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20-Year Depressive Trajectories among Older Women

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Abstract

Context—Despite the high occurrence of depressive symptoms in older adults, especially women, little is known about the long-term course of late-life depressive symptoms.

Objective—To characterize the natural course of depressive symptoms among elderly women followed for nearly 20 years, going from young old to oldest old.

Design—Using a latent class growth-curve analysis, we analyzed women enrolled in an ongoing prospective cohort study (1988–2009).

Setting—Clinic sites in Baltimore, MD, Minneapolis, MN, the Monongahela Valley near Pittsburgh, PA, and Portland, OR.

Participants—We studied 7240 community-dwelling women age 65 years or older.

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Main Outcome Measure—The Geriatric Depression Scale (GDS) short form (range: 0–15) was used to assess depressive symptoms repeatedly over follow-up.

Results—We identified four latent classes over 20 years, comprising an expected 28% of women with minimal depressive symptoms, 54% with persistently low symptoms, 15% with increasing symptoms, and 3% with persistently high symptoms. In an adjusted model for latent class membership, odds ratios (ORs) for belonging in the increasing and persistently high depressive symptom classes, respectively, compared with minimal symptom group were substantially and significantly ($P < .05$) elevated for baseline smoking (ORs, 4.69 and 7.97), physical inactivity (ORs, 2.11 and 2.78), small social network (ORs, 3.24 and 6.75), physical impairment (ORs, 8.11 and 16.43), myocardial infarction (ORs, 2.09 and 2.41), diabetes (ORs, 2.98 and 3.03), and obesity (ORs, 1.86 and 2.90).

Conclusions—Over 20 years, approximately 20% of older women experienced persistently high or increasing depressive symptoms. In addition, these women had more comorbidities, physical impairment, and negative lifestyle factors at baseline. These associations support the need for intervention and prevention strategies to reduce depressive symptoms into oldest-old years.

INTRODUCTION

While studies suggest that as many as 27% of community-dwelling older adults (aged 65 years and older) experience depressive symptoms,[1] little is known about the long-term course and heterogeneity of late-life depression. Given the projected expansion of the older population and the health and economic costs of depression,[2, 3] greater understanding of the chronic course of depressive symptoms into oldest-old years and the typologies that describe this chronic course will inform intervention and prevention strategies.

Most prior studies have assessed depressive symptoms at only one time point.[4] However, while depression peaks in young adulthood, it also tends to occur at a high and varying rate in late life.[5] Because of the association of depression and morbidity, poor health outcomes and mortality,[6–10] a persistent increase in depressive symptoms over time may have major health implications. Only a few studies have assessed trajectories of depressive symptoms in older participants and these have been limited by short follow-up.[11–16] In addition, since the oldest old (those age 80 years and older) are the fastest growing age group in the United States and a high incidence of depressive symptoms have been found among the oldest old,[17] long term investigation of depressive symptoms is needed in this group.

The primary objective of our study was to characterize the natural course of depressive symptoms among older women followed for nearly 20 years into their ninth and tenth decades of life. A secondary objective was to examine if lifestyle, function, and comorbidity factors known to be associated with late-life depression differentially predict more severe depressive symptom trajectories.

METHODS

Participants

We studied 7240 elderly community-dwelling women from the Study of Osteoporotic Fractures (SOF), a prospective cohort study of 9704 women age 65 years and older, originally recruited between September 1986 and October 1988 from population-based listings in 4 areas of the United States: Baltimore, MD; Minneapolis, MN; the Monongahela Valley near Pittsburgh, PA; and Portland, OR. Women were excluded if they were unable to walk without help or had had a bilateral hip replacement. At years 2 (1988–1990), 6 (1992–1994), 10 (1996–1998), 16 (2002–2004), and 20 (2007–2009) the subjects were administered a depression scale. Our study included 7240 women who had at least two

depression scale measures over the nearly 20 study years. The sample was 99.7% Caucasian, with mean (SD) age of 72.8 (4.7) years. During the study, 3654 women died and 622 ended the study early. The average number of depression measurements was 3.4 and the median length of follow up was 12.2 years. All women provided written informed consent, and the study was approved by the committees on human research at each site. In addition, current study analyses were approved by the institutional review board of the University of California, San Francisco.

Measures

Information on participants' age, education, marital status and living arrangements was collected at baseline. The Geriatric Depression Scale (GDS) short form, a 15-item questionnaire with scores ranging from 0 to 15 assessing the number of depressive symptoms based on binary item responses (i.e., 'yes' or 'no'), was used to determine the trajectories of depressive symptoms over follow-up. A final GDS score was determined for women with no more than 5 missing items (≤ 33%). This score was calculated by first taking the average of the non-missing items and then multiplying the average by 15. The GDS was initially administered during year 2 (defined as the baseline examination in this study) and repeated at follow-up years 6, 10, 16, and 20. It is a validated and reliable self-report scale used to detect depressive symptoms in older participants,[18] as the GDS scale is structured to minimize the measurement of common but nonspecific factors in older adults (e.g., fatigue, sleep disturbance, and poor concentration).[19] A GDS cut-off of ≥ 6 indicates depression.

