Journal of Affective Disorders 293 (2021) 338–346

Contents lists available at ScienceDirect

Journal of Affective Disorders

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

Research paper

Association between social network characteristics and prevalent and incident depression: The Maastricht Study

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ARTICLE INFO

Keywords:
Social network
Depressive symptoms
Depression
Prospective cohort study
Emotional support

ABSTRACT

Aims: Social network characteristics may provide a novel non-pharmaceutical target for the prevention of depression. We investigated the temporal association of a broad range of structural and functional social network characteristics with incident depressive symptoms over 5 years of follow-up.

Methods: We used data from The Maastricht Study, a population-based prospective cohort study (n=2,465, mean age 59.8±8.1 years, 49.1% women, 11,585 person-years of follow-up). Social network characteristics were assessed through a name generator questionnaire. Clinically relevant depressive symptoms (9-item Patient Health Questionnaire score≥10) were assessed at baseline and annually. We used multivariable logistic and Cox regression analyses, adjusted for sociodemographic, lifestyle and cardiovascular risk factors.

Results: In cross-sectional analyses less emotional support for discomfort and with important decisions, and less informational support were associated with prevalent depressive symptoms (OR[95%CI] 1.19 [1.01-1.40]; 1.22 [1.05-1.43], and 1.20 [1.04-1.39], respectively). Every fewer 10% of family members was associated with prevalent depressive symptoms (1.11 [1.01-1.23]). In longitudinal analyses, less emotional support on important decisions was also associated with higher risk of incident depressive symptoms (HR[95%CI] 1.13 [1.03-1.25]). In addition, every fewer 10% of the network that was a family member was associated with a higher hazard of incident depressive symptoms (1.07 [1.01-1.13]).

Conclusions: This study shows that less emotional support and fewer family members in the network were associated with higher risk of both prevalent and incident depression. The importance of emotional support and the role that family plays should be considered in treatment and prevention of depression.

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https://doi.org/10.1016/j.jad.2021.06.046
Received 28 January 2021; Received in revised form 9 May 2021; Accepted 19 June 2021
Available online 25 June 2021

1. Introduction

Depression is one of the most common psychiatric disorders, and is expected to become the leading cause of disease burden in 2030, globally (World Health Organization, 2008). In addition, depression results in a higher risk of premature mortality with a reduction of approximately 10 years in life expectancy (Walker et al., 2015). Despite the availability of psychological and pharmacological treatments, the clinical course of depression is highly recurrent (Burcusa and Iacono, 2007). Considering this, new (non-pharmaceutical) treatment and prevention opportunities are needed. Hereby, prevention strategies that involve individuals' social network could play an important role. The current COVID-19 pandemic further stresses the importance of social interactions and social isolation, especially in those individuals vulnerable for psychiatric conditions like depression.

Preliminary evidence highlights the association between social network characteristics and depression. However, prior studies are highly heterogeneous in terms of measurements, populations studied, and study design. Earlier findings have shown that some structural characteristics of social network, for instance, low number of contacts (Chao, 2011), small network size (Santini et al., 2015b), and lack of social participation (Chao, 2011) were associated with depression. Additionally, functional characteristics, particularly lack of social support (Levula et al., 2018; van den Brink et al., 2018), and social isolation (Cacioppo et al., 2011; Chao, 2011; Levula et al., 2018) were associated with depression as well. However, results were controversial (Noteboom et al., 2016; Schwarzbach et al., 2014), possibly due to potential limitations of individual studies or because of variability in methods to assess social network characteristics. Firstly, social network characteristics were mainly studied as single variables, frequently based on one (or limited) question (s), reducing the comprehensive understanding of the association of both structural and functional components of the social context with depression. This gave insight into the relevance of the social network to depression, but more in-depth insights are needed to develop preventive instruments. Secondly, most studies had a cross-sectional design limiting the possibilities to infer causality and temporality (Levula et al., 2018; Santini et al., 2015b), while social isolation might be both a risk factor and a consequence of depression. Moreover, longitudinal studies had a small sample size or used hospital-based (Teo et al., 2013) or convenience sampling (Santini et al., 2015b) populations, while population-based samples will enable a broader generalizability of findings. Finally, social network characteristics may modify lifestyle factors like smoking, alcohol use, physical activity, diet and obesity. However, previous studies were unable to adjust for lifestyle or cardiovascular risk (CVD) factors.

In light of this, our primary aim was to assess, if a wide range of both functional and structural social network characteristics, assessed using a validated method (name generator), were associated with prevalent and incident depression. Moreover, we adjusted our analysis for many potential confounding factors, including lifestyle and CVD risk factors. In addition, as both social network characteristics and depression are known to differ between men and women, we assessed whether any such associations differed by sex.

2. Methods

2.1. Study population and design

We used data from The Maastricht Study, a population-based observational prospective cohort study (Schram et al., 2014). In brief, the study focuses on the aetiology, pathophysiology, complications and comorbidities of type 2 diabetes mellitus (T2DM) and is characterized by an extensive phenotyping approach. Eligible participants were individuals aged 40-75 years and living in the southern part of the Netherlands, recruited through mass media campaigns, and from the municipal registries and the regional Diabetes Patient Registry via mailings. Recruitment was stratified according to known T2DM status, with an oversampling of individuals with T2DM, for reasons of efficiency. The baseline examinations of each participant were performed within three months. The study has been approved by the Institutional Medical Ethical Committee (NL31329.068.10) and the Ministry of Health, Welfare and Sports of the Netherlands (Permit 131088-105234-PG). All participants gave written informed consent. The present study includes longitudinal data from the first 3,451 participants, who completed the baseline survey between November 2010-September 2013. For cross-sectional analyses, full data on depression and social network characteristics at baseline was available in 2,685 participants (Figure 1). For longitudinal analysis, participants with depression at baseline (n=114) were excluded, resulting in a sample size of 2,465 participants. In this sample, follow-up data were available in 90.9% (year 1), 84.8% (year 2), 79.3% (year 3), 71.4% (year 4) and 75.7% (year 5) of the participants.

2.2. Social network

Social network characteristics were assessed at baseline through a name generator method (McCallister and Fischer, 1978). The respondent identifies a maximum of five persons for seven different types of contacts, followed by questions about these individuals (sex, age, type of relationship, and geographic distance). More details have been reported elsewhere (Brinkhues et al., 2017).

