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Online Supplement

Online Methods

Measurement of confounding variables

Education, income, employment, smoking, and physical activity were assessed in a standardized computer-assisted personal interview. Education was classified according to the International Standard Classification of Education[1] as total years of formal education, combining school and vocational training and classified into four categories, with the highest category of 18 and more years of education (equivalent to a University degree) and the lowest category of 10 and less years (equivalent to a basic school degree and no vocational training). Income was measured as the monthly household equivalent income calculated by dividing the total household net income by a weighting factor for each household member.[2] Employment was defined as currently having a job. Smoking was defined as history of cigarette smoking during the past year.[3] Regular physical activity was defined as regularly performing any type of sports activities. Depression and alcohol consumption were assessed via self-report paper-and-pencil questionnaire. Depression was measured with the Center for Epidemiological Studies - Depression Scale (CES-D).[4] Alcohol consumption was measured as pure alcohol intake in grams per week. Therefore, the frequency of drinking beer, wine, sparkling wine, and spirits and the amount of intake was assessed. For each beverage the consumed volume in milliliters per week was calculated and multiplied with the percent of alcohol (0.05 for beer, 0.1 for white/red/sparkling wine, and 0.4 for spirits). The result was then multiplied with 0.794 gram, which is the final specific gravity of alcohol. Blood pressure was measured with an automated oscillometric device (Omron 705-CP, Omron, Mannheim, Germany) and the mean value of the second and third of 3 measurements taken at least 2 minutes apart was used. Body-mass-index (BMI, kg/m²) was calculated from standardized measurements of height and weight. Total, low-density lipoprotein cholesterol and high-density lipoprotein cholesterol were measured with standardized enzymatic methods using the ADVIA 1650 System (Siemens Healthcare Diagnostics, Eschborn, Germany). HbA1c was measured using immunonephelometry at 340/700 nm (BNII nephelometer, Dade-Behring, Deerfield, Illinois, USA). History of stroke, coronary heart disease (myocardial infarction or coronary intervention), and peripheral artery disease was assessed with a standardized computer-assisted personal interview performed by a physician. Participants were asked to bring all the medications they had been taking during the 7 days prior to the examination appointment. These were coded according to the Anatomical Therapeutic Chemical Classification Index.[5] Antihypertensive drug treatment was defined according to the KORA study definition.[6] Lipid-lowering medications included all medications with ATC code C10, antidiabetic medications those with ATC code A10, antidepressants those with ATC code N06A and N06CA, and anxiolytics those with ATC Code N03AE, N05BA, N05CD, and N05CF.

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Study End Points and Verification of Study End Points

Morbidity status during follow-up was assessed by annual postal questionnaires. After 5 and 10 years, a second medical examination in the study center took place. Participants were followed over a median of 13.4 (IQR 10.5–14.2) years for cardiovascular events. Cardiovascular events comprised strokes (defined as focal neurological deficits over a period of >24 h of presumed cerebrovascular origin), coronary events (including non-fatal acute myocardial infarction and coronary death defined as clinical symptoms, signs on electrocardiography, increased enzymes [levels of creatinine kinase], and troponin T or I, as well, and necropsy changes), or independently coded causes of deaths according to diseases of the circulatory system (chapter 9 of ICD-10). For the validation of incident cardiovascular events, hospital and nursing home records including ECGs, laboratory values, and pathology reports were collected. Death certificates were collected and interviews with general practitioners, relatives, and eye-witnesses were undertaken, if possible, in those who died. An external end point committee blinded for risk factor status reviewed all documents and classified cardiovascular events at separate regular meetings twice a year; for the end point stroke, an additional expert panel consisting of 4 neurologists was created (see section criteria and endpoint committee in the manuscript).

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eTable 1. Association of different types of social support and social integration with cardiovascular events stratified by sex