Lifestyle factors were measured at baseline and included current smoking, number of drinks of alcohol, physical activity, and social networks. Alcohol use was assessed as the current number of drinks consumed per week with ≥ 7 drinks/week defined as frequent consumption.[20] Physical inactivity was defined as no low-, moderate-, or high-intensity physical activities as measured with a modified Paffenbarger scale.[21, 22] The Lubben Social Network Scale (LSNS),[23] a validated 10-item self-report inventory assessing type of relationships and size and frequency of contact, was used to determine an averaged social network score for each participant ranging from 0 to 5 (higher scores equated to larger networks). We defined participants as having a small social network if they fell below the median of the averaged LSNS (< 3.3). A similar cutoff defining small networks has been used in other SOF studies.[24]

Physical function was assessed at baseline for each of 5 activities (i.e., walking 2–3 blocks, climbing 10 steps without resting, preparing meals, shopping, and doing heavy housework). Global cognitive function was assessed by the modified version of the Mini-Mental State Examination (mMMSE)[25] with a maximum score of 26. Scores of less than 23 indicated cognitive impairment (equivalent to at least 1.5 standard deviations below the mean).[22] At baseline, medical history was obtained including myocardial infarction (MI), stroke, diabetes, and breast cancer and clinical measures of hypertension and obesity (body mass index ≥ 30 kg/m^2). Finally, participants were asked about current use (within the past 30 days) of medications including antidepressants; reports of current use were checked by examining the labels of drugs.

Statistical Analyses

Latent class growth-curve analysis (LCGA), as implemented in the Proc Traj procedure in SAS version 9.1.3 (SAS Institute Inc., Cary, NC),[26] was used to estimate mean trajectories of the GDS scores as a function of current age at each visit. In contrast to standard growth-curve analysis, LCGA estimates mean trajectories for two or more unobserved or latent classes, in combination with probability of membership in each latent class for every observation in the sample. Using Proc Traj, the repeated GDS scores were modeled as

censored normal. In addition to demographic variables, included for face validity, the multivariable Proc Traj sub-model used to estimate probabilities of latent class membership included covariates that were statistically significant ($P < .05$) in bivariate analyses. To describe bivariate associations, we estimated prevalence of baseline characteristics within latent classes and assessed differences in characteristics across latent classes using weighted repeated measures analyses. In these analyses, each participant contributed to each latent class in proportion to her predicted probability of class membership, based on the Proc Traj results. Robust standard errors were used to account for lack of independence of the weighted data across the four groups.

We hypothesized *a priori* that there would be five latent classes, four closely resembling the classes estimated by Proc Traj in the four-class model we selected, and an additional class with declining GDS scores. However, a five-class model did not include a declining trajectory, instead splitting one of the four other hypothesized classes into two similar subgroups. Moreover, the Bayesian Information Criteria (BIC), conventionally used to determine the number of latent classes, pointed to a large number of barely distinguishable classes. Thus, we selected the four-class model as a parsimonious description of the sample in best accord with our prior hypothesis. Statistical tests for models were two-tailed with $P < .05$ defining statistical significance.

RESULTS

Figure 1 presents the four latent class GDS mean trajectories estimated by the selected LCGA model, plotted by current age at each visit. The predicted probabilities of group membership totaled 28% with minimal depressive symptoms, 54% with persistently low symptoms, 15% with increasing symptoms, and 3% with persistently high symptoms.

Bivariate Analyses

Table 1, and Figures 2a, 2b, and 2c show the results for our weighted bivariate analyses characterizing the four latent classes. Women with the highest versus lowest depression trajectory over time were slightly younger at baseline (71.9 vs 73.1 years) and had less years of education (11.8 vs 13.1 years) (Table 1; $P < .01$ for trend). Current use of antidepressants was particularly low for all groups, but increased from respondents with minimal to persistently high symptoms (i.e., 0.6%, 1.5%, 3.5%, and 7.1%, respectively); ever use of antidepressants over the entire study period included 12% of women with minimal symptoms, 21% with persistently low symptoms, 31% with increasing symptoms, and 41% with persistently high symptoms.

We found that the highest disease burden was in the group with persistently high depressive symptoms (Figure 2a; MI = 13.6%, Stroke = 6.5%, Diabetes = 14.2%, Hypertension = 43.2%, and Obesity = 32.5%) and the lowest disease burden was in the minimal symptom group (MI = 3.8%, Stroke = 1.5%, Diabetes = 3.4%, Hypertension = 32.0%, and Obesity = 13.6%) (all $P < .001$ for trend). We also examined the prevalence of breast cancer, and in going from minimal to high symptoms the trend was statistically significant but less remarkable (i.e., 4 to 7%; $P = .01$ for trend). For “negative” lifestyle factors, prevalence of smoking, physical inactivity, and small social network increased with severity of trajectory (Figure 2b; $P < .001$ for trend), with physical inactivity and small social network having the largest differences (persistently high vs minimal symptoms: 34.5% vs 12% and 70.5% vs 41.3%, respectively). Frequent alcohol consumption (≥ 7 drinks/week) appeared to have a reverse relationship, where the persistently high group had the lowest prevalence (8.1%) compared with the other groups (10–13%) ($P = .02$ for trend). In addition, physical and cognitive impairment increased from minimal to persistently high groups (Figure 2c; $P < .001$ for trend).

