})] = \alpha_{jt} + \beta_{Lj} L_{ijt} + \beta_{Sj} S_{ijt} + \gamma_j^T X_{ijt} + \log(\Delta t_{ijt})$$

1

In Eq. (1), p is the probability of the relevant endpoint transition for person i in cohort j at starting wave t; L is standardized loneliness, S the isolation index, X the covariate vector, α the cohort-specific wave intercept and Δt the nominal interval in years. Distinct coefficients are estimated for onset and recovery. At fixed interval duration and covariates, a one-unit exposure contrast multiplies the transformed endpoint probability as follows:

$$\mathrm{CAR} = \exp(\beta_{Lj}) = \frac{-\log\{1-p(L+1)\}}{-\log\{1-p(L)\}}$$

2

Thus CAR > 1 indicates a higher conditional probability of the specified endpoint transition, but its percentage departure from 1 is not a percentage difference in risk or recovery speed. The duration offset imposes a working relationship with nominal observation length; it does not recover unobserved transitions or establish constant hazards. As sensitivity analyses, we restricted records to consecutive scheduled waves and fitted logistic endpoint models with log nominal interval duration entered as a covariate, reporting odds ratios separately. Continuous-time multistate analyses would require explicit assumptions about unobserved paths and additional modelling (Jackson, 2011).

2.6 Meta analysis and sensitivity analyses

Cohort log coefficients were pooled using restricted maximum likelihood (REML) random-effects meta-analysis. Conventional 95% confidence intervals used the normal distribution; I^2 was calculated from Cochran's Q, and prediction intervals used a t quantile with k − 2 degrees of freedom and variance equal

to the estimated between-cohort variance plus the variance of the pooled mean (Higgins et al., 2003; IntHout et al., 2016; Viechtbauer, 2010). The REML objective was checked at zero as well as the numerical optimum. Modified Hartung–Knapp intervals with the variance multiplier bounded below by 1 and k − 1 degrees of freedom assessed uncertainty from small k (Röver et al., 2015). Prediction intervals and I^2 remain imprecise with few heterogeneous cohorts.

Additional analyses covered adjustment sets (Supplementary Table S3), joint phenotypes (S4), baseline severity (S5), measurement type (S6), item-excluded outcomes (S7) and loneliness×isolation interaction (S8). Supplementary Figures S1–S4 display joint phenotypes, adjustment and severity comparisons, leave-one-cohort-out estimates, and observation-gap distributions, respectively. We did not conduct meta-regression with six cohorts. Baseline-severity adjustment used CHARLS/KLoSA scores after subtracting the loneliness item and unchanged SHARE EURO-D scores. For MHAS, the harmonized nine-item total included a binary loneliness item; the eight-item severity score was reconstructed by subtracting that item. We report both the corrected four-cohort sensitivity and a three-cohort analysis excluding MHAS (Supplementary Table S5). Within each comparison, primary and severity models used identical records. Because item-level scoring rules could not be reconstructed for every cohort, these sensitivity analyses were restricted to cohorts with a defensible modified score.

An exploratory outcome analysis used nine-item CHARLS/KLoSA scores after loneliness-item removal, with a working threshold ≥ 9; this rescaled threshold was not treated as an independently validated diagnostic cut-off. SHARE retained EURO-D. Sensitivity analyses addressing observation spacing, alternate link functions, small-k uncertainty and score overlap were exploratory and were not preregistered. No multiplicity correction was applied. All tests were two-sided, with emphasis on estimates and uncertainty.

3 Results

3.1 Study population and observed transitions

Table 1 describes the 127,408 participants contributing at least one eligible interval, at their first eligible observation. It therefore excludes people with only one eligible record. The six cohorts differed in age, symptom prevalence and structural isolation; Supplementary Table S2 reports the corresponding record, person and interval denominators.

Table 1
Characteristics of transition-contributing participants at their first eligible observation

Characteristic	CHARLS	ELSA	HRS	KLoSA	MHAS	SHARE
Participants	18,829	8,123	13,632	8,542	13,050	65,232
Age, years	59.1 (8.3)	65.4 (9.0)	65.0 (9.6)	63.7 (10.4)	63.8 (9.2)	65.1 (9.5)
Female, %	51.3	55.8	60.0	56.8	57.5	56.2
Elevated symptoms, %	35.2	13.2	13.0	28.9	31.4	26.2
Loneliness, raw score	1.5 (0.9)	1.4 (0.5)	1.5 (0.5)	1.5 (0.7)	0.3 (0.5)	1.3 (0.4)
Objective isolation, 0–3	0.6 (0.7)	1.2 (1.0)	1.0 (1.0)	0.6 (0.8)	0.9 (0.8)	1.0 (0.9)
Living alone, %	5.3	23.5	20.4	10.6	6.0	19.8
Partnered, %	88.7	67.0	63.1	79.0	70.8	72.3
Any social participation, %	53.0	33.1	60.8	69.8	42.9	47.3

Values are mean (SD) or percent unless stated. N = 127,408 people with at least one eligible observed interval, before model-specific covariate exclusions. Raw loneliness scales are not directly comparable; see Supplementary Table S1. Percentages use available observations for each variable.

The 276,045 intervals comprised 174,534 below→below pairs, 31,806 onsets, 39,400 elevated→elevated pairs and 30,305 recoveries. Covariate exclusions removed 6,636 intervals; primary models used 269,409 intervals from 125,892 people, with 30,998 onset and 29,572 recovery events. In total, 59,541 eligible intervals (21.6%) skipped at least one scheduled wave. Median nominal gaps were two years in CHARLS, ELSA, KLoSA and SHARE, three years in MHAS and four years in HRS; gaps ranged from two to 12 years overall. HRS had only 46 consecutive scheduled-wave intervals with the required measures. Cohort model estimates and row-conditional endpoint proportions are displayed in Figs. 2 and 3, respectively; the proportions are unweighted descriptions over unequal intervals, not annual risks (Supplementary Tables S2 and S9; Supplementary Figure S4).

