New onset of depression in aging women and men: contributions of social, psychological, behavioral, and somatic predictors in the community‡

Original Article

Manfred E. Beutel[1], Elmar Brähler[1], Joerg Wiltink[1], Jasmin Ghaemi Kerahrodi[1], Juliane Burghardt[1], Matthias Michal[1], Andreas Schulz[2,3], Phillipp S. Wild[2,3,4,5], Thomas Münzel[3,5,6], Irene Schmidtmann[7], Karl J. Lackner[8], Norbert Pfeiffer[9], Andreas Borta[10] and Ana N. Tibubos[1]

[1]Department of Psychosomatic Medicine and Psychotherapy, University Medical Center of the Johannes Gutenberg-University Mainz, Germany; [2]Preventive Cardiology and Preventive Medicine, Center for Cardiology, University Medical Center of the Johannes Gutenberg-University Mainz, Germany; [3]Center for Translational Vascular Biology (CTVB), University Medical Center of the Johannes Gutenberg-University Mainz, Germany; [4]Center for Thrombosis and Hemostasis, University Medical Center of the Johannes Gutenberg-University Mainz, Germany; [5]DZHK (German Center for Cardiovascular Research), partner site Rhine-Main, Mainz, Germany; [6]Center for Cardiology I, University Medical Center of the Johannes Gutenberg-University Mainz, Germany; [7]Institute for Medical Biostatistics, Epidemiology and Informatics, University Medical Center Mainz, Germany; [8]Institute of Clinical Chemistry and Laboratory Medicine, University Medical Center of the Johannes Gutenberg-University Mainz, Germany; [9]Department of Ophthalmology, University Medical Center of the Johannes Gutenberg-University Mainz, Germany and [10]Boehringer Ingelheim Pharma GmbH Co KG, Ingelheim am Rhein, Germany

Abstract

Background. Based on the vulnerability–stress model, we aimed to (1) determine new onset of depression in individuals who had not shown evidence of depression at baseline (5 years earlier) and (2) identify social, psychological, behavioral, and somatic predictors.

Methods. Longitudinal data of $N = 10\,036$ participants (40–79 years) were evaluated who had no evidence of depression at baseline based on Patient Health Questionnaire (PHQ-9), no history of depression, or intake of antidepressants. Multivariate logistic regression models were used to predict the onset of depression.

Results. Prevalence of new cases of depression was 4.4%. Higher rates of women (5.1%) than men (3.8%) were due to their excess incidence <60 years of age. Regression analyses revealed significant social, psychological, behavioral, and somatic predictors: loneliness [odds ratio (OR) 2.01; 95% confidence interval (CI) 1.48–2.71], generalized anxiety (OR 2.65; 1.79–3.85), social phobia (OR 1.87; 1.34–2.57), panic (OR 1.67; 1.01–2.64), type D personality (OR 1.85; 1.47–2.32), smoking (OR 1.35; 1.05–1.71), and comorbid cancer (OR 1.58; 1.09–2.24). Protective factors were age (OR 0.88; 0.83–0.93) and social support (OR 0.93; 0.90–0.95). Stratified by sex, cancer was predictive for women; for men smoking and life events. Entered additionally, the PHQ-9 baseline score was strongly predictive (OR 1.40; 1.34–1.47), generalized anxiety became only marginally, and panic was no longer predictive. Other predictors remained significant, albeit weaker.

Conclusions. Psychobiological vulnerability, stress, and illness-related factors were predictive of new onset of depression, whereas social support was protective. Baseline subclinical depression was an additional risk weakening the relationship between anxiety and depression by taking their overlap into account. Vulnerability factors differed between men and women.

Introduction

Depression is one of the most debilitating mental disorders in the general population, strongly associated with a reduced quality of life, work disability, cardiovascular disease (Beutel *et al.*, 2014), and premature death (Cuijpers *et al.*, 2013). Its prevalence was 7.2% in the general population aged 25–74 years based on the Patient Health Questionnaire (PHQ-9) (Beutel *et al.*, 2014). The vulnerability–stress model (Spijker *et al.*, 2004) posits sociodemographic, psychological, somatic, and behavioral risk factors.

