

Sex-Specific Longitudinal Pathways to Activities of Daily Living Disability in Older Adults with Cardiovascular Disease and/or Hypertension: Findings from the Health, Aging and Retirement in Thailand (HART) Study

Tanavij Pannoi¹ , Chardsumon Prutipinyo²  and Utoomporn Wongsin² 

¹Department of Pharmaceutical Care, School of Pharmacy, Walailak University, Nakhon Si Thammarat, Thailand;

²Department of Public Health Administration, Faculty of Public Health, Mahidol University, Bangkok, Thailand

Correspondence:

Utoomporn Wongsin, PhD,
Department of Public Health
Administration, Faculty of Public
Health, Mahidol University,
Bangkok, Thailand
E-mail: utoomporn.won@mahidol.ac.th

Received: March 13, 2026;

Revised: June 25, 2026;

Accepted: July 17, 2026

ABSTRACT

OBJECTIVE Cardiovascular diseases (CVDs) and/or hypertension (HTN) are a major contributor to activities of daily living (ADL) disability in ageing populations. Although sex differences in CVDs/HTN incidence and outcomes are well documented, less is known about sex-specific mechanisms underlying functional disability among older adults with CVDs/HTN.

METHODS We analysed longitudinal data from four waves (2015–2022) of the HART study using two lagged panels (2015–2017–2020; 2017–2020–2022) to assess whether associations vary across time contexts. Psycho-social exposures (depressive symptoms, physical activity, multimorbidity, and pain) and mobility impairment were examined using ordinal structural equation modelling (SEM) weighted least squares mean- and variance-adjusted (WLSMV), adjusting for baseline covariates. Sex- stratified and panel moderation analyses were performed, with inverse probability weighting in sensitivity analyses.

RESULTS A total of 999 and 1,066 participants were included in Panels A and B, respectively. Baseline ADL distributions were similar across panels, with predominantly mild ADL disability. In Panel A, multimorbidity was positively associated with ADL disability, while pain showed an inverse association. In Panel B, mobility impairment was strongly associated with ADL disability. No mediation was observed at the panel level. However, an exploratory indirect association between depressive symptoms and ADL disability through mobility impairment was observed among men in Panel B ($\beta = 0.07$, 95% CI: 0.05–0.10), whereas no corresponding association was observed among women.

CONCLUSION Longitudinal pathways to ADL disability among older adults with CVDs/HTN varied by sex and longitudinal observation window. An exploratory, panel-specific indirect association between depressive symptoms, mobility impairment, and ADL disability was observed only among men in Panel B. This finding should be interpreted cautiously and requires confirmation in future longitudinal studies with consistent mobility measurements.

KEYWORDS sex differences, risk factors of ADL disability, older adults with cardiovascular diseases

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INTRODUCTION

Cardiovascular diseases (CVDs) and/or hypertension (HTN) remain the leading cause of morbidity, mortality, and disability worldwide, reflecting the combined impact of aging populations and increased exposure to cardiometabolic risk factors (1, 2). Although improvements in treatment have reduced case-fatality rates, a growing number of adults are living longer with the long-term consequences of CVDs/HTN, including physical limitations, reduced social participation, and diminished quality of life (1). These outcomes make disability a critical component of CVDs/HTN burden, particularly in aging societies.

Sex differences are well documented across the cardiovascular disease continuum. Men generally exhibit earlier onset and higher incidence of CVDs/HTN, while women are more likely to present with atypical symptoms and receive sub-optimal preventive and therapeutic care (3). Such disparities have the potential to influence long-term recovery and functional outcomes. However, evidence on sex-specific patterns of activities of daily living (ADL) disability among individuals with CVDs/HTN remains mixed. While some population-based studies suggest similar levels of functional limitation between men and women after adjusting for comorbidities (4), others indicate that women with cardiometabolic multimorbidity are more likely than men to report ADL limitations, pain, and depressive symptoms (5). Such inconsistencies highlight the importance of examining not only ADL disability prevalence, but also the mechanisms through which ADL disability develops.

The disablement process framework describes how disease-related impairments progress to functional limitations, such as mobility impairment, and ultimately to ADL disability when compensatory strategies are insufficient (6–8). These pathways are dynamic and context dependent, influenced by psychosocial factors and stage of functional decline.

Thailand is experiencing rapid population ageing alongside a rising burden of CVDs/HTN, yet longitudinal evidence on sex-specific ADL disability pathways remains limited. Therefore, this study uses data from the Health, Aging, and Retirement in Thailand survey to examine whether psychosocial-mobility-ADL disability pathways differ by

sex and across different longitudinal observation windows.

METHODS

Study design and data source

This longitudinal cohort study used data from four waves (2015, 2017, 2020, and 2022) of the Health, Aging and Retirement in Thailand (HART) survey (9), a nationally representative study of community-dwelling Thai adults aged ≥ 45 years. The analysis examined temporal pathways linking psychosocial factors to functional ADL disability among adults with CVDs/HTN including hypertension using a lagged mediation framework. Two partially overlapping analytic panels were constructed to preserve temporal ordering between exposures, mediator, and outcome, and to minimise potential reverse causation.

Participants and panel construction

Wave-specific datasets were harmonised and reshaped into a person-wave long format using a unique participant identifier (PID). Because household identifiers may change across waves, longitudinal linkage relied exclusively on PID. At each wave, CVDs/HTN was defined as self-reported hypertension or cardiovascular disease. This definition prioritised statistical stability, and findings should be interpreted accordingly. A dynamic indicator (*cvd_ever*), defined as the cumulative maximum of wave-specific CVDs/HTN status, was used to identify participants with CVDs/HTN at or before each wave. Eligibility for each analytic panel required evidence of CVDs/HTN at or prior to the panel-specific baseline.

Panels were constructed as partially overlapping, time-lagged cohorts to examine whether psychosocial-mobility-ADL disability pathways vary across temporal contexts. We did not assume that panels represent discrete stages of ADL disability; rather, they provide complementary perspectives on how associations may change over time. Panel A included psychosocial exposures measured in 2015, mobility impairment assessed in 2017, and ADL disability assessed in 2020. Panel B was defined analogously, with exposures measured in 2017, mobility impairment in 2020, and ADL disability in 2022. Panel-specific analytic samples were assembled by linking baseline, mediator, and outcome waves by PID and restricting

analyses to participants with complete data on pre-specified variables. Pain was included only in Panel A due to differences in measurement availability across survey waves.

Variables

Functional ADL disability was assessed using four ADL items and summarized as an ADL score. Given pronounced ceiling effects, ADL was modelled primarily as an ordinal outcome, with baseline ADL included as a covariate as shown in Supplementary Figure 1–2 (Figure S1–S2). Psychosocial exposures included depressive symptoms, physical activity, multimorbidity, and pain. Depressive symptoms were derived from summed scale scores, physical activity from exercise behavior, multimorbidity from counts of chronic conditions, and pain from self-reported accident-related physical health impact. The mediator was constructed using a prespecified hierarchical approach integrating mobility status, mobility level (when available), and fatigue-related symptoms to capture overall functional limitation, accommodating variation in item availability across waves but potentially introducing measurement heterogeneity. Further details of variable construction is provided in supplementary Table 1 (Table S1).