Functional and structural characteristics were then computed from the questionnaire (Brinkhues et al., 2018c). In brief, participants indicated the names of contacts who provided informational support related to advice on any problems, emotional support related to discomfort, emotional support related to important decisions, practical support related to jobs, and practical support related to sickness (functional characteristics). For every type of support, participants could name a maximum of five network members. Network size (defined as total number of unique network members), contact frequency [including total contacts per half year (defined as the sum of all contacts per half year), percentage of daily-weekly contact], and type of relationship (including percentage of network members living within walking distance, percentage of family members, percentage of friends, and participation in social activities) were assessed (structural characteristics). Those variables assessed in percentages were defined in steps of 10%. Based on an average network size of 10 network members, a change in one network member corresponds to 10%. Living alone was defined as a person who lived alone in his/her household. Social participation was defined as membership of, for instance, a sports club, religious group, volunteer organization, discussion group, self-support group, internet club, or other organization.

2.3. Assessment of depression at baseline

At baseline, prevalent depressive symptoms were assessed by use of a validated Dutch version of the 9-item Patient Health Questionnaire (PHQ-9) (Kroenke et al., 2001). It comprises nine items rated on a four-point scale, ranging from 0 = "not at all" to 3 = "nearly every day". Response options are used to calculate a continuous total-score ranging from 0 (no symptoms) to 27 (all symptoms present nearly every day) (Smolderen et al., 2009). When one or two items were missing, the total-score was calculated as 9 × (total points/9−number of missing items) and rounded to the nearest integer. A pre-defined cut-off score of ≥10 was used as a dichotomous scoring system for defining clinically relevant depressive symptoms (Pettersson et al., 2015).

At baseline, a prevalent and lifetime episode of MDD was assessed by the Mini-International Neuropsychiatric Interview (MINI) (Sheehan et al., 1998). The MINI is a short diagnostic structured interview, used to assess the presence of minor or major depressive disorder in the preceding two weeks according to the DSM-IV. MDD is diagnosed (Onete et al., 2018) if participants had five symptoms, of which at least one was

a core symptom plus other symptoms of depression. Lifetime history of MDD was assessed by asking for the presence of symptoms during minimally two weeks over the lifetime.

2.4. Assessment of depression during follow-up

Incident depressive symptoms were assessed by use of the PHQ-9 questionnaire annually over five years of follow-up. Incident depressive symptoms were defined as no depressive symptoms at baseline and presence of depressive symptoms (PHQ-9≥10) on at least one follow-up moment.

2.5. Covariates

Questionnaires were used to assess educational level, smoking status, alcohol consumption (Health Council of the Netherlands, 2006), diet, and moderate-to-vigorous physical activity level (CHAMPS questionnaire) (Schram et al., 2014). Diet was assessed using a Food Frequency Questionnaire and a Dutch Health Diet Index was calculated in order to measure the adherence to the Dutch dietary guidelines of 2015 (Looman et al., 2017; Gianfredi et al., 2021). History of CVD was derived from the Rose questionnaire (Schram et al., 2014). An oral glucose tolerance test was used to determine glucose metabolism status (Kulinski et al., 2014), defined according to the WHO 2006 criteria (World Health Organization, 2006). Office blood pressure was calculated as the average of at least three blood pressure readings (Omron 705IT, Japan). Fasting blood samples were used for laboratory assessment of total cholesterol and HDL cholesterol.

2.6. Statistical analysis

For descriptive purposes, most social network variables were inverted (multiplied by −1) to indicate that lower values reflect an increased risk. We conducted multivariable logistic regression analyses to examine the cross-sectional association of the social network characteristics with depressive symptoms and MDD. We used negative binomial regression analyses to assess the association of social network characteristics and prevalent depressive symptoms (PHQ-9 score). Cox regression analysis was used to assess the association between social network characteristics and incident depressive symptoms over time. Analyses were adjusted for age, sex, level of education, and, because of the oversampling, type 2 diabetes (model 1), additionally for smoking, alcohol consumption, physical activity, diet and BMI (model 2), and additionally for history of CVD, hypertension and dyslipidaemia. In addition, we tested for interaction with sex, and because of the oversampling of diabetes, and type 2 diabetes, in model 3. Lastly, we assessed multicollinearity among the social network characteristics using multiple linear regression models. Multicollinearity was assessed using variance inflation factor (VIF). A VIF equal to 1 means no multicollinearity among regressors, a VIF greater than 1 indicates that regressors may be moderately correlated, and no actions are needed. A VIF between 5 and 10 indicates high correlation that may be problematic (Akinwande et al., 2015). All analyses were conducted using IBM SPSS software version 21.0 (IBM Corp. Armonk, NY, USA), a p-value ≤ 0.05 was considered statistically significant.

3. Results

3.1. Descriptive characteristics

Table 1 shows the general characteristics of the study population at baseline and follow-up, stratified for depression. Participants had a mean age of 59.8±8.1 years and 49.1% were women. Participants with prevalent or incident depression had a lower level of education, were more often smokers and alcohol users, had a higher BMI, had a lower adherence to the Dutch dietary guidelines, were less physically active, had a less favourable cardiovascular-risk profile compared to participants without depressive symptoms. During 11,585 person-years of follow-up, 259 (10.5%) participants developed depressive symptoms. No differences have been detected between the full cohort and included participants, while excluded participants showed a worse cardiovascular-risk profile compared to included participants. Data are reported in Supplementary Table S1.

