Journal of Affective Disorders 397 (2026) 120885

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research paper

Cross-sectional and longitudinal associations between subthreshold depressive symptoms and cognition, physical health, and quality of life in older adults aged 55+: a retrospective study

Julia Christl [a,b,*], Pascal Grumbach [a,e], Christiane Jockwitz [c,d], Natalia Wege [a], Svenja Caspers [c,d,1], Eva Meisenzahl [a,1]

[a] Department of Psychiatry and Psychotherapy, Medical Faculty, Heinrich Heine University, Bergische Landstr. 2, 40629, Düsseldorf, Germany
[b] Department of Psychiatry and Psychotherapy, LVR-Klinikum Essen, University of Duisburg-Essen, Medical Faculty, Essen, Germany
[c] Institut für Anatomie I, Medizinische Fakultät & Universitätsklinikum Düsseldorf, Heinrich-Heine-Universität Düsseldorf, Moorenstraße 5, 40221, Düsseldorf, Germany
[d] Institut für Neurowissenschaften und Medizin (INM-1), Forschungszentrum Jülich, Wilhelm-Johnen-Straße, 52428, Jülich, Germany
[e] Institut für Neurowissenschaften und Medizin, Brain & Behavior (INM-7), Forschungszentrum Jülich, Wilhelm-Johnen-Straße, 52428, Jülich, Germany

ARTICLE INFO

Keywords:
Cognition
Late-life depression
Clinical high-risk state of depression
Late life
Quality of life
Executive functioning
Physical health

ABSTRACT

Subthreshold depressive symptoms (SDS) increase with age and adversely affect cognition, physical health, and quality of life. Therefore, this retrospective study investigated the cross-sectional and longitudinal associations between the absence or presence of SDS and neuropsychological performance, physical health, and quality of life in a large, representative sample of older adults aged 55 + .

Data on cognition, physical variables, and psychosocial measures from a healthy subsample of participants aged 55 to 87 years from the population-based 1000BRAINS study were retrospectively analyzed. Cross-sectional data were available for 6691000BRAINS participants, and longitudinal data for 255 participants. The relationship between the absence or presence of SDS and neuropsychological, physical health, and psychosocial measures was examined by linear regression models and repeated-measures analysis of covariance, adjusted for age, sex, educational level, and multiple comparisons.

Greater severity of SDS at baseline was linked to poorer performance in cognitive domains, including processing speed, executive function, figural and verbal memory, and in the dementia screening test, lower physical activity levels, and more physical complaints. Increased SDS over time correlated with accelerated vascular ageing, higher body mass index, and lower quality of life.

In older adults, SDS are associated with impaired cognitive function and lower physical activity levels and quality of life. Further research in the field of early recognition of late-life depression should assess cognition and physical health to identify clinical factors and their interaction in the development of late-life depression.

1. Introduction

The importance of early detection of depressive disorders in the prodromal phase and the development of preventive strategies is emphasized due to demographic change (United Nations, 2022), the high healthcare costs associated with depression, including in older age (Olesen et al., 2012; Grochtdreis et al., 2019; Bock et al., 2016), and the high comorbidity with somatic diseases such as diabetes mellitus, coronary artery diseases, arterial hypertension (Köhler et al., 2018; Zhang et al., 2018; Alexopoulos, 2019). In addition, late-life depression (LLD), even after remission is associated with impairment in activities of daily living and executive functioning (Kiosses and Alexopoulos, 2005). A meta-analysis on prodromal symptoms in adults with unipolar depression showed that the duration of the prodromal phase varies from months to several years and found that common psychopathological symptoms are anxiety, tension, irritability and physical complaints

* Corresponding author: Department of Psychiatry and Psychotherapy, Medical Faculty, Heinrich-Heine-University, Bergische Landstr. 2, 40629, Düsseldorf, Germany.
E-mail addresses: julia.christl@lvr.de (J. Christl), pascal.grumbach@hhu.de (P. Grumbach), c.jockwitz@fz-juelich.de (C. Jockwitz), Natalia.wege@lvr.de (N. Wege), Svenja.Caspers@med.uni-duesseldorf.de (S. Caspers), Eva.Meisenzahl@lvr.de (E. Meisenzahl).
[1] These authors contributed equally.

https://doi.org/10.1016/j.jad.2025.120885
Received 11 June 2025; Received in revised form 5 November 2025; Accepted 13 December 2025
Available online 15 December 2025

(Benasi et al., 2021). One study found that depressive symptoms are present in 21.3 % of people aged 50 years and older (Christl et al., 2025), and a meta-analysis showed a global prevalence of depressive symptoms of 19.47 % in this age group (Volkert et al., 2013). Higher severity of depressive symptoms is associated with more physical illness and the use of certain medications, such as proton pump inhibitors and antihypertensives (Christl et al., 2025).

The term 'subthreshold depressive symptoms' (SDS) generally refers to patients who experience a cluster of depressive symptoms, but whose symptoms are not severe enough in terms of number, duration or quality to meet the DSM criteria for a diagnosis of major depressive disorder (MDD; Sadek and Bona, 2000). SDS may be part of the clinical high-risk state of depression, which implies prospective clinical risk identification (CHR—D; Meisenzahl et al., 2024a). Often, the CHR-D involves not only one but multiple stressors, with physical and mental health playing a particularly important role (Meisenzahl et al., 2024b). SDS may be part of the prodrome for LLD and are linked to functional decline, hopelessness, and increased mortality (Meisenzahl et al., 2024a; Biella et al., 2019; Benasi et al., 2021; Schoevers et al., 2006; Chopra et al., 2005). SDS have a high prevalence and are found in approximately 12 % of the general adult population and SDS are associated with an increased likelihood of developing MDD, dysthymia, social phobia, and generalized anxiety disorder over a 3-year follow-up (Tuithof et al., 2018). In the Berlin Ageing Study, which examined depression in participants aged 79 to 100 years, 9.1 % of participants showed a clinical manifest depressive disorder (Linden et al., 1998). When SDS were also included, the proportion of participants with depressive symptoms increased to 26.9 % and was even higher among people with multimorbidity. Another study found that people aged 65 years and older with SDS showed higher functional impairment than non-depressed people and had a similar medical burden as patients with minor depressive disorder or MDD (Lyness et al., 2007). Triolo et al. (2023) found that subsyndromal depression and MDD accelerate the accumulation of multimorbidity and that cognitive impairment negatively influences the development of depression. SDS were associated with an almost 40 % risk of developing depression and a number needed to treat of 5.8, highlighting the need for preventive strategies in primary care (Schoevers et al., 2006).

Impairments in the cognitive domains of psychomotor speed, attention, memory and executive functions are evident in the first episode of MDD. Furthermore, cognitive impairments are an early symptom in the course of depression and represent targets for prevention of further progression of depression (Lee et al., 2012). However, cognitive symptoms manifest differently in late and mid-life, i.e., decreased processing speed, executive function, selective attention, working memory, verbal fluency, and spatial planning are more prominent in LLD (Aziz and Steffens, 2017), raising the question whether prodromal cognitive symptoms are also different in late and mid-life.

The above findings underpin the need for further research on SDS and their association with cognitive impairment in the older general population with the aim to enable healthcare providers to identify this symptom-level categorization in late-life. Therefore, this study aimed to evaluate whether SDS are associated with cognitive performance, physical health, and quality of life in the general population aged 55+. To investigate the longitudinal course of SDS and the relationship of longitudinal changes in the severity of SDS with cognitive performance, physical health, and quality of life, we analyzed whether cognitive performance, physical health, and psychosocial factors may predict longitudinal changes in the severity of SDS.

2. Methods

2.1. Participants

We included participants aged 55+ from the 1000BRAINS cohort, a population-based investigation of structural and functional variability in the human brain during ageing (Caspers et al., 2014). Participants in 1000BRAINS were recruited from the 10-year follow-up of the Heinz Nixdorf Recall Study (Schmermund et al., 2002) and the Heinz Nixdorf Recall MultiGeneration Study (Kowall et al., 2021) and were only excluded if they had a contraindication for magnetic resonance imaging (see Caspers et al., 2014).

A total of 9691000BRAINS participants were aged 55 years or older (maximum age, 87 years; M = 67.24; SD 6.93) at the first visit (t0); 369 of these adults had participated in the second assessment (t1). The mean interval between visits was 3.8 years (SD 0.73).

Depressive symptoms were evaluated with the Beck Depression Inventory II (BDI-II), a self-rating instrument (Hautzinger et al., 2006), and categorized according to the BDI-II sum score (Storch et al., 2004). SDS were defined as minimal (BDI-II score 9 to 13) and mild depression (BDI-II score 14 to 19) according to the BDI-II (i.e., BDI-II score < 20). Only participants with no depressive symptoms or with SDS were included in the cross-sectional analyses (t0) (i.e., BDI-II score < 20).

Participants with prior or current psychiatric treatment at t0 ($n = 152$) were excluded from the present retrospective analysis, as were those with a prescription for antidepressants (n = 15), severe depressive symptoms ($n = 5$; Beck Depression Inventory II [BDI-II] score, > 19), current or past neurological treatment ($n = 38$), and suspected dementia (DemTect score, < 9; $n = 6$). An additional 84 participants were excluded because of missing data. Thus, 669 participants were eligible for inclusion in the cross-sectional analyses and 255 for inclusion in the longitudinal analyses.

All participants had given written informed consent to participate in the 1000BRAINS study. The study was approved by the ethics committee of the University of Essen (Germany) and performed in accordance with the Declaration of Helsinki.