Statistical analysis

Analyses followed a lagged mediation framework based on the disablement process model. Panels were analyzed both separately and jointly using multi-group structural equation modelling (SEM). Given the ordinal ADL outcome and ceiling effects, weighted least squares mean- and variance-adjusted (WLSMV) estimation was applied. Models specified exposure–mediator (a), mediator–outcome (b), and direct (c') paths, with indirect effects estimated as the product ($a \times b$). Confidence intervals for indirect effects were derived using the delta method under the WLSMV estimator.

To address potential selection bias from complete-case analysis, inverse probability weighting (IPW) was applied. Inclusion probabilities were estimated using baseline panel, age, sex, education, baseline ADL, depressive symptoms, multimorbidity, and physical activity. Stabilized weights were trimmed at the 1st and 99th percentiles and incorporated into weighted SEM models.

All models were adjusted for age, sex, education, and baseline ADL. Panel and sex differences evaluated by comparing nested multi-group models using scaled chi-square difference tests appropriate for WLSMV estimation in lavaan. Models allowing structural paths to vary across groups were compared with corresponding models in which the relevant paths were constrained to equality. As the models were just-identified ($df = 0$), global fit indices were not informative; inference therefore focused on parameter estimates and their consistency across analyses.

In addition to explanatory analyses, supplementary predictive evaluations were conducted to assess model discrimination and calibration for ADL disability severity. These analyses were intended to complement, but not replace, the primary causal mediation framework. Statistical significance was set at $\alpha = 0.05$.

RESULTS

Panel A included 999 participants and Panel B included 1,066 participants. A total of 1,454 individuals were excluded due to CVDs/HTN onset after the panel baseline, reflecting the dynamic cohort design in Table 1 and Supplementary Table 2 (Table S2). Table 1 summarises baseline characteristics of participants with cardiovascular disease in Panels A and B. Participants were predominantly older adults with low socioeconomic status and substantial cardiometabolic burden. Median monthly income was lower in Panel B than Panel A. Functional status was comparable, with identical median baseline ADL scores of 5.0 (IQR 5.0–5.0) and most participants reporting mild functional limitation. Depressive symptoms were higher in Panel B (median 16.0, IQR 14.0–18.0) than Panel A (14.0, IQR 12.0–17.0), with slightly higher physical activity. Age distributions were similar, women predominated, and education levels were low. In Panel A, 14.2% reported pain; data unavailable.

Regarding Table 2, in Panel A, multimorbidity was positively associated with subsequent ADL disability ($\beta = 0.16$, 95% CI: 0.01–0.31; $p = 0.04$), whereas pain showed a modest inverse association ($\beta = -0.36$, 95% CI: -0.71 to -0.01 ; $p = 0.04$) with stable effects as shown in supplementary Figure 3 (Figure S3). Mobility impairment was not associated with subsequent ADL disability

Table 1. Baseline characteristics of participants with cardiovascular disease and/or hypertension by panel

Baseline characteristics	Panel A	Panel B
Sex, n (%)		
Men	371 (37.1)	422 (39.6)
Women	628 (62.9)	644 (60.4)
Age group, n (%)		
45–59 years	200 (20.0)	189 (17.7)
60–69 years	358 (35.8)	366 (34.3)
70–79 years	260 (26.0)	311 (29.2)
≥ 80 years	181 (18.1)	200 (18.8)
Education level, n (%)		
No formal education	96 (9.6)	75 (7.0)
Primary education	783 (78.4)	835 (78.3)
Lower secondary (Grade 9)	42 (4.2)	63 (5.9)
Upper secondary (Grade 12)	36 (3.6)	57 (5.3)
Vocational certificate	2 (0.2)	7 (0.7)
Higher vocational/diploma	21 (2.1)	8 (0.8)
Bachelor's degree	17 (1.7)	19 (1.8)
Other	2 (0.2)	2 (0.2)
Income (THB/month), median (IQR)	9,000 (5,000–12,000)	5,800 (2,500–10,000)
ADL score, n (%)		
4 (no/very mild limitation)	13 (1.3)	0 (0.0)
5 (mild limitation)	965 (96.6)	1032 (96.8)
6–10 (moderate limitation)	15 (1.5)	28 (2.6)
≥ 11 (severe limitation)	6 (0.6)	6 (0.6)
Depressive symptoms	14.0 (12.0–17.0)	16.0 (14.0–18.0)
Physical activity score	2.0 (1.0–5.0)	3.0 (1.0–5.0)
Current pain, n (%)		
Pain	142 (14.2)	NA*
No pain	857 (85.8)	NA*
Comorbidities, n (%)		
Hypertension	949 (95.0)	871 (81.7)
Diabetes	280 (28.0)	250 (23.5)
Lung disease	4 (0.4)	21 (2.0)
Liver/Gastrointestinal disease	8 (0.8)	9 (0.8)
Kidney/urinary disease	26 (2.6)	41 (3.8)
Cardiovascular disease	131 (13.1)	130 (12.2)
Brain disease/dementia	9 (0.9)	15 (1.4)
Emotional/psychiatric/neuro disorder	1 (0.1)	2 (0.2)
Arthritis	64 (6.4)	85 (8.0)
Osteoporosis	46 (4.6)	42 (3.9)
Other disease	152 (15.2)	224 (21.0)

*NA, not available; Panel A, baseline in 2015 (n = 999); Panel B, baseline in 2017 (n = 1,066)

IQR, interquartile range; ADL, activities of daily living

($\beta = 0.01$, 95% CI -0.02 – 0.04 ; $p = 0.53$), while age remained a significant predictor of worse ADL outcomes ($\beta = 0.57$, 95% CI: 0.41 – 0.73 ; $p < 0.001$). Depression, physical activity, education, and baseline ADL were not significantly associated with ADL disability. In Panel B, mobility impairment likewise remained strongly associated with subsequent ADL disability ($\beta = 0.11$, 95% CI: 0.10 – 0.11 ; $p < 0.001$), and age was also significantly associated with worse ADL outcomes ($\beta = 0.47$, 95%

CI: 0.07 – 0.87 ; $p = 0.02$), whereas no other predictors reached statistical significance.

Panel-level mediation analyses (Table 3) showed no statistically significant indirect effects of depression, multimorbidity, physical activity, or pain on ADL disability through mobility impairment in either panel. In Panel A, indirect effects were close to zero with confidence intervals crossing the null (e.g., depression: $\beta = -0.000$, 95% CI: -0.001 to 0.001 ; $p = 0.97$). Similarly, in Panel B, no

Table 2. Direct associations between psychosocial factors, mobility impairment, and ADL disability across temporally distinct lagged panels

Predictor	Panel A	p-value	Panel B	p-value
	Standardized β coefficient (95% CI)		Standardized β coefficient (95% CI)	
Depression	-0.00 (-0.003, 0.003)	0.96	0.016 (-0.06, 0.09)	0.67
Multimorbidity	0.16 (0.01, 0.31)	0.04*	0.14 (-0.24, 0.51)	0.49
Physical activity	0.01 (-0.06, 0.08)	0.81	-0.01 (-0.06, 0.05)	0.97
Pain	-0.36 (-0.71, -0.01)	0.04*	—	—
Mobility impairment	0.01 (-0.02, 0.04)	0.53	0.11 (0.10, 0.11)	< 0.001*
Age	0.57 (0.41, 0.73)	< 0.001*	0.47 (0.07, 0.87)	0.02*
Education	-0.00 (-0.01, 0.01)	0.98	0.20 (-0.18, 0.58)	0.30
Baseline ADL	-0.11 (-0.27, 0.05)	0.17	-0.02 (-0.46, 0.43)	0.93