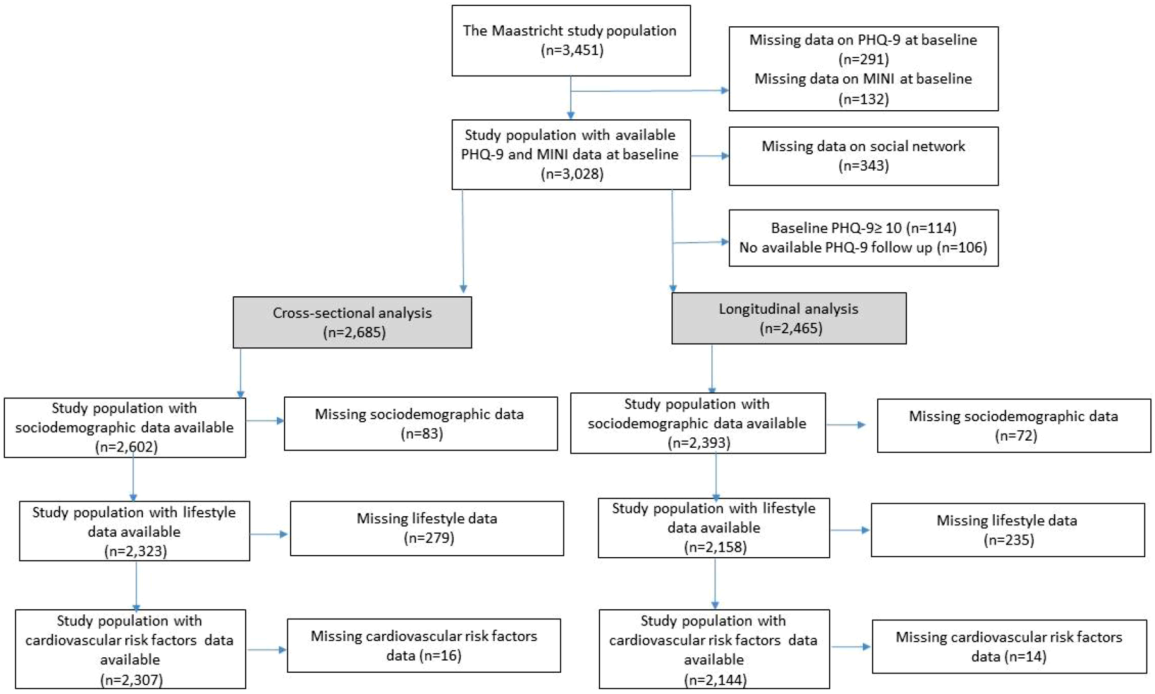

Fig. 1. Flowchart of the study population.

Table 1
Baseline characteristics of the study population stratified by prevalent and incident depression.

Characteristic	*Cross-sectional analysis* No depression at baseline (PHQ-9<10 and no MDD (MINI)) (n=2,529)	Prevalent depressive symptoms (PHQ-9≥10) (n=114)	Prevalent Major depressive disorder MDD (MINI) (n=87)	*Longitudinal analysis* No depression (PHQ-9<10 at baseline and follow-up) (n=2,206)	Incident depressive symptoms (PHQ-9≥10 during follow-up) (n=259)
Women	1,243 (49.1)	70 (61.4)	44 (50.6)	1,087 (49.3)	124 (47.9)
Age (years)	59.8 ± 8.2	56.6 ± 7.5	58.9 ± 8.1	59.8 ± 8.1	59.7 ± 8.3
Education					
Low/Medium/High	30.5/28.4/41.1	42.7/31.8/25.5	49.4/28.9/21.7	28.9/28.4/42.7	40.4/31.8/27.8
Smoking					
Never/Former/Current	36.2/52.0/11.8	21.8/50.9/27.3	22.4/56.5/21.2	37.1/52.6/10.3	28.1/51.6/20.3
Alcohol use					
None/Low/High	16.7/56.9/26.4	36.9/43.2/19.8	35.3/41.2/23.5	15.6/57.1/27.4	24.2/55.1/20.7
BMI (kg/m^2)	26.8 ± 4.4	29.1 ± 6.1	29.1 ±5.7	26.7 ± 4.2	28.0 ± 4.9
Dutch Diet score	84.1 ± 14.7	80.7 ±13.6	80.1 ± 13.7	84.6 ± 14.6	79.8 ± 14.8
MVPA (hours/week)	5.7 ± 4.4	4.3 ± 4.3	3.9 ± 3.4	5.8 ± 4.4	4.6 ± 4.2
Hypertension	1,387 (55.0)	71 (62.3)	56 (64.4)	1,192 (54.2)	161 (62.2)
Total cholesterol-to-HDL cholesterol ratio	3.6 ± 1.2	3.7 ±1.3	3.9 ± 1.2	3.6 ± 1.1	3.8 ± 1.3
Type 2 diabetes	664 (26.3)	50 (43.9)	39 (44.8)	530 (24.0)	104 (40.2)
History of CVD	385 (15.5)	26 (23.6)	18 (20.9)	313 (14.4)	62 (24.4)
Depression					
Depression score at baseline (PHQ-9 score)	2.2 ± 2.2	14.0 ± 3.9	11.2 ± 6.2	2.0±2.1	4.5 ± 2.7
Major depressive disorder at baseline (MINI)	0	45 (39.5)	87 (100)	21 (1.0)	18 (6.9)
Use of antidepressants at baseline	134 (5.3)	30 (26.3)	24 (27.6)	99 (4.5)	38 (14.7)
Functional characteristics of the social network					
Emotional support (discomfort)*	2.7 ± 1.6	2.4 ± 1.5	2.2 ± 1.5	2.8 ± 1.6	2.5 ± 1.6
Emotional support (important decisions)*	3.1 ± 1.6	2.6 ± 1.6	2.6 ± 1.7	3.2 ± 1.6	2.7 ± 1.6
Informational support*	3.3 ± 1.6	3.0 ± 1.6	2.8 ± 1.7	3.3 ± 1.6	3.1 ± 1.7
Practical support (jobs)*	2.3 ± 1.4	2.1 ± 1.3	2.0 ± 1.4	2.3 ± 1.4	2.1 ± 1.4
Practical support (sickness)*	2.8 ± 1.5	2.6 ± 1.5	2.4 ± 1.5	2.9 ± 1.5	2.6 ± 1.5
Structural characteristics of the social network					
Network size (n)	10.1 ± 5.2	8.5 ± 4.6	8.6 ± 4.4	10.3 ± 5.2	9.0 ± 4.9
Contact frequency					
Total contacts per half year (n)	232.0 ± 143.1	230.0 ± 147.4	213.3 ± 120.2	235.1 ± 144.0	219.4 ± 139.4
Percentage of daily-weekly contact	47.3 ± 25.7	56.1 ± 24.5	51.2 ± 24.0	46.9 ± 25.5	50.0 ± 26.4
Proximity					
Percentage of network members living within walking distance	43.5 ± 23.9	44.2 ± 23.9	45.4 ± 25.5	43.1 ± 23.6	46.3 ± 26.0
Type of relationship					
Percentage of family members	58.6 ± 23.3	59.3 ± 25.8	58.8 ± 25.0	58.5 ± 23.0	57.9 ± 25.3
Percentage of friends	27.8 ± 21.0	25.3 ± 23.6	28.5 ± 22.0	28.1 ± 20.6	26.2 ± 23.1
Living alone	448 (17.7)	30 (26.3)	13 (14.9)	374 (17.0)	55 (21.2)
Social participation	1,734 (67.6)	63 (55.3)	51 (58.6)	1,526 (69.2)	158 (61.0)

* Functional characteristics of social network range from 0 to 5. Results are presented as mean ± SD or n (%).

