

Sex-specific educational disparities in the odds and progression of depressive symptoms in Northern Sweden: A longitudinal study

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Abstract

Background: Educational attainment is considered a social protective factor against depression risk, but less is known about sex-specific associations between education and the odds, progression, and severity of depressive symptoms in older populations. This study investigated these associations among middle-aged and older adults in Northern Sweden.

Methods: We used data from the Betula longitudinal cohort study in Umeå, Sweden. Depressive symptoms were measured using the CES-D scale across multiple waves (1998-2014). We used mixed-effects logistic, linear and ordinal regression models. Marginal population means and exceedance probabilities were estimated.

Results: The study included 1013 individuals (men=503, women=510). Higher education, particularly secondary education, was associated with higher odds of depression (Odds ratio [OR] for secondary vs primary = 1.88, 95% CI 1.08–3.30). Sex-stratified analyses indicated positive associations (i.e., all ORs > 1, although not statistically significant), with a pronounced association in women with secondary education. Among women neither the linear mixed model nor the ordinal regression model showed any statistical evidence of educational differences in depression progression or severity. In men, the linear mixed model suggested decreasing symptom severity among higher-educated men and increasing severity among those with primary education over time (P for interaction < 0.05). Similar patterns appeared in the ordinal model.

Conclusions: Our study suggests higher education is associated with higher the odds of depression particularly in women. Evidence for educational differences in symptom progression was only evident among men. These findings highlight a complex relationship between education and depression in Swedish older adults, underscoring the need for validation in larger studies.

Introduction

Depression affects about 4–5% of the global population and accounted for approximately 56 million disability-adjusted life-years (DALYs) in 2023, with rising incidence (1–3). It shows clear sex-specific differences, being about 1.5 times more prevalent in women than men (prevalence of depression was 4.98% among women and 3.25% among men in 2023) (2, 4, 5). Between 2010 and 2021, depression has remained one of the leading contributors to the global disease burden (6).

Depression arises from a complex interplay of social, psychological, and biological factors (7–9). Investigating the social determinants of depression onset and progression can inform effective strategies to reduce the disease burden. Education, which is a well-established social determinant of health, offers significant potential for public health interventions (10, 11). Higher educational attainment is known to be a protective factor against the development of depression (12–18). This protective effect can be explained by the World Health Organization's conceptual framework on social determinants of health (19), as education improves socioeconomic outcomes, such as better jobs, increased income,

healthier lifestyles, and greater access to resources, which collectively mitigate psychosocial stressors. The association between educational attainment and risk of depression is bidirectional, that is depression can also negatively impact subsequent educational attainment, particularly among younger age groups (20).

Despite substantial evidence that higher education serves as a resilience factor against depression risk, previous studies mostly focused on education in relation to depression onset or prevalence (12–18), not on its progression and severity over time. In Sweden, though education and healthcare are tax-based and publicly financed, several studies have shown that socioeconomic disparities in mental health persist (21–25). However, few have examined the specific influence of education on depression risk (26, 27). These studies primarily focused on young adults (20 years) and middle-aged adults (31–64 years), and none have reported findings specifically for the older population in Northern Sweden. Older adults represent a particularly vulnerable group as depression in later life is associated with functional and cognitive decline, comorbidity, and increased mortality, yet later life depression remains under-recognized (28). Understanding educational inequalities in depression in Northern Sweden is particularly relevant, as the social and public health context of this relatively sparsely populated region may differ from that of the more densely populated southern regions (25). Given the well-established sex differences in depression, it is also important to investigate sex-specific differences in the association between education and depression.

To our knowledge, longitudinal evidence on sex-specific effects of education on depression progression and severity in middle and older age remains limited. Therefore, our study aims to investigate the effect of educational attainment on odds, progression, and severity of depressive symptoms over time among middle-aged and older adults in Northern Sweden as well as potential sex-specific differences in these associations.

Methods

Study setting

The participants in this investigation were from the Betula prospective cohort study, which is a population-based longitudinal study conducted in Umeå, on the northeast coast of Sweden. Established in 1988, the Betula study aimed to examine how health and memory develop over adult life including old age, to identify early signs of dementia, and to evaluate premorbid memory function. The Betula study adopted a cross-sequential design, following multiple age groups over time (e.g., five years intervals) to disentangle cohort and aging effect, and recruiting new sets of individuals at subsequent follow-ups to control for potential practice (retest) effects and attrition. This sequential design mitigates the limitations of standard cross-sectional and longitudinal studies, providing more accurate estimates of cognitive and health outcome trajectories (29, 30).

Betula participants were randomly selected from the population registry with a sex distribution representative of the general population. Ten age cohorts were recruited with five-year intervals (i.e. 35,

40, 45 ... 80 years; originally 100 participants per each age stratum). Those with dementia, non-native Swedish speakers, severe hearing/vision impairments, or intellectual disabilities were excluded and replaced with individuals of the same age and sex. Data collection took place between 1988 and 2014 across six waves: W1 (1988–1991), W2 (1993–1995), W3 (1998–2001), W4 (2003–2005), W5 (2008–2010), and W6 (2013–2014). The sample at W1 comprised 1,000 participants (Sample 1, S1) with an equal sex distribution. At W2, two additional groups of participants were recruited; Sample 2 (S2; n = 995), matched to the age and sex distribution of S1 at W1, and Sample 3 (S3; n = 963), matched to the age and sex distribution of S1 at W2 (ages 40, 45, 50 ... 85 years). Of note, S2 had only one follow-up assessment and was therefore not included in the current study. W2 was considered the baseline for this study.

Each participant underwent a comprehensive assessment including self-administered questionnaires on socioeconomic conditions, critical life events, and other health-related factors; medical examinations with blood samplings and anthropometric measurements; health surveys/interviews; and an extensive evaluation of memory functions as well as mental health. Health surveys and medical examinations were conducted by research nurses or assistant nurses as per standardized protocols, while cognitive evaluations were administered by investigators trained in basic psychology. Details of the Betula study are described elsewhere (29, 31, 32).

Exclusions

In addition to original exclusion criteria of the Betula study, individuals were required to have at least two visits (i.e. W2 and W3), resulting in the exclusion of 401 individuals. Participants with at least two self-reported depressive symptoms at baseline (e.g., feeling dispirited, fatigue, sleep problems, loss of appetite, loneliness or anxiety/worry), used as a proxy for depression (n = 314), and those diagnosed with dementia during the study period (n = 101) were excluded. Individuals with missing data on baseline exposure or covariates, as well as those missing outcome data at all time points (n = 134), were excluded. Details of the exclusions are depicted in Fig. 1.