*statistical significant ($p < 0.05$); ADL, activities of daily living

Table 3. Panel-level indirect effects of psychosocial exposures on ADL disability via mobility impairment

Exposure	Outcome	Panel	Indirect effect:	p-value
			Standardized β coefficient (95% CI)	
Depression	ADL disability	A	-0.000 (-0.001, 0.001)	0.97
Multimorbidity	ADL disability	A	-0.002 (-0.050, 0.046)	0.95
Physical activity	ADL disability	A	-0.000 (-0.006, 0.006)	0.99
Pain	ADL disability	A	-0.009 (-0.176, 0.159)	0.92
Depression	ADL disability	B	0.002 (-0.066, 0.070)	0.96
Multimorbidity	ADL disability	B	0.002 (-0.370, 0.374)	0.99
Physical activity	ADL disability	B	-0.001 (-0.043, 0.042)	0.98

ADL, activities of daily living

Table 4. Sex differences in the mediation of depression-ADL disability associations via mobility impairment

Exposure	Mediator	Outcome	Panel	Sex	Indirect effect:	p-value**
					Standardized β coefficient (95% CI)*	
Depression	Mobility	ADL disability	B	Male	0.07 (0.05, 0.10)	< 0.001
Depression	Mobility	ADL disability	B	Female	0.00 (-0.11, 0.11)	0.999

*Indirect effects estimated using ordinal SEM (WLSMV) with defined parameters ($a \times b$).; **Bold indicates statistical significance ($p < 0.05$); ADL, activities of daily living

indirect pathways reached significance, including depression ($\beta = 0.002$, 95% CI: -0.066 to 0.070; $p = 0.96$) and multimorbidity ($\beta = 0.002$, 95% CI: -0.370 to 0.374; $p = 0.99$). Consistent with these findings, panel moderation analyses in Supplementary Table 3 (Table S3) demonstrated significant heterogeneity between panels ($\chi^2 = 75.25$, $df = 13$, $p < 0.001$). Although mobility impairment was strongly associated with subsequent ADL disability in both panels, none of the upstream exposure-to-mobility pathways were statistically

significant in Panel A, explaining the absence of indirect effects despite the strong mobility-ADL association.

Table 4 reports sex moderation and sex-stratified mediation results. Scaled chi-square difference testing indicated no evidence of sex moderation in Panel A ($\chi^2 = 13.41$, $df = 15$, $p = 0.57$), but strong evidence of sex moderation in Panel B ($\chi^2 = 652.73$, $df = 13$, $p < 0.001$). Sex-stratified analyses in Panel B showed a significant indirect effect of depression on ADL disability through mobil-

ity impairment among men ($\beta = 0.074$, 95% CI: 0.046–0.103; $p < 0.001$), whereas no significant mediation was observed among women.

Inverse probability weighted sensitivity analyses in supplementary Table 4 (Table S4) yielded results that were broadly consistent with the complete-case analyses. In Panel A, multimorbidity remained positively associated with subsequent ADL disability, whereas pain showed a similar inverse but borderline association. In Panel B, mobility impairment remained positively associated with ADL disability, although the magnitude of the association was attenuated after weighting. No significant indirect effects through the mobility mediator were observed in either panel, supporting the robustness of the primary findings to potential selection bias.

Supplementary predictive analyses in supplementary Table 5 (Table S5) and supplementary Figure 4–5 (Figure S4–S5) demonstrated that the direct-effects model consistently achieved better predictive discrimination than the mediation model, particularly among men. All models in Panel A and B were just-identified ($df = 0$); therefore, fit indices indicate perfect fit by definition and are not informative as shown in Supplementary Table 6 (Table S6).

DISCUSSION

This longitudinal study examined sex-specific pathways to functional ADL disability among older adults with cardiovascular disease using a lagged panel design grounded in the disablement process framework. Our findings demonstrate that associations between psychosocial factors, mobility impairment, and activities of daily living disability are context dependent and differ by sex, even among individuals with similar baseline functional status. These results highlight the importance of examining ADL disability mechanisms, rather than ADL disability prevalence alone, when assessing functional decline in ageing populations with chronic cardiovascular conditions.

Despite initial conceptualisation along the disablement continuum, similar baseline ADL distributions do not support a strict staging interpretation. Age was a significant predictor of ADL disability among older adults with cardiovascular diseases in Thailand in both Panels A and B. This finding is consistent with previous findings (10–13). This

is because advancing age is linked to a decline in physical functioning, including decreased gait speed and impaired equilibrium, which subsequently restricts the capacity to carry out ADL.

Pain is commonly associated with functional ADL disability among older adults with cardiovascular disease; however, we observed an inverse association with subsequent ADL disability in Panel A. This contrasts with previous evidence linking chronic or severe pain to functional decline (14–16). In the present study, the variable used to represent pain reflects activity-limiting physical impact rather than chronic pain and may capture injury-related or activity-associated conditions. Residual confounding, activity-related bias, and potential selection bias—where individuals with more advanced ADL disability may be less likely to report activity-limiting physical impact—may also have contributed to this finding. Accordingly, this inverse association should not be interpreted as evidence that pain is protective, but rather as a finding that may reflect the operationalisation of the study variable and residual sources of bias.

Mobility impairment was strongly associated with subsequent ADL disability in both Panel A and Panel B. This finding is consistent with previous evidence showing that poorer mobility capacity is associated with subsequent disability among community-dwelling older adults (17, 18). However, mobility functioned as a mediator only in Panel B because none of the upstream psychosocial exposures were significantly associated with mobility impairment in Panel A. These findings suggest that while mobility is a robust predictor of subsequent disability, its role as a mediator may vary across longitudinal observation windows.

Multimorbidity has also been associated with functional disability in older populations, with evidence indicating that both the number and specific combinations of chronic conditions may influence disability risk. (19–23) In particular, multimorbidity patterns involving cardiovascular and metabolic conditions, often in combination with musculoskeletal or other chronic conditions, have been associated with functional disability and loss of independence (20–23). In the present study, multimorbidity was associated with subsequent ADL disability in Panel A, supporting the

relevance of coexisting chronic disease burden to functional decline. However, this association was not observed in Panel B, suggesting that the contribution of multimorbidity to subsequent ADL disability may also vary across longitudinal contexts.

In this longitudinal analysis, mobility impairment mediated the association between depression and subsequent ADL disability only in Panel B, with limited and context-specific evidence of sex-specific mediation, while no meaningful mediation was observed at the panel level or in Panel A. These findings indicate that mediation pathways are not consistent across contexts and support a context-dependent interpretation within the Disablement Process framework (24). Such differences may reflect variation in physical reserve, coping strategies, caregiving support, health-seeking behaviour, and social roles, which can influence how mobility limitations translate into disability across individuals and settings.

Although baseline ADL distributions were similar across panels (Table 1), panel-moderation analyses in supplementary Table 3 (Table S3) showed that mobility-related paths differed between panels, indicating heterogeneity in disablement mechanisms. This aligns with prior longitudinal evidence that depression–disability pathways are complex, non-linear, and context dependent (7). Likewise, evidence from the Longitudinal Aging Study Amsterdam further suggests that depressive symptoms may accelerate specific transitions within the disablement pathway rather than exert uniform effects across all stages of functional decline (6).