2.2. Neuropsychological variables

At t0 and t1, participants underwent a neuropsychological assessment that included a wide range of cognitive tests, i.e., the Trail Making Test parts A (visual attention, processing speed) and B (concept shifting), Stroop test (Jülich version; susceptibility to interference; note that the interference, processing speed, and concept shifting parts of the Stroop test are inversely scaled, i.e., elevated scores indicate lower cognitive performance), Benton test (visual and figural memory), Visual Pattern Test (Jülich version; visual memory), Block Tapping Test (visuospatial working memory), Five-Points Test (Jülich version; figural fluency), *Leistungsprüfungssystem 50+* (problem solving), Verbal Memory Test (verbal memory), Digitspan (forward and backward) from the *Nürnberger Alters-Inventar* (verbal working memory), Regensburger Verbal Fluency Test (semantic and phonemic verbal fluency), the Boston Naming Test (word retrieval, naming), and the Vocabulary Test (vocabulary). Participants were also evaluated with the DemTect (Kalbe et al., 2004), a cognitive screening test for mild cognitive impairment or early dementia. For a detailed description of all the included tests, see Caspers et al. (2014).

2.3. Physical variables

At t0 and t1, physical variables were assessed with a semi-structured interview. Participants were asked about physical activity (h/week), cigarette smoking (n/day), and alcohol consumption (units/week). Body mass index and systolic blood pressure were also recorded (for a detailed description, see Lehmann et al., 2018), and physical complaints were evaluated with the *Freiburger Personality Inventory* (Fahrenberg et al., 2010).

At t0, vascular ageing was calculated by estimating the risk for an atherosclerotic cardiovascular disease event with an algorithm that included age, sex, total and high-density lipoprotein (HDL) cholesterol, systolic blood pressure, treatment for hypertension, smoking, and diabetes status (D'Agostino Sr et al., 2008).

At t0, metabolic syndrome was assessed by measuring waist circumference, triglyceride levels, HDL cholesterol, blood pressure, and fasting blood glucose levels. Metabolic syndrome is defined as elevated values for three or more of these measurements, an HDL cholesterol value lower than the reference range (women <50 mg/dL, men <40 mg/dL), or use of medication to normalize these values.

2.4. Psychosocial questionnaires

At both time points, quality of life, daily activities, and behavioral characteristics were assessed with the *Nürnberger Lebensqualitäts-Fragebogen* (quality of life in general) and *Nürnberger Alters-Alltagsaktivitäten-Skala* (daily activities in older adults) from the *Nürnberger Alters-Inventar (*Oswald and Fleischmann, 1997*)*; the *Activities-specific Balance Confidence Scale* (ABC; balance confidence; Powell and Myers, 1995), and the *Frontal Behavioral Inventory* (FBI; Jülich version adapted from Kertesz et al., 1997; personality and behavioral changes related to decreases in frontal brain tissue). The ABC and FBI questionnaires are inversely scaled, i.e., higher values indicate reduced balance confidence and more pronounced changes of personality and behavior. For a detailed description of all included questionnaires, see Caspers et al. (2014).

2.5. Statistical analysis

First, we performed linear regression models to find cross-sectional associations of BDI-II scores with neuropsychological and sociodemographic variables at baseline (t0). Cognitive parameters that showed significant associations in these initial analyses were then simultaneously included into a multiple regression model to determine whether they were independently related to depressive symptoms. Next, we calculated a ΔBDI-II score ($BDI\text{-}II_{t1}$ – $BDI\text{-}II_{t0}$), where positive values indicated increased depressive symptoms over time, and performed a repeated-measures analysis of covariance (ANCOVA) with the cognitive tests or psychosocial measures at t0 and t1 as within-subject variables; sex as the between-subject factor; and age, educational level according to the International Standard Classification of Education 97 (ISCED 97; UNESCO United Nations Educational and Scientific and Cultural Organization, 2003), and ΔBDI-II as covariates. To evaluate the relationship between longitudinal changes in depressive symptoms and cognitive performance or psychosocial measures, we examined the interaction effect of ΔBDI-II score x time on the respective measure.

To predict longitudinal changes in depressive symptoms from neuropsychological, physical health, and psychosocial scores at baseline, we computed linear regression models between ΔBDI-II and the cognitive, physical, and psychosocial measures at t0.

All analyses were corrected for age, sex, and ISCED 97 educational level. To account for multiple comparisons, we applied the False Discovery Rate (FDR) correction by using the Benjamini-Hochberg procedure. Results were considered statistically significant if the FDR-adjusted p value (pFDR) was <0.05. Statistical analyses were performed with IBM SPSS Statistics 27 (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Sample characteristics of participants with or without SDS at t0 and t1

Table 1 shows the descriptive statistics of participants. The total sample comprised 669 people (303 women, 366 men) at t0 and 255 at t1 (117 women, 138 men). The sex distribution and educational level did not differ between the t0 and t1 subsamples, and no participants had severe depressive symptoms at t1 (highest BDI-II score, 17). A significant correlation was found between BDI-II scores at t0 and t1 ($r = 0.604$, $p <$ .001).

Five participants reported undergoing psychiatric treatment between the two assessments; however, none of them was prescribed antidepressants. Two additional participants were prescribed antidepressants at t1. All participants reported significantly lower quality of life at t1, but BDI-II and DemTect scores did not significantly change over time (Table 1). BDI-II scores correlated significantly with age ($\beta = 0.118$, $p =$ .002, $R^2 = 0.047$), ISCED97 educational level ($\beta = -0.120$, $p = .003$, $R^2 = 0.047$), and sex ($\beta = 0.111$, $p = .006$, $R^2 = 0.047$). No correlation was found between BDI-II scores and living alone ($\beta = -0.006$, $p = .871$, $R^2 = 0.045$). Longitudinal changes in depressive symptoms did not correlate significantly with age ($\beta = 0.115$, $p = .068$, $R^2 = 0.002$), ISCED97 educational level ($\beta = -0.018$, $p = .787$, $R^2 = 0.002$), sex ($\beta = 0.012$, $p = .854$, $R^2 = 0.002$), or living status ($\beta = -0.058$, $p = .381$, $R^2 = 0.001$). Consequently, linear regression models were adjusted for age, sex, and ISCED97 educational level.

Table 1
Descriptive statistics of participants included at T0 and T1.

Variables[1]	t0	t1	p (t0 vs t1)
N	669	255	
Age, mean (SD), y	67.6 (6.9)	70.8 (6.7)	< 0.001[2]
Female sex, n (%)	303 (45.3)	117 (45.9)	0.872[3]
ISCED 97, mean (SD)	6.5 (2.0)	6.7 (1.9)	0.065[2]
Psychiatric treatment, n (%)	0 (0)	5 (2.0)	< 0.001[3]
Psychotropic drug intake, n (%)	9 (1.3)	3 (1.2)	0.839[2]
Antidepressant intake, n (%)	0 (0)	2 (0.8)	0.022[3]
BDI-II, mean (SD)	4.4 (3.9)	4.2 (3.8)	0.386[2]
DemTect, mean (SD)	14.8 (2.4)	14.8 (2.6)	0.626[2]
NLQ, mean (SD)	135.1 (13.8)	138.3 (12.3)	0.002[2]

Note: [1] t-test (two-tailed), [2] X^2 test (two-tailed).

BDI-II, Beck Depression Inventory II; DemTect, screening test for dementia; ISCED 97, International Standard Classification of Education 97; NLQ, Nürnberger Lebensqualitäts-Fragebogen (quality of life); t0, baseline assessment; t1, follow-up assessment

3.2. Cross-sectional associations of the absence or presence of SDS with cognitive performance at t0

The presence of more depressive symptoms at t0 was associated with lower DemTect values. Furthermore, after FDR correction, higher depressive symptom severity was significantly negatively associated with the following cognitive domains: figural memory, semantic fluency (with and without switching), problem solving, figural fluency, visuospatial memory (backwards condition), naming, phonemic fluency (with and without switching), vocabulary, and verbal memory (Fig. 1, Table 2). Moreover, we observed a positive association between depressive symptoms and processing speed scores, suggesting that greater depressive symptom severity is linked to slower cognitive processing. To account for the correlations among the cognitive tests, we included all significant cognitive measures in a multiple linear regression model. The association between BDI-II and DemTect remained significant ($\beta = -0.103$, $p = .028$, $R^2 = 0.073$), and the results indicated that the strongest negative correlation between cognitive tests was between BDI-II and DemTect scores.

3.3. Cross-sectional associations of the absence or presence of SDS with physical variables at t0

Higher SDS scores correlated significantly with lower levels of physical activity and more physical complaints. However, no significant association was found between physical or age-related illnesses (see Table 3).