Assessment of depressive symptoms

In Betula cohort, depressive symptoms were assessed using the Center for Epidemiologic Studies Depression Scale (CES-D) (33), a 20-item self-reported questionnaire designed to screen depressive symptoms in the general population. Each item was rated on a 4-point scale ranging from 0 (rarely or never), 1 (a little or some of the time), 2 (moderately or much of the time), to 3 (most or almost all the time), reflecting the frequency of symptoms experienced during the past week. Four positively worded items (e.g., “I felt hopeful about the future,” “I was happy”) are reverse coded to ensure that higher total scores (range: 0–60) indicate greater depressive symptomatology. The CES-D has demonstrated excellent psychometric properties, including high internal consistency, reliable test–retest performance, high diagnostic accuracy, and strong correlations with clinical diagnoses of depression (34–37). A standard CES-D cutoff score of 16 or higher was used to classify individuals with depressive symptoms (binary yes/no depression outcome) (38). In addition to the continuous CES-D score, symptom severity

was categorized as follows: none (0–9), mild/subsyndromal (10–15), moderate (16–24), and severe (25–60), based on prior research (34, 36, 37). In the Betula cohort, CES-D data were collected starting from W3.

Educational attainment and other covariates

Educational attainment was categorized into compulsory/primary education (≤ 9 years), secondary education (10–12 years), and postsecondary education (≥ 13 years). Other covariates were preselected based on important factors linked to depression in previous studies (39–47), data availability and directed acyclic graph (DAG) (48) (supplementary Fig. 1). These included sociodemographic factors: cohort age (40–50, 55–65, 70–85 years), sex (women, men), occupational status (employed, retired/sick leave/unemployed), and marital status (married, not married, divorced/widowed), number of critical life events (0, 1–5, 6–10, ≥ 10); lifestyle factors and anthropometric measurements: smoking status (yes/no), alcohol consumption (yes/no), physical activity (never/few times ever, monthly, weekly, daily), body mass index (normal weight, overweight, obese), and waist–hip ratios (recommended, high risk); and comorbidities and other health-related factors: self-reported major illnesses including cardiovascular disease, stroke, diabetes, cancer, thyroid or other hormonal/metabolic disturbances (yes/no), blood pressure (hypertension/not), genetic predisposition (yes/no for APOE4 gene) and menopausal status (yes/no) in women. Except for menopausal status, educational variables and all covariate data were obtained from W2, which served as the baseline for this study. As menopause-related questions for women were introduced at W3, menopausal status at W2 was retrospectively derived based on age at menopause reported at W3.

Statistical analysis

Baseline characteristics of study participants and depression outcomes during follow-up were compared using Pearson's chi-square test for categorical variables and t-tests for continuous variables. To investigate the association between baseline educational attainment and odds of depressive symptoms (binary outcomes defined by a CES-D cutoff score of 16) during follow-up time points, mixed-effects logistic regression was used. Two statistical models were fitted. Model 1 was a minimally adjusted model that included potential confounding factors (key sociodemographic factors) based on DAG (supplementary Fig. 1) and test wave as a continuous variable, as it showed a lower Akaike Information Criterion (AIC) value than when included as a factor variable. Model 2 was a fully adjusted model that additionally incorporated other known risk factors for depression, including lifestyle, anthropometric measurements, comorbidities, and other health-related factors. Details of the adjusted variables in each model are described in the corresponding tables. Analyses were stratified by sex to understand sex-specific differences in the associations, and menopausal status was additionally adjusted in the analyses for women. Although Model 2 generally yielded lower AIC values than Model 1, Model 1 based on DAG was considered the final model for subsequent analyses as Model 2 may contain potential

mediators. A *post-hoc* cross-tabulation between education levels and test waves was also conducted to understand the study retention by education levels.

To further examine the baseline education in relation to the progression/severity of depressive symptoms during follow-up, we used a linear mixed-effects model for depressive symptoms in continuous CES-D scale and a cumulative link mixed model (also called ordered regression model) for depression severity categorized as none, mild, moderate, or severe. The mixed-effects regression models were performed using R software packages “lme4” (49) and “ordinal”(50). A two-level random-intercept model, with individual serial numbers included as a random effect (level two) to account for within-person correlations, was used because it yielded a lower AIC value than the two-level random-slope model. An exception was the ordered regression model in men, where the random-slope model showed the lowest AIC value. Interaction terms between test wave and educational attainment were included in the linear mixed and ordered regression models for men, as models with these interactions yielded the lowest AIC values.

The R package “emmeans”(51–53) was used to obtain estimated marginal population means from a linear mixed model and estimated exceedance probabilities (probability of being in higher symptom categories) from an ordered regression model, where higher values of these estimates indicate greater progression/severity of depressive symptoms. All statistical analyses were performed using R software (version 4.5.0; R Foundation for Statistical Computing, Vienna, Austria), with a statistical significance level of < 0.05 .

Results

Baseline characteristics and depression outcomes

After exclusions, the final study population comprised 1,013 individuals with somewhat equal sex distribution (men = 503, women = 510; Fig. 1). Table 1 presents participants’ baseline characteristics and depression outcomes (binary yes/no) during follow-up with 128 participants identified as having depression. Compared to non-depressed individuals, those with depression were more often women (60.9% vs. 48.8%, $P = 0.014$), on average two years younger (55 vs. 57 years, $P = 0.032$), and more likely to have higher education; secondary (28.9% vs. 21.6%) or postsecondary (42.2% vs. 34.9%; $P = 0.007$). They were also more likely to report little or no physical activity (33.6% vs. 22.3%; $P = 0.013$) and to have experienced more than five critical life events (57.8% vs. 35.9%; $P < 0.001$). Baseline characteristics and depression outcomes by sex are summarized in Supplementary Table 1. Among women, those with depression were more likely than non-depressed women to be younger, have higher education, report little or no physical activity, and experience a greater number of critical life events, consistent with findings in the total population. In contrast, no significant baseline differences were observed between depressed and non-depressed men, except for marital status, with divorced or widowed men more likely to be depressed. *Post-hoc* cross-tabulation between education levels and test waves showed that the proportions of women with primary education reduced from 42% in wave 2 to 27% in wave 6 while the

proportions of women with secondary and postsecondary education increased from 23–35% in wave 2 to 30–44% in wave 6 (Supplementary Table 2). Similar patterns were observed for men.