The sex-stratified mediation observed in Panel B, whereby depression influenced ADL disability through mobility impairment among men but not women, is broadly consistent with previous observations, although the evidence remains limited. Depressive symptoms have been linked to gait slowing and mobility decline, which may translate differently into ADL disability due to sex differences in physical reserve, social roles, and coping strategies (8). Recent longitudinal work further suggests that indirect effects of depression on ADL disability emerge only under specific behavioral and contextual conditions (25). Nevertheless, this significant indirect effect of depressive symptoms via mobility among men in Panel

B was not replicated and should be interpreted cautiously. Overall, findings do not support consistent sex-specific mediation pathways, but suggest that any such effects are small and vary depending on the panel.

In adults with CVDs/HTN, our findings extend prior research by identifying context- and sex-specific functional mechanisms, rather than focusing solely on overall ADL disability levels. Previous population-based research using WHODAS-II found broadly similar levels of functional disability between men and women with cardiovascular disease, defined as heart disease, heart attack, or stroke, despite higher levels of depressive symptoms among women (4). In contrast, the present study examined ADL disability among adults with a broader CVDs/HTN definition and focused on sex-specific longitudinal pathways rather than overall functional disability. Our longitudinal panel-based analysis showed that depressive symptoms were indirectly associated with subsequent ADL disability through mobility impairment only in Panel B and only among men. This exploratory finding suggests that in CVDs/HTN-related ADL disability may emerge at the level of functional pathways rather than ADL disability prevalence, and that the contribution of mobility depends on analytic context.

Nonetheless, this study distinguishes explanatory from predictive modelling approaches. The primary analyses evaluated longitudinal pathways linking psychosocial factors, mobility impairment, and subsequent ADL disability, whereas the supplementary ROC/AUC analyses assessed predictive performance. The mediation model did not improve predictive discrimination compared with the direct-effects model, indicating that variables useful for understanding longitudinal pathways are not necessarily useful for improving individual-level prediction of future ADL disability.

Key strengths include the use of multiple waves from a nationally representative cohort of Thai adults with CVDs/HTN and a lagged design preserving temporal ordering between psychosocial exposures, mobility impairment, and ADL disability. Panel-based structural equation modelling allowed formal testing of heterogeneity in disablement pathways, while ordinal modelling with WLSMV appropriately addressed ceiling effects

and non-normal outcome distributions common in older populations. Sex-stratified mediation analyses further clarified subgroup-specific mechanisms.

Several limitations, however, should be acknowledged. Depression and pain were self-reported, pain was available in only one panel, and unmeasured adaptive processes such as caregiving support or assistive device use may partly explain panel-specific findings. Although conducted in Thailand, these findings may have relevance for other ageing populations experiencing rising cardiometabolic burden.

This study relied on complete-case analysis across multiple waves, which may introduce selection bias in an ageing cohort with non-random attrition. Although inverse probability weighted sensitivity analyses yielded results broadly consistent with the primary models, some attenuation in effect estimates—particularly for mobility impairment in Panel B indicates that selection processes may have modestly influenced effect size estimates.

The operationalisation of key variables warrants caution. The pain measure reflects activity-limiting impact rather than chronic pain and may capture acute or situational limitations. The mobility/fatigue composite, constructed using a hierarchical approach, may introduce measurement heterogeneity and some overlap with depressive symptoms. Accordingly, the mediator should be interpreted as a broad functional limitation construct rather than a specific mobility measure.

A mobility-only sensitivity analysis could not be conducted because the mobility items (C102005 and C102006) were unavailable in the 2020 HART wave, precluding construction of a comparable mediator for Panel B. Consequently, the depression-mediated pathway should be interpreted cautiously and warrants confirmation in cohorts with consistent mobility measurements across all waves.

Furthermore, the definition of CVDs/HTN in this study included both hypertension and clinical cardiovascular conditions, which may reduce disease specificity. In this cohort, hypertension accounted for the majority of cases, while clinical CVDs alone was relatively uncommon. As a result, the findings may primarily reflect cardiometabolic risk rather than established cardiovascular disease, and should be interpreted accordingly.

Clinically, integrating mobility assessment with depression screening may help identify older adults with CVDs/HTN who are at increased risk of functional decline. Whether this approach should differ by sex requires further investigation.

CONCLUSIONS

This longitudinal study found that mobility impairment was consistently associated with subsequent activities of daily living (ADL) disability among older Thai adults with cardiovascular diseases and/or hypertension, whereas associations involving multimorbidity and psychosocial factors varied across panels. Evidence that mobility impairment mediated the association between depressive symptoms and later ADL disability was limited to Panel B and, in sex-stratified analyses, was observed among men only; this finding was not replicated and should be interpreted cautiously. The mediation model also did not improve predictive discrimination over the direct-effects model. These results support considering mobility and depressive symptoms together when assessing functional health in older adults, while not establishing a need for different approaches by sex. These pathways need to be confirmed and their clinical relevance assessed through further longitudinal studies with consistent measures of mobility, and where attrition and other contextual factors are taken into account.

ACKNOWLEDGMENTS

Authors express gratitude to HART Thailand for providing essential information for this study.

FUNDING

No funds were received for the work.

CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

AUTHOR CONTRIBUTIONS

T.P., U.W.: conceptualization; T.P., C.P., U.W.: conceptual methodology; T.P., U.W.: data curation; T.P.: formal analysis; C.P., U.W.: investigation; U.W.: supervision; T.P., C.P., U.W.: writing – original draft; T.P., C.P., U.W.: writing – review & editing.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DATA AVAILABILITY STATEMENT

Data are available from the corresponding author upon reasonable request.

INSTITUTIONAL REVIEW BOARD STATEMENT

This research has been reviewed and approved for the exemption by Ethical Review Committee for Human Research of Faculty of Public Health, Mahidol University. (Protocol No: MUPH 231/2025.) Date of issue 21 November 2025. The present secondary analysis complied with the Declaration of Helsinki.

INFORMED CONSENT STATEMENT

Informed consent was waived by the Ethics Committee because this study utilized secondary data that were fully anonymized and posed minimal risk to participants.

