

Original Research Article

Associations between Dementia Outcomes and Depressive Symptoms, Leisure Activities, and Social Support

Kathrin Hesper^a Michael Wagner^{a, b} Birgitt Wiese^c Jana Prokein^c
Annette Ernst^d Hans-Helmut König^e Christian Brettschneider^e
Steffi G. Riedel-Heller^f Melanie Lupp^f Siegfried Weyerer^g
Sandra Eifflaender-Gorfer^g Horst Bickel^h Edelgard Mösch^h
Michael Pentzekⁱ Angela Fuchsⁱ Wolfgang Maier^{a, b} Martin Scherer^d
Marion Eisele^d for the AgeCoDe Study Group

^aDepartment of Psychiatry, University of Bonn, and ^bGerman Center for Neurodegenerative Diseases (DZNE), Bonn, ^cWorking Group Medical Statistics and IT Infrastructure, Institute of General Practice, Hannover Medical School, Hannover, Departments of ^dPrimary Medical Care and ^eMedical Sociology and Health Economics, University Medical Centre, Hamburg-Eppendorf, ^fInstitute of Social Medicine, Occupational Health and Public Health, University of Leipzig, Leipzig, ^gCentral Institute of Mental Health, Medical Faculty Mannheim/Heidelberg University, Mannheim, ^hDepartment of Psychiatry, Technical University Munich, Munich, and ⁱInstitute of General Practice, Medical Faculty, Heinrich Heine University Düsseldorf, Düsseldorf, Germany

Key Words

Dementia · Alzheimer's dementia · Depressive symptoms · Cognitive activities · Physical activities · Social engagement · Social support · Emotional support · Practical support

Abstract

Background: Social relations and depressive symptoms are intertwined. They both predict subsequent dementia, but only few studies on the association between social life aspects and subsequent dementia exist. **Methods:** The risk of subsequent dementia was estimated over 2 follow-up assessments, each 18 months apart, depending on leisure activity, social support (general scale and the 3 factors emotional support, practical support, and social integration), and depressive symptoms, using proportional hazard models in a cohort of elderly patients (n = 2,300, with a mean age of 82.45 years) recruited for the study by their general practitioners. **Results:** Higher depressive symptoms and lower cognitive and physical activity were associated with an increased risk of subsequent all-cause dementia and Alzheimer's dementia (AD). While neither social engagement nor the general social support scale was associated with subsequent dementia, a higher level of social integration was associated with a lower

Kathrin Hesper
Department of Psychiatry, University of Bonn
Sigmund-Freud-Str. 25
DE-53105 Bonn (Germany)
E-Mail Kathrin.Hesper@ukb.uni-bonn.de

dementia risk. In combined models, the results for activity variables remained similar, but the strength of the association between depressive symptoms and the subsequent risk of dementia decreased, and the association with social integration disappeared. **Conclusions:** Depressive symptoms increased and activity variables decreased the risk of subsequent dementia; however, activity variables, namely cognitive and physical activity, partly mediated the effect of depressive symptoms on the subsequent risk of all-cause dementia and AD. In many cases, social support was not associated with a risk of subsequent dementia.

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Introduction

Associations between depressive symptoms and social relationships in the elderly have been found in various studies [for a review, see ref. 1]. The loss of social contacts or a decrease in mobility or physical abilities inherently associated with older age might be conditions that contribute to this close connection [2]. Both depressive symptoms [3, 4] and a deficiency in aspects of social life such as social networks [5–7] or social activities [8, 9] showed associations with an increased risk of subsequent dementia and Alzheimer's dementia (AD); however, research on the qualitative aspect of social relationships, namely social support, and the risk of subsequent dementia is scarce, although some studies on social networks and dementia included the risk factor 'satisfaction with social contacts' [5, 7, 10]. Low social support was related to worse depression outcomes [11, 12] and worse cognition or cognitive decline [13, 14]; however, studies on social support and dementia risk are missing. One qualitative aspect of social relations that proved to be a risk factor for subsequent AD is loneliness [15].

Byers and Yaffe [16] proposed vascular diseases, changes in glucocorticoid steroid levels that can result in hippocampal atrophy, accumulation of amyloid- β plaques, inflammatory processes, and lack of nerve growth factors as possible biological mechanisms linking depression and subsequent dementia. Social variables might positively influence depressive and cardiovascular disease symptoms [17, 18] which have been linked to dementia [16, 19] or might be associated with immune function, (neuro)endocrine processes [18], and stress response [20, 21], which, in turn, are also associated with cognition [22, 23]. Similarly, this was already outlined in the context of cognitive decline by Seeman et al. [24, p. 243f.].

Besides these neurophysiological mechanisms, an association between social variables, depressive symptoms, and subsequent dementia might be explained by either a 'stimulation hypothesis' or by an 'emotional buffer hypothesis'. The stimulation hypothesis assumes that social interaction and social engagement might positively influence, stimulate, and contribute to the maintenance of cognitive function and capacity [9, 25] and overlap with the principle of 'cognitive reserve' [26, 27]. The emotional buffer hypothesis posits that supportive aspects of social interaction might protect against the impact of adverse physiological stress processes or psychological conditions and thereby serve as protectors against cognitive decline and dementia [24, 25].