Social support	Person-years N	Cardiovascular events N	Crude incidence rate per 1000 person-years (95% CI)	Unadjusted HR (95% CI)	Minimal adjusted HR (95% CI)	Biological factors HR (95% CI)	Health behavior HR (95% CI)	Socioeconomic HR (95% CI)	Depression HR (95% CI)
Men									
Lack of instrumental support									
No	19,924	196	9.8 (8.5–11.3)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	2,188	21	9.6 (5.9–14.6)	0.97 (0.62–1.53)	0.75 (0.47–1.20)	0.70 (0.42–1.15)	0.74 (0.46–1.19)	0.71 (0.43–1.15)	0.78 (0.45–1.28)
Lack of emotional support									
No	18,887	182	9.6 (8.3–11.1)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	3,235	35	10.8 (7.5–15.0)	1.12 (0.78–1.61)	0.93 (0.63–1.35)	0.89 (0.59–1.33)	0.89 (0.61–1.31)	0.92 (0.63–1.35)	0.88 (0.59–1.32)
Lack of financial support									
No	17,020	148	8.7 (7.4–10.2)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	5,092	69	13.6 (10.6–17.1)	1.56 (1.17–2.07)	1.54 (1.14–2.07)	1.52 (1.11–2.07)	1.50 (1.12–2.03)	1.55 (1.15–2.11)	<u>1.51 (1.10–2.06)</u>
Lack of social integration									
No	21,372	205	9.6 (8.3–11.0)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	740	12	16.2 (8.4–28.2)	1.68 (0.94–3.01)	1.92 (1.07–3.46)	2.13 (1.17–3.88)	1.59 (0.88–2.89)	2.10 (1.15–3.85)	2.14 (1.18–3.86)
Women									
Lack of instrumental support									
No	22,508	106	4.7 (3.9–5.7)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	3,424	16	4.7 (2.7–7.6)	0.99 (0.58–1.67)	1.12(0.65–1.93)	1.20 (0.69–2.07)	1.09 (0.62–1.91)	1.10 (0.63–1.94)	1.23 (0.69–2.19)
Lack of emotional support									
No	21,661	110	5.1 (4.2–6.1)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	4,271	12	2.8 (1.5–4.9)	0.55 (0.30–1.01)	0.57 (0.31–1.06)	0.58 (0.31–1.08)	0.53 (0.28–1.01)	0.53 (0.28–1.01)	0.51 (0.26–1.02)
Lack of financial support									
No	20,921	100	4.8 (3.9–5.8)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	5,011	22	4.4 (2.8–6.6)	0.91 (0.58–1.45)	0.89 (0.55–1.42)	0.82 (0.50–1.33)	0.94 (0.58–1.51)	0.87 (0.53–1.43)	0.80 (0.47–1.34)
Lack of social integration									
No	23,402	106	4.5 (3.7–5.5)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	2,530	16	6.3 (3.6–10.2)	1.40 (0.83–2.37)	1.12 (0.66–1.90)	1.01 (0.59–1.73)	0.93 (0.52–1.64)	0.98 (0.57–1.67)	1.18 (0.67–2.09)

Minimally adjusted: adjusting for age and social integration or social support, respectively; Biological factors: minimally adjusted + systolic blood pressure, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, glycated hemoglobin, body-mass-index, antihypertensive medication, lipid-lowering medication, antidiabetic medication); Health behavior: minimally adjusted + alcohol consumption, current smoking, regular physical activity; Socioeconomic: minimally adjusted + income, education, employment; Depression: minimally adjusted + depression, antidepressants, anxiolytics. CI=confidence interval; HR=hazards ratio.

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eTable 2. Association of different types of social support and social integration with cardiovascular events stratified by age

Social support	Person-years N	Cardiovascular events N	Crude incidence rate per 1000 person-years (95% CI)	Unadjusted HR (95% CI)	Minimal adjusted HR (95% CI)	Biological factors HR (95% CI)	Health behavior HR (95% CI)	Socioeconomic HR (95% CI)	Depression HR (95% CI)
<65 years									
Lack of instrumental support									
No	32,390	157	4.8 (4.1–5.7)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	4,010	13	3.2 (1.7–5.5)	0.67 (0.38–1.17)	0.72 (0.40–1.30)	0.69 (0.37–1.29)	0.70 (0.39–1.27)	0.58 (0.30–1.09)	0.72 (0.39–1.34)
Lack of emotional support									
No	30,913	154	5.0 (4.2–5.8)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	5,488	16	2.9 (1.7–4.4)	0.58 (0.35–0.98)	0.58 (0.34–0.99)	0.57 (0.32–1.01)	0.58 (0.34–0.99)	0.62 (0.36–1.06)	0.52 (0.29–0.94)
Lack of financial support									
No	28,980	123	4.2 (3.5–5.1)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	7,421	47	6.3 (4.7–8.6)	1.49 (1.06–2.08)	1.53 (1.08–2.16)	1.50 (1.05–2.15)	1.53 (1.08–2.17)	1.58 (1.11–2.26)	1.52 (1.05–2.19)
Lack of social integration									
No	34,201	157	4.6 (3.9–5.4)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	2,200	13	5.9 (3.1–10.1)	1.28 (0.73–2.26)	1.79 (1.01–3.18)	1.85 (1.03–3.33)	1.61 (0.90–2.88)	1.87 (1.04–3.37)	1.90 (1.06–3.41)
≥65 years									
Lack of instrumental support									
No	10,042	145	14.4 (12.2–17.0)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	1,602	24	15.0 (9.6–22.2)	1.04 (0.67–1.60)	1.01 (0.64–1.59)	0.98 (0.61–1.56)	1.01 (0.63–1.59)	1.08 (0.68–1.70)	1.15 (0.71–1.86)
Lack of emotional support									
No	9,625	138	14.3 (12.1–16.9)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	2,018	31	15.4 (10.5–21.7)	1.07 (0.72–1.58)	0.98 (0.65–1.48)	0.93 (0.61–1.43)	0.91 (0.60–1.39)	0.90 (0.59–1.37)	0.92 (0.63–1.53)
Lack of financial support									
No	8,961	125	13.9 (11.6–16.6)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	2,682	44	16.4 (11.9–22.0)	1.17 (0.83–1.65)	1.12 (0.78–1.60)	1.07 (0.74–1.55)	1.13 (0.79–1.63)	1.07 (0.74–1.55)	1.04 (0.70–1.53)
Lack of social integration									
No	10,573	154	14.6 (12.4–17.0)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	1,070	15	14.0 (7.9–23.0)	0.97 (0.57–1.64)	1.10 (0.64–1.91)	1.14 (0.65–2.00)	0.86 (0.48–1.56)	1.02 (0.58–1.77)	1.26 (0.70–2.28)