3.4. Cross-sectional associations of to the presence or absence of SDS with psychosocial parameters at t0

For psychosocial measures, higher SDS at t0 showed a negative

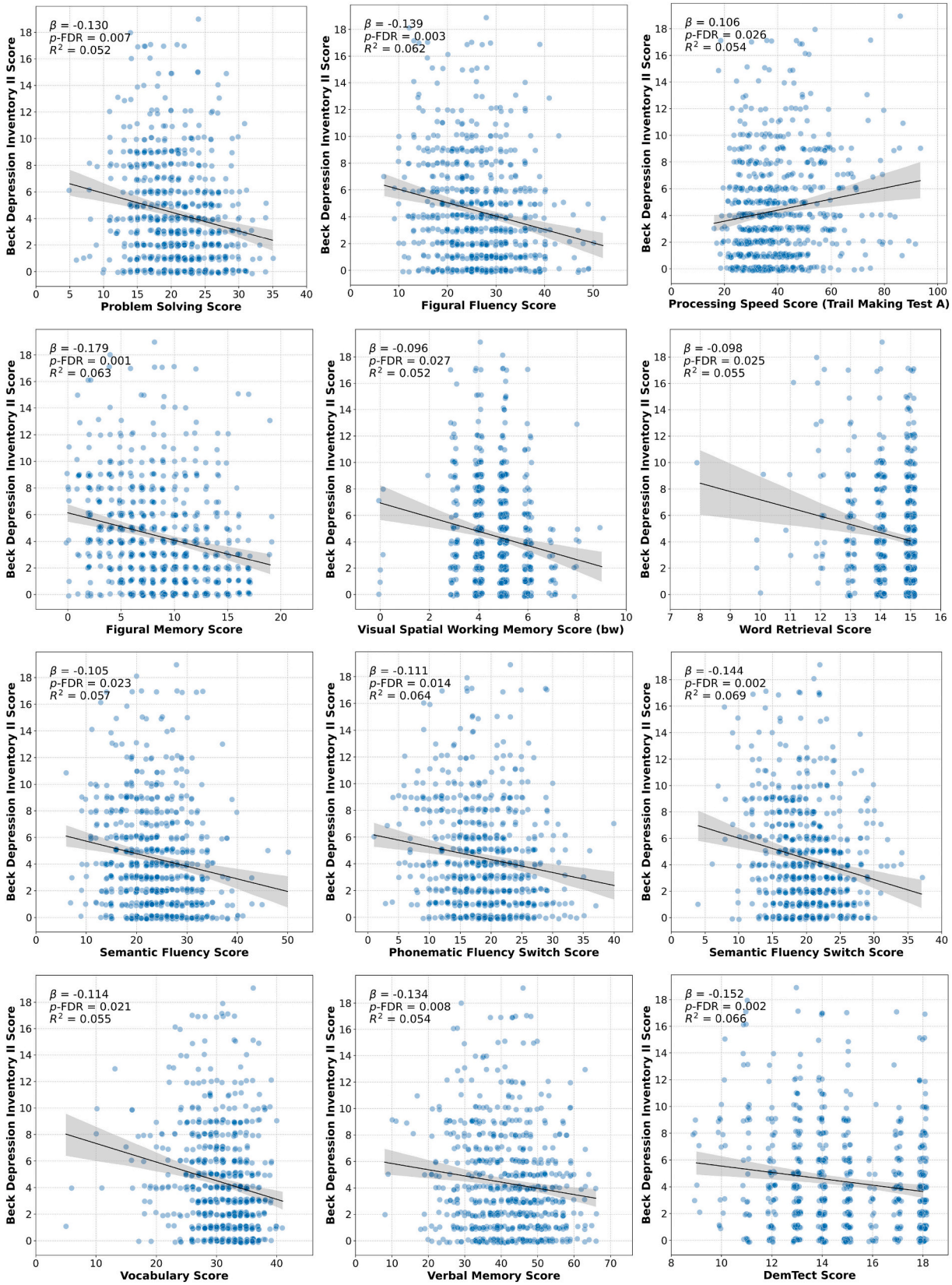

Fig. 1. Scatterplot illustrating the significant associations between baseline Beck Depression Inventory II (BDI-II) scores and different cognitive tests. The x-axis represents the unprocessed scores of the respective cognitive test, the y-axis shows the unprocessed BDI-II scores. Data points are semi-transparent and were slightly jittered to visualize overlapping observations. Trend lines represent the least-squares linear fit; shaded area denotes the 95 % confidence interval. In the top-left corner, results from the multiple regression analysis are displayed, including the β-value, FDR-corrected p-value (p-FDR), and R squared (R^2), reflecting the strength and significance of the associations.

Table 2
Cross-sectional linear regression analyses of Beck Depression Inventory-II scores versus cognitive, physical, and psychosocial variables.

Independent variables	B	SE	β	p	$pFDR$	R^2
Cognitive parameters						
Problem solving	−0.097	0.032	−0.130	0.002	**0.007**	0.052
Stroop test (interference)	0.001	0.006	0.009	0.830	0.830	0.047
Figural fluency	−0.070	0.021	−0.139	< 0.001	**0.003**	0.062
Processing speed (TMT A)	0.029	0.011	0.105	0.013	**0.026**	0.054
Concept shifting (TMT B/A)	0.003	0.004	0.031	0.446	0.495	0.047
Figural memory	−0.165	0.041	−0.179	< 0.001	**0.001**	0.063
Visuospatial memory forwards	−0.194	0.166	−0.046	0.243	0.347	0.047
Visuospatial memory backwards	−0.337	0.140	−0.096	0.016	**0.027**	0.052
Visual memory	−0.075	0.095	−0.034	0.430	0.506	0.047
Short-term memory forwards	−0.066	0.143	−0.018	0.645	0.679	0.047
Working memory backwards	−0.131	0.137	−0.037	0.342	0.456	0.049
Word retrieval	−0.417	0.169	−0.098	0.014	**0.025**	0.055
Phonemic fluency	−0.047	0.024	−0.076	0.053	0.081	0.057
Semantic fluency	−0.062	0.024	−0.105	0.010	**0.023**	0.057
Switching of phonemic fluency tasks	−0.072	0.026	−0.111	0.005	**0.014**	0.064
Switching of semantic fluency tasks	−0.120	0.033	−0.144	< 0.001	**0.002**	0.069
Vocabulary	−0.088	0.033	−0.114	0.008	**0.021**	0.055
Verbal memory	−0.051	0.016	−0.134	0.002	**0.008**	0.054
DemTect	−0.249	0.066	−0.152	< 0.001	**0.002**	0.066
Physical variables						
Physical activity, h/week	−0.063	0.028	−0.087	**0.023**		0.052
Cigarette smoking, n/day	0.027	0.031	0.034	0.383		0.046
Alcohol consumption, units/week	−0.006	0.014	−0.017	0.664		0.045
Body mass index	−0.018	0.037	−0.019	0.625		0.045
Systolic blood pressure	−0.016	0.009	−0.074	0.067		0.053
Vascular ageing, y	−0.016	0.009	−0.081	0.076		0.052
Metabolic syndrome	−0.002	0.007	−0.010	0.787		0.050
Physical complaints (FPI)	0.872	0.072	0.455	**< 0.001**		0.222
Cataract	−0.006	0.086	−0.003	0.942		0.045
Glaucoma	0.004	0.004	0.043	0.251		0.047
Age-related hearing loss	0.226	0.172	0.050	0.190		0.048
Hearing aid	0.085	0.164	0.020	0.602		0.046
Joint disease	0.388	0.203	0.072	0.057		0.050
Artificial joint	0.499	0.258	0.073	0.054		0.050
Disc prolapse	0.122	0.189	0.024	0.518		0.046
Polyneuropathy	0.353	0.200	0.067	0.079		0.050
Psychosocial variables						
NLQ	−0.176	0.009	−0.630	< 0.001	**< 0.001**	0.418
NAA	−0.481	0.056	−0.326	< 0.001	**< 0.001**	0.148
FBI	0.287	0.025	0.414	< 0.001	**< 0.001**	0.215
ABC	0.298	0.045	0.268	< 0.001	**< 0.001**	0.111

Note: Results of the linear regression analyses at baseline. Uncorrected p values and p values corrected for multiple comparisons by False Discovery Rate correction (pFDR) are reported.
ABC, Activities-specific Balance Confidence; B, regression coefficient; BDI-II, Beck Depression Inventory II; β, standardized regression coefficient; DemTect, screening test for dementia; FBI, Frontal Behavioral Inventory (Jülich version); pFDR, false discovery rate-adjusted p value; FPI, Freiburger Personality Inventory; NAA, Nürnberger Alters-Alltagsaktivitäten-Skala; NLQ, Nürnberger Lebensqualitäts-Fragebogen; R^2, adjusted quality measure of the linear model; SE, standard error; TMT, Trail Making Test

Table 3
Linear regression analyses for change in Beck Depression Inventor-II scores versus sociodemographic and physical variables at baseline (t0).

Independent variables	B	SE	β	p	R^2
Physical variables					
Physical activity, h/week	−0.021	0.035	−0.040	0.547	−0.001
Cigarette smoking, n/day	0.098	0.048	0.130	**0.042**	0.015
Alcohol consumption, units/week	0.002	0.018	0.007	0.918	−0.002
Body mass index	0.125	0.053	0.149	**0.018**	0.020
Systolic blood pressure, mmHg	0.015	0.012	0.081	0.224	0.001
Vascular ageing, y	0.034	0.014	0.189	**0.013**	0.020
Metabolic syndrome	0.004	0.017	0.016	0.797	−0.004
Physical complaints, FPI score	0.018	0.126	0.010	0.887	−0.002
Cataract	−0.018	0.114	−0.010	0.872	−0.002
Glaucoma	−0.073	0.112	−0.042	0.517	0.000
Age-related hearing loss	−0.161	0.211	−0.048	0.446	0.001
Hearing aid	−0.119	0.293	−0.026	0.684	−0.001
Joint disease	−0.311	0.257	−0.076	0.228	0.004
Artificial joint	−0.242	0.324	−0.047	0.455	0.000
Disc prolapse	−0.054	0.210	−0.016	0.797	−0.002
Polyneuropathy	−0.056	0.219	−0.016	0.799	−0.002

Note: Results of the linear regression analyses predicting change in Beck Depression Inventory II score from baseline sociodemographic and physical variables.
B, regression coefficient; BDI-II, Beck Depression Inventory II; ΔBDI-II, $BDI\text{-}II_{t1} - BDI\text{-}II_{t0}$; β, standardized regression coefficient; FPI, Freiburger Personality Inventory; ISCED97, International Standard Classification of Education 97; R^2, adjusted quality measure of the linear model; SE, standard error.

association with both quality of life ($\beta = -0.630$, $pFDR < 0.001$, $R^2 = 0.418$) and daily activities ($\beta = -0.481$, $pFDR < 0.001$, $R^2 = 0.148$). Conversely, they showed a positive association with the sum scores of ABC ($\beta = 0.268$, $pFDR < 0.001$, $R^2 = 0.111$) and FBI ($\beta = 0.414$, $pFDR < 0.001$, $R^2 = 0.215$; Fig. S1, Table 2).