We hypothesized that depressive symptoms increase the risk of subsequent dementia and AD, whereas it is decreased by leisure activities and social support. The association between depressive symptoms and a subsequent dementia risk might be conveyed by leisure activities and social support. To face the problem of 'reverse causation', i.e. that an early dementia process influences social engagement and leisure activities, social support, and depressive symptoms, we included cognitive status and daily functioning into the adjusted prediction models.

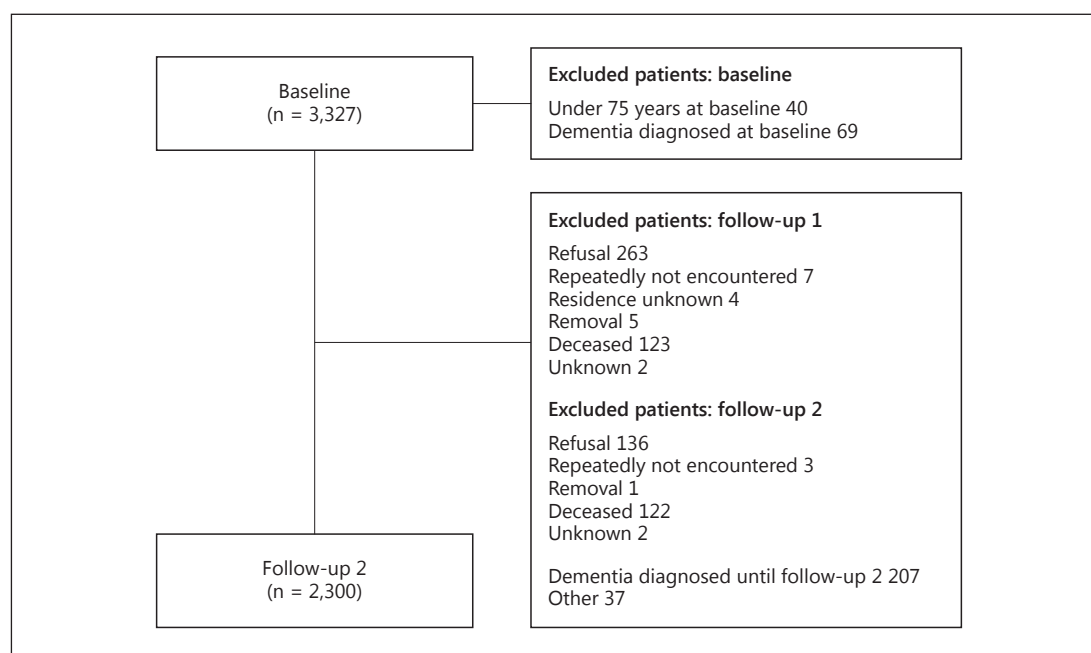


Fig. 1. Sample selection flowchart.

Materials and Methods

Sample

We present data from a prospective multi-centre study [the German Study on Aging, Cognition, and Dementia in Primary Care Patients (AgeCoDe)]. At baseline, participants aged ≥ 75 years were recruited via their general practitioners (GPs) in six German cities (Bonn, Düsseldorf, Hamburg, Leipzig, Mannheim, and Munich). Inclusion criteria were absence of dementia according to GP judgement and at least one contact with the GP within the past 12 months. Exclusion criteria were consultations only at home visits, severe illness, insufficient knowledge of the German language, deafness or blindness, and an inability to provide informed consent. The relevant ethics committees approved the study. The interview was conducted in person by a trained research assistant. Follow-up assessments after baseline evaluation in 2003/2004 were conducted every 1.5 years. We used follow-up 2 data on covariates and predictors as baseline values when the assessment of social support was introduced. Information on dementia status until follow-up 4 was included. Follow-up 4 was conducted approximately 3 years after follow-up 2. The sample initially consisted of 3,327 participants. We excluded participants aged < 75 years at baseline and participants with a diagnosis of dementia until follow-up 2. Other exclusion criteria were not applied. A sample selection flowchart is given in figure 1.

Assessment of Depressive Symptoms

The short version of the Geriatric Depression Scale (GDS-15) in German [28] was used at follow-up 2 to assess depressive symptoms. The GDS-15 consists of 15 questions that can be accepted or rejected. If more than 2 items were missing, the GDS-15 score could not be computed. If 1 or 2 items were missing, a weighted score was computed. The internal consistency of the GDS-15 scale was acceptable (Cronbach's $\alpha = 0.74$).