3.2 Loneliness and observed transitions

In primary models, higher loneliness was associated with a higher probability of observed onset in all six cohorts (Fig. 2A; Table 2). Cohort CARs ranged from 1.25 (95% CI 1.20–1.29) in CHARLS to 1.81 (1.72–1.90) in ELSA. The pooled CAR was 1.43 (1.27–1.61). Heterogeneity was substantial (I^2=97.7%); the 95% prediction interval crossed 1 (0.92–2.21), cautioning against assuming a uniform magnitude in other populations.

Higher loneliness was also associated with a lower probability of observed recovery in every cohort (Fig. 2B). The pooled CAR was 0.82 (0.78–0.85), with I^2=86.7% and a prediction interval of 0.71–0.94. This direction was consistent across cohorts, although effect magnitudes differed. The outcome refers to being below threshold at the next eligible observation and does not measure time to recovery.

Table 2
Primary-model analysis samples and cohort estimates

Cohort	Transition	People	Intervals	Events	Loneliness CAR (95% CI)	Isolation CAR (95% CI)
CHARLS	Onset	14,511	30,200	6,898	1.25 (1.20–1.29)	1.06 (1.03–1.10)
CHARLS	Recovery	9,439	16,261	6,341	0.87 (0.85–0.89)	0.97 (0.93–1.01)
ELSA	Onset	6,940	18,837	1,258	1.81 (1.72–1.90)	1.07 (1.01–1.14)
ELSA	Recovery	1,584	2,370	1,247	0.75 (0.71–0.79)	0.96 (0.90–1.03)
HRS	Onset	12,327	20,225	1,521	1.57 (1.50–1.65)	0.95 (0.90–1.00)
HRS	Recovery	2,277	2,720	1,395	0.80 (0.75–0.84)	0.92 (0.87–0.97)
KLoSA	Onset	7,709	25,650	3,815	1.47 (1.40–1.53)	1.13 (1.08–1.18)
KLoSA	Recovery	4,461	8,996	4,083	0.82 (0.79–0.84)	0.92 (0.88–0.96)
MHAS	Onset	10,040	14,965	2,863	1.26 (1.20–1.32)	1.00 (0.95–1.05)
MHAS	Recovery	5,129	6,679	2,849	0.80 (0.77–0.83)	1.06 (1.01–1.11)
SHARE	Onset	53,047	91,761	14,643	1.30 (1.27–1.33)	0.99 (0.97–1.00)
SHARE	Recovery	22,532	30,745	13,657	0.85 (0.83–0.86)	1.03 (1.01–1.05)

Each row is a separate complete-case model. People may appear in both outcome strata; counts must not be added to obtain unique people. CAR is exp(β), a ratio of − log(1 − p) at fixed covariates and interval length, not a directly observed hazard or risk ratio. Loneliness is per cohort reference SD; isolation is per component. Both exposures are mutually adjusted with primary covariates.

3.3 Objective isolation and joint phenotypes

For each additional objective-isolation component, pooled CARs were 1.03 (0.98–1.08) for onset (I^2=89.1%; prediction interval 0.87–1.23) and 0.98 (0.93–1.02) for recovery (I^2=87.8%; prediction interval 0.83–1.15) (Fig. 2C–D). Cohort estimates varied in direction. These results provide no stable pooled conditional association for this three-component index; they do not rule out total effects operating through loneliness or associations with broader measures of social connection.

Relative to neither high loneliness nor high isolation, pooled onset CARs were 2.06 (1.73–2.46) for loneliness only, 1.06 (0.96–1.17) for isolation only and 1.78 (1.28–2.47) for both. Recovery CARs were 0.65 (0.61–0.70), 0.96 (0.87–1.07) and 0.63 (0.57–0.70), respectively (Supplementary Figure S1;

Supplementary Table S4). The product-term CAR was 0.94 (0.91–0.97) for onset, with a prediction interval crossing 1, and 1.01 (1.00–1.02) for recovery (Supplementary Table S8). These exploratory link-scale interactions do not quantify additive-risk synergy or establish differences between phenotype estimates.

3.4 Sensitivity analyses

Loneliness estimates changed little across the demographic, primary and expanded specifications: pooled onset CARs were 1.48, 1.43 and 1.42, and recovery CARs were 0.80, 0.82 and 0.82. Same-record comparisons are included to distinguish additional adjustment from complete-case selection (Table 3; Supplementary Table S3; Supplementary Figure S2). Leave-one-cohort-out estimates remained directionally consistent (Supplementary Figure S3). Measurement-type strata each contained only three cohorts and had wide prediction intervals; they cannot establish equivalence of single-item and multi-item instruments (Supplementary Table S6).

After correcting the MHAS severity score, adding baseline symptom severity in the same four-cohort sample changed the loneliness CAR from 1.31 (1.22–1.41) to 1.23 (1.20–1.26) for onset, and from 0.84 (0.81–0.86) to 0.87 (0.83–0.91) for recovery. Recovery heterogeneity remained substantial (I^2=89.5%) and its prediction interval crossed 1 (0.69–1.10). Excluding MHAS gave recovery CAR 0.89 (0.88–0.91) in three cohorts, with I^2=0% and prediction interval 0.82–0.97; the contrast shows that the apparent absence of heterogeneity is not robust to the corrected MHAS contribution. Same-record comparisons and the scoring discrepancy are documented in Supplementary Table S5. The exploratory loneliness-excluded outcome analyses remained directionally similar, with threshold-validity limitations (Supplementary Table S7).

Restricting to consecutive scheduled waves retained 216,504 eligible intervals; HRS had insufficient observations for model fitting, leaving five cohorts. The loneliness CAR was 1.40 (1.22–1.61) for onset and 0.82 (0.79–0.85) for recovery. Logistic endpoint models in all six cohorts produced pooled loneliness odds ratios of 1.51 (1.34–1.71) and 0.76 (0.71–0.81), respectively. These different effect scales support direction rather than equality of magnitude. Modified Hartung–Knapp intervals for the primary loneliness associations were 1.22–1.67 and 0.77–0.86 (Supplementary Table S9).