3.5. Association of longitudinal changes in SDS with cognitive parameters

Repeated-measures ANCOVA showed no significant interaction between ΔBDI-II score x time and longitudinal changes in cognitive tests (see Table S1).

Regression analyses found significant positive associations for ΔBDI-II score as the dependent variable and semantic fluency ($\beta = 0.152$, $p = .022$, $pFDR = 0.263$, $R^2 = 0.020$) and vocabulary ($\beta = 0.152$, $p = .033$, $pFDR = 0.197$, $R^2 = 0.016$) at baseline as independent variables; however, these results were no longer significant after FDR correction.

3.6. Association of longitudinal changes in SDS with physical variables

Longitudinal changes in depressive symptoms correlated significantly with the number of cigarettes smoked per day, body mass index, and vascular ageing in years at t0 (Table 3).

3.7. Association of longitudinal changes in SDS with psychosocial parameters

A significant negative interaction effect of ΔBDI-II score x time was found for longitudinal changes in quality of life (NLQ; $F(1, 191) = 16.100$, $pFDR < 0.001$, partial $\eta^2 = 0.078$) and daily activities (NAA; F

(1,201) = 6.674, *pFDR* = 0.021, partial η^2 = 0.032). At t0, ΔBDI-II showed no significant association with psychosocial measures (see Fig. 2 and Table S2).

4. Discussion

This retrospective analysis of data from the general population-based 1000BRAINS study assessed possible associations of SDS with cognitive performance, physical health, and quality of life at baseline (t0) in adults aged 55+ and evaluated longitudinal changes in severity of SDS and their relationship with cognition, physical health, and psychosocial variables in this cohort. The study found that severity of SDS at baseline was linked to poorer performance in various cognitive domains (including processing speed, executive function, figural, and verbal memory) and in the dementia screening test (DemTect), lower physical activity, and higher physical complaints. Furthermore, an increase in SDS over time correlated with lower quality of life, more vascular ageing, and higher body mass index.

In the 1000BRAINS cohort, SDS were present in 14 % of the population aged 50 years and older (Christl et al., 2025). Lower mental functioning in individuals with SDS is associated with an increased likelihood of MDD (Pietrzak et al., 2013). Further characterization of SDS with regard to cognition, physical health, and psychosocial functioning may help to identify individuals at risk for further worsening of depressive symptoms and for CHR-D in late life and may support the development of preventive strategies (Judd et al., 2002; Cuijpers et al., 2007; Rosenberg et al., 2010).

At t1, five participants reported new undergoing psychiatric treatment and two were prescribed antidepressants. BDI-II scores at the two assessments of all participants highly correlated with each other, and

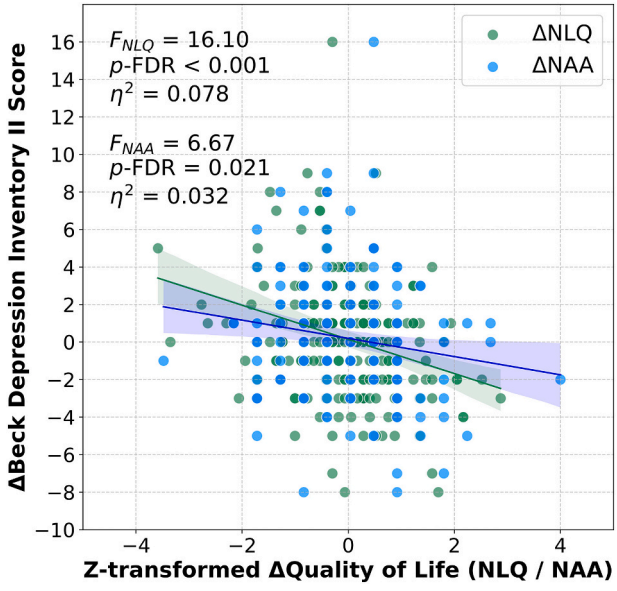

Fig. 2. Scatterplot illustrating the association between longitudinal changes in depressive symptoms (ΔBDI-II = BDI-II_{t1} – BDI-II_{t0}) and changes in quality-of-life measures (NLQ: Nürnberger Lebensqualitäts-Fragebogen; NAA: Nürnberger Alters-Alltagsaktivitäten-Skala). The x-axis shows z-transformed ΔNLQ (NLQ_{t1} – NLQ_{t0}; green) and ΔNAA (NAA_{t1} – NAA_{t0}; blue) scores. *Z*-transformation was performed by subtracting the mean of each measure from each individual score and dividing by its standard deviation, allowing direct comparison across measures on the same scale. The y-axis represents ΔBDI-II scores. Trend lines represent the least-squares linear fit; shaded area denotes the 95 % confidence interval. In the top-left corner, results from the repeated measures ANCOVA are displayed, including the F-value, FDR-corrected *p*-value (*p*-FDR), and partial eta squared (η^2), reflecting the strength and significance of the associations. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

BDI-II and DemTect scores did not significantly change over time. Of note, the small number of participants with manifest depressive symptoms and no increase in depressive symptom severity in our study may be due to the populations-based design, which did not focus on participants with a higher severity of depressive symptoms, and strict exclusion of participants with history of psychiatric and neurological treatment. Nevertheless, depressive symptom severity highly correlated between the two assessments, underscoring the importance of viewing depressive symptoms on a continuum, and imply that a dimensional conceptualization of depressive symptoms may help to identify individuals who may be at risk for developing MDD and related disorders (Pietrzak et al., 2013; Keller et al., 1992; Judd, 2012; Sadek and Bona, 2000; DeYoung et al., 2024).

4.1. SDS and cognition

After correction for age, sex, and educational level, SDS correlated significantly with poorer cognitive performance in processing speed, switching of phonemic and semantic fluency tasks, and figural and verbal memory. When all significant cognitive parameters were included in one regression model, the correlation between SDS and the DemTect score remained significant. This result indicates that after correction for other cognitive domains, SDS are most strongly associated with the DemTect.

Dillon et al. (2014) showed that patients with SDS in late-life present a mixed profile, i.e., they have cognitive deficits in cortical (language) and subcortical domains (memory), which could indicate that this group is at risk for dementia. Our findings support previous research linking depressive symptoms to declines in memory and processing speed (Clark et al., 2009), with specific impacts observed on semantic fluency and verbal memory. In addition, depressive symptoms in late life are often accompanied by impairments in various cognitive domains, particularly processing speed and executive function, rather than in one particular domain (Dillon et al., 2014; Butters et al., 2004; Alexopoulos, 2019; Lim et al., 2013). Furthermore, symptoms can persist even after remission of depression and can have a negative impact on quality of life in mid- and late-life (Gonda et al., 2015; Nebes et al., 2003; Conradi et al., 2011). Zhou et al. (2021) showed that depressive symptoms correlated negatively with the various categories in the Mini Mental Status Examination, which—similar to the DemTect—is a screening test for dementia and encompasses subtests on word fluency, intellectual flexibility, verbal and working memory (Kalbe et al., 2004). Therefore, the observed association may reflect a broader cognitive vulnerability in individuals with elevated depressive symptoms, potentially involving episodic memory, attentional control, and executive functioning. However, it could also be argued that SDS are an early risk for developing dementia, although our cross-sectional results prevent such a causal inference.

The question whether depression is a prodrome of dementia and/or an etiologic risk factor for the development of dementia remains unclear (Aziz and Steffens, 2013; Butters et al., 2004; Bennett and Thomas, 2014; Piras et al., 2021; Almeida et al., 2017; Livingston et al., 2020). The interval between a diagnosis of depression and an Alzheimer's disease diagnosis and the odds for developing dementia still correlate positively and significantly after adjusting for the length of the interval (Jorm, 2001; Ownby et al., 2006). Results from the Whitehall II cohort study of 10,308 persons (aged 35 to 55 years) showed that depressive symptoms emerge a decade before incipient dementia and that recurrent or chronic depression does not increase the risk for dementia (Singh-Manoux et al., 2017). A prospective cohort study of 354,313 participants aged 50 to 70 years found a reduced likelihood of developing dementia after treatment of depression and showed that this effect was significant in all groups of patients except those with chronically high levels of depressive symptoms (Yang et al., 2023). A large Korean population-based cohort study showed an increased risk for dementia in people aged 60 years and older with chronic or recurrent SDS over a follow-up period of 6 years (Oh et al., 2021). In our sample, longitudinal changes

in depressive symptoms did not correlate with changes in cognitive performance; the lack of a correlation may be associated with the shorter follow-up period and younger population.