Assessment of Social Variables

We included leisure activities and social support assessed at follow-up 2 as social variables in our analysis. Leisure activities were evaluated according to Verghese et al. [29], containing some modifications. Activities during the past 4 weeks were assessed, and its frequency was classified as daily, several times per week, once a week, less than once a week, and never (score range 0–4, with higher scores indicating more activity). Physical activities included bicycling, walking, swimming, gymnastics, chores/gardening, and a category of other physical activities (e.g., bowling, dancing, stationary bicycling, jogging, or golfing); cognitive activities included crossword puzzling, memory training/brainteasers, games (card games, board games, or individual games), reading, writing, and playing music, and social activities included taking care of others (such as relatives or friends) and social engagement (e.g., in the church, as a volunteer, in a party, or in a club). To provide comparability with other studies, we will refer to these social activity variables as social engagement. Global activity, including all activities that were assessed or the 3 activity domains social engagement, cognitive, and physical activity, were separately included as mean scores in the analyses representing their average frequency.

Social support was evaluated using the short form (K-14) of a German questionnaire called F-SozU (Fragebogen zur sozialen Unterstützung) by Fydrich et al. [30]. We identified a 3-factor model of social support by exploratory and confirmatory factor analysis. These 3 factors can be defined as emotional support (e.g., ‘I have a close person whom I can always count on for help’), practical support (e.g., ‘when necessary, I have the possibility of borrowing things from my neighbours’), and social integration (e.g., ‘I know several people with whom I enjoy sharing activities’). A modified dichotomous response format was provided. A total social support score including all K-14 items or the items of the 3 social support factors – emotional support, practical support, and social integration – were separately included as mean scores in the analyses. The internal consistency of the K-14 scale was good (Cronbach’s $\alpha = 0.84$).

Assessment of Dementia

Dementia assessment was based on the Structured Interview for Diagnosis of Dementia of Alzheimer Type, Multi-Infarct Dementia and Dementia of Other Aetiology according to DSM-IV and ICD-10 criteria (SIDAM) [31] implemented by a trained research assistant. When SIDAM could not be assessed, a Global Deterioration Scale [32] score of at least 4 and/or a Blessed Dementia Rating Scale [33] score were used. Each case of incident dementia and its aetiological subtype was validated by a geriatric expert on the basis of medical information relevant to the aetiology of dementia provided by the GP. AD was diagnosed according to the DSM-IV criteria [34]. Vascular dementia was diagnosed according to the NINDS-AIREN criteria [35]. Target variables of this publication were all-cause dementia that included all cases (i.e., AD, mixed forms, vascular dementia, specific types of dementia such as Lewy body dementia or dementia caused by substance abuse, and dementia not otherwise specified) and AD (including AD and mixed forms), whereas dementia of other aetiology was not included as separate aetiology due to small sample sizes. The presence or absence of dementia was diagnosed at every follow-up assessment. Only incident cases at follow-up 3 or 4 were considered, whereas prevalent cases until follow-up 2 were excluded.

Covariates

At follow-up 2, we entered age in years, sex, education according to CASMIN [36] in 3 stages (low, medium, high), dichotomous apolipoprotein E4 status (ApoE4; present or absent), the Mini-Mental State Examination (MMSE) [37] score to control for global cognition, and the instrumental activities of daily living (IADL) score according to Lawton and Brody

Table 1. Sample characteristics at follow-up 2 when none of the included participants had a dementia diagnosis grouped by dementia status at follow-up 4

	Participants without dementia diagnosis until follow-up 4	Participants with any dementia diagnosis until follow-up 4	Participants with AD diagnosis until follow-up 4
Participants	2,087	213	150
Age, years	82.31 ± 3.31	83.84 ± 3.51	84.02 ± 3.51
Sex			
Female	1,363 (65.3)	144 (67.6)	108 (72.0)
Male	724 (34.7)	69 (32.4)	42 (28.0)
Education ^a			
Low	1,248 (59.8)	138 (64.8)	101 (67.3)
Medium	588 (28.2)	58 (27.2)	37 (24.7)
High	251 (12.0)	17 (8.0)	12 (8.0)
ApoE4			
No ApoE4	1,620 (77.6)	145 (68.1)	97 (64.7)
ApoE4	389 (18.6)	59 (27.7)	46 (30.7)
Missing	78 (3.7)	9 (4.2)	7 (4.7)
MMSE ^b	28.07 ± 1.58	26.25 ± 1.88	26.05 ± 1.82
Missing	8 (0.4)	3 (1.4)	2 (1.3)
IADL ^c	6.94 ± 1.48	6.54 ± 1.81	6.65 ± 1.71
Missing	3 (0.1)	0 (0.0)	0 (0.0)
GDS-15 ^d	2.40 ± 2.38	3.22 ± 2.94	3.16 ± 2.82
Missing	8 (0.4)	6 (2.8)	6 (4.0)
Global activity ^e	1.21 ± 0.42	0.95 ± 0.36	0.94 ± 0.36
Missing	5 (0.2)	1 (0.5)	1 (0.7)
Social engagement ^e	0.38 (0.67)	0.30 (0.61)	0.29 (0.61)
Cognitive activity ^e	1.44 (0.55)	1.19 (0.48)	1.17 (0.48)
Physical activity ^e	1.27 (0.63)	0.94 (0.58)	0.93 (0.57)
K-14 ^f	0.88 ± 0.18	0.87 ± 0.18	0.87 ± 0.18
Missing	12 (0.6)	2 (0.9)	2 (1.3)
K-14 factor 1 ^g	0.90 (0.19)	0.91 (0.19)	0.90 (0.20)
K-14 factor 2 ^g	0.91 (0.20)	0.93 (0.17)	0.93 (0.16)
K-14 factor 3 ^g	0.78 (0.32)	0.72 (0.35)	0.71 (0.34)