Primary depression-state definitions were internally consistent with the stated score thresholds, and complete objective-isolation scores agreed with their three component indicators. However, the harmonized dataset did not permit independent reconstruction of every original questionnaire item, source-specific missing-item rule or recoding step. These measurement limitations are summarized in Supplementary Table S12. Single-exposure models retaining the duration offset but excluding demographic, health and mutual-exposure adjustment are reported in Supplementary Table S13.

Table 3
Pooled primary associations and focused sensitivity analyses

Analysis	Transition	Exposure	k	CAR (95% CI)	I^2, %	95% PI
Primary	Onset	Loneliness	6	1.43 (1.27–1.61)	97.7	0.92–2.21
Primary	Onset	Isolation	6	1.03 (0.98–1.08)	89.1	0.87–1.23
Primary	Recovery	Loneliness	6	0.82 (0.78–0.85)	86.7	0.71–0.94
Primary	Recovery	Isolation	6	0.98 (0.93–1.02)	87.8	0.83–1.15
Same-record comparator	Onset	Loneliness	4	1.31 (1.22–1.41)	91.5	0.93–1.86
Same-record comparator	Recovery	Loneliness	4	0.84 (0.81–0.86)	82.6	0.71–0.98
Corrected severity	Onset	Loneliness	4	1.23 (1.20–1.26)	34.8	1.14–1.33
Corrected severity	Recovery	Loneliness	4	0.87 (0.83–0.91)	89.5	0.69–1.10
Severity excluding MHAS	Onset	Loneliness	3	1.23 (1.20–1.27)	56.4	0.90–1.69
Severity excluding MHAS	Recovery	Loneliness	3	0.89 (0.88–0.91)	0.0	0.82–0.97
Scheduled waves only	Onset	Loneliness	5	1.40 (1.22–1.61)	97.7	0.80–2.45
Scheduled waves only	Recovery	Loneliness	5	0.82 (0.79–0.85)	85.1	0.71–0.95

Corrected severity and its same-record comparator use CHARLS, KLoSA, MHAS and SHARE; the three-cohort analysis excludes MHAS. Scheduled-wave restriction excludes HRS from synthesis because too few eligible intervals were available. Full adjustment-set, severity, alternate-link and small-k results appear in Supplementary Tables S3, S5 and S9. PI, prediction interval.

4 Discussion

Across six ageing cohorts, loneliness was associated with both observed onset and reduced recovery of elevated depressive symptoms after mutual adjustment for a common structural-isolation index. Loneliness estimates had a consistent direction, but the onset prediction interval crossed the null and heterogeneity was high. Objective-isolation estimates were less consistent across cohorts. These findings concern conditional endpoint associations, not event-time hazards, first lifetime incidence, clinical remission or treatment effects. Extending the analysis to people already above a symptom threshold identifies a distinct question that onset-only designs cannot address.

The distinction between loneliness and objective isolation is theoretically consequential. Structural isolation captures observable features of social organization—partnership, living arrangements, participation, and contact—whereas loneliness is an appraisal of whether available relationships satisfy emotional and relational needs (Berkman et al., 2000; Hughes et al., 2004; Cornwell and Waite, 2009; National Academies of Sciences, Engineering, and Medicine, 2020). Earlier work found that perceived

isolation could be more closely related to mental health than social disconnectedness (Cornwell and Waite, 2009), and Cacioppo et al. identified loneliness as a specific longitudinal risk factor for depressive symptoms (Cacioppo et al., 2006). The present results are consistent with those observations and with systematic evidence of longitudinal associations (Van As et al., 2022) and quantitative evidence of reciprocal loneliness–depression links (Chen et al., 2023). They also refine recent cross-national evidence in which loneliness, social activity, and socioeconomic position predicted incident depressive symptoms across ageing studies (Wang et al., 2024): after subjective and structural social disconnection were placed in the same transition model, loneliness showed a more consistent direction of association.

Several processes could explain the pattern. Loneliness may reflect threat appraisal, negative social expectations, sleep disruption and diminished emotionally meaningful support (Hawkley and Cacioppo, 2010). Clinical research distinguishes emotional and social loneliness in relation to depression (Peerenboom et al., 2015), while evidence on support and resilience suggests possible pathways without establishing causation (Wen et al., 2024). Depression can also influence social withdrawal and appraisal, creating reciprocal associations (Chen et al., 2023). The same-record severity analyses attenuated loneliness associations towards 1, consistent with confounding or shared affective content, while associations with subsequent state remained. Conditioning on baseline depression and health may itself induce selection or remove parts of a social pathway, so residual associations should not be interpreted as isolated causal effects.

The recovery findings are compatible with earlier clinical evidence of poorer depression prognosis among lonely older adults (Holvast et al., 2015) and with heterogeneous later-life symptom courses (Johnco et al., 2024; Qiu and Zhu, 2026; Harber-Aschan et al., 2026). They do not demonstrate predictive value beyond established clinical measures: calibration, discrimination, incremental prediction and clinical utility were not evaluated. Nor can a participant with two elevated endpoints be assumed continuously depressed. Future work with more frequent assessments, explicit relapse histories and death information could distinguish persistence from unobserved recovery and recurrence.

Objective social isolation behaved differently, and the heterogeneity is itself informative. Structural circumstances do not necessarily have the same meaning across societies. Living alone may represent autonomy in one context and social vulnerability in another; non-participation may reflect disability, local opportunity structures, caregiving roles, cultural norms, or preferences rather than social deprivation per se. Prior cross-national research has shown that social-isolation associations can vary across settings (Noguchi et al., 2021), and recent JAD studies have emphasized heterogeneity in social-isolation profiles and functional context (Liu et al., 2025). Our three-component index was intentionally conservative to maximize comparability; it therefore captured a common structural core at the cost of some locally meaningful network detail. The absence of a stable pooled association should not be read as evidence that objective isolation is harmless. Rather, its interpretation depends on the restricted index, measurement reliability, covariate conditioning and populations studied. Different exposure units also prevent a direct ranking of their importance.