Multivariable Model

For the multivariable model, the strongest association was seen with physical impairment, where the odds of increasing and persistently high symptoms over 20 years was eight times (odds ratio [OR], 8.11; 95% confidence interval [CI], 5.98–11.02) and sixteen times (OR, 16.43; 95% CI, 10.29–26.23) higher for those with any physical (IADL) difficulty compared to those with no physical impairment (Table 2). In addition, "negative" lifestyle factors were strong predictors of increasing and persistently high trajectories. Those who smoked were 5- and 8-fold more likely to have increasing and persistently high symptoms (ORs, 4.69 and 7.97; 95% CIs, 2.96–7.43 and 4.37–14.54, respectively). Women who were physically inactive were over twice as likely to have increasing symptoms and almost three times more likely to have persistently high symptoms than women who were active (ORs, 2.11 and 2.78; 95% CIs, 1.52–2.93 and 1.77–4.36, respectively). Women who had a small social network had nearly a 7-fold increased odds of persistently high symptoms (OR, 6.75; 95% CI, 4.33–10.53).

We found a 2 to 5-fold increased odds of persistently high trajectory of depressive symptoms for those women who had myocardial infarction (OR, 2.41; 95% CI, 1.18–4.90), stroke (OR, 5.12; 95% CI, 1.63–16.08), diabetes (OR, 3.03; 95% CI, 1.49–6.14), obesity (OR, 2.90; 95% CI, 1.88–4.48), and breast cancer (OR, 2.51; 95% CI, 1.24–5.09) (Table 2). Myocardial infarction, diabetes, and obesity were also significantly ($P < .05$) and independently associated with increasing symptoms. However, stroke and breast cancer were only associated with persistently high symptoms, while hypertension was only significantly associated with increasing symptoms (OR, 1.63; 95% CI, 1.29–2.07), independent of other covariates.

COMMENT

We identified four trajectories of depressive symptoms among older women followed for nearly 20 years (minimal depressive symptoms, persistently low symptoms, increasing symptoms, and persistently high symptoms). The prominent characteristics describing increasing and persistently high depressive trajectories compared with minimal symptoms were negative life style factors (i.e., smoking, physical inactivity, and small social network), physical impairment, and comorbidities (i.e., myocardial infarction, diabetes, and obesity). This study confirms that high and increasing depressive symptoms occur with concerning frequency over the course of elderly years with survival to oldest old having increased symptom burden.

Few prior studies have considered the heterogeneity and natural course of depressive symptomatology in older adults. Our findings are supported by a 6-year study from the Longitudinal Aging Study Amsterdam in which four depression trajectory patterns were identified: remission, remission plus recurrence, chronic-intermittent, and chronic.[27] By utilizing a latent class cluster approach, we were able to characterize individuals by subtypes; identifying trajectories that may more realistically reflect the long-term course of late-life depression. Most previous latent class analyses describing heterogeneity in depressive symptoms have examined one point in time,[28–33] while the few studies that have investigated trajectories over multiple years have used one or two years of data,[14, 15] used a one-item question to assess depression,[12] or had limited sample size to accurately assess follow up.[16]

Two studies that assessed 10 and 12 years of depressive symptoms had inconsistent results. Our findings provide evidence supporting the 10-year study of 3922 older community-dwelling adults aged 60 years and older, where the study identified four distinct trajectories (i.e., persistent low, persistent mild, late peak, and high-chronic).[13] In contrast, the 12-year

study identified six latent trajectories in 1260 community-dwelling adults aged 65 years and older.[11] Unlike our results, this study found that two of the trajectories started high and declined with time. Finally, unlike this previous research, we had a very large sample size (over 7000 women) which provided information on a substantial number of oldest-old women, despite attrition due to dropouts and death.