Data are numbers with percentages in parentheses or means ± SDs. Participants with any dementia diagnosis until follow-up 4 were older ($p < 0.001$), more likely to carry at least one ApoE4 allele ($p = 0.002$), had lower MMSE ($p < 0.001$) and IADL scores ($p = 0.002$), higher GDS-15 scores ($p < 0.001$), and lower global activity ($p < 0.001$) compared to participants without dementia diagnosis until follow-up 4 (no statistical differences for sex, education, and K-14 scores); participants with AD were a subpopulation of participants with any dementia diagnosis.

^a Classification of education according to CASMIN.

^b Score range 0–30, Folstein et al. [37].

^c Score range 0–8, Lawton and Brody [38].

^d Score range 0–15, Sheikh and Yesavage [28].

^e Global activity (score range 0–4), social engagement (score range 0–4), cognitive activity (score range 0–4), physical activity (score range 0–4).

^f Score range 0–1, social support scale, Fydrich et al. [30].

^g Factor 1 (score range 0–1), emotional support; factor 2 (score range 0–1), practical support; factor 3 (score range 0–1), social integration.

[38] to control for functional status as a continuous variable (with higher values indicating better performance) as covariates into our models. The covariates were included to control for a potentially confounding effect (age, education), a genetic risk factor (ApoE4), and the possibility of reverse causation (MMSE, IADL).

Statistical Analysis

Cox regression analyses were used to investigate the effect of leisure activities, social support, depressive symptoms, and covariates assessed at follow-up 2 on the time until dementia was diagnosed in crude and adjusted proportional hazards models. In model 1, no covariates were included. Model 2 was adjusted for age, sex, education, ApoE4, MMSE, and IADL. Prediction of subsequent dementia by leisure activities, social support, and depressive symptoms was regarded separately and combined with and without adjustment for covariates. Interaction terms (global activity \times depressive symptoms and social support \times depressive symptoms) were entered into additional prediction models. In supplementary analyses, specific leisure activities were entered as a categorical variable of frequency to predict the subsequent all-cause dementia risk. The level of significance was set at $\alpha = 0.05$.

Results

Sample characteristics at follow-up 2 are given in table 1. Higher depressive symptom scores were associated with a significantly increased risk of subsequent all-cause dementia and AD in the unadjusted model (all-cause dementia: HR 1.14, 95% CI 1.09–1.20, $p < 0.001$; AD: HR 1.14, 95% CI 1.08–1.21, $p < 0.001$) and in the model adjusted for age, sex, education, ApoE4, MMSE, and IADL (all-cause dementia: HR 1.09, 95% CI 1.03–1.14, $p = 0.001$; AD: HR 1.08, 95% CI 1.01–1.15, $p = 0.018$). Higher overall activity scores were associated with a significantly decreased risk of subsequent all-cause dementia and AD in the unadjusted (all-cause dementia: HR 0.18, 95% CI 0.13–0.26, $p < 0.001$; AD: HR 0.16, 95% CI 0.10–0.24, $p < 0.001$) and the adjusted model (all-cause dementia: HR 0.33, 95% CI 0.22–0.49, $p < 0.001$; AD: HR 0.29, 95% CI 0.18–0.47, $p < 0.001$). Further analysis of separate activities showed that both cognitive (all-cause dementia: unadjusted HR 0.48, 95% CI 0.37–0.63, $p < 0.001$, and adjusted HR 0.66, 95% CI 0.50–0.87, $p = 0.004$; AD: unadjusted HR 0.44, 95% CI 0.33–0.60, $p < 0.001$, and adjusted HR 0.62, 95% CI 0.44–0.87, $p = 0.006$) and physical activity (all-cause dementia: unadjusted HR 0.44, 95% CI 0.34–0.56, $p < 0.001$, and adjusted HR 0.57, 95% CI 0.44–0.74, $p < 0.001$; AD: unadjusted HR 0.43, 95% CI 0.32–0.57, $p < 0.001$, and adjusted HR 0.54, 95% CI 0.39–0.74, $p < 0.001$) was associated with a decreased risk of both dementia outcomes, whereas social engagement was not associated with any dementia risk. K-14 (social support) and K-14 factor 1 (emotional support) were not associated with the subsequent risk of all-cause dementia or AD. After adjustment for covariates, K-14 factor 2 (practical support) was associated with a significantly increased AD risk (HR 3.18, 95% CI 1.05–9.66, $p = 0.041$). K-14 factor 3 (social integration) was associated with a decreased subsequent all-cause dementia and AD risk in the unadjusted (all-cause dementia: HR 0.43, 95% CI 0.28–0.67, $p < 0.001$; AD: HR 0.42, 95% CI 0.25–0.71, $p = 0.001$) but not in the adjusted models.