With regard to *sociodemographic factors*, women were about twice as likely to develop depression during their life time as men (Timm *et al.*, 2017). While older cohorts of men and women had a decreased incidence of depression, incidence remained higher in women. However,

evidence for late-onset depression (>60 years) has been scarce (Aziz and Steffens, 2013), and the greatest gender gap in incident depression has been found in middle age (Bogren *et al.*, 2017).

In a meta-analysis on the associations with socioeconomic status (SES) (Lorant *et al.*, 2003), prevalence studies ($N = 51$) prevailed over incidence and persistence studies ($N = 5$, each). Odds of a new episode of depression were increased in low SES. However, compared with the odds of persistent depression [odds ratio (OR) = 2.06], the magnitude was lower (OR = 1.24); dose–response relationships were found for lower education, income, and SES (Groffen *et al.*, 2013).

As *psychological factors*, early childhood adversity in addition to a family history of depression (Timm *et al.*, 2017), increased the risk for depressive and anxiety disorders later in life (Gibb *et al.*, 2007). Further, neuroticism and negative emotionality predicted the onset of major depressive disorder (MDD) episodes in community samples (Klein *et al.*, 2011). Major stressful life events (SLE) have been identified as precursors of depression (Kendler *et al.*, 1999). While men reported more work-related and legal problems and women reported more interpersonal problems (Kendler *et al.*, 2001), life event categories had similar depressogenic effects in men and women (Vrshek-Schallhorn *et al.*, 2015). Loneliness as an important social stress factor (Beutel *et al.*, 2017*b*) was a risk factor for incident depression (Green *et al.*, 1992), whereas social support was associated with lower depressive symptoms (Beutel *et al.*, 2017*a*). In a twin study, women reported higher levels of social support than men. However, social support reduced the risk of subsequent depression only in women (Kendler *et al.*, 2005).

Generalized anxiety disorder has a high lifetime comorbidity with depressive disorders (Coplan *et al.*, 2015); due to their early age of onset, anxiety disorders may precede depression. For example, anxious adolescents with a tendency to ruminate were more vulnerable to subsequent depressive symptoms (Starr *et al.*, 2016). A systematic review (Hardeveld *et al.*, 2010) found that larger numbers of previous depressive episodes and residual symptoms increased the risk of recurrence. Subclinical depression adversely affected functioning and quality of life, which may contribute to an increased incidence of depression (Rodriguez *et al.*, 2012).

The relationship between depression and *behavioral factors* is complex: depression has been related to physical inactivity and increased consumption of tobacco and alcohol. Recent meta-analyses found more incident depression in obesity (ORs between 1.21 and 5.18), particularly in women (Rajan and Menon, 2017). In a recent study, baseline smoking was associated with incident depression 5 years later (Cabello *et al.*, 2017).

Regarding *somatic factors*, increased depressive symptoms were found in cardiovascular disease, diabetes (Wiltink *et al.*, 2011), cancer (Hartung *et al.*, 2017), chronic obstructive pulmonary disease (COPD), and other chronic diseases. Given the link between multimorbidity and depression (Spangenberg *et al.*, 2011), in an aging sample, somatic conditions need to be ascertained. However, studies investigating the significance of chronic disease for the onset of depression in the general population have been scarce. In a recent systematic review (Bernardini *et al.*, 2017), out of 12 studies predicting MDD, five focused on patients with medical disorders, and only two were from the general population.

This paper is based on a unique, comprehensive large longitudinal population-based aging sample, analyzing the effects of sociodemographic, psychological, behavioral, and somatic baseline data on new onset of depression 5 years later. We took care to exclude participants who were depressed at baseline, who had reported a previous diagnosis of depression or who had taken antidepressants. Our aims were:

(1) To determine the point prevalence of depression in individuals who had not shown evidence of depression at baseline 5 years earlier,
(2) To determine the combined impact of a broad range of social, psychological, behavioral, and somatic predictors of new onset of depression.