Intervention evidence should be considered separately. Reviews report heterogeneous effects of interventions on loneliness and social connection (Cohen-Mansfield and Perach, 2015; Chua et al., 2024; Duffner et al., 2024), and the JoyAge programme studied integrated prevention in older adults (Liu et al., 2026). The present associations motivate evaluating social connection during depression follow-up, but do not show that reducing loneliness accelerates recovery or that structural interventions are ineffective. Trials would need to assess depressive symptom trajectories and potential harms as well as changes in connection.

Strengths include six large longitudinal cohorts, explicit conditioning on starting symptom state, mutual exposure adjustment, complete reporting of observed transitions and cohort-specific synthesis with prediction intervals. Sensitivity analyses included same-record covariate comparisons, restricted-wave analyses, an alternative endpoint link and small-k uncertainty checks, each addressing a distinct modelling or measurement concern.

Several limitations remain. Symptom scales and cut-offs differ and do not establish clinical diagnosis; item overlap, varying missing-item rules and source recoding may affect measurement. Standardization within cohort aligns numerical units without establishing measurement invariance. Long and unequal gaps permit unobserved reversals; the offset is a modelling assumption, not a correction that resolves them. Selecting complete exposures at both endpoints and complete covariates may introduce informative selection, while death and dropout were not jointly modelled. The associations are unweighted, SHARE is pooled across countries, and neither country-level transportability nor population-standardized risks were assessed. Residual and time-varying confounding, common reporting tendencies, conditioning on baseline state and exploratory multiplicity constrain interpretation. Finally, the harmonized dataset could not support independent reconstruction of every source-item transformation across all parent cohorts.

In conclusion, loneliness was consistently associated with observed depressive symptom onset and reduced observed recovery across six ageing cohorts, whereas the common objective-isolation index showed heterogeneous conditional associations. The results support investigating symptom recovery alongside onset and distinguishing subjective from structural social connection. They do not establish causal superiority, clinical prediction or recovery speed.

Abbreviations

ADL
activities of daily living
CAR
cloglog association ratio
CES-D
Center for Epidemiologic Studies Depression Scale
CHARLS

China Health and Retirement Longitudinal Study
CI
confidence interval
ELSA
English Longitudinal Study of Ageing
EURO-D
European Union Initiative to Compare Symptoms of Depression scale
HRS
Health and Retirement Study
KLoSA
Korean Longitudinal Study of Aging
MHAS
Mexican Health and Aging Study
PI
prediction interval
REML
restricted maximum likelihood
SD
standard deviation
SHARE
Survey of Health, Ageing and Retirement in Europe
STROBE
Strengthening the Reporting of Observational Studies in Epidemiology

Declarations

Ethics approval and consent to participate

This study was a secondary analysis of de-identified data obtained from publicly accessible research datasets, including the China Health and Retirement Longitudinal Study (CHARLS), English Longitudinal Study of Ageing (ELSA), Health and Retirement Study (HRS), Korean Longitudinal Study of Aging (KLoSA), Mexican Health and Aging Study (MHAS), and Survey of Health, Ageing and Retirement in Europe (SHARE). The original cohort studies obtained ethical approval from their respective institutional review boards or ethics committees and obtained informed consent from all participants in accordance with their study protocols. The present study involved no new recruitment, intervention, direct contact with participants, or collection of identifiable personal information, and used only de-identified secondary data. Therefore, no additional informed consent was required for the present secondary analysis.

Consent for publication

Not applicable. This study used only de-identified secondary data and did not involve individual identifiable information.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Funding

This work was supported by Shandong Second Medical University (Project No. 2026RZB0704). The funder had no role in the study design; data acquisition, analysis, or interpretation; preparation of the manuscript; or the decision to submit the manuscript for publication.

Author Contribution

L.G., J.Y., S.L., and Y.L. conceived and designed the study. L.G., J.Y., and Y.L. contributed to data curation, formal analysis, and statistical analysis. J.Y. developed the software. L.G. and Y.L. wrote the original draft. L.G. and J.Y. performed visualization. S.L. and Y.L. contributed to validation. S.L. was responsible for supervision, project administration, and funding acquisition. All authors contributed to methodology and writing—review and editing. All authors read and approved the final manuscript.

Acknowledgements

The authors gratefully acknowledge the investigators, staff, and participants of the China Health and Retirement Longitudinal Study (CHARLS), English Longitudinal Study of Ageing (ELSA), Health and Retirement Study (HRS), Korean Longitudinal Study of Aging (KLoSA), Mexican Health and Aging Study (MHAS), and Survey of Health, Ageing and Retirement in Europe (SHARE) for making their data available for research.

Data Availability

Data availabilityThe data used in this study were obtained from the publicly accessible repositories of the China Health and Retirement Longitudinal Study (CHARLS), English Longitudinal Study of Ageing (ELSA), Health and Retirement Study (HRS), Korean Longitudinal Study of Aging (KLoSA), Mexican Health and Aging Study (MHAS), and Survey of Health, Ageing and Retirement in Europe (SHARE). These data are available to researchers through the respective study repositories, subject to their applicable registration, access, and data-use requirements. The authors do not redistribute participant-level source

data. The harmonized variables and analytical procedures used in the present study are described in the manuscript and supplementary materials.