When depressive symptoms, leisure activities, and social support variables were entered into combined prediction models (table 2), depressive symptoms were still significantly associated with an increased risk of all-cause dementia but not of AD, whereas global activities were associated with a highly significantly decreased risk of subsequent all-cause dementia and AD, and social support showed no association with any dementia risk. In a next step, activity domains and social support factors instead of global scores were entered into the models. The results for depressive symptoms remained similar. Cognitive and physical activ-

Table 2. Combined prediction of subsequent all-cause dementia and AD by depressive symptoms, activity variables, and social support entered into covariate-unadjusted and -adjusted models

	Model 1 (not adjusted for covariates)				Model 2 (adjusted for age, sex, education, ApoE4, MMSE, and IADL)			
	all-cause dementia		AD		all-cause dementia		AD	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Depressive symptoms, activities, and social support (combined prediction)								
GDS-15	1.08**	1.02–1.14	1.07	0.999–1.14	1.07*	1.01–1.13	1.05	0.98–1.13
Global activities	0.21***	0.14–0.31	0.19***	0.12–0.29	0.37***	0.25–0.57	0.33***	0.20–0.55
K-14	1.83	0.82–4.08	1.58	0.62–4.07	1.94	0.80–4.69	1.61	0.57–4.57
Depressive symptoms, activity domains, and social support factors (combined prediction)								
GDS-15	1.08**	1.02–1.14	1.06	0.995–1.14	1.07*	1.00–1.13	1.05	0.98–1.14
Social engagement	0.97	0.77–1.21	0.94	0.71–1.25	0.94	0.73–1.21	0.91	0.67–1.23
Cognitive activities	0.51***	0.39–0.67	0.46***	0.34–0.64	0.70*	0.52–0.93	0.65*	0.45–0.92
Physical activities	0.49***	0.38–0.63	0.49***	0.36–0.66	0.62***	0.47–0.80	0.59**	0.43–0.82
K-14 factor 1	1.80	0.71–4.54	1.25	0.43–3.66	1.02	0.39–2.66	0.54	0.19–1.55
K-14 factor 2	1.66	0.71–3.90	2.28	0.79–6.56	2.34	0.91–6.02	3.57*	1.12–11.44
K-14 factor 3	0.76	0.47–1.22	0.75	0.43–1.33	0.92	0.56–1.52	1.02	0.55–1.87
Factor 1 = Emotional support; factor 2 = practical support; factor 3 = social integration. * p < 0.05; ** p < 0.01; *** p < 0.001.								

Table 3. Prediction of subsequent all-cause dementia and AD by depressive symptoms, activity variables, and social support entered pairwise into covariate-unadjusted and -adjusted models

	Model 1 (not adjusted for covariates)				Model 2 (adjusted for age, sex, education, ApoE4, MMSE, and IADL)			
	all-cause dementia		AD		all-cause dementia		AD	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Depressive symptoms and activities (combined prediction)								
GDS-15	1.06*	1.01–1.12	1.06	0.99–1.12	1.05	0.99–1.10	1.03	0.97–1.10
Global activities	0.21***	0.15–0.31	0.19***	0.12–0.30	0.37***	0.25–0.57	0.33***	0.20–0.54
Depressive symptoms and social support (combined prediction)								
GDS-15	1.16***	1.10–1.22	1.15***	1.08–1.22	1.11***	1.05–1.17	1.09*	1.02–1.17
K-14	1.59	0.73–3.47	1.35	0.54–3.39	1.82	0.76–4.36	1.50	0.54–4.20
* p < 0.05; *** p < 0.001.								

ities were associated with a reduced risk of subsequent all-cause dementia and AD, whereas social engagement was again not associated with any subsequent dementia risk. K-14 factor 1 (emotional support) and factor 3 (social integration) were not associated with any subsequent risk of dementia. After adjustment for covariates (model 2), K-14 factor 2 (practical support) was associated with a significantly increased AD risk.

Analyses that included depressive symptoms and activities and depressive symptoms and social support pairwise as predictors of subsequent all-cause dementia and AD in unadjusted models suggested that activities and not social support were associated with a reduced influence of depressive symptoms on subsequent dementia risk (table 3).