In the present sample, we found no significant association between longitudinal changes in SDS and cognitive tests at baseline, i.e., cognitive impairment at baseline was not associated with a worsening of depressive symptoms. However, Hopper et al. (2024) demonstrated that cognitive impairment predicted a worsening in depressive symptoms at follow-up. The results may differ from ours because this study included participants with higher levels of depressive symptoms at baseline. A longitudinal, population-based study found that depression in participants older than 50 years was related to cognitive functioning. However, depression was not associated with faster cognitive decline. In individuals with a higher cognitive reserve, however, depression was found to have a harmful effect on memory performance (Lara et al., 2022). A longitudinal examination of depressive events (depressive symptoms/depressive syndrome/MDD) in 4509 participants from the population-based Rotterdam Study showed that higher cognitive and brain reserve was associated with a lower incidence of depressive events, although these effects decreased when participants with depressive symptoms at baseline were excluded (Zijlmans et al., 2023).

The above findings may indicate that depressive symptoms are a risk factor for development of a depressive disorder, but they do not appear to indicate that they are a risk factor for a reduction in cognitive and brain reserve and therefore an increase in the risk for dementia. Furthermore, a reduction in brain reserve due to reduced neuroplasticity, oxidative stress, inflammatory processes, and vascular changes such as increased white matter lesions appears to be relevant for the development of a depressive episode in late life (Alexopoulos, 2019; Weisenbach and Kumar, 2014). These underlying pathomechanisms of depression in late life are shared with neurodegenerative processes that lead to mild cognitive impairment and dementia (Alexopoulos, 2019; Byers and Yaffe, 2011). Neuroimaging studies concluded that LLD presents along a continuum of common neurobiological substrates (Lavretsky et al., 2004; Kumar et al., 1998; Allan et al., 2016; DeYoung et al., 2024). For example, the Research Domain Criteria aims to promote research to validate the dimensions defined by neurobiology and behavioral measures that cut across current disorder categories. These can then inform future revisions of our diagnostic systems (Cuthbert, 2014). In addition, LLD often has a chronic course, and these pathomechanisms may contribute to the longitudinal course of the disease (Weisenbach and Kumar, 2014; Comijs et al., 2015; de la Torre-Luque et al., 2019). To conclude, in SDS, preventive strategies may be extremely effective in reducing the risk of progression of not only depressive symptom severity but also cognitive decline.

4.2. SDS and physical health

In the cross-sectional analysis, higher severity of depressive symptoms in participants with SDS were associated with less physical activity and more physical complaints. Over the longitudinal course, after correcting for age, sex, and educational level, an increase in severity of SDS correlated with a higher vascular age, greater number of cigarettes smoked per day, and higher body mass index at baseline; however, the effects were only small.

In patients with depression, older age is associated with a higher risk for physical inactivity (Vancampfort et al., 2017). A comparative epidemiological study in older adults with depression and SDS also found that people with depression exercised less (Oh et al., 2020). Longitudinal analyses of depressive trajectories in late-life showed that physical activity increased the hazard ratio of recovery from SDS and depression (Triolo et al., 2024). In addition, higher activity-based cognitive reserve was associated with a lower risk for development of depressive symptoms in late-life (Triolo et al., 2025). In summary, these results provide further support for a possible association of low physical activity with increased depressive symptoms.

In accordance with our results, a meta-analysis showed that depression and obesity have a bidirectional association, i.e., obesity at baseline increased the risk for developing depression, and depression increased the risk for developing obesity (Luppino et al., 2010). A previous cross-sectional analysis of the total 1000BRAINS cohort at t0 also found a significant positive correlation between depressive symptom severity and obesity (Christl et al., 2025). A prospective study on adults aged 50 to 70 showed that somatic and vegetative symptoms of the BDI-II (e.g. fatigue, sleep disturbances and changes in appetite) were associated with insulin resistance and increased the risk of developing diabetes, partly by increasing body mass index (Khambaty et al., 2014).

A higher level of vascular ageing was associated with longitudinal changes in depressive symptoms. To our knowledge, the relationship between SDS and vascular ageing has not previously been described. However, the relationship between SDS and blood pressure variability has been investigated, revealing that elevated diastolic blood pressure variability is associated with SDS (Sible et al., 2022). Similar to our study, Zhang et al. (2018) found that arterial hypertension, coronary artery disease, and diabetes mellitus increase the risk for development of LLD. Vascular ageing could be an early biomarker for deterioration of depressive symptoms. Compared with not having depressive symptoms, having SDS affects health and the self-rating of one's health as poor (Ayuso-Mateos et al., 2010; Judd et al., 1996). Furthermore, SDS and MDD accelerate the accumulation of multimorbidity (Triolo et al., 2023).

Even in SDS, i.e., the symptoms do not fulfil the diagnostic criteria for depression, depressive symptoms are associated with physical complaints and lower physical activity. This association may imply that physical complaints and lower physical activity increase the progression of depressive symptoms and, vice versa, that SDS may increase the risk of multimorbidity.

4.3. SDS and quality of life

Similar to prior studies linking depressive episodes to reduced quality of life and increased mortality (Köhler et al., 2018), our findings highlight that SDS are significantly associated with lower quality of life, fewer daily activities, and poorer balance confidence. Longitudinal changes in SDS were associated with a decrease in quality of life and daily activities. Thus, our findings indicate that a decrease in quality of life reflects an increase in depressive symptoms and that SDS and the changes of SDS over time are strongly associated with quality of life.

We found no significant association between quality of life at baseline and changes in depressive symptoms, indicating that quality of life may not predict changes in depressive symptoms. However, our study showed that quality of life and depressive symptomatology are highly correlated with each other; this finding is in accordance with other studies that found a significant impact of mild depressive symptoms and SDS on quality of life, social relationships, and well-being (Judd et al., 1997; Judd et al., 1996). SDS are associated with psychosocial impairment and disability, and depressive symptom severity shows a linear correlation with the degree of impairment. In conclusion, adopting a symptom- rather than a cut-off-level approach to viewing depression (Lavretsky et al., 2004; Judd et al., 2002; DeYoung et al., 2024) reveals that SDS are strongly associated with impairment in quality of life, similar to LLD.

4.4. Limitations

A limitation of the study is that depressive symptoms were evaluated by a self-rating instrument, the BDI-II. Nevertheless, this instrument has high internal consistency (coefficient alpha, 0.89), and in this age group and population, the prevalence of depression determined by a physician correlates with mean BDI-II scores (Steer et al., 2000; Gallagher et al., 1982; Segal et al., 2008; Balsamo et al., 2018; Veerman et al., 2009). Additionally, in our previous work we showed that the prevalence rates

of depressive symptoms in the 1000BRAINS sample were comparable to those in other large population-based studies (Christl et al., 2025) Depressive symptoms were evaluated at two time points at a mean interval of 3.8 years. Limitations include the limited availability of data at the second time point, which could result in attrition bias. However, as expected, the samples at the two measurement points differed only in terms of age and previous psychiatric treatment. This is because subjects with previous psychiatric treatment were excluded at t0, and the remaining subjects became older. Perhaps because of the relatively short interval between the two measurements, longitudinal changes in cognitive parameters did not correlate with changes in depressive symptoms. Furthermore, the approach to calculating the change in BDI-II score may have masked clinically meaningful heterogeneity (e.g. stable high symptoms vs. increasing low symptoms). Further analyses with a longer interval between tests of SDS and cognition are essential to further elucidate the association between cognition and SDS.

5. Conclusion

In summary, cross-sectional analysis showed that SDS in late life are associated with cognitive impairment and reduced physical health and quality of life. The longitudinal analysis showed that worsening of depressive symptoms correlates with a decrease in physical health and quality of life. SDS are associated with higher socioeconomic burden, more physical illnesses, and impairment in daily functioning and may be part of a prodrome for LLD (Meisenzahl et al., 2024a; Biella et al., 2019; Benasi et al., 2021; Schoevers et al., 2006; Chopra et al., 2005; Judd et al., 1996; Sadek and Bona, 2000). The results highlight the significant medical burden of SDS, which is linked to poorer cognitive performance, quality of life, and physical health. As SDS preventive strategies are likely to reduce the risk of depression and the associated medical burden, they are of great importance. Further research is required to elucidate the pathomechanisms of SDS. In addition, treatment of SDS may reduce the risk for further cognitive decline and physical complaints in late life.

CRediT authorship contribution statement

Julia Christl: Writing – original draft, Methodology, Conceptualization. **Pascal Grumbach:** Writing – review & editing, Visualization, Methodology, Data curation. **Christiane Jockwitz:** Writing – review & editing, Validation, Methodology, Investigation, Data curation. **Natalia Wege:** Writing – review & editing, Validation. **Svenja Caspers:** Writing – review & editing, Supervision, Project administration, Conceptualization. **Eva Meisenzahl:** Writing – review & editing, Supervision, Investigation, Conceptualization.

Funding

This project was partially funded by the German National Cohort and the 1000BRAINS Study of the Institute of Neuroscience and Medicine, Research Centre Jülich, Germany. Furthermore, this project received funding from the European Union's Horizon 2020 Research and Innovation Program under Grant Agreement No. 945539 (HBP SGA3; SC).

Declaration of competing interest

The authors declare that there are no conflicts of interest.

Acknowledgements

The authors thank Jacquie Klesing, Board-certified Editor in the Life Sciences (ELS), for editing assistance with the manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jad.2025.120885.

Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

References

Alexopoulos, G.S., 2019. Mechanisms and treatment of late-life depression. Transl. Psychiatry 9 (1), 188. https://doi.org/10.1038/s41398-019-0514-6.