3.2. Functional social network characteristics and prevalent depression

Table 2 shows that in cross-sectional analysis, less emotional support on discomfort and with important decisions were consistently associated with prevalent clinically relevant depressive symptoms in model 3: (OR [95%CI] 1.19 [1.01-1.40]; 1.22 [1.05-1.43], respectively and MDD (1.22 [1.01-1.46]; 1.20 [1.01-1.43], respectively). One unit less in emotional support was also associated with more depressive symptoms on a continuous scale (RR 1.04 [1.00-1.07]). Less informational support was significantly associated with clinically relevant depressive symptoms (1.20 [1.04-1.39]), but not with MDD (1.16 [0.99-1.37]). Both measures of less practical support (jobs and sickness) were not significantly associated with prevalent depressive symptoms or MDD after full adjustment, although a similar trend of less support being associated with prevalent clinically relevant depressive symptoms was observed. Moreover, one unit less in practical support (sickness) was associated with more depressive symptoms on a continuous scale (RR 1.05 [1.02-1.09]).

3.3. Structural social network characteristics and prevalent depression

The majority of the structural network characteristics were not associated with prevalent depressive symptoms or MDD in cross-sectional analyses (Table 2), as they lost statistical significance after adjustment for lifestyle risk factors (model 2). A lower percentage of family members was associated with clinically relevant depressive symptoms (OR 1.11 [1.01-1.23] per 10%) and each fewer network member reported was also associated with more depressive symptoms on a continuous scale (RR 1.03 [1.03-1.05]). Living alone was associated with clinically relevant depressive symptoms (1.75 [1.03-2.96]) and more depressive symptoms on a continuous scale (1.23 [1.08-1.40]), also after adjustment for lifestyle and CVD risk factors. The association of having fewer family members in general with MDD pointed towards the same direction, albeit not statistically significant, while the association for living alone and MDD was in the opposite direction and not statistically significant.

Table 2
Cross-sectional association of structural and functional social network characteristics with prevalent depressive symptoms and major depressive disorder.

Models	Depressive symptoms (PHQ-9>10 109 cases) OR (95% CI)	p-value	Major depressive disorder (MINI, 83 cases) OR (95% CI)	p-value	Depressive symptoms (PHQ-9 score) Rate ratio (95% CI)	p-value
Functional characteristics of the social network						
Less emotional support (discomfort)*						
Model 1	**1.17 (1.02-1.34)**	**0.028**	**1.19 (1.01-1.39)**	**0.038**	**1.04 (1.01-1.07)**	**0.022**
Model 2	**1.18 (1.01-1.38)**	**0.043**	**1.21 (1.01-1.46)**	**0.038**	1.03 (0.99-1.07)	0.061
Model 3	**1.19 (1.01-1.40)**	**0.033**	**1.22 (1.01-1.46)**	**0.037**	**1.04 (1.00-1.07)**	**0.035**
Less emotional support (important decisions)*						
Model 1	**1.25 (1.09-1.43)**	**0.001**	1.14 (0.97-1.33)	0.109	**1.03 (1.00-1.07)**	**0.034**
Model 2	**1.23 (1.05-1.44)**	**0.009**	**1.20 (1.01-1.43)**	**0.044**	1.02 (0.99-1.06)	0.233
Model 3	**1.22 (1.05-1.43)**	**0.012**	**1.20 (1.01-1.43)**	**0.046**	1.02 (0.99-1.06)	0.235
Less informational support*						
Model 1	**1.16 (1.02-1.31)**	**0.024**	1.14 (0.99-1.31)	0.067	1.03 (1.00-1.06)	0.065
Model 2	**1.19 (1.03-1.38)**	**0.017**	1.16 (0.99-1.36)	0.071	1.03 (0.99-1.06)	0.096
Model 3	**1.20 (1.04-1.39)**	**0.014**	1.16 (0.99-1.37)	0.063	1.03 (0.99-1.06)	0.092
Less practical support (jobs)*						
Model 1	1.11 (0.95-1.29)	0.177	1.10 (0.92-1.31)	0.308	1.03 (0.99-1.06)	0.105
Model 2	1.18 (0.99-1.42)	0.072	1.16 (0.94-1.43)	0.164	1.03 (0.99-1.07)	0.115
Model 3	1.18 (0.99-1.42)	0.072	1.16 (0.94-1.43)	0.156	1.03 (0.99-1.07)	0.083
Less practical support (sickness)*						
Model 1	1.15 (0.99-1.32)	0.055	**1.19 (1.01-1.40)**	**0.038**	**1.05 (1.02-1.08)**	**0.002**
Model 2	1.15 (0.98-1.35)	0.094	1.17 (0.97-1.41)	0.094	**1.05 (1.01-1.09)**	**0.005**
Model 3	1.15 (0.98-1.36)	0.086	1.18 (0.98-1.42)	0.081	**1.05 (1.02-1.09)**	**0.003**
Structural characteristics of the social network						
Smaller network size (for every fewer network member)						
Model 1	**1.07 (1.02-1.12)**	**0.008**	1.04 (0.98-1.10)	0.168	**1.01 (1.00-1.02)**	**0.015**
Model 2	1.05 (0.99-1.11)	0.075	1.03 (0.97-1.09)	0.381	1.01 (0.99-1.02)	0.244
Model 3	1.05 (0.99-1.11)	0.093	1.03 (0.97-1.09)	0.394	1.01 (0.99-1.02)	0.254
Contact frequency						
Total contacts per half year (for every 10 additional contacts)						
Model 1	1.00 (0.99-1.02)	0.790	1.01 (0.99-1.03)	0.333	1.00 (0.99-1.01)	0.167
Model 2	1.00 (0.98-1.02)	0.871	1.01 (0.99-1.03)	0.430	1.00 (0.99-1.01)	0.317
Model 3	1.00 (0.98-1.02)	0.850	1.01 (0.99-1.03)	0.415	1.00 (0.99-1.01)	0.239
Percentage of daily-weekly contact (for every additional 10%)						
Model 1	**1.09 (1.01-1.18)**	**0.025**	1.00 (0.92-1.09)	0.973	1.01 (0.99-1.03)	0.444
Model 2	1.07 (0.98-1.17)	0.110	0.96 (0.87-1.06)	0.427	1.00 (0.98-1.02)	0.719
Model 3	1.06 (0.97-1.16)	0.195	0.96 (0.87-1.06)	0.397	0.99 (0.97-1.01)	0.454
Proximity						
Percentage of network members living within walking distance (for every fewer 10%)						
Model 1	1.00 (0.93-1.09)	0.927	1.00 (0.92-1.10)	0.981	0.99 (0.97-1.01)	0.247
Model 2	0.97 (0.89-1.07)	0.577	0.97 (0.87-1.07)	0.512	0.99 (0.97-1.01)	0.263
Model 3	0.97 (0.88-1.06)	0.510	0.96 (0.87-1.06)	0.438	0.99 (0.97-1.01)	0.454
Type of relationship						
Percentage family members (for every fewer 10%)						
Model 1	1.04 (0.96-1.14)	0.359	1.07 (0.97-1.17)	0.177	**1.03 (1.00-1.05)**	**0.017**
Model 2	1.09 (0.99-1.21)	0.077	1.11 (0.99-1.23)	0.065	**1.03 (1.01-1.05)**	**0.014**
Model 3	**1.11 (1.01-1.23)**	**0.040**	1.10 (0.99-1.23)	0.069	**1.03 (1.01-1.05)**	**0.008**
Percentage friends (for every fewer 10%)						
Model 1	1.04 (0.94-1.15)	0.453	0.93 (0.84-1.03)	0.166	0.99 (0.97-1.01)	0.399
Model 2	1.01 (0.90-1.13)	0.854	0.91 (0.81-1.02)	0.109	0.99 (0.97-1.01)	0.399
Model 3	1.00 (0.89-1.12)	0.983	0.91 (0.81-1.02)	0.102	0.99 (0.96-1.01)	0.311
Living alone (%)						
Model 1	**1.80 (1.15-2.82)**	**0.010**	0.82 (0.45-1.51)	0.526	**1.25 (1.11-1.41)**	**0.000**
Model 2	**1.87 (1.11-3.13)**	**0.018**	0.73 (0.36-1.48)	0.386	**1.24 (1.09-1.41)**	**0.001**
Model 3	**1.75 (1.03-2.96)**	**0.038**	0.72 (0.36-1.47)	0.370	**1.23 (1.08-1.40)**	**0.001**
Lack of social participation (%)						
Model 1	1.32 (0.89-1.97)	0.171	1.17 (0.74-1.85)	0.503	**1.13 (1.02-1.24)**	**0.019**
Model 2+	1.18 (0.76-1.84)	0.452	0.90 (0.53-1.53)	0.704	1.04 (0.93-1.15)	0.502
Model 3+	1.20 (0.77-1.87)	0.425	1.10 (0.66-1.81)	0.718	1.01 (0.91-1.13)	0.854