In unadjusted prediction models that contained depressive symptoms, global activity, and the interaction term depressive symptoms × global activity, although the interaction term was no significant predictor (all-cause dementia: HR 1.09, 95% CI 0.96–1.23, p = 0.211;

Table 4. Prediction of all-cause dementia by specific leisure activities separately entered as categorical variables of frequency (adjusted for depressive symptoms, social support, and covariates, i.e., age, sex, education, ApoE4, MMSE, and IADL)

	Never, ref.	Less than once a week	Once a week	Several times a week	Daily
Physical activities					
Bicycling	1.00	0.74 (0.34–1.61)	0.60 (0.22–1.66)	0.64 (0.36–1.12)	0.61 (0.31–1.21)
Walking ^a	1.00	0.54* (0.33–0.87)	0.64 (0.36–1.15)	1.00 (0.69–1.44)	0.58* (0.35–0.98)
Swimming	1.00	0.71 (0.40–1.27)	0.78 (0.36–1.67)	0.46 (0.11–1.85)	0.00 (0.00–1.553E+101 ^b)
Gymnastics	1.00	1.47 (0.74–2.93)	1.29 (0.79–2.09)	0.93 (0.56–1.55)	0.80 (0.55–1.18)
Chores/gardening ^c	1.00	1.17 (0.63–2.18)	0.41 (0.13–1.32)	0.91 (0.58–1.42)	0.52*** (0.37–0.73)
Others	1.00	0.34* (0.14–0.82)	0.55 (0.18–1.73)	0.23 (0.03–1.67)	1.42 (0.52–3.86)
Cognitive activities					
Crossword puzzling	1.00	0.79 (0.42–1.50)	1.57 (0.92–2.67)	0.85 (0.56–1.27)	0.73 (0.51–1.04)
Memory training/brain teasers	1.00	0.68 (0.32–1.45)	0.75 (0.33–1.70)	0.59 (0.26–1.33)	0.25* (0.08–0.78)
Games	1.00	0.84 (0.55–1.29)	0.89 (0.51–1.53)	1.08 (0.62–1.90)	0.98 (0.46–2.11)
Reading	1.00	1.75 (0.55–5.53)	0.79 (0.20–3.11)	0.97 (0.41–2.30)	0.75 (0.35–1.62)
Writing	1.00	1.02 (0.75–1.40)	0.73 (0.38–1.43)	0.85 (0.38–1.88)	0.84 (0.30–2.33)
Playing music	1.00	0.73 (0.29–1.79)	0.74 (0.23–2.39)	0.00 (0.00–2.563E–107 ^b)	1.16 (0.28–4.74)
Social activities					
Taking care of others	1.00	0.48 (0.20–1.17)	1.03 (0.38–2.81)	1.22 (0.45–3.32)	0.73 (0.23–2.31)
Social engagement	1.00	0.84 (0.52–1.36)	0.76 (0.41–1.40)	0.70 (0.30–1.59)	1.57 (0.57–4.27)

Data are HRs with 95% CIs given in parentheses, unless otherwise specified. ref. = Reference. * $p < 0.05$; *** $p < 0.001$.

^a Overall significance, $p < 0.05$.

^b The upper limit of the CI could not be observed due to the small number of participants.

^c Overall significance, $p < 0.01$.

AD: HR 1.13, 95% CI 0.97–1.32, $p = 0.124$), depressive symptoms did not predict dementia outcomes anymore (all-cause dementia: HR 0.99, 95% CI 0.88–1.12, $p = 0.902$; AD: HR 0.95, 95% CI 0.81–1.11, $p = 0.506$), whereas the association between global activity and dementia risk remained stable (all-cause dementia: HR 0.17, 95% CI 0.10–0.29, $p < 0.001$; AD: HR 0.13, 95% CI 0.07–0.25, $p < 0.001$). When depressive symptoms, social support, and the interaction term depressive symptoms \times social support were entered in unadjusted models, none of the predictors were associated with subsequent all-cause dementia and AD risk.

Additionally, to provide a better interpretability of dementia risk reduction by activities, specific leisure activities were entered as categorical variables in unadjusted and adjusted models to predict all-cause dementia. In the unadjusted models, bicycling, walking, swimming, chores/gardening, the category of other physical activities, crossword puzzling, memory training/brain teasers, games, and reading were associated with a reduced risk of subsequent all-cause dementia. After adjustment for covariates and the other predictors (depressive symptoms, social support), walking and chores/gardening were associated with a reduced risk of all-cause dementia (table 4). Participants who reported to have walked daily during the previous 4 weeks showed a 40% reduced risk, and participants who reported doing chores/gardening daily showed about a 50% reduced risk of all-cause dementia compared to participants who reported that they never exhibited these activities.

Discussion

Activity variables, especially cognitive and physical activities, showed the strongest association with subsequent all-cause dementia and AD even when different covariates were controlled, whereas social engagement and social support did not predict all-cause dementia

and AD risk in many cases. The averaged frequency of diverse activities besides specific activities of rather low intensity, such as walking and doing chores, were associated with a reduced risk of subsequent dementia and AD. The increased risk of dementia and AD by depressive symptoms was (partly) mediated through the activity level, whereas more activities were associated with a reduced risk of subsequent dementia independent of depressive symptoms. Thus, in our sample, the activity-related variance of depressive symptoms seemed to be relevant for an increased subsequent dementia and AD risk. Although speculative, we assumed that different results emerged for all-cause dementia and AD due to power issues as the magnitude of HRs for both dementia outcomes were comparable; however, the associations were significant just for the larger all-cause dementia target group.