Allan, C.L., Sexton, C.E., Filippini, N., Topiwala, A., Mahmood, A., Zsoldos, E., Singh-Manoux, A., Shipley, M.J., Kivimaki, M., Mackay, C.E., Ebmeier, K.P., 2016. Subthreshold depressive symptoms and brain structure: a magnetic resonance imaging study within the Whitehall II cohort. J. Affect. Disord. 204, 219–225. https://doi.org/10.1016/j.jad.2016.06.049.

Almeida, O.P., Hankey, G.J., Yeap, B.B., Golledge, J., Flicker, L., 2017. Depression as a modifiable factor to decrease the risk of dementia. Transl. Psychiatry 7 (5), e1117. https://doi.org/10.1038/tp.2017.90.

Ayuso-Mateos, J.L., Nuevo, R., Verdes, E., Naidoo, N., Chatterji, S., 2010. From depressive symptoms to depressive disorders: the relevance of thresholds. The British journal of psychiatry : the journal of mental science 196 (5), 365–371. https://doi.org/10.1192/bjp.bp.109.071191.

Aziz, R., Steffens, D., 2017. Overlay of late-life depression and cognitive impairment. Focus (American Psychiatric Publishing) 15 (1), 35–41. https://doi.org/10.1176/appi.focus.20160036.

Aziz, R., Steffens, D.C., 2013. What are the causes of late-life depression? Psychiatr. Clin. North Am. 36 (4), 497–516. https://doi.org/10.1016/j.psc.2013.08.001.

Balsamo, M., Cataldi, F., Carlucci, L., Padulo, C., Fairfield, B., 2018. Assessment of late-life depression via self-report measures: a review. Clin. Interv. Aging 13, 2021–2044. https://doi.org/10.2147/CIA.S178943.

Benasi, G., Fava, G.A., Guidi, J., 2021. Prodromal symptoms in depression: a systematic review. Psychother. Psychosom. 90 (6), 365–372. https://doi.org/10.1159/000517953.

Bennett, S., Thomas, A.J., 2014. Depression and dementia: cause, consequence or coincidence? Maturitas 79 (2), 184–190. https://doi.org/10.1016/j.maturitas.2014.05.009.

Biella, M.M., Borges, M.K., Strauss, J., Mauer, S., Martinelli, J.E., Aprahamian, I., 2019. Subthreshold depression needs a prime time in old age psychiatry? A narrative review of current evidence. Neuropsychiatr. Dis. Treat. 23 (15), 2763–2772. https://doi.org/10.2147/NDT.S223640.

Bock, J.O., Brettschneider, C., Weyerer, S., Werle, J., Wagner, M., Maier, W., Scherer, M., Kaduszkiewicz, H., Wiese, B., Moor, L., Stein, J., Riedel-Heller, S.G., König, H.H., 2016. Excess health care costs of late-life depression - results of the AgeMooDe study. J. Affect. Disord. 199, 139–147. https://doi.org/10.1016/j.jad.2016.04.008.

Butters, M.A., Whyte, E.M., Nebes, R.D., Begley, A.E., Dew, M.A., Mulsant, B.H., Zmuda, M.D., Bhalla, R., Meltzer, C.C., Pollock, B.G., Reynolds 3rd, C.F., Becker, J. T., 2004. The nature and determinants of neuropsychological functioning in late-life depression. Arch. Gen. Psychiatry 61 (6), 587–595. https://doi.org/10.1001/archpsyc.61.6.587.

Byers, A.L., Yaffe, K., 2011. Depression and risk of developing dementia. Nat. Rev. Neurol. 7 (6), 323–331. https://doi.org/10.1038/nrneurol.2011.60.

Caspers, S., Moebus, S., Lux, S., Pundt, N., Schütz, H., Mühleisen, T.W., Gras, V., Eickhoff, S.B., Romanzetti, S., Stöcker, T., Stirnberg, R., Kirlangic, M.E., Minnerop, M., Pieperhoff, P., Mödder, U., Das, S., Evans, A.C., Jöckel, K.H., Erbel, R., Cichon, S., et al., 2014. Studying variability in human brain aging in a population-based German cohort-rationale and design of 1000BRAINS. Front. Aging Neurosci. 6, 149. https://doi.org/10.3389/fnagi.2014.00149.

Chopra, M.P., Zubritsky, C., Knott, K., Have, T.T., Hadley, T., Coyne, J.C., Oslin, D.W., 2005. Importance of subsyndromal symptoms of depression in elderly patients. The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry 13 (7), 597–606. https://doi.org/10.1176/appi.ajgp.13.7.597.

Christl, J., Grumbach, P., Jockwitz, C., Wege, N., Caspers, S., Meisenzahl, E., 2025. Prevalence of depressive symptoms in people aged 50 years and older: a retrospective cross-sectional study. J. Affect. Disord. 373, 353–363. https://doi.org/10.1016/j.jad.2024.12.099.

Clark, L., Chamberlain, S.R., Sahakian, B.J., 2009. Neurocognitive mechanisms in depression: implications for treatment. Annu. Rev. Neurosci. 32, 57–74. https://doi.org/10.1146/annurev.neuro.31.060407.125618.

Comijs, H.C., Nieuwesteeg, J., Kok, R., van Marwijk, H.W., van der Mast, R.C., Naarding, P., Voshaar, R.C., Verhaak, P., de Waal, M.W., Stek, M.L., 2015. The two-year course of late-life depression; results from the Netherlands study of depression in older persons. BMC Psychiatry 15, 20. https://doi.org/10.1186/s12888-015-0401-5.

Conradi, H.J., Ormel, J., de Jonge, P., 2011. Presence of individual (residual) symptoms during depressive episodes and periods of remission: a 3-year prospective study. Psychol. Med. 41 (6), 1165–1174. https://doi.org/10.1017/S0033291710001911.