Methods

Procedure and study sample

As described by Wild *et al.* (2012), the Gutenberg Health Study (GHS) is a population-based, prospective, observational single-center cohort study in the Rhine-Main-Region, Germany. Its primary aim is to analyze and improve cardiovascular risk factors and their stratification. The study protocol and documents were approved by the ethics committee of the Medical Chamber of Rhineland-Palatinate and the local data safety commissioner. All study investigations were conducted in line with the Declaration of Helsinki and principles outlined in recommendations for Good Clinical Practice and Good Epidemiological Practice. Participants were included after informed consent. The sample was drawn randomly from the local registry in the city of Mainz and the district of Mainz-Bingen, stratified 1:1 for gender and residence and in equal strata for decades of age. Inclusion criterion was age 35–74 years. Insufficient knowledge of German language, psychological, or physical impairment with regard to participation led to exclusion.

At baseline, 15 010 participants were examined between 2007 and 2012. Of those, 14 732 (98.1%) filled out the PHQ-9. A total of 12 422 took part in the follow-up (82.8%). Of those, $N = 12 140$ filled out the PHQ-9 (97.7%). Thus, 12 061 filled out the PHQ-9 on both occasions. Eight hundred seventy-seven were excluded due to a PHQ-9 ⩾ 10 at baseline, 971 had reported a history of depression, and 177 took antidepressant medication (N07a). Thus, analyses were based on $N = 10 036$ participants. Participants who fulfilled inclusion criteria and were lost to follow-up ($N = 1850$) were slightly more often female, older, had a lower SES, and suffered more frequently from chronic disease and cardiovascular risk factors; however, there were no differences regarding depression, generalized anxiety, or panic at baseline; social phobia was even slightly lower in drop-outs.

Materials and assessment

The 5-h baseline examination in the study center comprised the evaluation of prevalent classical cardiovascular risk factors and clinical variables, a computer-assisted personal interview, laboratory examinations from venous blood samples, blood pressure, and anthropometric measurements. All examinations were performed according to standard operating procedures by certified medical technical assistants.

Measures

Sociodemographic variables and psychological measures were assessed via self-report: sex, age in years, employment (no/yes), income, living with partner (no/yes), and SES. SES was defined according to Lampert *et al.* (2009) from 3 (lowest SES) to 21 (highest SES) based on education, profession, and income.

Psychological measures

The *Social Readjustment Rating Scale* (SRRS), a widely used checklist (Scully *et al.*, 2000; Hobson and Delunas, 2001),

provides a standardized measure of the impact of a wide range of SLE. An adapted German version with 36 items was administered (Cronbach's $\alpha = 0.81$); the latter were rated based on their occurrence in the past years (0 = no, 1 = yes). For analyses, we used the unweighted scores.

Loneliness was assessed by a single item 'I am frequently alone/ have few contacts' rated as 0 = no, does not apply; 1 = yes it applies, but I do not suffer from it; 2 = yes, it applies, and I suffer slightly; 3 = yes, it applies, and I suffer moderately; 4 = yes, it applies, and I suffer strongly. Loneliness was recoded combining 0 and 1 = no loneliness or distress; 2 = slight; 3 = moderate; and 4 = severe loneliness (Beutel *et al.*, 2017*b*).

Social support was assessed by the Brief Social Support Scale (BS6; Beutel *et al.*, 2017*a*). Six items (three per scale) assessed emotional and tangible support with good reliability (total scale $\alpha = 0.86$). Items were rated from 1 = never, 2 = occasionally, 3 = mostly to 4 = always available.

Depression was assessed with the PHQ-9 at baseline and follow-up. Caseness at follow-up was defined by a score $\geqslant 10$. Lowe *et al.* (2004) found a sensitivity of 81% and a specificity of 82% for depressive disorder determined by this cut-off. Internal consistency for the PHQ-9 was good (Cronbach's $\alpha = 0.80$).

Generalized anxiety was assessed with the two-item short form of the Generalized Anxiety Disorder-7 (GAD-7; Kroenke *et al.*, 2007). A sum score of 3 or higher (range 0–6) among these two items indicated generalized anxiety with good sensitivity (86%) and specificity (83%) (Kroenke *et al.*, 2007).

The German version of the *Mini-Social Phobia Inventory* (Mini-Spin) was used to detect *social anxiety*. A cut-off score of 6 (range 0–12) separated individuals with generalized social anxiety disorder and controls with good sensitivity (89%) and specificity (90%) (Wiltink *et al.*, 2017).

Panic disorder was screened with the brief PHQ panic module. Caseness was defined if at least two of the first four PHQ panic questions were answered with 'yes' (Lowe *et al.*, 2003).