Table 1
Baseline characteristics and binary depression outcomes during follow-up

Baseline characteristics	Depression outcome (CES-D score ≥ 16)		
	No (N = 885)	Yes (N = 128)	P-value ¹
Sex, N (%)			
women	432 (48.8)	78 (60.9)	0.014
men	453 (51.2)	50 (39.1)	
Age at assessment, mean (SD)	57 (12.36)	55 (11.77)	0.032
Cohort age, N (%)			
40–50	365 (41.2)	62 (48.4)	0.237
55–65	322 (36.4)	44 (34.4)	
70–85	198 (22.4)	22 (17.2)	
Educational attainment, N (%)			
compulsory/primary education (≤ 9 years)	385 (43.5)	37 (28.9)	0.007
secondary education (10–12 years)	191 (21.6)	37 (28.9)	
postsecondary education (≥ 13 years)	309 (34.9)	54 (42.2)	
Occupation status, N (%)			
employed	745 (84.2)	113 (88.3)	0.283
retired/unemployed/sick leave	140 (15.8)	15 (11.7)	
Marital status, N (%)			
married	698 (78.9)	101 (78.9)	0.854
not married	46 (5.2)	8 (6.2)	
divorced/widow/er	141 (15.9)	19 (14.8)	
APOE4 genes, N (%)			
no	638 (72.1)	92 (71.9)	1.000
yes	247 (27.9)	36 (28.1)	
Smoking, N (%)			
¹ Pearson's chi-square test for categorical variables and t-tests for continuous variables			

Baseline characteristics	Depression outcome (CES-D score ≥ 16)		
	No (N = 885)	Yes (N = 128)	P-value ¹
no	464 (52.4)	58 (45.3)	0.158
yes	421 (47.6)	70 (54.7)	
Alcohol, N (%)			
no	145 (16.4)	24 (18.8)	0.586
yes	740 (83.6)	104 (81.2)	
Body mass index, N (%)			
normal weight (18.5–24.9)	389 (44.0)	50 (39.1)	0.514
overweight (25–29.9)	381 (43.1)	58 (45.3)	
obese (≥ 30)	115 (13.0)	20 (15.6)	
Waist hip circumference, N (%)			
recommended	504 (56.9)	84 (65.6)	0.078
high risk	381 (43.1)	44 (34.4)	
Physical activity, N (%)			
never/few times ever	197 (22.3)	43 (33.6)	0.013
few times a month	146 (16.5)	20 (15.6)	
weekly	378 (42.7)	52 (40.6)	
daily	164 (18.5)	13 (10.2)	
Hypertension, N (%)			
no	421 (47.6)	65 (50.8)	0.559
yes	464 (52.4)	63 (49.2)	
Any comorbidities, N (%)			
no	274 (31.0)	35 (27.3)	0.467
yes	611 (69.0)	93 (72.7)	
Number of critical life events, N (%)			
None	63 (7.1)	3 (2.3)	< 0.001
¹ Pearson's chi-square test for categorical variables and t-tests for continuous variables			

Baseline characteristics	Depression outcome (CES-D score ≥ 16)		
	No (N = 885)	Yes (N = 128)	P-value ¹
1–5	504 (56.9)	51 (39.8)	
6–10	246 (27.8)	54 (42.2)	
11–23	72 (8.1)	20 (15.6)	
¹ Pearson's chi-square test for categorical variables and t-tests for continuous variables			

Regarding observed depressive symptoms in CES-D scores (Supplementary Fig. 2), sex-specific differences were observed across follow-up waves, with women consistently reporting higher symptom scores than men throughout follow-up. Age- and wave-adjusted linear mixed model also showed that men had lower mean CES-D scores than women across follow-up ($\beta = -0.82$; 95% CI: -1.37 to -0.26; $P = 0.004$). While mean depressive symptom scores in women showed a slight increase across waves 3 to 5 before declining in wave 6, mean scores in men gradually decreased over the same period. Further analyses by educational level (Fig. 2) showed that, among women, those with secondary and postsecondary education generally had higher observed mean scores than women with primary education across the study waves. In contrast, among men, the observed mean scores tended to decline overtime for those with secondary and postsecondary education, whereas men with primary education showed a more stable or slightly increasing pattern.

Association between educational attainment and odds of depression

For the whole population, both Model 1 and Model 2 showed positive associations between higher education categories and higher odds of depression, particularly among participants with secondary education, who had 1.88 (95% CI 1.08–3.30) times higher odds in Model 1 and 2.08 (95% CI 1.17–3.68) in Model 2 compared with primary education (Table 2). In subgroup analyses by sex, women with secondary education showed a pronounced positive association with higher odds of depression in Model 2 (odds ratio (OR) for secondary versus primary education = 2.33, 95% CI 1.03–5.27) (Table 2). Across both sexes, although not statistically significant in all models, higher education categories consistently showed odds ratios above one, indicating potential positive associations. Although Model 2 had lower AIC value in overall analyses, covariates included in Model 1 were selected for subsequent analyses because Model 2 likely included potential mediators.

Table 2
Association between educational attainment and odds of depression outcomes

	Educational attainment	Depressive episodes	Total number of observations	Model 1 ¹ OR (95% CI)	Model 2 ² OR (95% CI)
All	Primary (≤ 9 years)	40	948	Reference	Reference
	Secondary (10–12 years)	57	667	1.88 (1.08–3.30)	2.08 (1.17–3.68)
	Postsecondary (≥ 13 years)	65	1062	1.40 (0.80–2.47)	1.70 (0.95–3.04)
	AIC			1167.87	1165.51
Women ³	Primary (≤ 9 years)	20	470	Reference	Reference
	Secondary (10–12 years)	42	355	1.92 (0.88–4.20)	2.33 (1.03–5.27)
	Postsecondary (≥ 13 years)	40	525	1.22 (0.55–2.74)	1.64 (0.70–3.83)
	AIC			695.74	695.73
Men	Primary (≤ 9 years)	20	478	Reference	Reference
	Secondary (10–12 years)	15	312	1.43 (0.61–3.33)	1.49 (0.63–3.55)
	Postsecondary (≥ 13 years)	25	537	1.47 (0.65–3.34)	1.83 (0.78–4.27)
	AIC			480.96	491.89

¹Model 1 adjusted for sociodemographic factors: cohort age (40–50, 55–65, 70–85 years), sex (women, men), occupational status (employed, retired/sick leave/unemployed), and marital status (married, not married, divorced/widowed), number of critical life events (0, 1–5, 6–10, ≥ 10) and test wave in continuous variable.