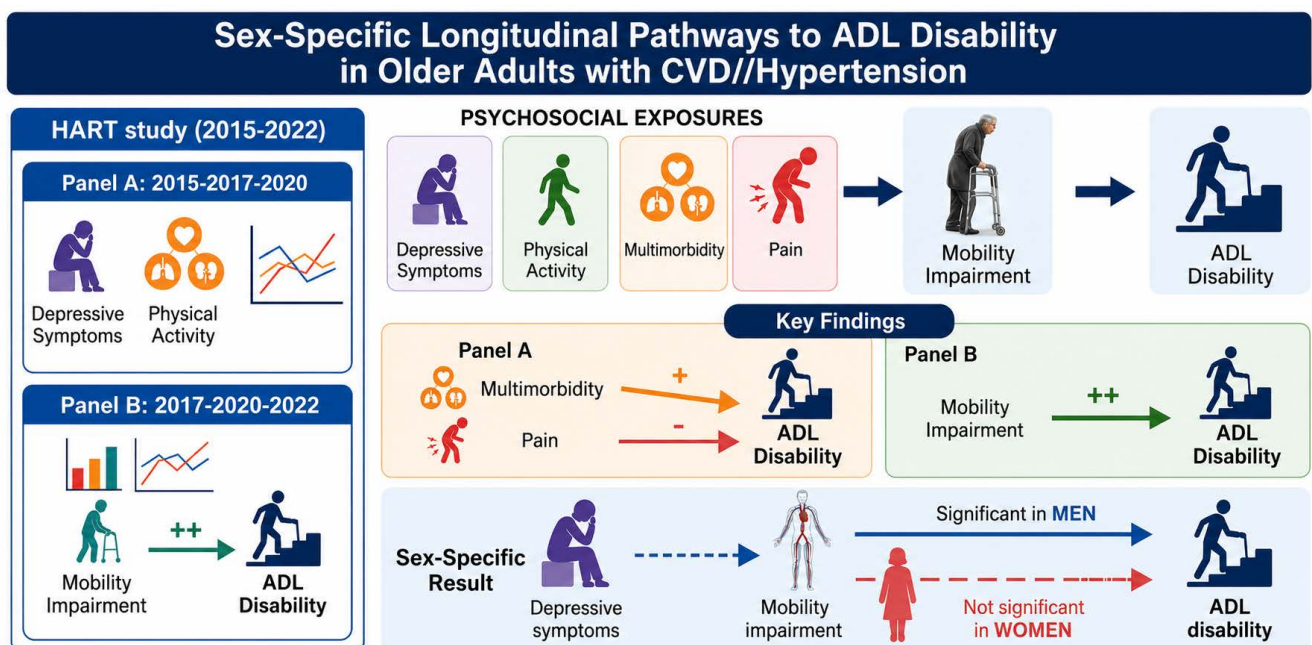
SUPPLEMENTARY MATERIALS

The following supporting information can be downloaded at: [Supplementary appendix](#)

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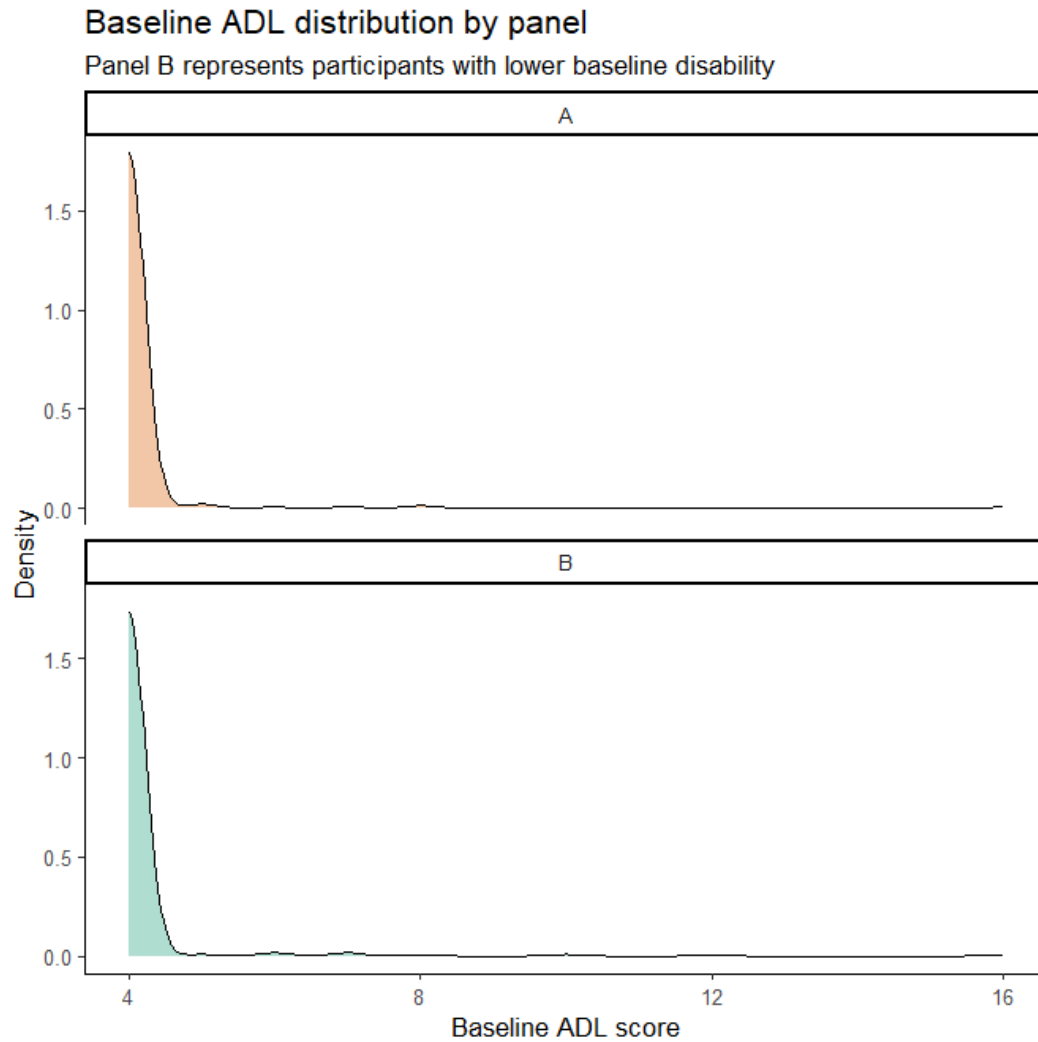


Figure S1. Baseline ADL distribution by panel. Kernel density plots show the distribution of baseline ADL scores after exclusion of non-comparable negative values. While median ADL was similar across panels, Panel A exhibited a broader upper tail, indicating a higher proportion of participants with moderate-to-severe baseline disability. In contrast, Panel B showed a more concentrated distribution at lower ADL scores, indicating a different baseline functional profile across the two temporally distinct analytic panels.