Type D personality was assessed with the German version of the DS14 (Denollet, 2005) comprising two reliable subscales with seven items each for negative affectivity and social inhibition, rated on a five-point Likert scale (0 = false to 4 = true). Type D was defined by a cut-off of 10 on both subscales.

Behavioral measures
Health behavior included *smoking*, which was dichotomized into non-smokers (never smoker and ex-smoker) and smokers (occasional smoker, i.e. cigarette/day, and smoker, i.e. cigarette/day).

Obesity was defined as a body mass index (BMI) $\geqslant 30$ kg/m^2 (0 = no, 1 = yes).

Alcohol consumption was measured in gram per day; alcohol abuse was defined as daily consumption $\geqslant 60$ mg for men and $\geqslant 40$ mg for women.

Physical activity was inquired with the Short Questionnaire to Assess Health-Enhancing Physical Activity (SQUASH; Peters *et al.*, 2012). The SQUASH captures commuting, leisure time, household, work, and school activities. Sleeping, lying, sitting, and standing were classified as inactivity (Peters *et al.*, 2012). Active sports was presented in quartiles with Q1 denominating the lowest and Q4 the highest quartile of physical activity.

Interview assessments
During the computer-assisted personal interview, participants were asked whether they had ever received a definite diagnosis of any depressive or anxiety disorder by a physician (medical history of lifetime diagnosis of any depressive, respectively, anxiety disorder). The presence of coronary heart disease was assessed by the question: 'Were you diagnosed with a stenosis of your coronary vessels?' Self-reported myocardial infarction, heart failure, stroke, deep vein thrombosis, pulmonary embolism, and peripheral arterial disease were summarized as cardiovascular risk diseases (CVD); cancer and COPD were assessed the same way.

Diabetes was defined in individuals with a definite diagnosis of diabetes by a physician or a blood glucose level of $\geqslant 126$ mg/dl in the baseline examination after an overnight fast of at least 8 h or a blood glucose level of >200 mg/dl after a fasting period of 8 h.

Medications were registered on site at the GHS study center by scanning the bar codes from the original packages of the drugs of participants. Medication use was described by the ATC code. Three classes of antidepressants were selected and entered as dichotomous variables (yes/no): non-selective monoamine reuptake inhibitors (ATC N06AA), selective serotonin reuptake inhibitors (ATC N06AB), and other antidepressants (ATC N06AX).

Statistical analysis
Descriptive analyses were performed as absolute and relative proportions for categorical data, means, and standard deviations for continuous variables and median with interquartile range if not fulfilling normal distribution. Inference tests between depression groups (no/yes) were calculated with *t* tests or χ^2 tests.

In order to determine new onset of depression at follow-up, based on the baseline data, we excluded subjects with a medical history of depression, intake of antidepressant medication, and increased depression scores (PHQ $\geqslant 10$) at baseline. In order to identify predictors of new onset of depression, we performed logistic regression analysis with depression (PHQ-9 sum score $\geqslant 10$) as the criterion at follow-up including sociodemographic, psychological, behavioral, and somatic factors assessed at baseline (model 1). In order to determine the effect of subclinical depression, we additionally included the PHQ-9 score at baseline (model 2). In order to identify sex effects, we also analyzed women and men separately.

The $p < 0.05$ was considered significant. Because of the explorative nature of the study, no Bonferroni tests were conducted. All *p* values should be regarded as continuous parameters that reflect the level of statistical evidence, and they are therefore reported exactly. Statistical analysis was carried out using R version 3.3.1.

Results
Table 1 gives an overview of the study participants according to the presence of depression at follow-up (separate tables for men and for women cf. online Supplementary Tables S1 and S2).

Table 1 shows the overall rate of new onset of depression as 4.4%. Depression was significantly associated with female sex, younger age, lower SES, income, and living without a partner. A higher rate of employment may be due to younger age of depressed participants. As psychological vulnerability factors, they had an increased proportion of type D personality. Participants with new onset of depression reported more life events at baseline, more loneliness, generalized anxiety, social phobia, panic and history of anxiety, and less social support. They smoked more often and reported less physical activity; there was no difference regarding obesity. Overall, there were no differences regarding the prevalence rates of somatic diseases.