Model 1 adjusted for sociodemographic characteristics (age, sex, level of education, and diabetes status).
Model 2 additional adjustment for lifestyle (MVPA, smoking, alcohol consumption, BMI and diet).
Model 3 additional adjustment for cardiovascular risk factors (hypertension, cholesterol, history of CVD).
* Functional characteristics of social network range from zero to five.
+ MVPA was not included in the analyses of social participation as membership of a sports club is part of the definition of social participation.

3.4. Functional social network characteristics and incident depressive symptoms

Table 3 shows that less emotional support on important decisions was associated with incident depressive symptoms after full adjustment (HR [95%CI] 1.13 [1.03-1.25]). The association of emotional support on discomfort lost significance after adjustment for lifestyle risk factors, while practical or informational support were not significantly associated with incident depressive symptoms.

3.5. Structural social network characteristics and incident depressive symptoms

A smaller network size was associated with a 4% higher hazard of incident depressive symptoms for every one person less in the network (Table 3); however, this association was attenuated after adjustment for lifestyle and cardiovascular-risk factors, and no longer statistically significant. The percentage of family members was consistently associated with incident depressive symptoms and remained so after adjustment for lifestyle and cardiovascular-risk factors. Every 10% fewer family members within the network was associated with a 7% higher hazard for incident depressive symptoms (1.07 [1.01-1.13]).

No statistically significant interactions were found with sex or diabetes.

Table 3
Longitudinal association of functional and structural social network characteristics at baseline with incident depressive symptoms during 5-years of follow-up.

Models	Incident depressive symptoms (PHQ-9≥10) HRs (95% CI)	p-value
Functional characteristics of the social network		
Less emotional support (discomfort)*		
Model 1	**1.11 (1.01-1.21)**	**0.025**
Model 2	1.08 (0.98-1.18)	0.135
Model 3	1.07 (0.97-1.18)	0.159
Less emotional support (important decisions)*		
Model 1	**1.18 (1.08-1.29)**	**0.000**
Model 2	**1.14 (1.04-1.26)**	**0.007**
Model 3	**1.13 (1.03-1.25)**	**0.011**
Less informational support*		
Model 1	1.06 (0.98-1.15)	0.150
Model 2	1.03 (0.94-1.12)	0.553
Model 3	1.02 (0.94-1.11)	0.644
Less practical support (jobs)*		
Model 1	1.06 (0.96-1.16)	0.281
Model 2	1.04 (0.93-1.15)	0.527
Model 3	1.03 (0.92-1.14)	0.629
Less practical support (sickness)*		
Model 1	1.08 (0.99-1.18)	0.071
Model 2	1.05 (0.95-1.16)	0.323
Model 3	1.04 (0.95-1.15)	0.395
Structural characteristics of the social network		
Smaller network size (for every fewer member)		
Model 1	**1.04 (1.01-1.07)**	**0.022**
Model 2	1.03 (0.99-1.06)	0.101
Model 3	1.03 (0.99-1.06)	0.120
Contact frequency		
Total contacts per half year (for every 10 additional contacts)		
Model 1	1.01 (0.99-1.02)	0.191
Model 2	1.01 (0.99-1.02)	0.158
Model 3	1.01 (0.99-1.02)	0.134
Percentage of daily-weekly contact (for every additional 10%)		
Model 1	1.01 (0.96-1.06)	0.745
Model 2	0.99 (0.94-1.05)	0.784
Model 3	0.99 (0.94-1.04)	0.586
Proximity		
Percentage of network members living within walking distance (for every fewer 10%)		
Model 1	1.03 (0.98-1.09)	0.229
Model 2	1.04 (0.98-1.10)	0.168
Model 3	1.03 (0.98-1.09)	0.227
Type of relationship		
Percentage of family members (for every fewer 10%)		
Model 1	1.06 (1.00-1.12)	0.054
Model 2	**1.06 (1.00-1.13)**	**0.048**
Model 3	**1.07 (1.01-1.13)**	**0.036**
Percentage of friends (for every fewer 10%)		
Model 1	1.01 (0.94-1.07)	0.900
Model 2	0.99 (0.93-1.07)	0.898
Model 3	0.99 (0.93-1.06)	0.855
Living alone (%)		
Model 1	1.31 (0.97-1.78)	0.082
Model 2	1.15 (0.81-1.62)	0.435
Model 3	1.14 (0.81-1.61)	0.456
Lack of social participation (%)		
Model 1	1.23 (0.95-1.60)	0.113
Model 2^{+}	1.16 (0.88-1.52)	0.299
Model 3^{+}	1.18 (0.90-1.56)	0.232

Model 1 adjusted for sociodemographic characteristics (age, sex, level of education, and diabetes status).
Model 2 additional adjustment for lifestyle (MVPA, smoking, alcohol consumption, BMI and diet).
Model 3 additional adjustment for cardiovascular risk factors (hypertension, cholesterol, history of CVD).