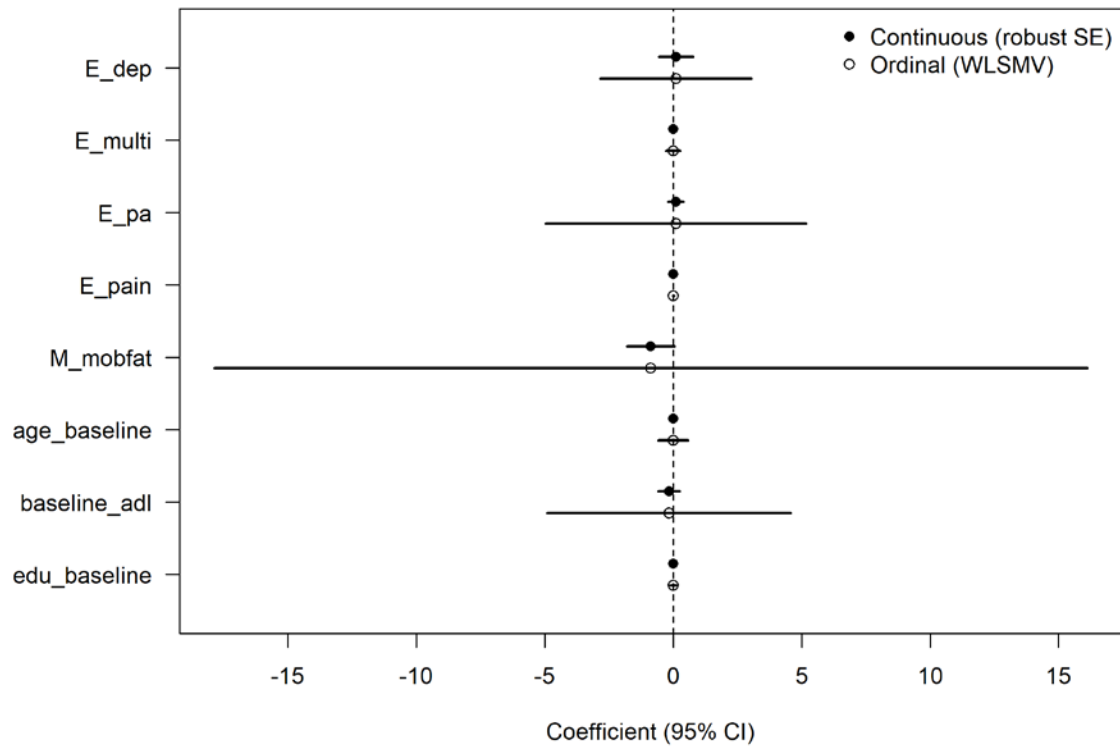


Figure S2 (Panel A). Direct effect estimates were highly consistent between models treating ADL as a continuous outcome and those treating ADL as an ordinal outcome using WLSMV. The direction and relative magnitude of effects were preserved across specifications, indicating that the main findings are robust to distributional assumptions of the disability outcome.

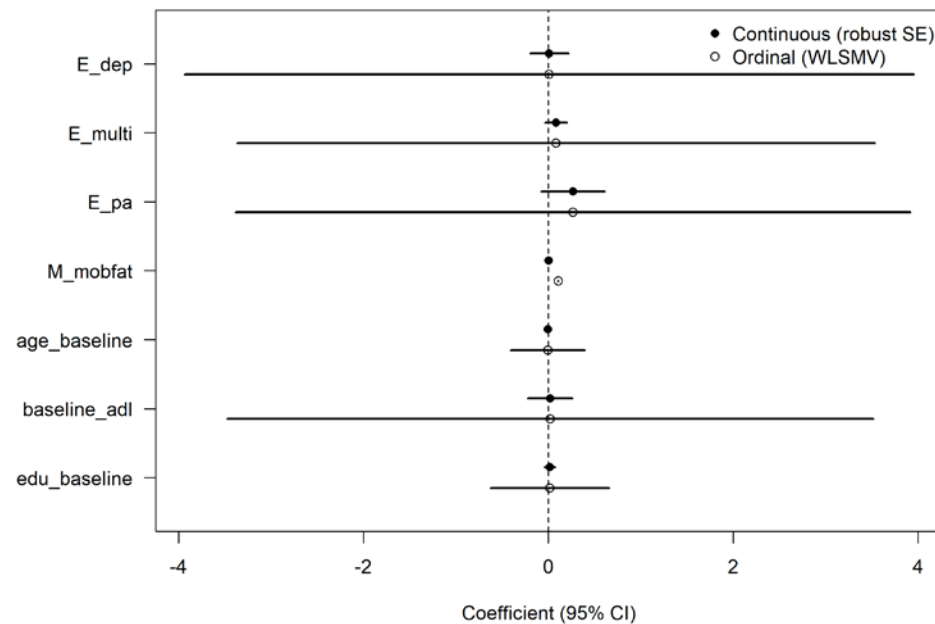


Figure S2 (Panel B). Direct effects estimated using continuous and ordinal specifications of ADL disability were highly consistent in direction and relative magnitude. Estimates in Panel B were generally more precise than those in Panel A, supporting the use of ordinal SEM for subsequent mediation analyses in this subgroup.

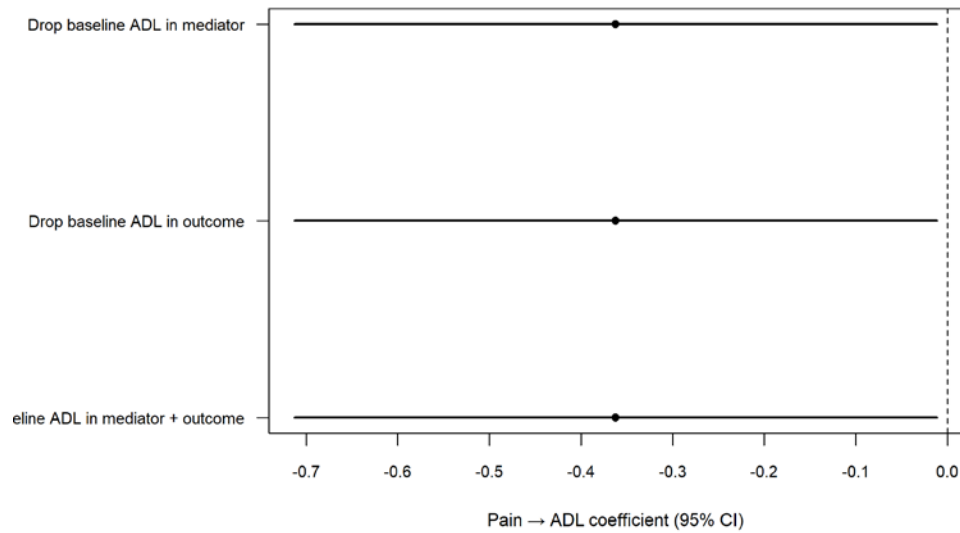


Figure S3. The association between pain and ADL disability in Panel A remained stable across alternative baseline ADL adjustment strategies, indicating that the observed effect is not attributable to over-adjustment or suppression by baseline functional status.

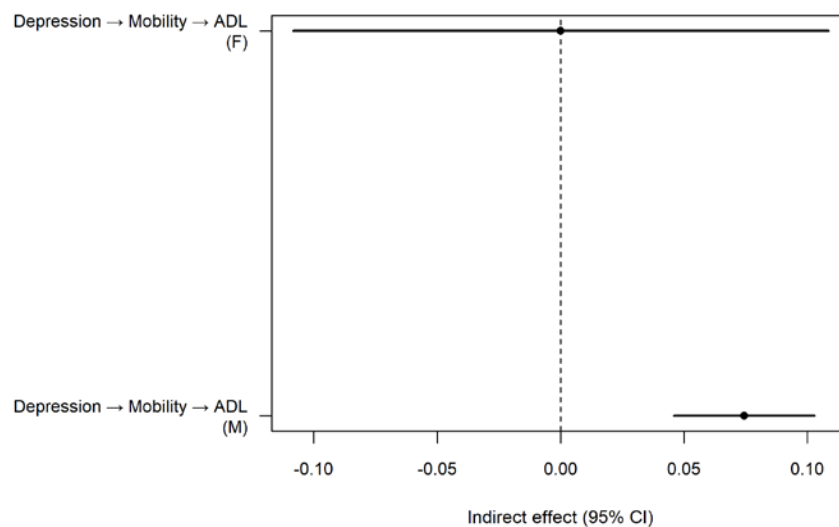


Figure S4. In Panel B, the indirect effect of depression on ADL disability via mobility impairment was evident in men but not in women. This sex-specific mediation suggests that mobility decline represents a relevant pathway linking depression to functional disability during the longitudinal observation period represented by Panel B

Supplementary results: robustness, sensitivity, and mechanistic analyses

Across both panels, direct effect estimates on ADL disability were highly consistent when ADL was modeled as a continuous outcome using robust standard errors or as an ordinal outcome using WLSMV (Figure S1). The direction and relative magnitude of associations were preserved across specifications, indicating that the main findings were not driven by distributional assumptions of the disability outcome. Estimates were generally more precise in Panel B, consistent with greater variability and reduced ceiling effects in this subgroup.