References

1. Aguilar-Navarro SG, Fuentes-Cantú A, Ávila-Funes JA, García-Mayo EJ. Validez y confiabilidad del cuestionario del ENASEM para la depresión en adultos mayores. Salud pública de México. 2007;49(4):256–62. https://doi.org/10.1590/S0036-36342007000400005.
2. Andresen EM, Malmgren JA, Carter WB, Patrick DL. Screening for depression in well older adults: evaluation of a short form of the CES-D. Am J Prev Med. 1994;10(2):77–84. https://doi.org/10.1016/S0749-3797(18)30622-6.
3. Berkman LF, Glass T, Brissette I, Seeman TE. From social integration to health: Durkheim in the new millennium. Soc Sci Med. 2000;51(6):843–57. https://doi.org/10.1016/S0277-9536(00)00065-4.
4. Börsch-Supan A, Brandt M, Hunkler C, et al. Data Resource Profile: the Survey of Health, Ageing and Retirement in Europe (SHARE). Int J Epidemiol. 2013;42(4):992–1001. https://doi.org/10.1093/ije/dyt088.
5. Cacioppo JT, Hughes ME, Waite LJ, Hawkley LC, Thisted RA. Loneliness as a specific risk factor for depressive symptoms: cross-sectional and longitudinal analyses. Psychol Aging. 2006;21(1):140–51. https://doi.org/10.1037/0882-7974.21.1.140.
6. Chen Z, Song X, Lee TMC, Zhang R. The robust reciprocal relationship between loneliness and depressive symptoms among the general population: evidence from a quantitative analysis of 37 studies. J Affect Disord. 2023;343:119–28. https://doi.org/10.1016/j.jad.2023.09.035.
7. Christl J, Grumbach P, Jockwitz C, Wege N, Caspers S, Meisenzahl E. Prevalence of depressive symptoms in people aged 50 years and older: a retrospective cross-sectional study. J Affect Disord. 2025;373:353–63. https://doi.org/10.1016/j.jad.2024.12.099.
8. Chua CMS, Chua JYX, Shorey S. Effectiveness of home-based interventions in improving loneliness and social connectedness among older adults: a systematic review and meta-analysis. Aging Ment Health. 2024;28(1):1–10. https://doi.org/10.1080/13607863.2023.2237919.
9. Cohen-Mansfield J, Perach R. Interventions for alleviating loneliness among older persons: a critical review. Am J Health Promotion. 2015;29(3):e109–25. https://doi.org/10.4278/ajhp.130418-LIT-182.
10. Cornwell EY, Waite LJ. Social disconnectedness, perceived isolation, and health among older adults. J Health Soc Behav. 2009;50(1):31–48. https://doi.org/10.1177/002214650905000103.
11. Duffner LA, Janssen N, Deckers K, et al. Facing the next 'geriatric giant'—a systematic literature review and meta-analysis of interventions tackling loneliness and social isolation among older adults. J Am Med Dir Assoc. 2024;25(9):105110. https://doi.org/10.1016/j.jamda.2024.105110.
12. Harber-Aschan L, Sjöberg L, Triolo F, Dekhtyar S. Trajectories of depressive symptoms in older adults: correlates and consequences for mortality. J Affect Disord. 2026;404:121409. https://doi.org/10.1016/j.jad.2026.121409.

13. Hawkley LC, Cacioppo JT. Loneliness matters: a theoretical and empirical review of consequences and mechanisms. Ann Behav Med. 2010;40(2):218–27. https://doi.org/10.1007/s12160-010-9210-8.
14. Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003;327(7414):557–60. https://doi.org/10.1136/bmj.327.7414.557.
15. Holt-Lunstad J, Smith TB, Baker M, Harris T, Stephenson D. Loneliness and social isolation as risk factors for mortality: a meta-analytic review. Perspect Psychol Sci. 2015;10(2):227–37. https://doi.org/10.1177/1745691614568352.
16. Holvast F, Burger H, de Waal MMW, van Marwijk HWJ, Comijs HC, Verhaak PFM. Loneliness is associated with poor prognosis in late-life depression: longitudinal analysis of the Netherlands Study of Depression in Older Persons. J Affect Disord. 2015;185:1–7. https://doi.org/10.1016/j.jad.2015.06.036.
17. Hughes ME, Waite LJ, Hawkley LC, Cacioppo JT. A short scale for measuring loneliness in large surveys: results from two population-based studies. Res Aging. 2004;26(6):655–72. https://doi.org/10.1177/0164027504268574.
18. IntHout J, Ioannidis JPA, Rovers MM, Goeman JJ. Plea for routinely presenting prediction intervals in meta-analysis. BMJ Open. 2016;6(7):e010247. https://doi.org/10.1136/bmjopen-2015-010247.
19. Jackson CH. Multi-State Models for Panel Data: The msm Package for R. J Stat Softw. 2011;38(8):1–28. https://doi.org/10.18637/jss.v038.i08.
20. Johnco CJ, Zagic D, Rapee RM, Kangas M, Wuthrich VM. Long-term remission and relapse of anxiety and depression in older adults after cognitive behavioural therapy (CBT): a 10-year follow-up of a randomised controlled trial. J Affect Disord. 2024;358:440–8. https://doi.org/10.1016/j.jad.2024.05.033.
21. Lee J. KLoSA—Korean Longitudinal Study of Aging. Korean J Family Med. 2020;41(1):1–2. https://doi.org/10.4082/kjfm.41.1E.
22. Liu T, Leung DKY, Wong D, et al. Effectiveness of an integrated prevention programme (JoyAge) for depressive symptoms, anxiety, and loneliness in older adults in Hong Kong: a pragmatic quasi-experimental trial. J Affect Disord. 2026;402:121333. https://doi.org/10.1016/j.jad.2026.121333.
23. Liu X, Chen JH, Gao B, Zhang WJ. Social isolation and depressive symptoms among older adults with different functional status in China: a latent class analysis. J Affect Disord. 2025;375:478–85. https://doi.org/10.1016/j.jad.2025.01.156.
24. National Academies of Sciences, Engineering, and Medicine. Social Isolation and Loneliness in Older Adults: Opportunities for the Health Care System. Washington, DC: National Academies; 2020. https://doi.org/10.17226/25663.
25. Noguchi T, Saito M, Aida J, et al. Association between social isolation and depression onset among older adults: a cross-national longitudinal study in England and Japan. BMJ Open. 2021;11(3):e045834. https://doi.org/10.1136/bmjopen-2020-045834.