Given our large sample size, we were able to study a comprehensive list of covariates known to be associated with late-life depression as potential predictors of high and increasing depressive trajectories. Studies have consistently found that various medical conditions, lifestyle factors, and functional impairment are associated with late-life depression or increased depressive symptoms;[4, 6, 34–37] however, most of these studies are either cross-sectional or describe factors related to a single mean trajectory of depression or depressive symptoms over time. In contrast, we described multiple trajectories and generated a set of characteristics, in combination, that best predict belonging to more severe depressive trajectories over the long term. To this end, we determined that physical impairment, myocardial infarction, diabetes, obesity, smoking, physical inactivity, and small social networks differentially predict high and increasing trajectories over two decades, going from young old to oldest old. Although some previous latent trajectory studies have examined the association between depressive trajectories and related factors, results have been mixed with most not considering these and other important covariates in combination.[11, 12, 14, 16]

The identification of four distinct trajectories of depressive symptoms over the course of 20 years has important implications. First, these trajectories provide new information concerning the heterogeneity of late-life depression. Second, the findings suggest that if left unresolved the natural course of depressive symptoms in older women will become more burdensome, where approximately 20% of women are expected to have high or increasing symptoms over the long term. Since the trajectories were determined by the latent class model, there were no specific cutoffs assigned to the groups. However, the upper two trajectory groups (increasing and persistently high symptoms) suggest a trend toward clinically significant depression (i.e., GDS $\geq$ 6).

Third, by identifying important predictors of these trajectories, we are able to determine risk factors that may be targets for prevention and intervention. In particular, our study suggests that modifiable risk factors, such as increased physical activity or exercise, increased social engagement or connectedness, or reduction of obesity may help to reduce the progression of symptom burden. Although an association between chronic conditions such as myocardial infarction and diabetes and risk of depression has been supported by prior research,[34, 38, 39] few studies have considered the importance of lifestyle factors as predictors of depression above and beyond morbidity. In our study, lifestyle factors (i.e., smoking, physical inactivity, and small social networks) had an impressive impact on increasing and persistently high depressive symptoms. Future studies on the impact of changes in lifestyle factors associated with changes in depressive symptoms are needed in order to target lifestyle factors for prevention and intervention of late-life depression. In general, research investigating positive lifestyle factors as a modality for combating depression or depressive symptoms in older adults has been modest.[40] Furthermore, current antidepressant use was low in our study and ‘ever use’ was less than 50% for those in the highest trajectory group. Although the literature has shown that the use of antidepressants has increased since our study baseline (1988),[41] our results suggest greater need for early recognition and treatment of depression symptoms in late life. Moreover, our results have implications for increasing the use of maintenance regimens of antidepressant pharmacotherapy in older adults in order to reduce depressive symptoms over the long term. Such maintenance treatment is also strongly supported by the maintenance trials from Pittsburgh and elsewhere.[42, 43] In

summary, investigation into combating symptom burden through managing cardiovascular conditions, improving physical function, and promoting positive lifestyle factors either alone or in combination with antidepressant use is suggested by our findings.

Of note, our results support evidence linked to the 'vascular depression hypothesis,'[44] showing that vascular disorders and vascular risk factors may precipitate and perpetuate the severity and chronicity of depression into late life. Because the risk of vascular disease increases in post-menopausal women,[45] our findings may suggest an increased risk of late onset depression or change in the course of pre-menopause depression after the onset of vascular disease. This implicates medications besides or in addition to antidepressants (e.g., drugs used for prevention and treatment of cerebrovascular disease), as well as lifestyle changes, to prevent and intervene on vascular depression in older women.

The strengths of this study include a large sample of community-dwelling older women, information on depressive symptoms over nearly two decades, and carefully measured potential predictors. To our knowledge, our study is the first to characterize the natural course of depressive symptoms over two decades in elderly women—the group at greatest risk of living with high rates of late-life depression and related illness and disability.[46, 47]

There are some limitations of this study. Our sample was restricted to women. Although women are at much higher risk of developing depressive disorders and comprise a larger proportion of the oldest old, gender differences in trajectories of depressive symptoms may be important, especially considering potentially different targets of prevention and intervention. One prior study found that depressive trajectories in men were affected by perceived health and disability, while trajectories in women were influenced by disability and social support.[16] In addition, the results of this study are not generalizable to nonwhite older adults or less healthy women. Moreover, we did not have a complete set of covariates available to investigate other potentially important baseline predictors of high and emerging depressive symptoms. This included incomplete information on socioeconomic status (e.g., income), sleep disturbance or sleep disorders, and medical history of cancer. Although the SOF study collected information on breast cancer at baseline, information specific to other cancers that have been found to be associated with geriatric depression, such as colon cancer,[48] was not available. Also, we had limited information on depression treatment and, therefore, we were unable to investigate the impact of treatment on changing trajectories. For example, we did not have information available on when the subjects initiated antidepressant treatment (only that they were taking antidepressants in the prior 30 days from the interview date) nor did we have information available on their use of non-pharmacological treatment for depression. Furthermore, we did not have information on prior history of depression and, thus, could not determine whether the baseline covariates were consequences of previous depression. Finally, because data on the GDS was collected at visits that were approximately 4 years apart, variation of depressive symptomatology during these gaps in time is unknown.