Minimally adjusted: adjusting for sex and social integration or social support, respectively; Biological factors: minimally adjusted + systolic blood pressure, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, glycated hemoglobin, body-mass-index, antihypertensive medication, lipid-lowering medication, antidiabetic medication); Health behavior: minimally adjusted + alcohol consumption, current smoking, regular physical activity; Socioeconomic: minimally adjusted + income, education, employment; Depression: minimally adjusted + depression, antidepressants, anxiolytics. CI=confidence interval; HR=hazards ratio.

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eTable 3. Association of different types of social support and social integration with all-cause mortality stratified by sex

Social support	Person-years N	Deaths N	Crude incidence rate per 1000 person-years (95% CI)	Unadjusted HR (95% CI)	Minimal adjusted HR (95% CI)	Biological factors HR (95% CI)	Health behavior HR (95% CI)	Socioeconomic HR (95% CI)	Depression HR (95% CI)
Men									
Lack of instrumental support									
No	21,184	263	12.4 (11.0–14.0)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	2,343	35	14.9 (10.4–20.7)	1.21 (0.85–1.73)	0.86 (0.59–1.25)	0.76 (0.51–1.12)	0.85 (0.58–1.22)	0.73 (0.49–1.08)	0.82 (0.55–1.22)
Lack of emotional support									
No	20,124	238	11.8 (10.4–13.4)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	3,403	60	17.6 (13.5–22.6)	1.51 (1.14–2.01)	1.24 (0.92–1.66)	1.32 (0.97–1.81)	1.26 (0.94–1.70)	1.14 (0.84–1.56)	1.23 (0.91–1.67)
Lack of financial support									
No	17,961	211	11.7 (10.2–13.4)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	5,566	87	15.6 (12.5–19.2)	1.34 (1.04–1.72)	1.17 (0.90–1.52)	1.17 (0.89–1.53)	1.10 (0.85–1.44)	1.17 (0.90–1.54)	1.21 (0.92–1.59)
Lack of social integration									
No	22,701	278	12.2 (10.9–13.8)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	826	20	24.2 (14.9–37.2)	2.08 (1.32–3.27)	2.45 (1.54–3.87)	2.90 (1.79–4.69)	1.87 (1.17–2.99)	1.99 (1.20–3.29)	2.46 (1.51–4.00)
Women									
Lack of instrumental support									
No	23,400	190	8.1 (7.0–9.4)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	3,625	42	11.6 (8.4–15.6)	1.46 (1.05–2.04)	1.31(0.92–1.87)	1.37 (0.96–1.97)	1.26 (0.87–1.81)	1.37 (0.95–1.97)	1.18 (0.80–1.75)
Lack of emotional support									
No	22,613	189	8.4 (7.2–9.6)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	4,412	43	9.7 (7.1–13.1)	1.18 (0.85–1.65)	1.17 (0.82–1.67)	1.17 (0.82–1.69)	1.14 (0.79–1.65)	1.10 (0.76–1.60)	1.20 (0.82–1.77)
Lack of financial support									
No	21,772	183	8.4 (7.2–9.7)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	5,254	49	9.3 (6.9–12.3)	1.14 (0.83–1.56)	0.99 (0.71–1.36)	0.93 (0.66–1.29)	0.86 (0.61–1.21)	1.01 (0.72–1.41)	0.91 (0.64–1.29)
Lack of social integration									
No	24,316	199	8.2 (7.1–9.4)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	2,710	33	12.2 (8.4–17.1)	1.52 (1.05–2.19)	1.11 (0.77–1.62)	0.99 (0.68–1.45)	0.94 (0.63–1.39)	1.00 (0.68–1.48)	1.03 (0.68–1.55)