²Model 2 additionally adjusted for lifestyle factors and anthropometric measurements: smoking status (yes/no), alcohol consumption (yes/no), exercise frequency (never/few times ever, monthly, weekly, daily), body mass index (normal weight, overweight, obese), and waist–hip ratios (recommended, high risk) self-reported major illnesses/comorbidities (yes/no), blood pressure (hypertension/not), genetic predisposition (yes/no for APOE4 gene)

³Menopausal status (yes/no) was included in both models for women.

OR= Odds ratios, CI=confidence intervals, AIC= Akaike Information Criterion value, Bold; Marks statistically significant results

Educational attainment and depression progression/severity (linear-mixed model)

Table 3 and Fig. 3 present the educational attainment in relation to mean depressive symptom score changes overtime by sex. Among women, no statistically significant association was observed between education and changes in mean CES-D scores over time (Table 3). Although marginal mean scores were slightly higher in women with higher education across all waves, overlapping confidence intervals and stable trajectories indicated no progression or increased severity (Fig. 3). On the other hand, compared to men with primary education, those with secondary and postsecondary education exhibited significant higher mean CES-D scores during follow-up (3.03, 95% CI: 0.59–5.46; and 3.53, 95% CI: 1.39–5.67, respectively). However, men in higher education categories showed reduced symptom progression, with mean scores declining by approximately 0.4 points per wave (0.36 minus 0.75 or 0.73), whereas those in the primary education category exhibited an average increase of 0.36 points per wave (Table 3) (P for interaction < 0.05, Fig. 3).

Table 3
Association between educational attainment and depression symptom progression/severity and estimated marginal means of CES-D scores

		Linear mixed model ¹ , Mean (95% CI)	Estimated marginal means (95% CI)			
Women	Educational attainment		Wave 3	Wave 4	Wave 5	Wave 6
	Primary (≤ 9 years)	Reference	6.94 (5.73–8.16)	6.92 (5.72–8.12)	6.90 (5.66–8.14)	6.87 (5.55–8.20)
	Secondary (10–12 years)	0.67 (-0.57–1.91)	7.61 (6.33–8.90)	7.59 (6.33–8.85)	7.57 (6.28–8.86)	7.54 (6.18–8.91)
	Postsecondary (≥ 13 years)	0.37 (-0.84–1.58)	7.32 (6.07–8.56)	7.29 (6.07–8.52)	7.27 (6.01–8.53)	7.25 (5.91–8.58)
	Test wave	-0.02 (-0.27–0.23)				
Men ²	Educational attainment		Wave 3	Wave 4	Wave 5	Wave 6
	Primary (≤ 9 years)	Reference	6.23 (5.24–7.22)	6.59 (5.64–7.55)	6.95 (5.89–8.02)	7.31 (6.03–8.59)
	Secondary (10–12 years)	3.03 (0.59–5.46)	7.02 (5.84–8.19)	6.63 (5.53–7.72)	6.24 (5.07–7.41)	5.85 (4.47–7.23)
	Postsecondary (≥ 13 years)	3.53 (1.39–5.67)	7.58 (6.54–8.62)	7.21 (6.21–8.20)	6.84 (5.80–7.88)	6.47 (5.29–7.65)
	Test wave	0.36 (-0.02–0.74)				
	Test wave x Secondary education	-0.75 (-1.31–-0.18)				
	Test wave x Postsecondary education	-0.73 (-1.22–-0.24)				

¹Linear mixed-effects models were used for depressive symptom outcomes in continuous CES-D scale. The models adjusted for sociodemographic factors: cohort age (40–50, 55–65, 70–85

years), sex (women, men), occupational status (employed, retired/sick leave/unemployed), and marital status (married, not married, divorced/widowed), number of critical life events (0, 1–5, 6–10, ≥ 10) and test wave in continuous variable. Menopausal status (yes/no) was included in the analyses for women. A two-level random-intercept model, with individual serial numbers included as a random effect (level two), was used.

²Interaction terms between test wave and education were included in the analyses for men as the models with interactions showed the lowest AIC values in men.

Bold; Marks statistically significant results

Educational attainment and depression progression/severity (order regression model)

The associations between educational attainment and the odds of being in higher depressive symptom categories, as well as the exceedance probabilities, are shown in Table 4 and Fig. 4. In both sexes, higher education was associated with higher odds of being in a more severe symptom category, although not statistically significant. For women, exceedance probabilities were generally higher in the higher education categories across all waves, but the confidence intervals overlapped, and trajectories showed only modest declines over time. Among men, the exceedance probabilities showed an overall declining pattern across waves. Men in the higher education categories had higher exceedance probabilities in wave 3, followed by lower probabilities than those with primary education in later waves, but confidence intervals overlapped.

Table 4

Association between educational attainment and depression symptom progression/severity and exceedance probabilities (ordinal outcomes)

		Ordered regression model ¹ , OR (95% CI)	Exceedance probabilities (95% CI)			
Women ²	Educational attainment		Wave 3	Wave 4	Wave 5	Wave 6
	Primary (≤ 9 years)	Reference	0.088 (0.044–0.131)	0.085 (0.043–0.128)	0.083 (0.041–0.126)	0.081 (0.036–0.125)
	Secondary (10–12 years)	1.28 (0.71–2.29)	0.106 (0.055–0.158)	0.104 (0.054–0.153)	0.101 (0.051–0.151)	0.098 (0.046–0.150)
	Postsecondary (≥ 13 years)	1.13 (0.63–2.01)	0.097 (0.050–0.143)	0.094 (0.049–0.139)	0.092 (0.046–0.137)	0.089 (0.041–0.137)
	Test wave	0.97 (0.84–1.10)				
Men ³	Educational attainment		Wave 3	Wave 4	Wave 5	Wave 6
	Primary (≤ 9 years)	Reference	0.094 (0.055–0.133)	0.079 (0.045–0.113)	0.066 (0.025–0.106)	0.054 (0.006–0.102)
	Secondary (10–12 years)	3.41 (0.57–20.37)	0.114 (0.065–0.164)	0.078 (0.039–0.117)	0.051 (0.012–0.089)	0.032 (0.000–0.068)
	Postsecondary (≥ 13 years)	2.60 (0.56–12.12)	0.112 (0.068–0.156)	0.080 (0.043–0.118)	0.056 (0.018–0.094)	0.038 (0.000–0.076)

¹Cumulative link mixed models (ordered regression models) were used for depression severity categorized as none (0–9), mild/subsyndromal (10–15), moderate (16–24), and severe (25–60). The models adjusted for sociodemographic factors: cohort age (40–50, 55–65, 70–85 years), sex (women, men), occupational status (employed, retired/sick leave/unemployed), and marital status (married, not married, divorced/widowed), number of critical life events (0, 1–5, 6–10, ≥ 10) and test wave in continuous variable. ²Menopausal status (yes/no) was included in the analyses for women. A two-level random-intercept model with individual serial numbers as random effects was used for women to account for within-person correlations, while two-level random-slope model (additionally included test wave as random slope), which showed the lowest AIC values, was used for men.