Understanding the long term course of depressive symptoms among those who live into their ninth and tenth decades of life is imperative. The results of this study help to describe these patterns by identifying four trajectories of depressive symptomatology; highlighting the persistence of symptoms in the oldest old. Although we determined key predictors of more severe depressive trajectories (i.e., comorbidities, physical impairment, and negative lifestyle factors at baseline), further investigation into combating increased burden over the long term is needed. In addition, these associations may be bidirectional, which suggests further investigation in longitudinal analyses. It is important that future research tests the bidirectionality of such associations as physical/cognitive impairment and depressive symptoms, elucidating the etiological relationship and where to intervene. Furthermore,

future research needs to examine other important covariates not accounted for in the current study (e.g., socioeconomic gradient) and investigate whether associations differ by gender and racial/ethnic diversity. Finally, because the number of trajectory classes selected was driven by prior hypothesis, our findings need to be carefully interpreted and confirmed by future work.

Given the projected expansion of the elderly population, increased life expectancy, and the health and economic costs of depression, the potential public health burden of late-life depressive disorders implicated by this study are concerning. These findings emphasize the importance of improving the recognition, monitoring and treatment of depressive symptoms over the long term, and of developing better interventions to forestall their development.

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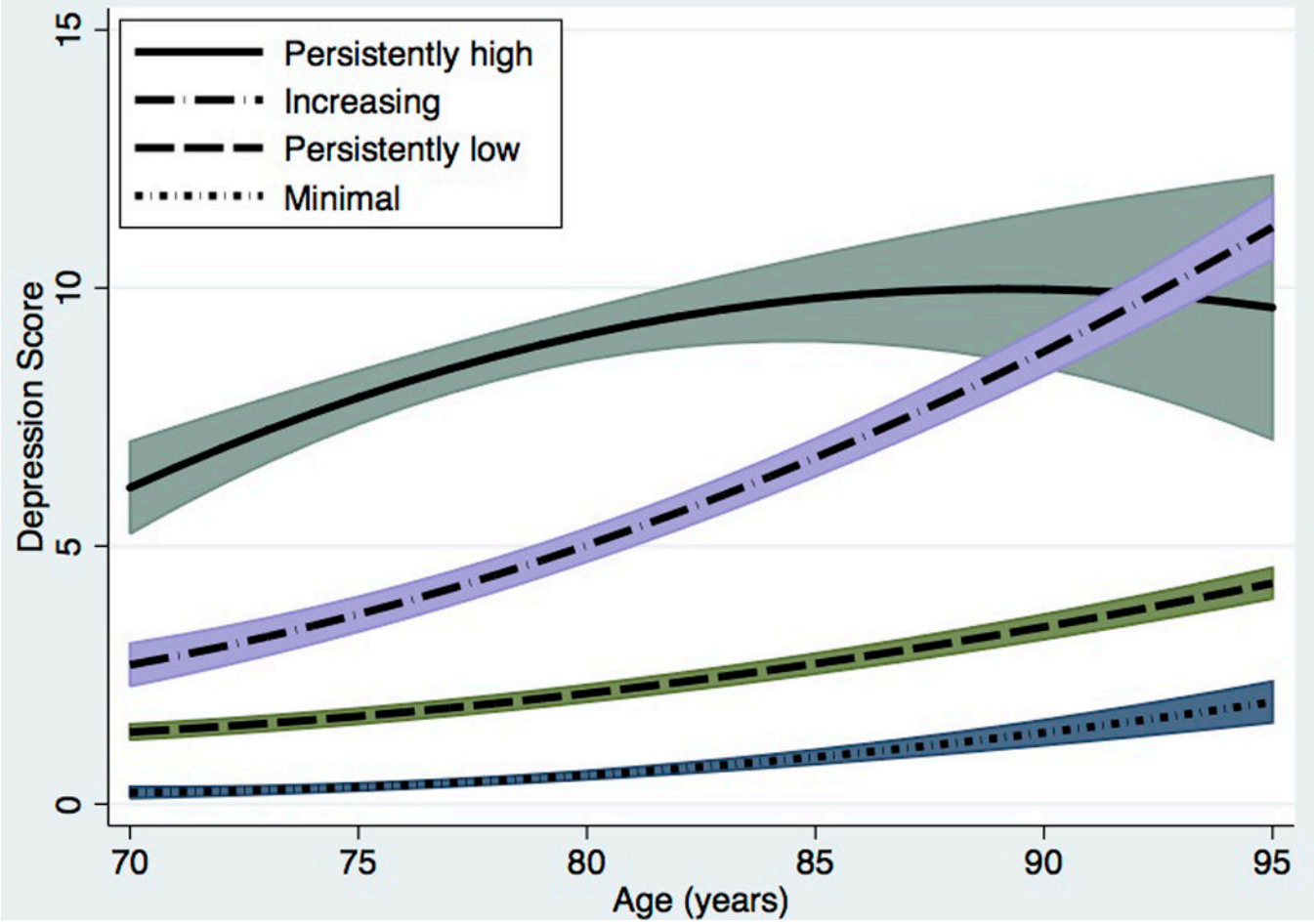
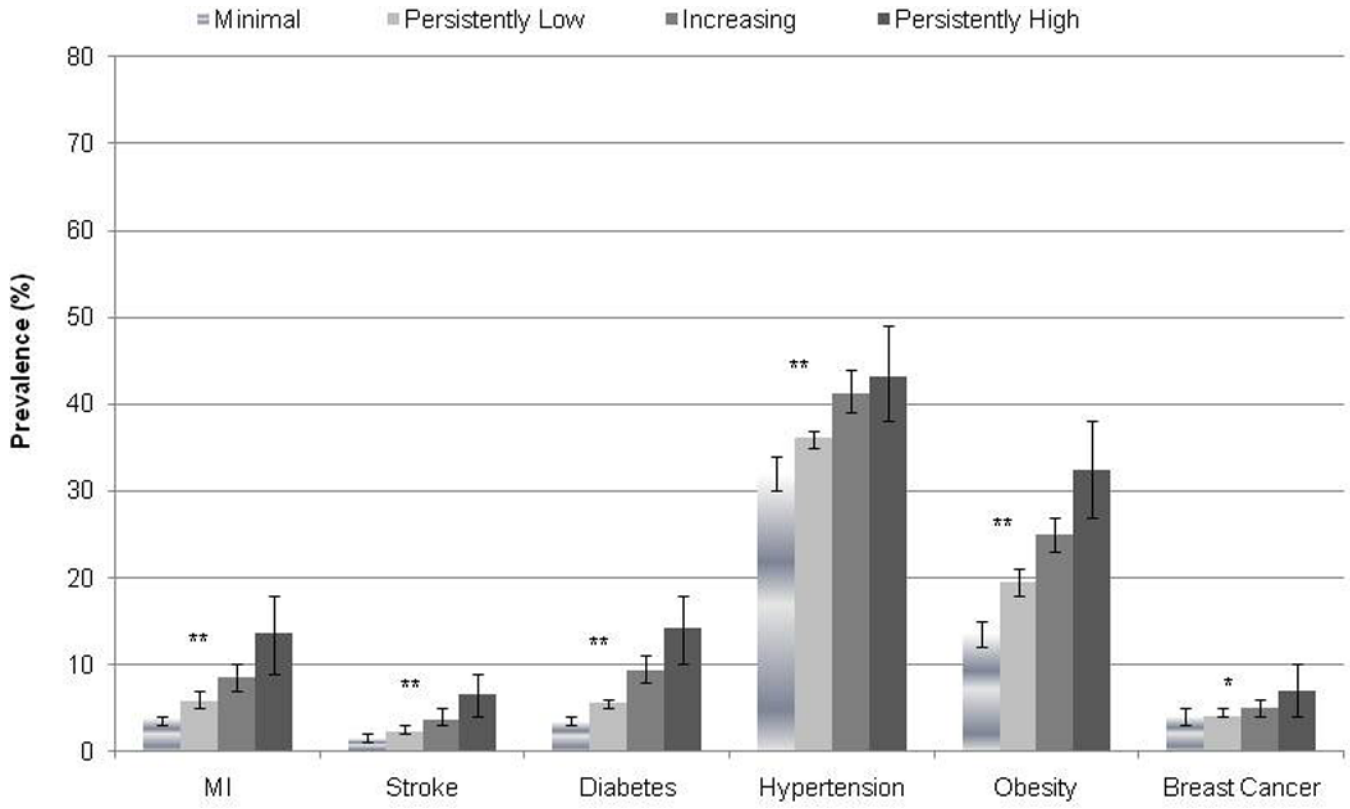
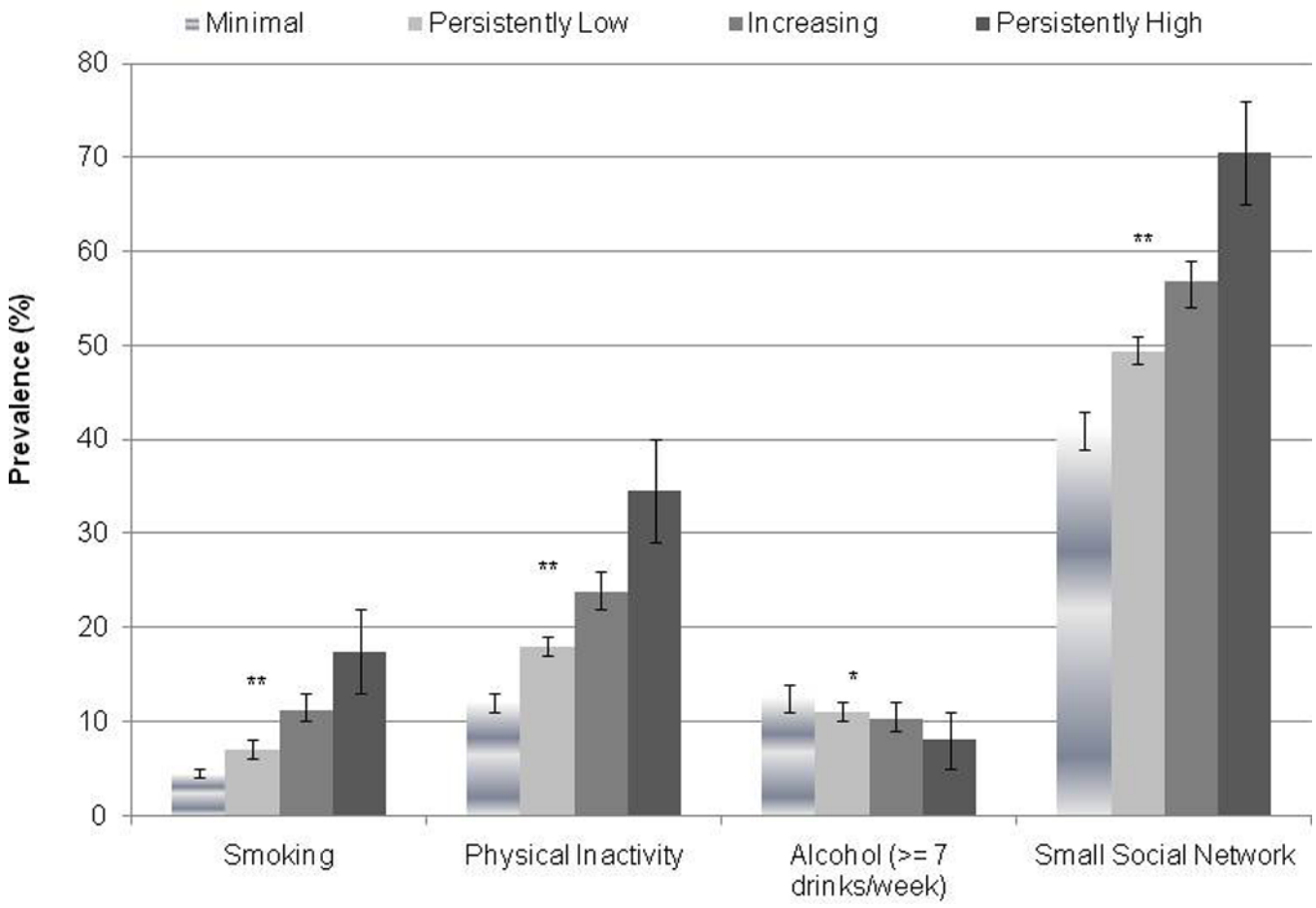