Table 1. Baseline characteristics stratified for new onset of depression

	All (N = 10 036)	No depression (N = 9599; 95.6%)	Depression (N = 437; 4.4%)	Sign.
Sociodemographic				
Sex (women, %)	46.1 (4628)	45.8 (4396)	53.1 (232)	0.0032
Age (years)	54.3 ± 10.9	54.4 ± 10.9	51.3 ± 10.4	<0.0001
SES (baseline)	13.48 ± 4.38	13.50 ± 4.38	13.02 ± 4.25	0.022
Employment (%)	65.4 (6545)	65.0 (6226)	73.5 (319)	0.00024
Income (baseline, €)	1875.00 (1125.00/2875.00)	1875.00 (1125.00/2875.00)	1625.00 (875.00/2375.00)	0.00019
Living with partner (%)	84.5 (8481)	84.7 (8129)	80.5 (352)	0.021
Psychological				
Type D (%)	19.4 (1936)	18.5 (1766)	39.2 (170)	<0.0001
Life events (past 12 months)	2.63 ± 2.52	2.60 ± 2.49	3.22 ± 3.12	<0.0001
Loneliness (%)	6.6 (662)	6.1 (581)	18.7 (81)	<0.0001
Social support	20.86 ± 3.34	20.93 ± 3.28	19.30 ± 4.04	<0.0001
Anxiety (GAD-2 ⩾ 3, %)	2.7 (269)	2.3 (222)	10.8 (47)	<0.0001
Social phobia (Mini-Spin ⩾ 6, %)	5.1 (511)	4.7 (445)	15.2 (66)	<0.0001
Panic (%)	2.2 (219)	2.1 (194)	6.0 (25)	<0.0001
History anxiety disorder (%)	2.9 (287)	2.8 (266)	4.8 (21)	0.018
Behavioral				
Smoking (%)	17.2 (1726)	16.9 (1620)	24.4 (106)	<0.0001
BMI (kg/m^2, mean, s.d.)	26.3 (23.8/29.6)	26.3 (23.8/29.6)	26.3 (23.7/29.8)	0.81
Active sports (%)	52.3 (5251)	52.5 (5044)	47.4 (207)	0.035
Alcohol abuse	2.8% (278)	2.8% (267)	2.5% (11)	0.88
Somatic				
CVD (%)	9.7 (975)	9.7 (932)	10.1 (43)	0.93
COPD (%)	3.9 (390)	3.8 (368)	5.0 (22)	0.20
Cancer (%)	7.9 (796)	7.9 (756)	9.2 (40)	0.32
Diabetes (%)	7.3 (726)	7.2 (690)	8.3 (36)	0.39

Comparing supplementary baseline Table 1 for men and Table 2 for women, baseline differences emerged. Depressed men, but not women, had a lower SES, lived less often with a partner, had a higher BMI, and performed active sports less often.

Figure 1 shows the comparison of new onset of depression of men and women by age decade.

The figure shows that the higher rate of depression in women was due to their excess morbidity in the younger age groups. In the youngest age group, women's proportion exceeded men's by 73%, in middle age by 30%, and in the elderly population, there was no more difference, while the proportion of participants with new-onset depression declined.

Table 2 shows multivariate logistic regression analyses of new onset of depression for all participants. Model 1 excludes and model 2 includes depression score at baseline.

According to model 1, younger age was a demographic predictor of depression, while female sex was no longer significant. Among the psychological factors, type D personality, comorbid cancer, and smoking were predictive of new onset of depression. This also applied to loneliness and to SLE (trend), whereas social support was protective. The strongest predictor was comorbid generalized anxiety, followed by loneliness, social phobia, type

D personality, and panic disorder. Among behavioral risk factors, smoking was a significant predictor, and comorbid cancer among the somatic factors. Protective factors were age and social support.

When the baseline depression score was additionally entered (model 2), a similar pattern ensued. Baseline subclinical depression was one of the strongest predictors of depression at follow-up. Psychological, behavioral, and somatic factors remained significant predictors, and age and social support were still significantly protective, although the magnitude was diminished in most. Particularly, generalized anxiety, the strongest predictor in model 1, was only marginally significant.