³Interaction terms between test wave and education were included in the analyses for men as the models with interactions showed the lowest AIC values in men.

Test wave	0.77 (0.52–1.15)
Test wave x Secondary education	0.73 (0.45–1.18)
Test wave x Postsecondary education	0.79 (0.53–1.19)

¹Cumulative link mixed models (ordered regression models) were used for depression severity categorized as none (0–9), mild/subsyndromal (10–15), moderate (16–24), and severe (25–60). The models adjusted for sociodemographic factors: cohort age (40–50, 55–65, 70–85 years), sex (women, men), occupational status (employed, retired/sick leave/unemployed), and marital status (married, not married, divorced/widowed), number of critical life events (0, 1–5, 6–10, ≥ 10) and test wave in continuous variable. ²Menopausal status (yes/no) was included in the analyses for women. A two-level random-intercept model with individual serial numbers as random effects was used for women to account for within-person correlations, while two-level random-slope model (additionally included test wave as random slope), which showed the lowest AIC values, was used for men.

³Interaction terms between test wave and education were included in the analyses for men as the models with interactions showed the lowest AIC values in men.

Discussion

In this longitudinal study of 1,013 participants, higher educational attainment was associated with increased odds of depression, particularly among those with secondary education, compared to primary education. Indications of potential sex-specific differences in depression symptoms were also observed. Individuals with depression were more likely to be women, who also had higher depressive symptom scores than men across waves. We found limited statistical evidence for educational differences in the progression and severity of depressive symptoms in women. In men, however, CES-D mean scores decreased over time among those with secondary and postsecondary education but increased among those with primary education.

The positive association between educational attainment and depression is unexpected and contrasts with the prior understanding that education is a resilience factor for mental health (12–18). However, the findings are not implausible. A large European study of more than 100,000 adults reported the protective effect of education against depressive symptoms was weakest among Scandinavian populations, and became non-significant after full adjustment for relevant covariates (12). In the same study, education was protective among men whereas in women, higher educational attainment was related with higher odds of depressive symptoms. Similarly, a cohort study from the Swedish Longitudinal Occupational Survey of Health reported that higher educational attainment was associated with increased odds of having higher depressive symptom level trajectories in both men and women (54). The potential explanations for these findings include that strong welfare systems in Scandinavian countries may reduce socioeconomic inequalities, thereby limiting the additional mental health benefits of education (12) and a potential link between higher educational level and higher internal and external demands and

more responsibility (54). Another study indicates that the beneficial effects of education have diminished among later-born US cohorts of middle-aged adults, and the authors' proposed reason was that a number of midlife challenges tend to permeate all educational levels, thereby diminishing differences across groups (55). Another study, from Russia, indicates similar direction of associations, but these findings were from younger adults (56). A report by the Organization for Economic Co-operation and Development (OECD, 2018) on education and depression also showed that although higher educational attainment is generally associated with lower depression across most OECD countries, this educational gradient was not statistically significant or somewhat different in Sweden, Finland and a few other countries (57).

Our study findings generally suggest that the mental health benefits of education are not universal; instead, higher education was associated with higher odds of depression among middle-age or older native Swedes in Northern Sweden. The reasons for this remain unclear. Narrower socioeconomic inequalities may reduce the relative advantages of higher education. However, self-reporting bias and healthy-user bias cannot be ruled out. For example, individuals with higher education may be more aware of their depressive symptoms and more capable of understanding and accurately reporting them in questionnaires. Supporting this, a psychometric study evaluating the depression questionnaires, including CES-D items, found that the accuracy of symptom reporting varies by educational level (58). Moreover, the Betula cohort originally excluded individuals with dementia or severe hearing, vision, or intellectual disabilities, which may have excluded depression cases, perhaps to a larger extent among those with only primary education. *Post hoc* analysis on education level and test waves also revealed that participants with primary education were more likely to drop out across follow-up than those with higher education. This education-related differences in study retention or health seeking behaviors may result in underrepresentation of depression in the lower-education group, potentially biasing the association toward higher odds among more highly educated participants. Therefore, the observed findings do not imply that educational attainment has no mental health benefits. Instead, our findings suggest that the relationship between education and depression among middle-aged and older Nordic populations is complex.

In our study, women were more likely than men to have depression, and their observed mean CES-D scores were higher across test waves, reflecting sex-specific mental health differences well-documented in several epidemiological, preclinical and clinical studies (2, 4, 5, 59, 60). Sex-specific disparities in depression may arise from a combination of biological factors (e.g., genetic risk, hormones, pregnancy, and physiological stress response), psychological characteristics (temperament and personality), and environmental influences such as societal norms and structural gender inequality (61). Of note, Chlapecka et al. (2020) found that educational attainment was negatively associated with depression in men, while a potential positive association was observed in women, particularly among those with middle education (12). This broadly aligns with our findings, which also showed a potential positive association in women with secondary education.

To our knowledge, no previous studies have examined sex-specific associations between educational attainment and depression progression/severity, particularly in Northern Sweden. Among women, neither the linear mixed model nor the ordered regression model provided sufficient statistical evidence of educational differences in depression progression or severity; trajectories were relatively stable, with overlapping confidence intervals across educational groups. For men, though not statistically significant in the ordered regression model, the linear mixed model suggested declining depression severity in those with higher education and increasing symptom severity among those with primary education. These findings point to potential sex-specific differences in the progression of depressive symptoms in relation to educational attainment.

Our study has several strengths. We used longitudinal data from the Betula cohort, a cross-sequential study with participants randomly selected to reflect the general population. Betula provides rich information on age-related health changes, including repeated measures of depressive symptoms and key determinants of depression. Using these data, we examined sex-specific associations between educational attainment and both depression onset and symptom progression among middle-aged and older adults in Northern Sweden, offering an important contribution to existing knowledge. The CES-D-based depression measures have strong psychometric properties, including good diagnostic accuracy and sensitivity to mild symptoms (34–37), although self-reporting of symptoms may vary by educational level (58).