Figure 1.
Mean trajectories of depressive symptoms by increasing age among older women





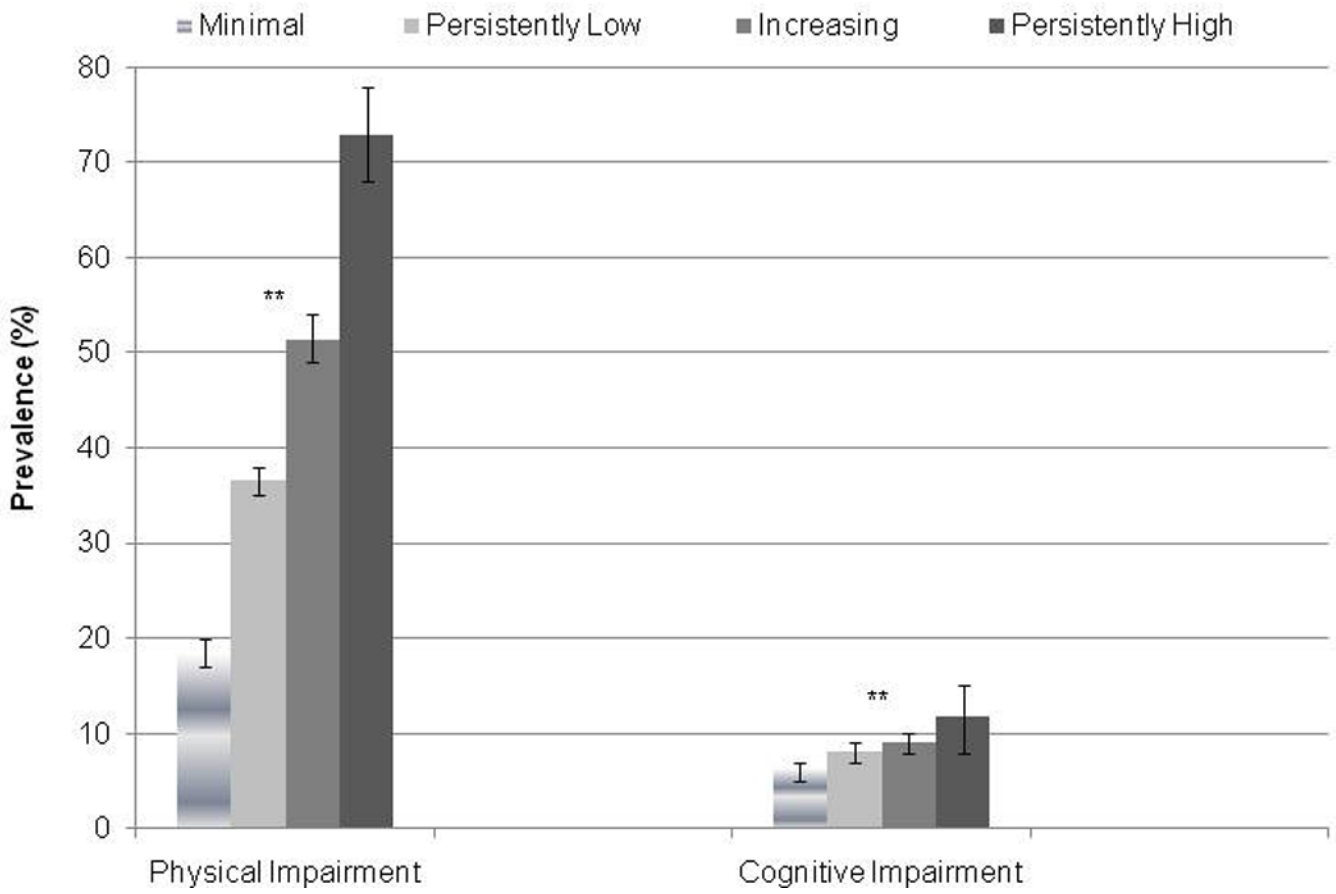


Figure 2.

a. Prevalence of comorbidities across trajectory groups of depressive symptoms
**P* < .05; ***P* < .001 (Test for trend, based on orthogonal contrasts in weighted GEE models); the I bars indicate 95% confidence intervals.

b. Prevalence of lifestyle factors across trajectory groups of depressive symptoms
**P* < .05; ***P* < .001 (Test for trend, based on orthogonal contrasts in weighted GEE models); the I bars indicate 95% confidence intervals.

c. Prevalence of functional impairment across trajectory groups of depressive symptoms
***P* < .001 (Test for trend, based on orthogonal contrast in weighted GEE models); the I bars indicate 95% confidence intervals.

Table 1

Baseline Demographic Characteristics of 7240 Older Women According to Depressive Symptom Trajectories

	Weighted mean (SE) or % (SE)				
Characteristic	**Minimal Symptoms (n = 1,928)**	**Persistently Low (n = 4,137)**	**Increasing Symptoms (n = 939)**	**Persistently High (n = 236)**	***P* Value[a]**
Age, years	73.1 (0.09)	72.9 (0.07)	72.3 (0.11)	71.9 (0.22)	<.001
Education, years	13.1 (0.05)	12.7 (0.04)	12.3 (0.07)	11.8 (0.16)	<.001
Married, % (SE)	48.0 (1.0)	49.3 (0.75)	48.8 (1.3)	42.4 (3.0)	.08
Living alone, % (SE)	43.9 (1.0)	42.6 (0.74)	42.8 (1.3)	45.3 (3.0)	.64