Cuijpers, P., Smit, F., van Straten, A., 2007. Psychological treatments of subthreshold depression : a meta-analytic review. Acta Psychiatr. Scand. 115, 434–441.
Cuthbert, B.N., 2014. The RDoC framework: facilitating transition from ICD/DSM to dimensional approaches that integrate neuroscience and psychopathology. World Psychiatry 13, 28–35. https://doi.org/10.1002/wps.20087.
D'Agostino Sr., R.B., Vasan, R.S., Pencina, M.J., Wolf, P.A., Cobain, M., Massaro, J.M., Kannel, W.B., 2008. General cardiovascular risk profile for use in primary care: the Framingham heart study. Circulation 117 (6), 743–753, 10.1161/CIRCULATIONAHA.107.699579)10.1161/CIRCULATIONAHA.107.699579).
de la Torre-Luque, A., de la Fuente, J., Sanchez-Niubo, A., Caballero, F.F., Prina, M., Muniz-Terrera, G., Haro, J.M., Ayuso-Mateos, J.L., 2019. Stability of clinically relevant depression symptoms in old-age across 11 cohorts: a multi-state study. Acta Psychiatr. Scand. 140 (6), 541–551. https://doi.org/10.1111/acps.13107.
DeYoung, C.G., Blain, S.D., Latzman, R.D., Grazioplene, R.G., Haltigan, J.D., Kotov, R., Michelini, G., Venables, N.C., Docherty, A.R., Goghari, V.M., Kallen, A.M., Martin, E. A., Palumbo, I.M., Patrick, C.J., Perkins, E.R., Shackman, A.J., Snyder, M.E., Tobin, K.E., 2024. The hierarchical taxonomy of psychopathology and the search for neurobiological substrates of mental illness: a systematic review and roadmap for future research. Journal of psychopathology and clinical science 133 (8), 697–715. https://doi.org/10.1037/abn0000903.
Dillon, C., Tartaglini, M.F., Stefani, D., Salgado, P., Taragano, F.E., Allegri, R.F., 2014. Geriatric depression and its relation with cognitive impairment and dementia. Arch. Gerontol. Geriatr. 59 (2), 450–456. https://doi.org/10.1016/j.archger.2014.04.006.
Fahrenberg, J., Hampel, R., Selg, H., 2010. FPI-R Freiburger Persönlichkeitsinventar, 8th Expanded Edn. Hogrefe, Göttingen.
Gallagher, D., Nies, G., Thompson, L.W., 1982. Reliability of the Beck depression inventory with older adults. J. Consult. Clin. Psychol. 50 (1), 152–153. https://doi.org/10.1037//0022-006x.50.1.152.
Gonda, X., Pompili, M., Serafini, G., Carvalho, A.F., Rihmer, Z., Dome, P., 2015. The role of cognitive dysfunction in the symptoms and remission from depression. Ann. General Psychiatry 14, 27. https://doi.org/10.1186/s12991-015-0068-9.
Grochtdreis, T., Brettschneider, C., Bjerregaard, F., Bleich, C., Boczor, S., Härter, M., Hölzel, L.P., Hüll, M., Kloppe, T., Niebling, W., Scherer, M., Tinsel, I., König, H.H., 2019. Cost-effectiveness analysis of collaborative treatment of late-life depression in primary care (GermanIMPACT). European psychiatry : the journal of the Association of European Psychiatrists 57, 10–18. https://doi.org/10.1016/j.eurpsy.2018.12.007.
Hautzinger, M., Keller, F., Kühner, C., 2006. BDI-II Beck Depressions-Inventar, 2nd Edn. Harcourt Test Services, Frankfurt.
Hopper, S., Grady, A., Best, J.R., Stinchcombe, A., 2024. Bidirectional associations between memory and depression moderated by sex and age: findings from the CLSA. Arch. Gerontol. Geriatr. 116, 105154. https://doi.org/10.1016/j.archger.2023.105154.
Jorm, A.F., 2001. History of depression as a risk factor for dementia: an updated review. Aust. N. Z. J. Psychiatry 35, 776–781.
Judd, L.L., 2012. Dimensional paradigm of the long-term course of unipolar major depressive disorder. Depress. Anxiety 29 (3), 167–171. https://doi.org/10.1002/da.21934.
Judd, L.L., Akiskal, H.S., Paulus, M.P., 1997. The role and clinical significance of subsyndromal depressive symptoms (SSD) in unipolar major depressive disorder. J. Affect. Disord. 45 (1–2), 5–18. https://doi.org/10.1016/s0165-0327(97)00055-4.
Judd, L.L., Paulus, M.P., Wells, K.B., Rapaport, M.H., 1996. Socioeconomic burden of subsyndromal depressive symptoms and major depression in a sample of the general population. Am. J. Psychiatry 153 (11), 1411–1417. https://doi.org/10.1176/ajp.153.11.1411.
Judd, L.L., Schettler, P.J., Akiskal, H.S., 2002. The prevalence, clinical relevance, and public health significance of subthreshold depressions. Psychiatr. Clin. North Am. 25 (4), 685–698. https://doi.org/10.1016/s0193-953x(02)00026-6.
Kalbe, E., Kessler, J., Calabrese, P., Smith, R., Passmore, A.P., Brand, M., et al., 2004. DemTect: a new, sensitive cognitive screening test to support the diagnosis of mild cognitive impairment and early dementia. Int. J. Geriatr. Psychiatry 19, 136–143. https://doi.org/10.1002/gps.1042.
Keller, M.B., Lavori, P.W., Mueller, T.I., Endicott, J., Coryell, W., Hirschfeld, R.M., Shea, T., 1992. Time to recovery, chronicity, and levels of psychopathology in major depression. A 5-year prospective follow-up of 431 subjects. Arch. Gen. Psychiatry 49 (10), 809–816. https://doi.org/10.1001/archpsyc.1992.01820100053010.
Kertesz, A., Davidson, W., Fox, H., 1997. Frontal behavioral inventory: diagnostic criteria for frontal lobe dementia. Can. J. Neurol. Sci. 24, 29–36.
Khambaty, T., Stewart, J.C., Muldoon, M.F., Kamarck, T.W., 2014. Depressive symptom clusters as predictors of 6-year increases in insulin resistance: data from the Pittsburgh healthy heart project. Psychosom. Med. 76 (5), 363–369. https://doi.org/10.1097/PSY.0000000000000063.
Kiosses, D.N., Alexopoulos, G.S., 2005. IADL functions, cognitive deficits, and severity of depression: a preliminary study. The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry 13 (3), 244–249. https://doi.org/10.1176/appi.ajgp.13.3.244.
Köhler, C.A., Evangelou, E., Stubbs, B., Solmi, M., Veronese, N., Belbasis, L., Bortolato, B., Melo, M.C.A., Coelho, C.A., Fernandes, B.S., Olfson, M., Ioannidis, J.P. A., Carvalho, A.F., 2018. Mapping risk factors for depression across the lifespan: an umbrella review of evidence from meta-analyses and Mendelian randomization studies. J. Psychiatr. Res. 103, 189–207. https://doi.org/10.1016/j.jpsychires.2018.05.020.
Kowall, B., Lehnich, A.T., Schramm, S., Schmidt, B., Erbel, R., Jöckel, K.H., Stang, A., 2021. Family aggregation of sleep characteristics: results of the Heinz Nixdorf Recall and the multi-generation study. PLoS One 16 (6), e0252828. https://doi.org/10.1371/journal.pone.0252828.
Kumar, A., Jin, Z., Bilker, W., Udupa, J., Gottlieb, G., 1998. Late-onset minor and major depression: early evidence for common neuroanatomical substrates detected by using MRI. Proc. Natl. Acad. Sci. USA 95 (13), 7654–7658. https://doi.org/10.1073/pnas.95.13.7654.
Lara, E., Martín-María, N., Miret, M., Olaya, B., Haro, J.M., Ayuso-Mateos, J.L., 2022. Is there a combined effect of depression and cognitive reserve on cognitive function? Findings from a population-based study. Psychol. Health 37 (9), 1132–1147. https://doi.org/10.1080/08870446.2021.1927030.
Lavretsky, H., Kurbanyan, K., Kumar, A., 2004. The significance of subsyndromal depression in geriatrics. Curr. Psychiatry Rep. 6 (1), 25–31. https://doi.org/10.1007/s11920-004-0034-8.
Lee, R.S., Hermens, D.F., Porter, M.A., Redoblado-Hodge, M.A., 2012. A meta-analysis of cognitive deficits in first-episode major depressive disorder. J. Affect. Disord. 140 (2), 113–124. https://doi.org/10.1016/j.jad.2011.10.023.
Lehmann, N., Erbel, R., Mahabadi, A.A., Rauwolf, M., Möhlenkamp, S., Moebus, S., Kälsch, H., Budde, T., Schmermund, A., Stang, A., Führer-Sakel, D., Weimar, C., Roggenbuck, U., Dragano, N., Jöckel, K.H., Heinz Nixdorf Recall Study Investigators, 2018. Value of progression of coronary artery calcification for risk prediction of coronary and cardiovascular events: result of the HNR study (Heinz Nixdorf Recall). Circulation 137 (7), 665–679. https://doi.org/10.1161/CIRCULATIONAHA.116.027034.
Lim, J., Oh, I.K., Han, C., Huh, Y.J., Jung, I.K., Patkar, A.A., Steffens, D.C., Jang, B.H., 2013. Sensitivity of cognitive tests in four cognitive domains in discriminating MDD patients from healthy controls: a meta-analysis. Int. Psychogeriatr. 25 (9), 1543–1557. https://doi.org/10.1017/S1041610213000689.
Linden, M., Kurtz, G., Baltes, M.M., Geiselmann, B., Lang, F.R., Reischies, F.M., Helmchen, H., 1998. Depression bei Hochbetagten. Ergebnisse der Berliner Altersstudie [depression in the very elderly]. Nervenarzt 69 (1), 27–37. https://doi.org/10.1007/s001150050235.
Livingston, G., Huntley, J., Sommerlad, A., Ames, D., Ballard, C., Banerjee, S., Brayne, C., Burns, A., Cohen-Mansfield, J., Cooper, C., Costafreda, S.G., Dias, A., Fox, N., Gitlin, L.N., Howard, R., Kales, H.C., Kivimäki, M., Larson, E.B., Ogunniyi, A., Orgeta, V., Mukadam, N., 2020. Dementia prevention, intervention, and care: 2020 report of the lancet commission. Lancet (London, England) 396 (10248), 413–446. https://doi.org/10.1016/S0140-6736(20)30367-6.
Luppino, F.S., de Wit, L.M., Bouvy, P.F., Stijnen, T., Cuijpers, P., Penninx, B.W., Zitman, F.G., 2010. Overweight, obesity, and depression: a systematic review and meta-analysis of longitudinal studies. Arch. Gen. Psychiatry 67 (3), 220–229. https://doi.org/10.1001/archgenpsychiatry.2010.2.
Lyness, J.M., Kim, J., Tang, W., Tu, X., Conwell, Y., King, D.A., Caine, E.D., 2007. The clinical significance of subsyndromal depression in older primary care patients. The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry 15 (3), 214–223. https://doi.org/10.1097/01.JGP.0000235763.50230.83.
Meisenzahl, E., Schultze-Lutter, F., Stegmüller, V., Schulte-Körne, G., Greimel, E., Klingele, C., Dannlowski, U., Hahn, T., Romer, G., Romanos, M., Deserno, L., Theisen, C., Kujovic, M., Ruhrmann, S., Forstner, A.J., Wege, N., 2024a. Stressors during the prodromal phase of major depressive episode (CHR-D). Front. Psychiatry 15, 1389370, 10.3389/fpsyt.2024.1389370b.
Meisenzahl, E., Wege, N., Stegmüller, V., Schulte-Körne, G., Greimel, E., Dannlowski, U., Hahn, T., Romer, G., Romanos, M., Deserno, L., Klingele, C., Theisen, C., Kieckhäfer, C., Forstner, A., Ruhrmann, S., Schultze-Lutter, F., 2024b. Clinical high risk state of major depressive episodes: assessment of prodromal phase, its occurrence, duration and symptom patterns by the instrument the DEpression early prediction-INventory (DEEP-IN). J. Affect. Disord. 351, 403–413. https://doi.org/10.1016/j.jad.2023.12.084 a.
Nebes, R.D., Pollock, B.G., Houck, P.R., Butters, M.A., Mulsant, B.H., Zmuda, M.D., Reynolds 3rd, C.F., 2003. Persistence of cognitive impairment in geriatric patients following antidepressant treatment: a randomized, double-blind clinical trial with nortriptyline and paroxetine. J. Psychiatr. Res. 37 (2), 99–108. https://doi.org/10.1016/s0022-3956(02)00085-7.
Oh, D.J., Han, J.W., Bae, J.B., Kim, T.H., Kwak, K.P., Kim, B.J., Kim, S.G., Kim, J.L., Moon, S.W., Park, J.H., Ryu, S.H., Youn, J.C., Lee, D.Y., Lee, D.W., Lee, S.B., Lee, J. J., Jhoo, J.H., Kim, K.W., 2021. Chronic subsyndromal depression and risk of dementia in older adults. Aust. N. Z. J. Psychiatry 55 (8), 809–816. https://doi.org/10.1177/0004867420972763.
Oh, D.J., Han, J.W., Kim, T.H., Kwak, K.P., Kim, B.J., Kim, S.G., Kim, J.L., Moon, S.W., Park, J.H., Ryu, S.H., Youn, J.C., Lee, D.Y., Lee, D.W., Lee, S.B., Lee, J.J., Jhoo, J.H., Kim, K.W., 2020. Epidemiological characteristics of subsyndromal depression in late life. Aust. N. Z. J. Psychiatry 54 (2), 150–158. https://doi.org/10.1177/0004867419879242.
Olesen, J., Gustavsson, A., Svensson, M., Wittchen, H.U., Jönsson, B., CDBE2010 study group, European Brain Council, 2012. The economic cost of brain disorders in Europe. Eur. J. Neurol. 19 (1), 155–162. https://doi.org/10.1111/j.1468-1331.2011.03590.x.
Oswald, W.D., Fleischmann, U.M., 1997. Nürnberger-Alters-Inventar (NAI). Hogrefe, Göttingen.
Ownby, R.L., Crocco, E., Acevedo, A., John, V., Loewenstein, D., 2006. Depression and risk for Alzheimer disease: systematic review, meta-analysis, and metaregression analysis. Arch. Gen. Psychiatry 63 (5), 530–538. https://doi.org/10.1001/archpsyc.63.5.530.
Pietrzak, R.H., Kinley, J., Afifi, T.O., Enns, M.W., Fawcett, J., Sareen, J., 2013. Subsyndromal depression in the United States: prevalence, course, and risk for incident psychiatric outcomes. Psychol. Med. 43 (7), 1401–1414. https://doi.org/10.1017/S0033291712002309.