In addition to the aforementioned self-reporting bias and healthy-user bias, a number of further limitations warrant consideration. The study has limited generalizability as the Betula cohort included only middle-aged and older native Swedish speaking participants. The relatively small sample size in subgroup analyses may reduce the precision of the estimates. The CES-D depressive scores were available only from wave 3 onward, and depressive symptoms may change between waves. Missing data, particularly for the outcome, as well as residual or unmeasured confounding, may also have influenced the observed associations.

Conclusions

In this longitudinal cohort of 1,013 middle-aged and older Swedish adults in Northern Sweden, higher education was associated with increased odds of depression, especially in women who had significant higher depressive symptoms score overall. Evidence for educational differences in symptom progression was limited in women, but for men, those with higher educations showed decreasing depressive symptoms score over time, in contrast to those with primary education. These observed associations should not be interpreted in the sense that education lacks mental-health benefits; rather the findings suggest a complex relationship between education and depression in middle-age and older population of Northern Sweden. Validation studies using register-based or other population-based cohort data, considering age, gender, and geographical aspects, are warranted to confirm and further elucidate these associations.

Abbreviations

AIC	Akaike Information Criterion
APOE4	Apolipoprotein E ε4
CES-D	Center for Epidemiologic Studies Depression Scale
CI	Confidence Interval
DAG	Directed Acyclic Graph
DALYs	Disability-adjusted life-years
OECD	Organization for Economic Co-operation and Development
OR	Odds ratio
S1–S3	Samples 1–3
W1–W6	Waves 1–6

Declarations

Ethical approval and consent to participate

Ethical approval was obtained from the Swedish Ethical Review Authority (Etikprövningsmyndigheten) (reference number: 2022-04608-01, Amendment: 2023-03633-02). This study used secondary data from the Betula cohort study, Umeå, Sweden, and was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants prior to their inclusion in the Betula cohort.

Consent for publication

Not applicable (no identifiable data)

Availability of data and materials

The data used in the study are confidential and can be requested from the steering committee of Betula study (Umeå University), subject to relevant ethical approvals. For further information, please contact the corresponding authors.

Competing interests

All authors declare no competing interests.

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Authors’ contributions

Sai San Moon Lu: Writing – original draft, Conceptualization, Methodology, Data curation, Formal analysis, Visualization. **Anna Sundström:** Writing – review & editing, Data curation, Methodology. **Theo Rein:** Writing –review & editing, Methodology. **Johan Nilsson Sommar:** Writing – review & editing, Methodology. **Sara Pudas:** Writing – review & editing. **Sophia Harlid:** Writing – review & editing. **Ivan Nalvarte:** Writing – review & editing. **Joëlle Rüegg:** Writing – review & editing, Funding acquisition, Project administration. **Anna Oudin:** Writing – review & editing, Funding acquisition, Conceptualization, Methodology, Formal analysis, Project administration, Supervision.