[a] *P*-values for trend, based on orthogonal contrasts in weighted Generalized Estimating Equation (GEE) models.

Table 2

Multivariable Model: Factors Independently Associated with Trajectories of Depressive Symptoms Over 20 Years Compared with Minimal Symptoms[a]

		OR (95% CI)		
Characteristic	**Minimal Symptoms**	**Persistently Low**	**Increasing Symptoms**	**Persistently High**
Lifestyle				
Smoking	1.0	2.09 (1.34–3.26)	4.69 (2.96–7.43)	7.97 (4.37–14.54)
Alcohol (≥ 7 drinks/week)	1.0	1.02 (0.77–1.35)	0.99 (0.69–1.43)	0.85 (0.44–1.63)
Physical inactivity	1.0	1.69 (1.25–2.27)	2.11 (1.52–2.93)	2.78 (1.77–4.36)
Small social network	1.0	2.14 (1.72–2.67)	3.24 (2.45–4.30)	6.75 (4.33–10.53)
Functional Impairment				
Physical	1.0	4.79 (3.66–6.28)	8.11 (5.98–11.02)	16.43 (10.29–26.23)
Cognitive	1.0	1.47 (0.99–2.20)	1.39 (0.88–2.20)	1.43 (0.74–2.79)
Comorbidity				
Myocardial infarction	1.0	1.60 (0.92–2.76)	2.09 (1.19–3.66)	2.41 (1.18–4.90)
Stroke	1.0	2.18 (0.80–5.94)	2.58 (0.93–7.16)	5.12 (1.63–16.08)
Diabetes	1.0	1.33 (0.76–2.34)	2.98 (1.75–5.10)	3.03 (1.49–6.14)
Hypertension	1.0	1.13 (0.93–1.38)	1.63 (1.29–2.07)	1.08 (0.73–1.60)
Obesity	1.0	1.51 (1.15–1.99)	1.86 (1.37–2.53)	2.90 (1.88–4.48)
Breast cancer	1.0	1.25 (0.79–1.99)	1.10 (0.62–1.94)	2.51 (1.24–5.09)

[a]Model additionally adjusted for demographic variables (education, married, living alone); results additionally adjusted for antidepressant use were similar.