* Functional characteristics of social network range from zero to five.
+ MVPA was not included in the analyses of social participation as membership of a sports club is part of the definition of social participation. crude n=259 cases; model 1 n=251 cases; model 2 n=216 cases; model 3 n=214 cases.

3.6. Additional analyses

To minimize selection bias and confirm the robustness of findings, several sensitivity analyses were performed. Similar associations were found after 1) additional adjustment for antidepressant drugs use, 2) additional adjustment for MDD at baseline, 3) excluding participants with antidepressant drugs use at baseline, 4) excluding participants with MDD at baseline, 5) excluding participants with lifetime MDD, using a control group with 6) no missing or only 7) one missing follow-up measurement; 8) excluding individuals with type 2 diabetes; 9) additional adjustment for occupational status; 10) additional adjustment for social network size. The associations between social network characteristics and incident depressive symptoms became slightly stronger after excluding participants with any missing PHQ-9 data over 5 follow-up measurements, while other analyses did not materially change the results (Supplementary Table S2). A moderate collinearity has been found for network size, total contacts per half year and percentage of daily-weekly contact. This result can be explained by these variables being derived from the network size. Results are reported in Supplementary Table S3.

4. Discussion

This study is the first to assess the association between a broad range of functional and structural social network characteristics and the risk of prevalent and incident depression in a population-based setting. This study shows that emotional support is associated with both prevalent and incident depression. In addition, the proportion of family members, whom may be crucial in the delivery of emotional support, was significantly associated with both prevalent and incident depression. These associations were independent of a large range of potential confounders. Within the current COVID-19 pandemic, we fell this paper adds important information on which social ties are essential to maintain for individuals with or at risk of depression during regional or national lockdowns.

4.1. Functional social network characteristics and depression

In this study, less emotional support on discomfort and with important decisions were consistently associated with both prevalent MDD, and prevalent and incident depressive symptoms. Our results are in line with the meta-analysis by Santini et al (Santini et al., 2015b), and two more recent studies (Santini et al., 2015a; Schwarzbach et al., 2014) where lower informational and emotional support were associated with depression.

It is important to appreciate that cross-sectional analyses provide a snapshot of the distribution of social network characteristics among depressed versus non-depressed participants. Knowledge on this distribution is useful to improve social network characteristics of depressed individuals. Longitudinal analyses provide insights into the temporality of these associations and may help to identify which social network characteristics could be considered in prevention. However, since our data confirmed a statistical association between less emotional support, fewer family members and depression, even in cross-sectional analysis, we can speculate that these associations may be bidirectional. Thus, less emotional support and fewer family members might be considered both cause (as suggested by our longitudinal data) and consequence of depression (considering that depressed people show less interest in social interaction).

4.2. Structural social network characteristics and depression

Even if a mixed network of friends and family is important, we found a consistent association between fewer family members within the network and a higher risk of depression in both prevalent and incident depressive symptoms. This fits well with the observation that less emotional support is associated with depression, as family members are an important source of emotional support, and is in line with previous studies (Santini et al., 2015b; Shanas, 1979; van den Brink et al., 2018). Moreover, our results support the convoy model, where the most supportive members are nuclear family members which are consistent over time, and with whom sociohistorical experiences are shared (Fuller et al., 2020). In light of this, we believe that educating family members about their important role in depression could be an important strategy in reducing the burden of depression. We do not have data to confirm in which way the family support can reduce depression, or which is the best way to educate family members. Future studies, exploring this relationship in more detail, are needed to provide new insights in the etiology and prevention of depression. Moreover, it should be considered that, in general, social support is thought to have beneficial effects on wellbeing, health and (mainly chronic) diseases management, particularly during the late stage of the life (Schwarzbach et al., 2014; Wrzus et al., 2013). Previous studies showed that more social support might be associated with lower risk of diabetes (Brinkhues et al., 2017) and its complications (such as micro- and macrovascular complications) (Brinkhues et al., 2018a), self-health-promoting behaviors, better use of services and well-being among type 2 diabetes subjects (Schiotz et al., 2012).

We only found a weak association of (the frequently studied) network size with depression. Prior studies reported great differences of this association in both cross-sectional and longitudinal analysis (Santini et al., 2015b), which may be due to different methods used to assess network size.

In our analysis, living alone was significantly associated with prevalent but not with incident depressive symptoms, contrasting previous studies (Bisschop et al., 2004; Sonnenberg et al., 2013). Given that our findings are based on a limited number of individuals who lived alone and had depression, the power to detect a potential association was limited and this result should be interpreted with caution. In our study, social contacts as well as the other structural characteristics were not associated with depression in both cross-sectional and longitudinal analyses.

4.3. Implications and mechanism

Our results highlight the importance to comprehensively assess structural and functional social networks characteristics in depression as this provides useful new insights for developing future (intervention) approaches. For the prevention of depression, two aspects may prove important: 1) to improve support, in particular emotional support and 2) to enhance existing social network ties, in particular with family members.

One major question is how emotional support by family members may prevent the development of depression. According to the buffering hypothesis (Berkman et al., 2015), emotional support may reduce stress, which is a well-known source of depression. In addition, family members are considered the core of human relationships, with whom uniformity of background, perception and action are shared (Fuller et al., 2020). Family is often a source of support, even if it may be a source of social strain, sharing the same sociohistorical experiences, as ,within the family, is presumed to facilitate the receipt of social support (Fuller et al., 2020). Thus, family members may be best equipped to capitalize

social support (Latkin and Knowlton, 2015), particularly in light of the socioemotional selectivity theory, according to which elderly people focus their emotional contacts on mostly close family members (Carstensen et al., 1999).

The current COVID-19 pandemic highlights the importance of social interactions, especially for those individuals with psychiatric disorders like depression (Amerio et al., 2020). Our study provides essential information on the social ties and social support that are most relevant for those with prevalent depression and those at high depression risk. This information is highly relevant during times of social isolation that results from the regional or national lockdowns and may guide clinicians towards clear advice to their depressed patients to uphold their family ties.