26. Peerenboom L, Collard RM, Naarding P, Comijs HC. The association between depression and emotional and social loneliness in older persons and the influence of social support, cognitive functioning and personality: a cross-sectional study. J Affect Disord. 2015;182:26–31. https://doi.org/10.1016/j.jad.2015.04.033.
27. Perissinotto CM, Stijacic Cenzer I, Covinsky KE. Loneliness in older persons: a predictor of functional decline and death. Arch Intern Med. 2012;172(14):1078–83. https://doi.org/10.1001/archinternmed.2012.1993.
28. Prentice RL, Gloeckler LA. Regression analysis of grouped survival data with application to breast cancer data. Biometrics. 1978;34(1):57–67. https://doi.org/10.2307/2529588.
29. Prince MJ, Reischies F, Beekman ATF, et al. Development of the EURO-D scale—a European Union initiative to compare symptoms of depression in 14 European centres. Br J Psychiatry. 1999;174(4):330–8. https://doi.org/10.1192/bjp.174.4.330.
30. Qiu Y, Zhu X. Interpretable machine learning models for predicting depression status and remission three years later in older adults in China: a longitudinal study. J Affect Disord. 2026;394(Pt A):120536. https://doi.org/10.1016/j.jad.2025.120536.
31. Röver C, Knapp G, Friede T. Hartung-Knapp-Sidik-Jonkman approach and its modification for random-effects meta-analysis with few studies. BMC Med Res Methodol. 2015;15:99. https://doi.org/10.1186/s12874-015-0091-1.
32. Singer JD, Willett JB. It's about time: using discrete-time survival analysis to study duration and the timing of events. J Educational Stat. 1993;18(2):155–95. https://doi.org/10.3102/10769986018002155.
33. Sonnega A, Faul JD, Ofstedal MB, Langa KM, Phillips JWR, Weir DR. Cohort Profile: the Health and Retirement Study (HRS). Int J Epidemiol. 2014;43(2):576–85. https://doi.org/10.1093/ije/dyu067.
34. Steptoe A, Breeze E, Banks J, Nazroo J. Cohort Profile: the English Longitudinal Study of Ageing. Int J Epidemiol. 2013a;42(6):1640–8. https://doi.org/10.1093/ije/dys168.
35. Steptoe A, Shankar A, Demakakos P, Wardle J. Social isolation, loneliness, and all-cause mortality in older men and women. Proc Natl Acad Sci USA. 2013b;110(15):5797–801. https://doi.org/10.1073/pnas.1219686110.
36. Turvey CL, Wallace RB, Herzog R. A revised CES-D measure of depressive symptoms and a DSM-based measure of major depressive episodes in the elderly. Int Psychogeriatr. 1999;11(2):139–48. https://doi.org/10.1017/S1041610299005694.
37. Van As BAL, Imbimbo E, Franceschi A, Menesini E, Nocentini A. The longitudinal association between loneliness and depressive symptoms in the elderly: a systematic review. Int Psychogeriatr. 2022;34(7):657–69. https://doi.org/10.1017/S1041610221000399.
38. Viechtbauer W. Conducting meta-analyses in R with the metafor package. J Stat Softw. 2010;36(3):1–48. https://doi.org/10.18637/jss.v036.i03.
39. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement:

guidelines for reporting observational studies. Lancet. 2007;370(9596):1453–7. https://doi.org/10.1016/S0140-6736(07)61602-X.

40. Wang Y, Liu M, Yang F, Chen H, Wang Y, Liu J. The associations of socioeconomic status, social activities, and loneliness with depressive symptoms in adults aged 50 years and older across 24 countries: findings from five prospective cohort studies. Lancet Healthy Longev. 2024;5(9):100618. https://doi.org/10.1016/j.lanhl.2024.07.001.
41. Wen Z, Wang H, Liang Q, Liu L, Zhang W, Zhang X. Mediating effect of social support and resilience between loneliness and depression in older adults: a systematic review and meta-analytic structural equation modeling. J Affect Disord. 2024;365:246–57. https://doi.org/10.1016/j.jad.2024.08.062.
42. Wong R, Michaels-Obregon A, Palloni A. Cohort Profile: the Mexican Health and Aging Study (MHAS). Int J Epidemiol. 2017;46(2):e2. https://doi.org/10.1093/ije/dyu263.
43. World Health Organization. From loneliness to social connection: charting a path to healthier societies. Report of the WHO Commission on Social Connection. Geneva: World Health Organization. 2025. ISBN 978-92-4-011236-0. https://iris.who.int/handle/10665/381746 (accessed 20 September 2026).
44. World Health Organization. Mental health of older adults. Geneva: World Health Organization; 2026. https://www.who.int/news-room/fact-sheets/detail/mental-health-of-older-adults. (accessed 20 September 2026). Updated 20 July 2026.
45. Zhao Y, Hu Y, Smith JP, Strauss J, Yang G. Cohort Profile: the China Health and Retirement Longitudinal Study (CHARLS). Int J Epidemiol. 2014;43(1):61–8. https://doi.org/10.1093/ije/dys203.
46. Zhu S, Kong X, Han F, et al. Association between social isolation and depression: evidence from longitudinal and Mendelian randomization analyses. J Affect Disord. 2024;350:182–7. https://doi.org/10.1016/j.jad.2024.01.106.