Online Supplementary Table S3 presents findings for men, and online Supplementary Table S4 for women. In model 1, generalized anxiety, loneliness, social phobia, and type D personality were significant predictors of depression, whereas social support remained protective. Among men, smoking was a predictor. Among women, cancer was a predictor of depression, whereas age was associated with less new onset of depression only among women. After entering baseline subclinical depression scores (model 2), in men and women, only age was strongly predictive of a lower incidence of depression. For men, social support remained significant, whereas it was only marginally significant

Table 2. Logistic regression models of new onset of depression: model 1 excluding depression measure (PHQ-9) at baseline *v.* model 2 including subclinically depressed participants (PHQ-9 < 10) at baseline

	Model 1 (*N* = 9543; *N* = 400 events)				Model 2 (*N* = 9543; *N* = 400 events)			
	Odds ratio	L (95% CI)	U (95% CI)	*p*	Odds ratio	L (95% CI)	U (95% CI)	*p*
PHQ-9_baseline	–	–	–		1.401	1.336	1.470	<0.0001
Sociodemographic								
Sex (women)	1.230	0.995	1.521	0.056	1.130	0.911	1.404	0.27
Age (5 years)	0.882	0.833	0.934	<0.0001	0.887	0.837	0.941	<0.0001
SES	0.981	0.956	1.008	0.16	0.995	0.969	1.023	0.73
Partnership	1.262	0.954	1.689	0.11	1.170	0.880	1.574	0.29
Psychological								
Type D	1.848	1.469	2.317	<0.0001	1.316	1.040	1.659	0.021
Life events	1.208	0.987	1.471	0.063	1.023	0.832	1.253	0.83
Loneliness	2.012	1.479	2.709	<0.0001	1.551	1.135	2.099	0.0051
Social support	0.926	0.900	0.954	<0.0001	0.954	0.927	0.984	0.0021
GAD-2⩾3	2.653	1.788	3.850	<0.0001	1.462	0.982	2.133	0.054
Social phobia (Mini-Spin⩾6)	1.872	1.341	2.574	0.00016	1.467	1.044	2.032	0.024
Panic	1.665	1.006	2.643	0.038	1.103	0.665	1.757	0.69
History of anxiety disorder	1.180	0.685	1.921	0.53	1.156	0.673	1.878	0.58
Behavioral								
Active sports	0.886	0.717	1.095	0.26	0.925	0.746	1.148	0.48
Obesity	1.137	0.882	1.453	0.31	1.045	0.808	1.342	0.73
Smoking	1.347	1.047	1.721	0.018	1.324	1.023	1.701	0.030
Alcohol abuse	1.086	0.547	1.944	0.64	1.066	0.533	1.925	0.84
Somatic								
CVD	1.226	0.831	1.763	0.29	1.127	0.757	1.633	0.54
COPD	1.203	0.712	1.917	0.46	1.126	0.663	1.807	0.64
Cancer	1.583	1.091	2.240	0.012	1.594	1.094	2.269	0.012
Diabetes	1.238	0.802	1.846	0.31	1.194	0.767	1.798	0.41

in women as a protective variable. Only in women, loneliness, social phobia, and cancer were retained as predictors; generalized anxiety was only marginally significant.

Discussion

Compared with studies focusing on recurrence of depression, few community studies have predicted incident depression in the general population (Bernardini *et al.*, 2017). Detailed analyses of men and women have been scarce. Based on a unique, comprehensive data set of a large longitudinal cohort of over 10 000 participants from the community aged 40–79 years, we determined the new onset of depression over 5 years and the combined effects of sociodemographic, psychological, behavioral, and somatic baseline characteristics. We took care to exclude participants who were depressed at baseline, who had reported a previous diagnosis of depression or who had taken antidepressants. Overall, we found a substantial rate of 4.4% of new onset of depression. Higher rates of women (Kuehner, 2017), however,

were only found below the age of 60 years, whereas the percentage of depression declined to similar levels for men and women above 60 years (Bogren *et al.*, 2017).