Piras, F., Banaj, N., Porcari, D.E., Piras, F., Spalletta, G., 2021. Later life depression as risk factor for developing dementia: epidemiological evidence, predictive models, preventive strategies and future trends. Minerva Med. 112 (4), 456–466. https://doi.org/10.23736/S0026-4806.21.07571-6.

Powell, L.E., Myers, A.M., 1995. The activities-specific balance confidence (ABC) scale. J. Gerontol. A Biol. Sci. Med. Sci. 50A, M28–M34.

Rosenberg, D., Depp, C.A., Vahia, I.V., Reichstadt, J., Palmer, B.W., Kerr, J., Norman, G., Jeste, D.V., 2010. Exergames for subsyndromal depression in older adults : a pilot study of a novel intervention. Am. J. Geriatr. Psychiatr. 18, 221–226.

Sadek, N., Bona, J., 2000. Subsyndromal symptomatic depression: a new concept. Depress. Anxiety 12 (1), 30–39. https://doi.org/10.1002/1520-6394(2000)12:1<30:AID-DA4>3.0.CO;2-P.

Schmermund, A., Möhlenkamp, S., Stang, A., Grönemeyer, D., Seibel, R., Hirche, H., Mann, K., Siffert, W., Lauterbach, K., Siegrist, J., Jöckel, K.H., Erbel, R., 2002. Assessment of clinically silent atherosclerotic disease and established and novel risk factors for predicting myocardial infarction and cardiac death in healthy middle-aged subjects: rationale and design of the Heinz Nixdorf RECALL study. Risk factors, evaluation of coronary calcium and lifestyle. Am. Heart J. 144 (2), 212–218. https://doi.org/10.1067/mhj.2002.123579. Copy.

Schoevers, R.A., Smit, F., Deeg, D.J., Cuijpers, P., Dekker, J., van Tilburg, W., Beekman, A.T., 2006. Prevention of late-life depression in primary care: do we know where to begin? Am. J. Psychiatry 163 (9), 1611–1621. https://doi.org/10.1176/ajp.2006.163.9.1611.

Segal, D.L., Coolidge, F.L., Cahill, B.S., O'Riley, A.A., 2008. Psychometric properties of the Beck depression inventory II (BDI-II) among community-dwelling older adults. Behav. Modif. 32 (1), 3–20. https://doi.org/10.1177/0145445507303833.

Sible, I.J., Jang, J.Y., Sultzer, D.L., Nation, D.A., Alzheimer's Disease Neuroimaging Initiative, 2022. Visit-to-visit blood pressure variability and subthreshold depressive symptoms in older adults. Am. J. Geriatr. Psychiatry 30 (10), 1110–1119. https://doi.org/10.1016/j.jagp.2022.03.006.

Singh-Manoux, A., Dugravot, A., Fournier, A., Abell, J., Ebmeier, K., Kivimäki, M., Sabia, S., 2017. Trajectories of depressive symptoms before diagnosis of dementia: a 28-year follow-up study. JAMA Psychiatry 74 (7), 712–718. https://doi.org/10.1001/jamapsychiatry.2017.0660.

Steer, R.A., Rissmiller, D.J., Beck, A.T., 2000. Use of the Beck depression inventory-II with depressed geriatric inpatients. Behav. Res. Ther. 38 (3), 311–318. https://doi.org/10.1016/s0005-7967(99)00068-6.

Storch, E.A., Roberti, J.W., Roth, D.A., 2004. Factor structure, concurrent validity, and internal consistency of the Beck depression inventory-second edition in a sample of college students. Depress. Anxiety 19 (3), 187–189. https://doi.org/10.1002/da.20002.

Triolo, F., Grande, G., Ekström, I., Laukka, E.J., Fors, S., Marseglia, A., Dekhtyar, S., 2025. Cognitive reserve types and depressive symptoms development in late-life: a population-based cohort study. Cortex; a journal devoted to the study of the nervous system and behavior 185, 74–83. https://doi.org/10.1016/j.cortex.2025.02.001.

Triolo, F., Sjöberg, L., Calderón-Larrañaga, A., Belvederi Murri, M., Vetrano, D.L., Fratiglioni, L., Dekhtyar, S., 2023. Late-life depression and multimorbidity trajectories: the role of symptom complexity and severity. Age Ageing 52 (2), afac315. https://doi.org/10.1093/ageing/afac315.

Triolo, F., Vetrano, D.L., Trevisan, C., Sjöberg, L., Calderón-Larrañaga, A., Belvederi Murri, M., Fratiglioni, L., Dekhtyar, S., 2024. Mapping 15-year depressive symptom transitions in late life: population-based cohort study. The British journal of psychiatry : the journal of mental science 225 (2), 321–327. https://doi.org/10.1192/bjp.2024.840.

Tuithof, M., Ten Have, M., van Dorsselaer, S., Kleinjan, M., Beekman, A., de Graaf, R., 2018. Course of subthreshold depression into a depressive disorder and its risk factors. J. Affect. Disord. 241, 206–215. https://doi.org/10.1016/j.jad.2018.08.010.

UNESCO United Nations Educational, Scientific and Cultural Organization, 2003. International Standard Classification of Education, ISCED 1997. Advances in Cross-National Comparison: A European Working Book for Demographic and Socio-Economic Variables.195–220.

United Nations Department of Economic and Social Affairs, Population Division, 2022. World Population Prospects 2022: Summary of Results. In: UN DESA/POP/2022/TR/NO. wpp2022_summary_of_results.pdf (un.org), p. 3 accessed 6 august 2024.

Vancampfort, D., Stubbs, B., Firth, J., Hallgren, M., Schuch, F., Lahti, J., Rosenbaum, S., Ward, P.B., Mugisha, J., Carvalho, A.F., Koyanagi, A., 2017. Physical activity correlates among 24,230 people with depression across 46 low- and middle-income countries. J. Affect. Disord. 221, 81–88. https://doi.org/10.1016/j.jad.2017.06.012.

Veerman, J.L., Dowrick, C., Ayuso-Mateos, J.L., Dunn, G., Barendregt, J.J., 2009. Population prevalence of depression and mean Beck depression inventory score. The British journal of psychiatry : the journal of mental science 195 (6), 516–519. https://doi.org/10.1192/bjp.bp.109.066191.

Volkert, J., Schulz, H., Härter, M., Wlodarczyk, O., Andreas, S., 2013. The prevalence of mental disorders in older people in Western countries - a meta-analysis. Ageing Res. Rev. 12 (1), 339–353. https://doi.org/10.1016/j.arr.2012.09.004.

Weisenbach, S.L., Kumar, A., 2014. Current understanding of the neurobiology and longitudinal course of geriatric depression. Curr. Psychiatry Rep. 16 (9), 463. https://doi.org/10.1007/s11920-014-0463-y.

Yang, L., Deng, Y.T., Leng, Y., Ou, Y.N., Li, Y.Z., Chen, S.D., He, X.Y., Wu, B.S., Huang, S.Y., Zhang, Y.R., Kuo, K., Feng, W., Dong, Q., Feng, J.F., Suckling, J., Smith, A.D., Li, F., Cheng, W., Yu, J.T., 2023. Depression, depression treatments, and risk of incident dementia: a prospective cohort study of 354,313 participants. Biol. Psychiatry 93 (9), 802–809. https://doi.org/10.1016/j.biopsych.2022.08.026.

Zhang, Y., Chen, Y., Ma, L., 2018. Depression and cardiovascular disease in elderly: current understanding. Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia 47, 1–5. https://doi.org/10.1016/j.jocn.2017.09.022.

Zhou, L., Ma, X., Wang, W., 2021. Relationship between cognitive performance and depressive symptoms in Chinese older adults: the China health and retirement longitudinal study (CHARLS). J. Affect. Disord. 281, 454–458. https://doi.org/10.1016/j.jad.2020.12.059.

Zijlmans, J.L., Vernooij, M.W., Ikram, M.A., Luik, A.I., 2023. The role of cognitive and brain reserve in late-life depressive events: the Rotterdam study. J. Affect. Disord. 320, 211–217. https://doi.org/10.1016/j.jad.2022.09.145.