4.4. Strengths and limitations

A major strength of this study is the comprehensive assessment of both functional and structural social network characteristics by use of the name generator method (Brinkhues et al., 2018b; Marin, 2004), its population-based longitudinal design, large sample size, the extensive adjustment for confounding factors, and the assessment of depression with both the PHQ-9 questionnaire and the MINI (the gold standard). Although the PHQ-9 is not a diagnostic tool of MDD, it is a validated instrument with high sensitivity and specificity. Therefore, misclassification is expected to be low, and cross-sectional analyses with the MINI showed remarkably similar results (Kroenke et al., 2001). Regarding social network characteristics, despite the high number of variables, we did not detect multicollinearity aside from a moderate multicollinearity for network size, total contacts per half year and percentage of daily-weekly contact. Having this in mind, in sensitivity analysis we further adjusted for social network size, but our results did not change. However, it should be considered that multicollinearity results in unnecessary inflation of the confidence intervals, with the risk of losing the statistical significance (Akinwande et al., 2015).

This study has certain limitations. Participants who are more socially-isolated or who suffer from depression are less prone to take part in the study. Participants with incomplete data on social network characteristics and/or depression were found to have a worse cardiovascular-risk profile. Though we adjusted for a range of covariates that are related to being lost-to follow-up, some selection bias might be present. However, considering the type of enrollment, we believe that if any selection bias has occurred, this would have resulted in selecting more health-conscious people, which would result in an underestimation of the true association. Moreover, as people with a worse social network and higher PHQ-9 scores at baseline are more likely to be right-censored, this likely resulted in an underestimation of the true association. Social network characteristics have only been measured at baseline. However, evidence shows that social network characteristics remain stable during adulthood (Wrzus et al., 2013). The population of our study is mainly Caucasian, limiting the generalizability of the results, particularly considering the potential cultural differences in social network characteristics. Fourthly, data collected by questionnaires might be prone to recall bias or social desirability bias, particularly because both exposure and outcome were self-reported.

5. Conclusions

In conclusion, we show that both functional, in particular less emotional support, and structural social network characteristics (a lower proportion of family members), were associated with prevalent and incident depressive symptoms, independent of lifestyle and CVD risk factors. These findings indicate that social network characteristics like emotional support and proportion of family members are important for the prevention of depression.

Declaration of Competing Interest

None to declare.

Acknowledgments

The researchers are indebted to the participants for their willingness to participate in the study.

Financial support

This study was supported by the European Regional Development Fund via OP-Zuid, the Province of Limburg, the Dutch Ministry of Economic Affairs (grant 31O.041), Stichting De Weijerhorst (Maastricht, The Netherlands), the Pearl String Initiative Diabetes (Amsterdam, The Netherlands), the Cardiovascular Center (CVC, Maastricht, the Netherlands), CARIM School for Cardiovascular Diseases (Maastricht, The Netherlands), CAPHRI Care and Public Health Research Institute (Maastricht, The Netherlands), NUTRIM School for Nutrition and Translational Research in Metabolism (Maastricht, the Netherlands), Stichting Annadal (Maastricht, The Netherlands), Health Foundation Limburg (Maastricht, The Netherlands), and by unrestricted grants from Janssen-Cilag B.V. (Tilburg, The Netherlands), Novo Nordisk Farma B.V. (Alphen aan den Rijn, the Netherlands), and Sanofi-Aventis Netherlands B.V. (Gouda, the Netherlands).

Ethics standard

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All procedures involving human subjects were approved by Institutional Medical Ethical Committee (NL31329.068.10) and the Ministry of Health, Welfare and Sports of the Netherlands (Permit 131088-105234-PG).

Author statement

Drs MTS and VG have full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design VG, AK, MTS. Acquisition, analysis, or interpretation of data: All authors. Drafting of the manuscript: VG, MTS. Critical revision of the manuscript for important intellectual content: All authors. Statistical analysis: VG. Supervision: AK, MTS

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2021.06.046.

References

Akinwande, M., Dikko, H., Samson, A., 2015. Variance inflation factor: As a condition for the inclusion of suppressor variable (s) in regression analysis. Open J. Statistics 5, 754–767.

Amerio, A., Odone, A., Aguglia, A., Gianfredi, V., Bellini, L., Bucci, D., Gaetti, G., Capraro, M., Salvati, S., Serafini, G., Signorelli, C., Amore, M., Ghaemi, S.N., 2020. La casa de papel: a pandemic in a pandemic. J. Affect. Disord. 277, 53–54.

Berkman, L.F., Kawachi, I., Glymour, M.M., 2015. Social Epidemiology, 2 Ed. Oxford University Press.

Bisschop, M.I., Kriegsman, D.M., Beekman, A.T., Deeg, D.J., 2004. Chronic diseases and depression: the modifying role of psychosocial resources. Soc. Sci. Med. 59, 721–733.

Brinkhues, S., Dukers-Muijrers, N., Hoebe, C., van der Kallen, C.J.H., Dagnelie, P.C., Koster, A., Henry, R.M.A., Sep, S.J.S., Schaper, N.C., Stehouwer, C.D.A., Bosma, H., Savelkoul, P.H.M., Schram, M.T., 2017. Socially isolated individuals are more prone to have newly diagnosed and prevalent type 2 diabetes mellitus - the Maastricht study. BMC Public Health 17, 955.

Brinkhues, S., Dukers-Muijrers, N., Hoebe, C., van der Kallen, C.J.H., Koster, A., Henry, R.M.A., Stehouwer, C.D.A., Savelkoul, P.H.M., Schaper, N.C., Schram, M.T.,