The association between the social support factor ‘social integration’ and a decreased risk of subsequent dementia and AD disappeared after MMSE and IADL were included, which could possibly be explained by reverse causation due to social withdrawal caused by an early dementia process. Practical support was associated with an increased risk of subsequent dementia, specifically AD, when several covariates were controlled for, which could reflect an early increased need for help due to the disease but capture a different need for assistance than the statistically controlled for IADL. Emotional support did not predict subsequent all-cause dementia and AD, although other authors found an association with cognitive function [24, 25]. However, another AgeCoDe cohort study found no longitudinal association between the social support scale and cognitive change [39]. Instead of subjective measures of social interaction, objective indicators such as social network size might show stronger associations with subsequent dementia and AD.

The results pointed to the importance of activity in line with the stimulation hypothesis, whereas the emotional buffer hypothesis was not supported. An active lifestyle might also provide a buffer against the negative impact of stress [40], which corresponds to what we defined as the stimulation hypothesis. We found an association between cognitive activity and subsequent dementia outcomes in accordance with other studies that provided evidence for a reduced subsequent dementia risk [29, 41] or a delayed onset of dementia [42, 43] by cognitive activities. Additionally, we found a decreased risk of subsequent dementia by physical activity as already discovered by other authors [44, 45] as well as in a former publication on the present cohort [46], although some negative reports also exist [29, 42].

As our follow-up period was rather short considering the often long-lasting development of dementia, especially of AD, we cannot decide with certainty whether reduced activity was already an early sign of the disease, whether more activity would have delayed disease onset, or whether activity truly reduced the risk. However, we explored the possibility of reverse causation by controlling for IADL and MMSE, which can detect cognitive and functional deficits, and did not find evidence of a reduced activity level due to early dementia impairment.

Our study holds several strengths. We used a longitudinal design in a rather large sample. A wide range of variables representing an engaged or disengaged lifestyle was assessed (activities, social support, depressive symptoms), and potential confounders (age, sex, education, ApoE4, MMSE, IADL) were controlled for. Dementia was diagnosed according to established criteria. Besides these strengths, there are also some limitations. The classification of different activity domains seemed reasonable but was accompanied by the problem of unequal item numbers and frequency differences, resulting in psychometrical problems. Additionally, the activities might include shared social, cognitive, and physical aspects (e.g., walking alone or in a group). Different quality, besides frequency, was not considered (e.g., reading an advertisement or scientific literature). Perhaps we failed to find an association between social activities and dementia because of its insufficient operationalization. The social engagement activities in our study were rather uncommon compared to those assessed

in other studies [8, 9] and rarely occurred in our sample. Factor analysis of the social support scale K-14 revealed 3 factors, whereas Fydrich et al. [30] described it as unidimensional. Affirmation of the social support scale items was rather high. This ceiling effect was particularly true for the emotional and the practical support factor. Either the participants of our sample pronounced a high level of social support or their answers were influenced by social desirability bias. Unfortunately, social network size as an objective measure of social relation structure was not assessed at follow-up 2. In addition to these specific limitations, there are some general problems of longitudinal studies such as a positive selection bias when recruiting participants and sample attrition effects because some participants were lost during the course of the study.

The absence of an association between social engagement activities and subsequent dementia risk has to be interpreted with caution due to the uncommon operationalization which has possibly led to an underestimated importance. Although social support did not reliably predict the risk of subsequent dementia in our study, other studies showed that it is an important and health-promoting aspect of quality of life. As this was an observational study, we cannot rule out that results might be explained by reverse causation, although we statistically controlled for it. Nonetheless, a higher frequency especially of cognitive and physical activities was associated with a strongly reduced risk of subsequent dementia and AD independent of depressive symptoms through a follow-up period of up to 3 years. Experimental research and clinical trials in addition to the existing observational studies could help to study the causal direction of the associations. Recommending a generally active lifestyle with special emphasis on cognitive and physical aspects seems to be appropriate, as the risk of any harm is low.

Appendix

Members of the AgeCoDe Study Group

Principal Investigators (Hendrik van den Bussche, 2002–2011): Wolfgang Maier, Martin Scherer.

Heinz-Harald Abholz, Christian Brettschneider, Cadja Bachmann, Horst Bickel, Wolfgang Blank, Hendrik van den Bussche, Sandra Eifflaender-Gorfer, Marion Eisele, Annette Ernst, Angela Fuchs, Kathrin Heser, Frank Jessen, Hanna Kaduszkiewicz, Teresa Kaufeler, Mirjam Köhler, Hans-Helmut König, Alexander Koppa, Carolin Lange, Tobias Luck, Melanie Lupp, Manfred Mayer, Edelgard Mösch, Julia Olbrich, Michael Pentzek, Jana Prokein, Anna Schumacher, Steffi G. Riedel-Heller, Janine Stein, Susanne Steinmann, Franziska Tebarth, Michael Wagner, Klaus Weckbecker, Dagmar Weeg, Jochen Werle, Siegfried Weyerer, Birgitt Wiese, Steffen Wolfsgruber, and Thomas Zimmermann.