In Panel A, the inverse association between pain and ADL disability remained stable across alternative baseline ADL adjustment strategies, including models excluding baseline ADL from the mediator equation, the outcome equation, or both (Figure S2). The persistence of this effect suggests that it is unlikely to reflect over-adjustment or suppression due to baseline functional status, supporting a substantive interpretation rather than a modeling artifact.

Finally, sex-stratified mediation analyses in Panel B demonstrated a significant indirect effect of depression on ADL disability through mobility impairment in men, whereas no corresponding mediation was observed in women (Figure S3). This pattern indicates that mobility decline represents a sex-specific and context-dependent pathway linking depressive symptoms with ADL disability.

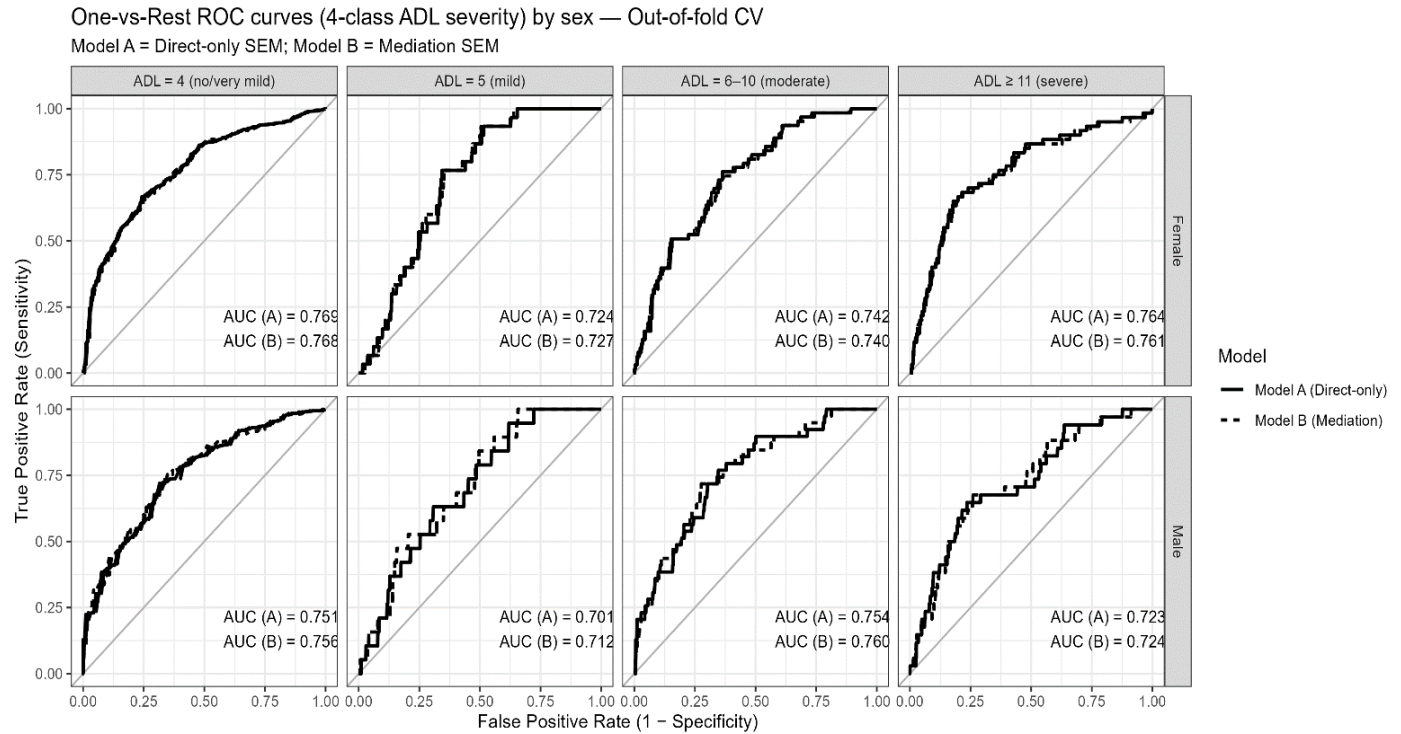


Figure S5. Sex-stratified one-vs-rest ROC curves for predicting four levels of ADL disability severity using structural equation models. One-vs-rest receiver operating characteristic (ROC) curves derived from out-of-fold cross-validation are shown for each ADL severity category (ADL = 4 [no/very mild], ADL = 5 [mild], ADL = 6–10 [moderate], and ADL ≥ 11 [severe]), stratified by sex. Model (A) represents the direct-effects structural equation model, while Model (B) represents the mediation structural equation model incorporating mobility limitation. Area under the ROC curve (AUC) values for both models are displayed within each panel. Both direct-effects and mediation structural equation models showed comparable, moderate discrimination for ADL disability severity across sexes, with higher accuracy for moderate and severe disability and minimal incremental gain from incorporating mobility limitation.

Table S1. Construction of analytic variables and panel-specific data arrangement in the Health, Aging and Retirement in Thailand (HART) study.

Construct (role)	Variable name in dataset	HART code(s)	Operational definition / derivation	Coding / range	Wave(s) used
Identifier	PID	PID	Unique participant identifier; used for all longitudinal joins	Character	All
Household context	HHID_baseline	HHID	Household identifier captured at baseline wave only; retained as context (not used to join waves)	Character	Baseline of each panel
Wave year	Wave	Wave	Survey wave year	2015/2017/2020/2022	All
CVD at wave	cvd_dx	C103001, C103107	1 if hypertension (C103001=1) OR cardiovascular disease (C103107=1) at that wave	0/1	All
Dynamic CVD cohort	cvd_ever	cvd_dx	Cumulative maximum of cvd_dx across waves per PID (CVD at or before wave)	0/1	All
CVD entry wave	cvd_entry_wave	cvd_dx, Wave	Earliest wave with cvd_dx=1 for each PID	2015/2017/2020/2022	All
Depressive symptoms (Exposure)	E_dep	C112001–C112010; reverse: C112004, C112007	Reverse code positive items: 3–item; sum all 10 items only when all present (within-scale complete case)	Sum score (higher=worse)	Panel A baseline 2015; Panel B baseline 2017
Physical activity (Exposure)	E_pa	C111001	Numeric proxy from exercise behavior item	As coded in HART	Panel A baseline 2015; Panel B baseline 2017
Pain proxy (Exposure)	E_pain	C105001	Accident resulting in physical health impact (past 1 year), used as pain/activity-limiting proxy	As coded in HART	Panel A baseline 2015; Panel B baseline 2017
Multimorbidity (Exposure)	E_multi	C103001, C103086, C103100, C103114, C103128, C103156 C103008, C103093, C103107, C103121, C103135,	Count of chronic condition indicators; missing treated as 0 before summing	Integer count	Panel A baseline 2015; Panel B baseline 2017