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Figures

Figure 1

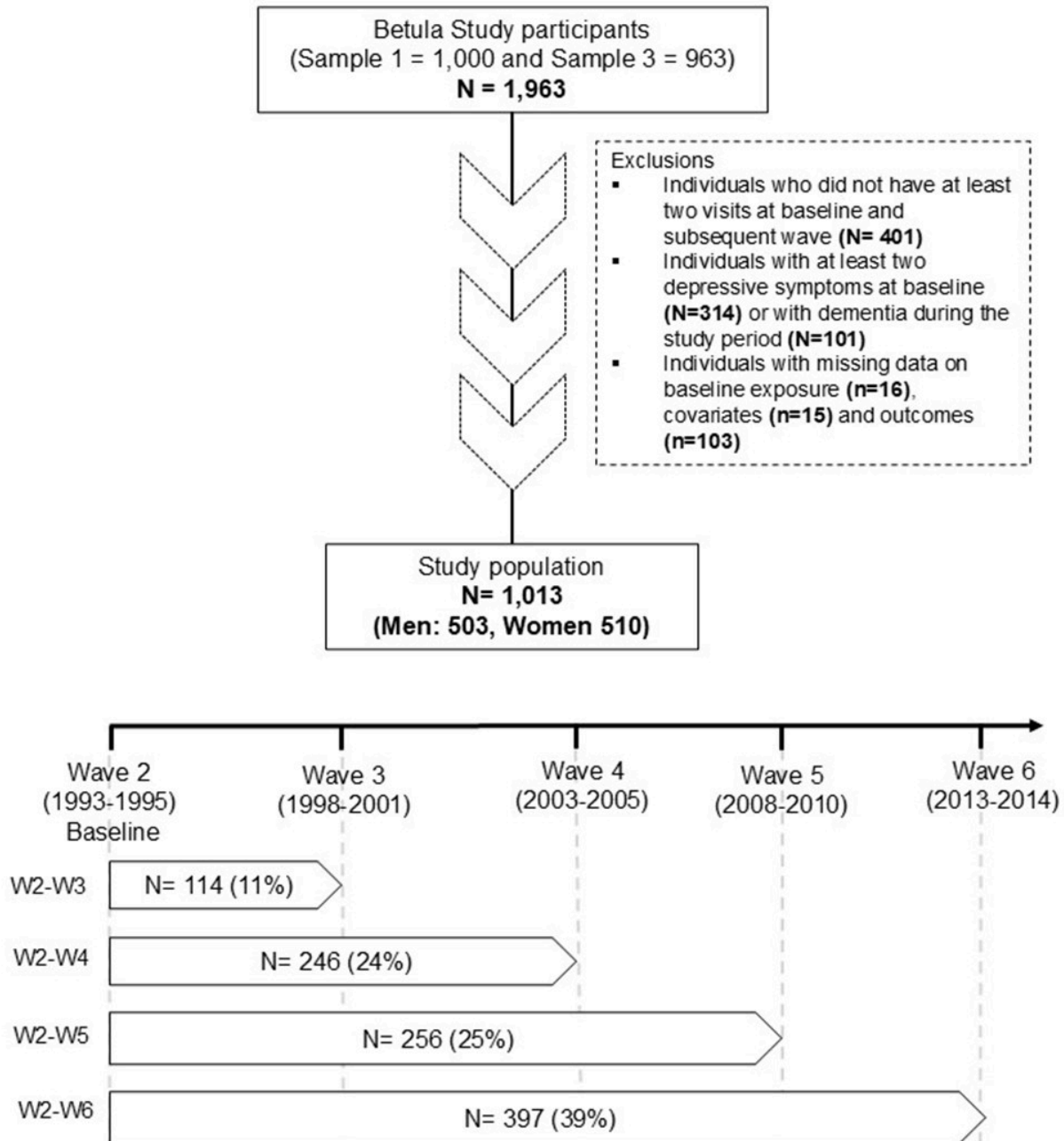


Figure 1

Flow chart of study participant selection and test waves

N= number, W=wave

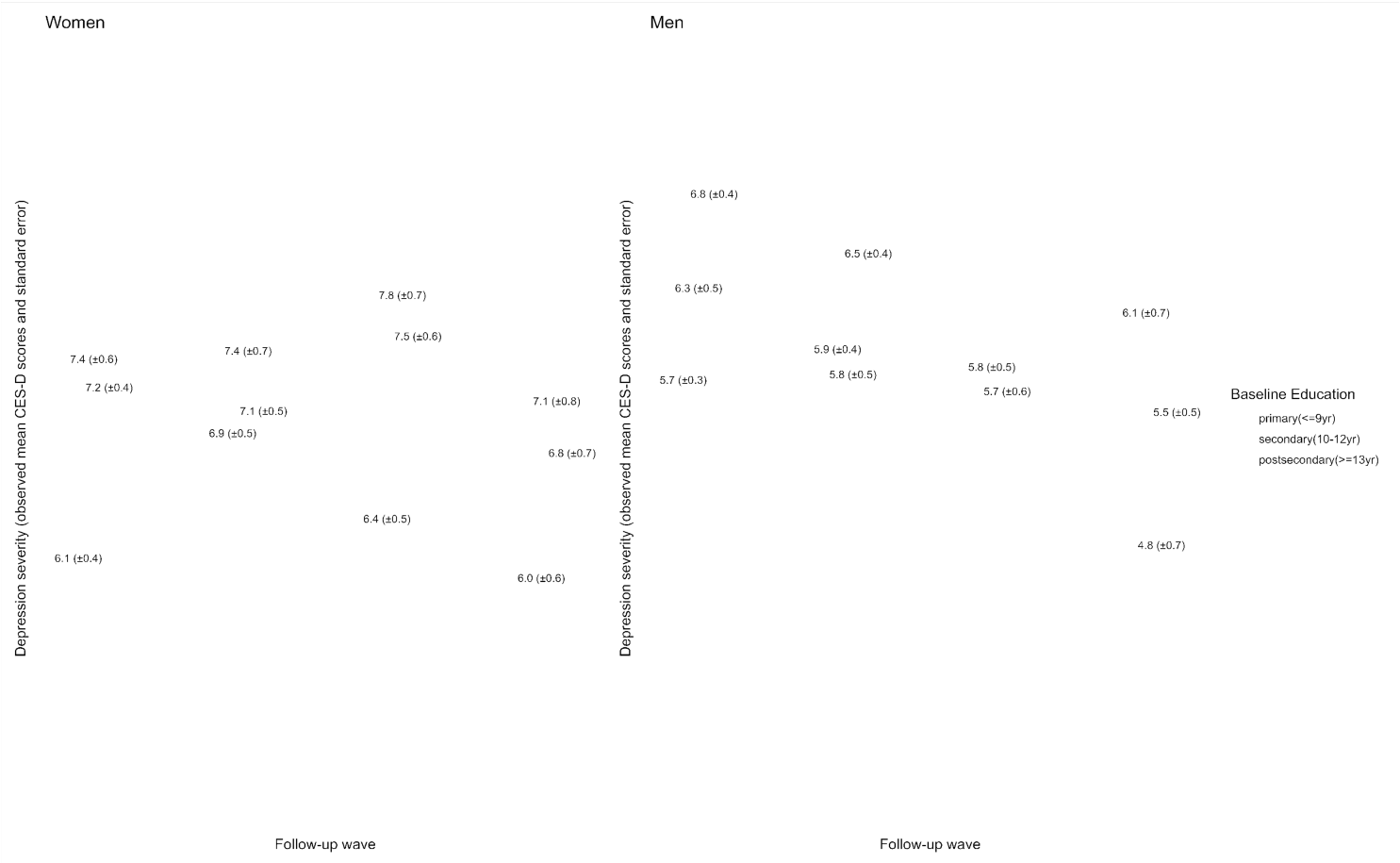


Figure 2

Observed mean CES-D scores across follow-up waves by baseline education

CES-D = Center for Epidemiologic Studies Depression scale

Wave 2 is baseline, and CES-D scores were collected from Wave 3 onward in the Betula cohort.