Figures

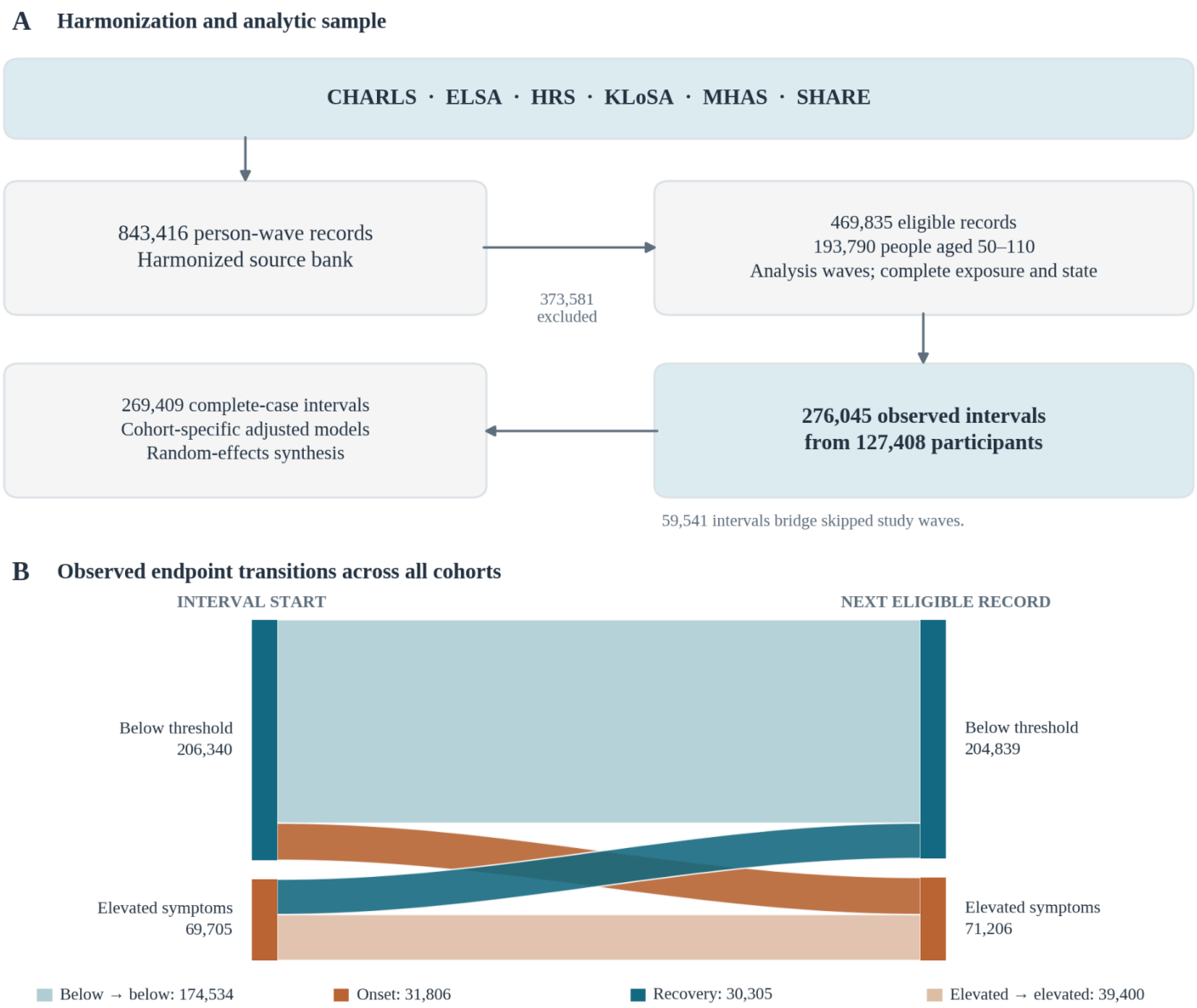


Figure 1

Study selection and observed transition framework

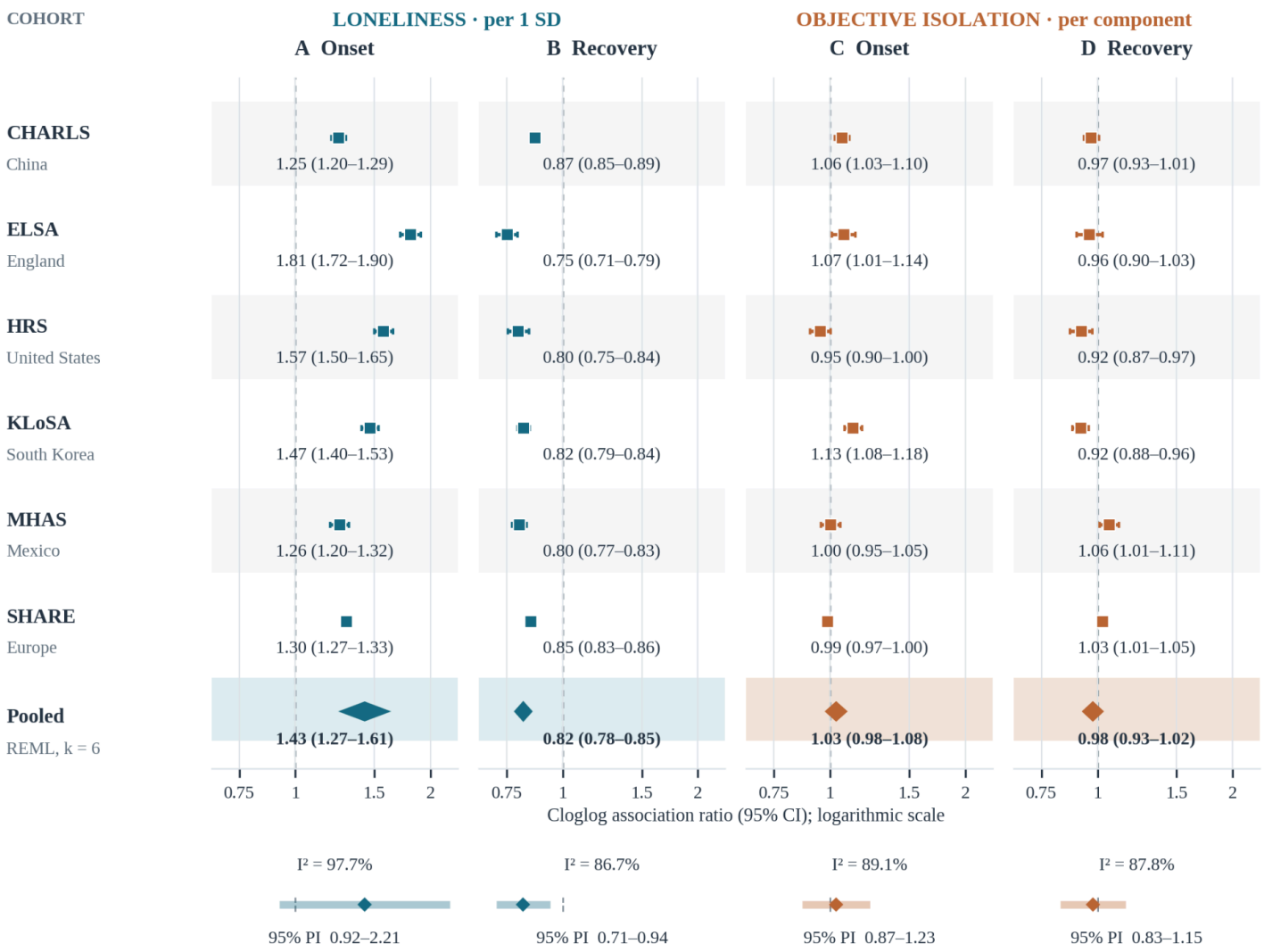


Figure 2

Integrated cohort-specific and pooled primary associations

A, loneliness and onset. B, loneliness and recovery. C, objective isolation and onset. D, objective isolation and recovery. All six cohorts are shown on logarithmic axes; points and lines show CARs and 95% confidence intervals, pooled diamonds show