Minimally adjusted: adjusting for age and social integration or social support, respectively; Biological factors: minimally adjusted + systolic blood pressure, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, glycated hemoglobin, body-mass-index, antihypertensive medication, lipid-lowering medication, antidiabetic medication); Health behavior: minimally adjusted + alcohol consumption, current smoking, regular physical activity; Socioeconomic: minimally adjusted + income, education, employment; Depression: minimally adjusted + depression, antidepressants, anxiolytics. CI=confidence interval; HR=hazards ratio.

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eTable 4. Association of different types of social support and social integration with mortality stratified by age

Social support	Person-years N	Deaths N	Crude incidence rate per 1000 person-years (95% CI)	Unadjusted HR (95% CI)	Minimal adjusted HR (95% CI)	Biological factors HR (95% CI)	Health behavior HR (95% CI)	Socioeconomic HR (95% CI)	Depression HR (95% CI)
<65 years									
Lack of instrumental support									
No	33,829	206	6.1 (5.3–7.0)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	4,200	32	7.6 (5.2–10.7)	1.28 (0.88–1.86)	1.21 (0.81–1.80)	1.27 (0.84–1.90)	1.04 (0.69–1.57)	1.08 (0.71–1.65)	1.18 (0.77–1.79)
Lack of emotional support									
No	32,341	196	6.1 (5.2–7.0)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	5,688	42	7.4 (5.3–10.0)	1.23 (0.88–1.72)	1.18 (0.82–1.68)	1.20 (0.83–1.73)	1.18 (0.82–1.70)	1.13 (0.78–1.63)	1.11 (0.76–1.63)
Lack of financial support									
No	30,142	186	6.2 (5.3–7.1)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	7,887	52	6.6 (4.9–8.6)	1.09 (0.80–1.48)	0.94 (0.68–1.29)	0.96 (0.69–1.33)	0.89 (0.64–1.23)	0.96 (0.69–1.33)	0.99 (0.72–1.38)
Lack of social integration									
No	35,673	214	6.0 (5.2–6.9)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	2,356	24	10.2 (6.5–15.1)	1.73 (1.14–2.64)	1.87 (1.22–2.88)	1.92 (1.24–2.98)	1.57 (1.02–2.43)	1.74 (1.12–2.71)	1.96 (1.27–3.04)
≥65 years									
Lack of instrumental support									
No	10,755	247	23.0 (20.2–26.0)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	1,769	45	25.4 (18.6–33.9)	1.10 (0.80–1.51)	0.96 (0.67–1.33)	0.86 (0.60–1.21)	0.96 (0.68–1.35)	0.95 (0.67–1.34)	0.84 (0.58–1.21)
Lack of emotional support									
No	10,397	231	22.2 (19.5–25.2)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	2,127	61	28.7 (22.0–36.7)	1.32 (0.99–1.75)	1.21 (0.90–1.63)	1.29 (0.95–1.76)	1.24 (0.92–1.68)	1.10 (0.81–1.50)	1.30 (0.95–1.78)
Lack of financial support									
No	9,591	208	21.7 (18.9–24.8)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	2,933	84	28.6 (22.9–35.3)	1.33 (1.03–1.71)	1.22 (0.94–1.60)	1.15 (0.87–1.52)	1.13 (0.85–1.49)	1.21 (0.91–1.59)	1.16 (0.88–1.54)
Lack of social integration									
No	11,343	263	23.2 (20.5–26.1)	Reference	Reference	Reference	Reference	Reference	Reference
Yes	1,180	29	24.6 (16.5–35.1)	1.08 (0.74–1.59)	1.17 (0.78–1.74)	1.06 (0.69–1.63)	0.99 (0.65–1.51)	0.96 (0.62–1.48)	0.97 (0.61–1.55)

Minimally adjusted: adjusting for sex, and social integration or social support, respectively; Biological factors: minimally adjusted + systolic blood pressure, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, glycated hemoglobin, body-mass-index, antihypertensive medication, lipid-lowering medication, antidiabetic medication); Health behavior: minimally adjusted + alcohol consumption, current smoking, regular physical activity; Socioeconomic: minimally adjusted + income, education, employment; Depression: minimally adjusted + depression, antidepressants, anxiolytics. CI=confidence interval; HR=hazards ratio.

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