Construct (role)	Variable name in dataset	HART code(s)	Operational definition / derivation	Coding / range	Wave(s) used
Mediator: mobility/fatigue composite	M_mobfat	C102005, C102006, fatigue items: C112006, C112001, C112002	Primary: (C102005 + fatigue_sum) if C102006 missing; else (C102005 + C102006 + fatigue_sum). Fallback if primary missing: mobility-only (C102005 ± C102006), else fatigue-only. Fatigue_sum requires complete items.	Continuous composite	Panel A mediator 2017; Panel B mediator 2020
ADL disability (Outcome, continuous)	Y_adl	C113001–C113004	Sum ADL items only when all four present (within-scale complete case)	Sum score	Panel A outcome 2020; Panel B outcome 2022
ADL disability (Outcome, binary)	Y_adl_bin	C113001–C113004	1 if adl_sum ≥1; 0 if adl_sum=0; missing if adl_sum missing	0/1	Panel A outcome 2020; Panel B outcome 2022
Sex (Covariate)	sex	A201001	Baseline sex	As coded in HART	Panel baselines
Age range (Covariate)	age_baseline	A201003	Baseline age category/range	As coded in HART	Panel baselines
Education (Covariate)	edu_baseline	A201004	Baseline education level	As coded in HART	Panel baselines
Income (Covariate)	income_baseline	D101008	Total monthly income at baseline; included but not required due to missingness	As coded in HART	Panel baselines
Panel indicator	panel	—	Panel membership indicator (A or B)	“A”/“B”	Derived

Table S2. Baseline cardiovascular disease and/or hypertension status by panel*

HTN/CVD status at baseline wave	Panel A (2015 baseline) N= 999	Panel B (2017 baseline) N = 1065
Both HTN + CVD	81 (8.1%)	83 (7.8%)
HTN only	868 (86.9%)	788 (74.0%)
CVD only	50 (5.0%)	47 (4.4%)
Neither	0 (0.0%)	147 (13.8%)

* Panel A participants were selected based on hypertension or cardiovascular disease reported at or before the 2015 baseline; therefore, no participants were classified as having neither condition at baseline. Panel B participants were selected based on cumulative history up to 2017, and some did not report hypertension or cardiovascular disease at the 2017 interview.; HTN = Hypertension, CVD = Cardiovascular Diseases

Table S3. Panel moderation (A vs B) and panel-specific standardized path estimates

(i) Panel moderation test (A vs B)

Analysis	Pain included	Constraints	χ^2 diff	df	p-value
Likelihood-ratio test: equal vs free regressions across panels	No	Regressions	75.25	13	<0.001

(ii) Key panel-specific standardized paths (free multi-group model)*

Path	Path type	Panel A β (95% CI)	p	Std. β	Panel B β (95% CI)	p	Std. β
Depression → Mobility	a: Exposure → Mediator	−0.002 (−0.117, 0.112)	0.968	−0.012	0.017 (−0.623, 0.657)	0.959	0.010
Multi morbidities → Mobility	a: Exposure → Mediator	−0.135 (−4.831, 4.562)	0.955	−0.009	0.020 (−3.473, 3.514)	0.991	0.002
Physical activity → Mobility	a: Exposure → Mediator	−0.003 (−0.619, 0.613)	0.992	−0.003	−0.005 (−0.403, 0.392)	0.979	−0.005
Mobility → ADL disability	b: Mediator → Outcome	0.083 (0.079, 0.086)	<0.001	0.838	0.107 (0.104, 0.109)	<0.001	0.862
Depression → ADL disability (direct)	c': Direct	0.000 (−0.010, 0.010)	0.976	0.008	0.016 (−0.057, 0.090)	0.665	0.077
Multi morbidities → ADL disability (direct)	c': Direct	0.175 (−0.242, 0.593)	0.411	0.123	0.135 (−0.245, 0.516)	0.485	0.114
Physical Activity → ADL disability (direct)	c': Direct	0.010 (−0.085, 0.105)	0.844	0.094	−0.001 (−0.057, 0.054)	0.968	−0.008

* Estimates derived from **ordinal SEM (WLSMV)**. Panel A and Panel B were modeled simultaneously using a multi-group framework. χ^2 difference test compares constrained (equal paths) vs unconstrained (free paths) models. Std. β = standardized coefficient. Panel moderation indicates that at least one structural path differs between panels.

Table S4. Comparison of complete-case and IPW-weighted SEM results for key pathways

Panel	Pathway	Complete-case β	IPW-weighted β	Interpretation
A	Multimorbidity $\rightarrow$ ADL disability	0.16	0.18	Consistent positive association
A	Pain $\rightarrow$ ADL disability	-0.36	-0.35	Similar inverse/borderline association
A	Mobility $\rightarrow$ ADL disability	0.01	0.01	No material association
B	Mobility $\rightarrow$ ADL disability	0.11	0.03	Direction preserved; weaker after weighting
B	Multimorbidity $\rightarrow$ ADL disability	0.14	0.14	Similar magnitude
B	Depression indirect effect via mobility	NS	NS	No panel-level mediation

Only key structural and indirect pathways are shown. Stabilised inverse probability weights were estimated for complete-case inclusion using panel, baseline age, sex, education, baseline ADL, depressive symptoms, multimorbidity, and physical activity, then trimmed at the 1st and 99th percentiles. Complete IPW estimates are available on request.

Table S5. Sex-specific predictive performance of structural equation models for moderate-to-severe ADL disability (ADL ≥ 6)

Sex	Model	n	AUC (95% CI)	RMSE	Brier score	Log loss	Calibration intercept	Calibration slope
Male	Model A (Direct-only)	793	0.751 (0.690–0.812)	0.272	0.0738	0.303	–1.055	0.495
	Model B (Mediation)	793	0.573 (0.499–0.647)	0.355	0.1261	2.435	–2.172	0.007
Female	Model A (Direct-only)	1,272	0.768 (0.724–0.812)	0.281	0.0787	0.300	–0.717	0.625
	Model B (Mediation)	1,272	0.711 (0.655–0.766)	0.286	0.0815	0.696	–2.058	0.025

- Model A includes direct effects of psychosocial and clinical factors on ADL disability.
- Model B additionally incorporates mobility limitation as a mediator.
- Predictive performance was evaluated using **out-of-fold cross-validation** stratified by sex.
- AUC indicates discrimination; RMSE and Brier score indicate overall probability accuracy (lower values indicate better performance).
- Calibration intercepts < 0 indicate systematic overestimation of risk; calibration slopes < 1 indicate overly extreme predictions.

Predictive analyses were conducted as supplementary evaluations to contrast explanatory and predictive performance and were not intended to assess the clinical utility of the mediation model. Overall, the direct-effects structural equation model (Model A) consistently demonstrated superior predictive performance compared with the mediation model (Model B) in both sexes. Model A showed moderate discrimination, with AUC values of 0.75 in men and 0.77 in women, whereas discrimination was lower for Model B, particularly among men. The reduction in discrimination associated with the mediation model was more pronounced in men ($\Delta\text{AUC} = -0.18$) than in women ($\Delta\text{AUC} = -0.06$). Measures of overall accuracy similarly favoured Model A, with lower RMSE and Brier scores in both sexes, indicating more accurate probability estimates. In contrast, Model B exhibited higher prediction error and substantially worse log loss, especially among men. Calibration analyses indicated systematic risk overestimation in both models, with more severe miscalibration observed for the mediation model. These findings suggest that while mediation modelling provides insight into pathways to disability, the direct-effects model offers more reliable predictive performance for moderate-to-severe ADL disability.

Table S6. Standard Model Fit Indices

Model	CFI	TLI	RMSEA	SRMR	df
Panel A	1.00	1.00	0.00	0.00	0
Panel B	1.00	1.00	0.00	0.00	0

All models were just-identified ($\text{df} = 0$); therefore, fit indices indicate perfect fit by definition and are not informative.