random-effects estimates, and distinct pooled interval marks show 95% prediction intervals. Loneliness is per cohort reference SD and isolation per component. CARs are exponentiated complementary log-log coefficients; they are not observed rates or percentage changes in risk.

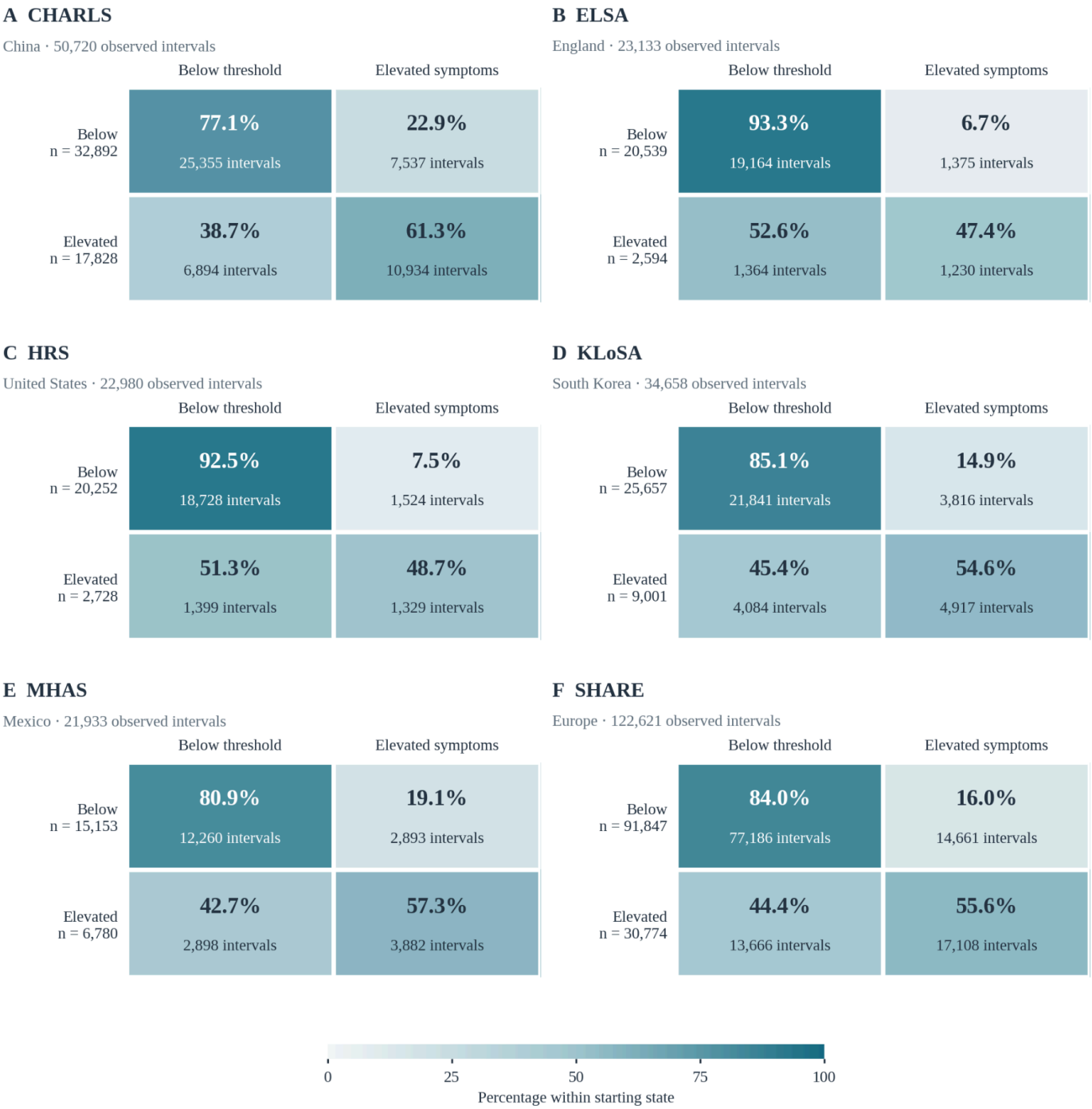


Figure 3

Observed depressive symptom transitions by cohort

Supplementary Files

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

- SupplementaryMaterial.docx