In univariate analyses, new onset of depression was significantly associated with *sociodemographic* factors (Lorant *et al.*, 2003) such as female sex, younger age, lower SES and income, and living without a partner. When stratified for sex, social disadvantage, however, was only associated with depression in men. As *psychological* predictors for depression, both in men and in women, we identified anxiety symptoms and a history of anxiety disorders, type D personality, life events, loneliness (Beutel *et al.*, 2017b), and low social support (Green *et al.*, 1992). Among the *behavioral* factors, smoking was associated with depression. A higher BMI and less active sports were linked to depression only in men. Surprisingly, somatic illnesses did not seem to be useful markers for future depressive episodes. In contrast, single sociodemographic and especially psychological measures, both narrow (e.g. panic) and broad (e.g. social support) concepts, showed significant effects on future depression.
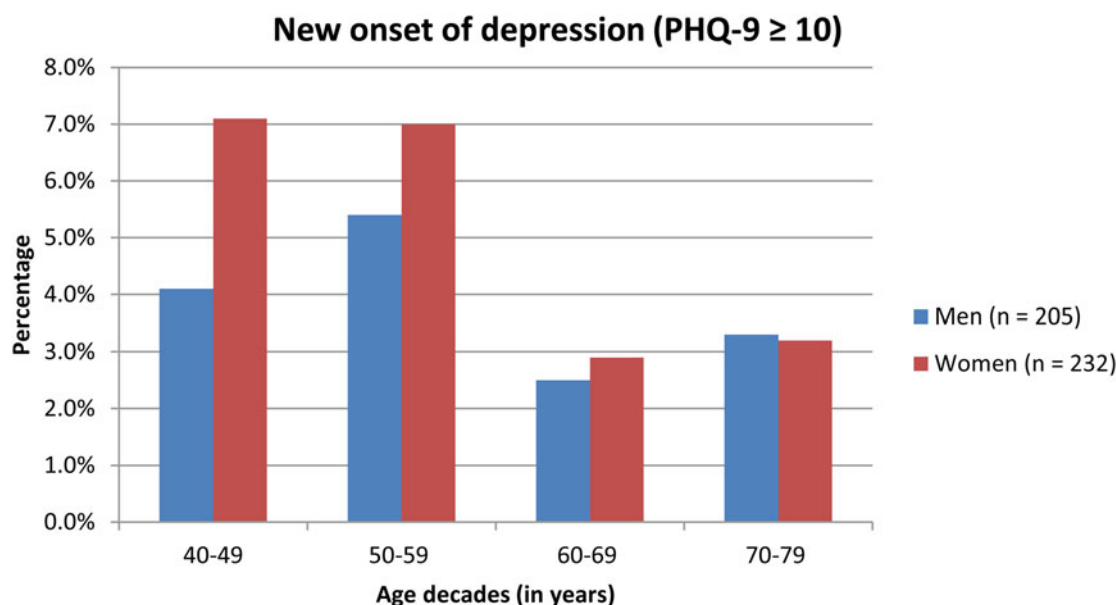
New onset of depression (PHQ-9 ≥ 10)

Fig. 1. Comparison of new onset of depression in men and women across age decades.

Taking intercorrelations of the predictor variables into account, multivariate logistic regression models were evaluated. In the overall model, female sex was no longer significant as a *sociodemographic* predictor of depression. The strongest *psychological* predictors of new onset of depression were generalized anxiety (Hardeveld *et al.*, 2010; Starr *et al.*, 2016), loneliness with a more than twofold risk (Beutel *et al.*, 2017*b*), and social phobia. Consistent with the role of personality in depression (Klein *et al.*, 2011), substantially elevated risks were also found for type D personality, along with panic disorder. In the multivariate model, life events only increased the risk for men. Among *behavioral* risk factors, smoking was a significant predictor. Cancer turned out to be predictive (Hartung *et al.*, 2017) among the *somatic* factors in the regression model (for all and for women), which was not the case in univariate analyses. Hence, shared variance of cancer with at least one of the other predictor variables seems to reveal the effect of cancer on depression in terms of a suppressor effect. This result emphasizes the relevance of joint analyses of determinants of depression, which is in line with the vulnerability–stress model (Spijker *et al.*, 2004) emphasizing reciprocal effects of psycho-bio-social variables and the role of the link between multimorbid somatic conditions and depression in aging (Kemp *et al.*, 2017). In aging, protective factors were age and social support (Beutel *et al.*, 2017*a*). Unlike Cabello *et al.* (2017), the role of unhealthy lifestyles was evident in men, but not in women. Among men, smoking and lack of exercise were predictors, and among women, cancer was a predictor of depression. Findings regarding depression in aging are contradictory (Spangenberg *et al.*, 2011). Taking into account sex, in our sample, increasing age was associated with less new onset of depression only among women.