GPs Participating at the Time of Follow-Up 5

Bonn: Claudia Adrian, Hanna Liese, Inge Bürfent, Johann von Aswege, Wolf-Dietrich Honig, Peter Gölle, Heribert Schützendorf, Elisabeth Benz, Annemarie Straimer, Arndt Uhlenbrock, Klaus-Michael Werner, Maria Göbel-Schlatholt, Hans-Jürgen Kaschell, Klaus Weckbecker, Theodor Alfen, Markus Stahlschmidt, Klaus Fischer, Wolf-Rüdiger Weisbach, Martin Tschoke, Jürgen Dorn, Helmut Menke, Erik Sievert, Ulrich Kröckert, Gabriele Salingré, Christian Mörchen, Peter Raab, Angela Baszenski, Clärli Loth, Christian Knaak, Peter Hötte, Jörg Pieper, Dirk Wassermann, Hans Josef Leyendecker, Gerhard Gohde, Barbara Simons, Achim Brünger, Uwe Petersen, Heike Wahl, Rainer Tewes, Doris Junghans-Kullmann, Angela Grimm-Kraft, Harald Bohnau, Ursula Pinsdorf, Thomas Busch, Gisela Keller, Susanne Fuchs-Römer, and Wolfgang Beisel.

Düsseldorf: Birgitt Richter-Polynice, Florinela Cupsa, Roland Matthias Unkelbach, Gerhard Schiller, Barbara Damanakis, Michael Frenkel, Klaus-Wolfgang Ebeling, Pauline Berger, Kurt Gillhausen, Uwe Hellmessen, Helga Hümmerich, Hans-Christian Heede, Boguslaw-Marian Kormann, Wolfgang Josef Peters, Ulrich Schott, Dirk Matzies, Andre Schumacher, Tim Oliver Flettner, Winfried Thraen, Harald Siegmund, Claus Levacher, Tim Blankenstein, Eliane Lamborelle, Ralf Hollstein, Edna Hoffmann, Ingeborg Ghane, Regine Claß, Stefan-Wolfgang Meier, Leo W. Moers, Udo Wundram, Klaus Schmitt, Rastin Missghian, Karin Spallek, and Christiane Schlösser.

Hamburg: Kathrin Groß, Winfried Bouché, Ursula Linn, Gundula Bormann, Gerhard Schulze, Klaus Stelter, Heike Gatermann, Doris Fischer-Radizi, Otto-Peter Witt, Stefanie Kavka, Günther Klötzl, Karl-Christian Münter, Michael Baumhöfener, Maren Oberländer, Cornelia Schiewe, Jörg Hufnagel, Anne-Marei Kressel, Michael Kebschull, Christine Wagner, Fridolin Burkhardt, Martina Hase, Matthias Büttner, Karl-Heinz Houcken, Christiane Zebidi, Johann Bröhan, Christiane Russ, Frank Bethge, Gisela Rughase-Block, Margret Lorenzen, Arne Elsen, Lerke Stiller, Angelika Giovanopoulos, Daniela Korte, Ursula Jedicke, Rosemarie Müller-Mette, Andrea Richter, Sanna Rauhala-Parrey, Constantin Zoras, Gabriele Pfeil-Woltmann, Annett Knöppel-Frenz, Martin Kaiser, Johannes Bruns, Joachim Homann, Georg Gorgon, Niklas Middendorf, Kay Menschke, Hans Heiner Stöver, Hans H. Bayer, Rüdiger Quandt, Gisela Rughase-Block, Hans-Michael Köllner, Enno Strohbehn, Thomas Haller, Nadine Jesse, Martin Domsch, and Marcus Dahlke.

Leipzig: Thomas Lipp, Ina Lipp, Martina Amm, Horst Bauer, Gabriele Rauchmaul, Hans Jochen Ebert, Angelika Gabriel-Müller, Hans-Christian Taut, Hella Voss, Ute Mühlmann, Holger Schmidt, Gabi Müller, Eva Hager, Bettina Tunze, Barbara Bräutigam, Thomas Paschke, Heinz-Michael Assmann, Ina Schmalbruch, Gunter Kässner, Iris Pförtzsch, Brigitte Ernst-Brennecke, Uwe Rahnefeld, Petra Striegler, Marga Gierth, Anselm Krügel, Margret Boehm, Dagmar Harnisch, Simone Kornisch-Koch, Birgit Höne, Lutz Schönherr, Frank Hambsch, Katrin Meitsch, Britta Krägelin-Nobahar, Cornelia Herzig, Astrid Georgi, Erhard Schwarzmann, Gerd Schinagl, Ulrike Pehnke, Mohammed Dayab, Sabine Müller, Jörg-Friedrich Onnasch, Michael Brosig, Dorothea Frydetski, Uwe Abschke, Volkmar Sperling, Ulrich Gläser, Frank Lebusser, and Detlef Hagert.

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The authors declare no conflicts of interest in relation to this study.

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