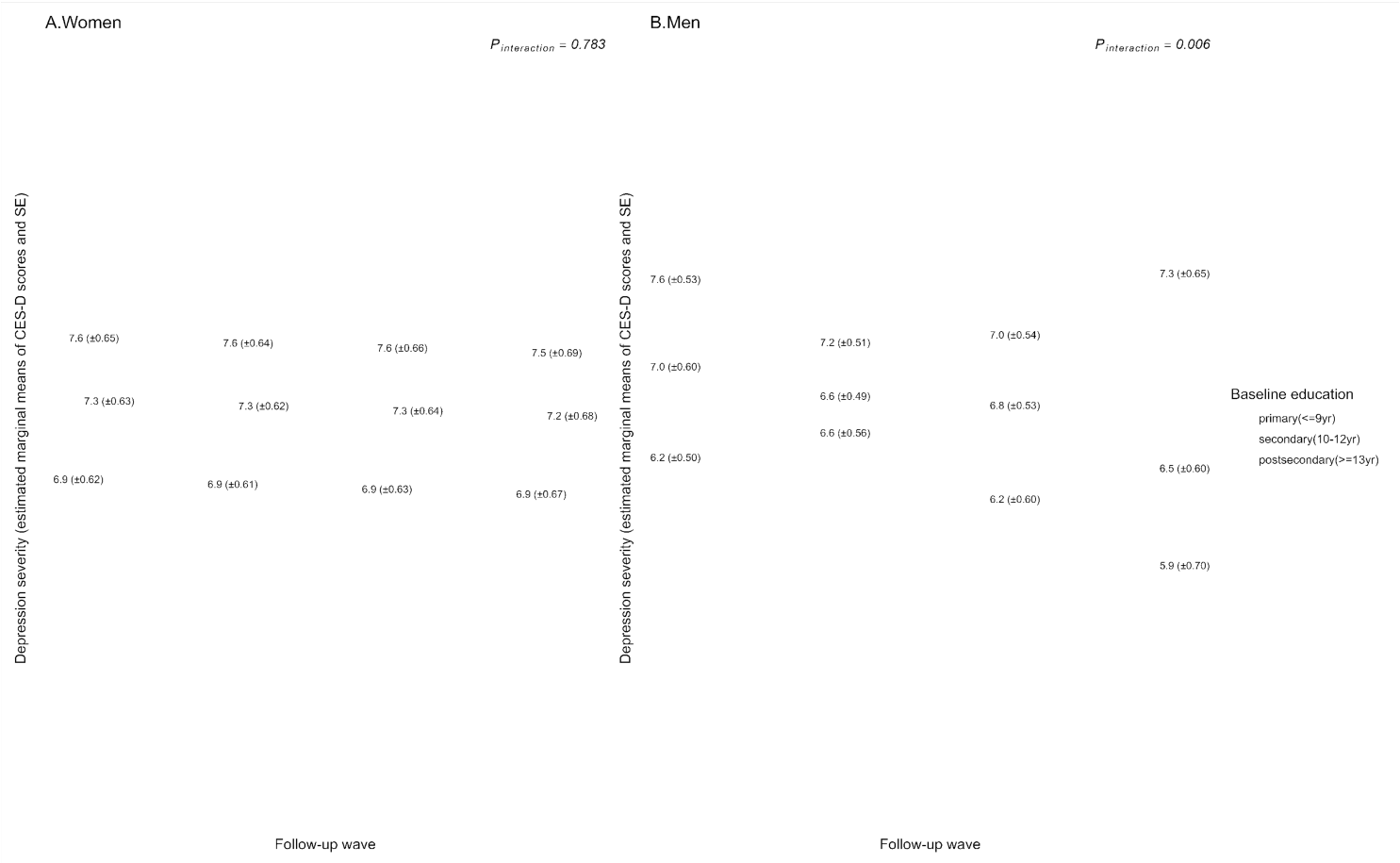


Figure 3

Estimated marginal means of CES-D scores across follow-up waves

CES-D = Center for Epidemiologic Studies Depression scale, SE = standard error

Wave 2 is baseline, and CES-D scores were collected from Wave 3 onward in the Betula cohort. Estimated marginal means were obtained from linear mixed models adjusted for covariates included in Model 1. Menopausal status was additionally adjusted for in women. Interaction terms between test wave and education were included only in the analyses for men.

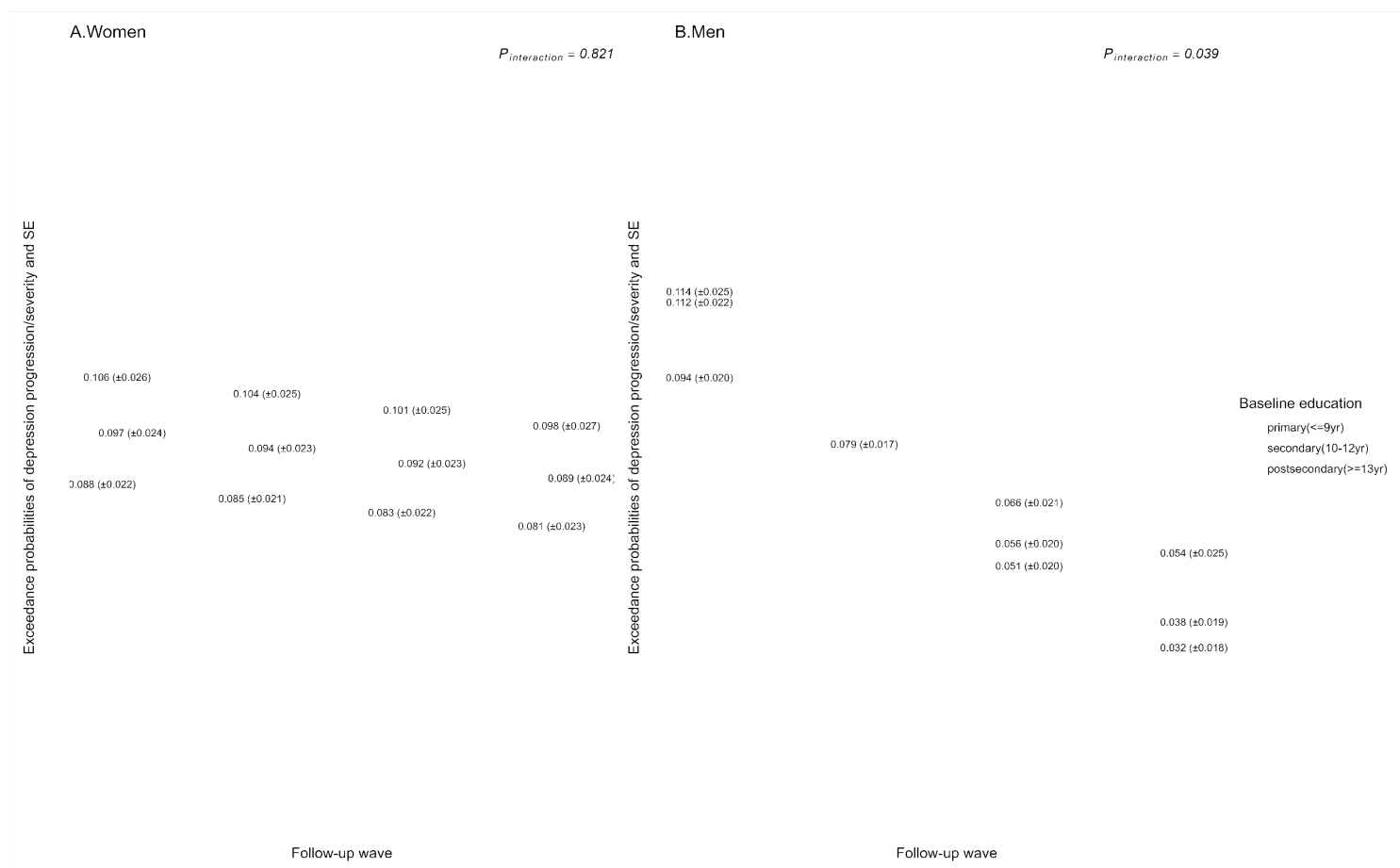


Figure 4

Exceedance probabilities of depression progressing/severity across follow-up waves

CES-D = Center for Epidemiologic Studies Depression scale, SE = standard error

Wave 2 is baseline, and CES-D scores were collected from Wave 3 onward in the Betula cohort. Exceedance probabilities (probability of being in higher symptom categories) were obtained from ordered regression models adjusted for covariates included in Model 1. Menopausal status was additionally adjusted for in women. Interaction terms between test wave and education were included only in the analyses for men.

Supplementary Files

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