When the baseline depression score was entered into the model, a similar pattern ensued. Consistent with the literature (Rodriguez *et al.*, 2012), baseline subclinical depression was one of the strongest predictors of new onset of depression at follow-up. Psychological, behavioral, and somatic factors remained significant predictors, and age and social support were still significantly protective, although the magnitude was diminished in most.

Particularly, generalized anxiety, the strongest predictor in the previous model, was statistically not predictive any more. The strong overlap of generalized anxiety and depression (Kohlmann *et al.*, 2016) has been discussed in terms of shared negative affectivity, respectively, neuroticism, genetic predisposition, and common neurobiology (Goodwin, 2015) leading to the recent development of transdiagnostic treatment manuals (Barlow *et al.*, 2013). After entering baseline subclinical depression scores, age (overall and both sexes) and social support (overall and men) were still predictive of a lower probability of depression. Few other risk factors were retained: At the *psychological* level, type D personality, loneliness, and social phobia (overall and for women) were still predictive. At *somatic* level, cancer (overall and for women) remained statistically relevant as risk factor, and smoking (overall) at the *behavioral* level. With regard to sex differences after statistically controlling the baseline depression score, only the depression buffering factors age and social support were relevant for men. For female individuals, psychological components and cancer additionally represented risk factors. Thus, the interplay of psychological and somatic determinants seems to be more important for women.

As we had already excluded participants with PHQ-9 scores ≥10 at baseline, we entered the baseline PHQ-9 scores into our model and additionally adjusted for any signs of depressive symptoms. This can be interpreted as a sensitivity analysis eliminating any overlap between depressive and anxiety symptoms and reduced any association between stressful sociodemographic, psychological, behavioral, and somatic factors.

Limitations

We used the PHQ-9, which is one of the most-used self-report questionnaires, to assess depression. While we inquired previous medical diagnoses of depression, respectively anxiety, we did not ascertain medical diagnoses of depression and anxiety from medical files. Given the limited time frame of 2 weeks of the PHQ-9, we cannot preclude that participants were depressed at other times during follow-up. While we used all information

available to exclude subjects who had been depressed, previously, an unknown proportion of participants included may actually have fulfilled the criteria of depression in the past without proper medical diagnosis. While we covered a substantial numbers of predictors from the literature, other predictors such as family history of depression were not assessed.

Conclusion

Following the vulnerability–stress model (Spijker *et al.*, 2004), a comprehensive model was tested to predict new onset of depression in an aging population, including sociodemographic, psychological, behavioral (Cabello *et al.*, 2017), and somatic factors (Wiltink *et al.*, 2011; Hartung *et al.*, 2017). Benefits of our study refer to the large sample of participants over a wide age range of middle and old age enabling us to identify a comprehensive set of predictors. Findings alert us to the complex interplay of factors and will be helpful to identify subjects at risk for developing depression. They underline the need to take signs of the major kinds of anxiety disorders (generalized, social anxiety, panic disorder) seriously as potential precursors of depression. They also underscore the role of social factors in addition to type D personality, with loneliness as a negative and social support as a positive factor. Among somatic disorders, cancer appears to cause new onset of depression in the context of these additional risk factors. Following gender-sensitive clinical research, which is a first step toward tailored treatment, we also analyzed data separately for men and women. Differential preventive efforts are likely indicated, e.g. treating smoking in men, and giving psychosocial support to women with cancer. Based on a recent trial with acceptance and commitment therapy, smoking cessation was associated with a decline of anxiety and depression in male smokers (Davoudi *et al.*, 2017). Findings that exercising has a small, but consistent positive effect on depression may need to be reconsidered separately for men and for women (Cooney *et al.*, 2013). Findings of our study have predictive validity due to the longitudinal study design in a large community sample. Future analyses might take a closer look at potential indicators of social disadvantage (e.g. employed single mothers, low-income participants) and specific life events in order to gain a better understanding of why trajectories of depression differ between women and men in midlife, but not in old age.

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