2018a. Social network characteristics are associated with type 2 diabetes complications: the maastricht study. Diabetes Care. 41, 1654–1662.
Brinkhues, S., Schram, M.T., Hoebe, C., Kretzschmar, M.E.E., Koster, A., Dagnelie, P.C., Sep, S.J.S., van Kuijk, S.M.J., Savelkoul, P.H.M., Dukers-Muijrers, N., 2018b. Social networks in relation to self-reported symptomatic infections in individuals aged 40-75 - the Maastricht study. BMC Infect. Dis. 18, 300.
Brinkhues, S., van Kuijk, S.M.J., Hoebe, C., Savelkoul, P.H.M., Kretzschmar, M.E.E., Jansen, M.W.J., de Vries, N., Sep, S.J.S., Dagnelie, P.C., Schaper, N.C., Verhey, F.R. J., Bosma, H., Maes, J., Schram, M.T., Dukers-Muijrers, N., 2018c. Development of prediction models for upper and lower respiratory and gastrointestinal tract infections using social network parameters in middle-aged and older persons -The Maastricht Study. Epidemiol. Infect. 146, 533–543.
Burcusa, S.L., Iacono, W.G., 2007. Risk for recurrence in depression. Clin. Psychol. Rev. 27, 959–985.
Cacioppo, J.T., Hawkley, L.C., Norman, G.J., Berntson, G.G., 2011. Social isolation. Ann. N. Y. Acad. Sci. 1231, 17–22.
Carstensen, L.L., Isaacowitz, D.M., Charles, S.T., 1999. Taking time seriously. A theory of socioemotional selectivity. Am. Psychol. 54, 165–181.
Chao, S.F., 2011. Assessing social support and depressive symptoms in older Chinese adults: a longitudinal perspective. Aging Ment. Health 15, 765–774.
Fuller, H.R., Ajrouch, K.J., Antonucci, T.C., 2020. The convoy model and later-life family relationships. J. Fam Theory Rev. 12, 126–146.
Gianfredi, V., Koster, A., Odone, A., Amerio, A., Signorelli, C., Schaper, N.C., Bosma, H., Kohler, S., Dagnelie, P.C., Stehouwer, C.D.A., Schram, M.T., Dongen, M., Eussen, S., 2021. Associations of dietary patterns with incident depression: the maastricht study. Nutrients 13.
Health Council of the Netherlands, 2006. Guidelines for a healthy diet 2006. publication no. 2006/21.
Kroenke, K., Spitzer, R.L., Williams, J.B., 2001. The PHQ-9: validity of a brief depression severity measure. J. Gen. Intern. Med. 16, 606–613.
Kulinski, J.P., Khera, A., Ayers, C.R., Das, S.R., de Lemos, J.A., Blair, S.N., Berry, J.D., 2014. Association between cardiorespiratory fitness and accelerometer-derived physical activity and sedentary time in the general population. Mayo Clin. Proc. 89, 1063–1071.
Latkin, C.A., Knowlton, A.R., 2015. Social network assessments and interventions for health behavior change: a critical review. Behav. Med. 41, 90–97.
Levula, A., Harre, M., Wilson, A., 2018. The association between social network factors with depression and anxiety at different life stages. Community Ment. Health J. 54, 842–854.
Looman, M., Feskens, E.J., de Rijk, M., Meijboom, S., Biesbroek, S., Temme, E.H., de Vries, J., Geelen, A., 2017. Development and evaluation of the Dutch Healthy Diet index 2015. Public Health Nutr. 20, 2289–2299.
Marin, A., 2004. Are respondents more likely to list alters with certain characteristics?: Implications for name generator data. Social Networks 26, 289–307.
McCallister, L., Fischer, C., 1978. A procedure for surveying personal networks. Sociol. Methods Res. 131–148.
Noteboom, A., Beekman, A.T.F., Vogelzangs, N., Penninx, B., 2016. Personality and social support as predictors of first and recurrent episodes of depression. J. Affect. Disord. 190, 156–161.
Onete, V., Henry, R.M., Sep, S.J.S., Koster, A., van der Kallen, C.J., Dagnelie, P.C., Schaper, N., Kohler, S., Reesink, K., Stehouwer, C.D.A., Schram, M.T., 2018. Arterial stiffness is associated with depression in middle-aged men - the Maastricht Study. J. Psychiatry Neurosci. 43, 111–119.
Pettersson, A., Bostrom, K.B., Gustavsson, P., Ekselius, L., 2015. Which instruments to support diagnosis of depression have sufficient accuracy? A systematic review. Nord. J. Psychiatry 69, 497–508.
Santini, Z.I., Koyanagi, A., Tyrovolas, S., Haro, J.M., 2015a. The association of relationship quality and social networks with depression, anxiety, and suicidal ideation among older married adults: findings from a cross-sectional analysis of the Irish Longitudinal Study on Ageing (TILDA). J. Affect. Disord. 179, 134–141.
Santini, Z.I., Koyanagi, A., Tyrovolas, S., Mason, C., Haro, J.M., 2015b. The association between social relationships and depression: a systematic review. J. Affect. Disord. 175, 53–65.
Schiotz, M.L., Bogelund, M., Almdal, T., Jensen, B.B., Willaing, I., 2012. Social support and self-management behaviour among patients with Type 2 diabetes. Diabet. Med. 29, 654–661.
Schram, M.T., Sep, S.J., van der Kallen, C.J., Dagnelie, P.C., Koster, A., Schaper, N., Henry, R.M., Stehouwer, C.D., 2014. The Maastricht Study: an extensive phenotyping study on determinants of type 2 diabetes, its complications and its comorbidities. Eur. J. Epidemiol. 29, 439–451.
Schwarzbach, M., Luppa, M., Forstmeier, S., Konig, H.H., Riedel-Heller, S.G., 2014. Social relations and depression in late life-a systematic review. Int. J. Geriatr. Psychiatry 29, 1–21.
Shanas, E., 1979. The family as a social support system in old age. Gerontologist 19, 169–174.
Sheehan, D.V., Lecrubier, Y., Sheehan, K.H., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., Dunbar, G.C., 1998. The mini-international neuropsychiatric interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J. Clin. Psychiatry 59 (Suppl 20), 34–57, 22-33;quiz.
Smolderen, K.G., Spertus, J.A., Reid, K.J., Buchanan, D.M., Krumholz, H.M., Denollet, J., Vaccarino, V., Chan, P.S., 2009. The association of cognitive and somatic depressive symptoms with depression recognition and outcomes after myocardial infarction. Circulation 2, 328–337.
Sonnenberg, C.M., Deeg, D.J., van Tilburg, T.G., Vink, D., Stek, M.L., Beekman, A.T., 2013. Gender differences in the relation between depression and social support in later life. Int. Psychogeriatr. 25, 61–70.
Teo, A.R., Choi, H., Valenstein, M., 2013. Social relationships and depression: ten-year follow-up from a nationally representative study. PLoS One 8, e62396.
van den Brink, R.H.S., Schutter, N., Hanssen, D.J.C., Elzinga, B.M., Rabeling-Keus, I.M., Stek, M.L., Comijs, H.C., Penninx, B., Oude Voshaar, R.C., 2018. Prognostic significance of social network, social support and loneliness for course of major depressive disorder in adulthood and old age. Epidemiol. Psychiatr. Sci. 27, 266–277.
Walker, E.R., McGee, R.E., Druss, B.G., 2015. Mortality in mental disorders and global disease burden implications: a systematic review and meta-analysis. JAMA Psychiatry 72, 334–341.
World Health Organization, 2006. Definition and diagnosis of Diabetes Mellitus and Intermediate Hyperglycemia. World Health Organization, Geneva, Switzerland, pp. 1–3.
World Health Organization, 2008. The Global Burden of Disease: 2004 Update. Health Statistics and Information Systems, Geneva.
Wrzus, C., Hanel, M., Wagner, J., Neyer, F.J., 2013. Social network changes and life events across the life span: a meta-analysis. Psychol. Bull. 139, 53–80.