**Determinants of social health trajectories during the COVID-19 pandemic in older adults: The Rotterdam Study**

**Supplementary material**

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**Appendix A.** Supplemental methods

**Supplementary Table 1.** Physical distancing measures for COVID-19 prevention in the Netherlands in March – July 2020.

**Supplementary Table 2.** Associations of determinants with rate of change of perceived social isolation and loneliness trajectories

**Supplementary Table 3.** Associations of determinants with rate of change of social connectedness trajectories

**Supplementary Table 4.** Associations of determinants with rate of change of loneliness trajectories (CES-D)

**Supplementary Figure 1.** Flow chart of the study population

**Appendix A. Supplemental methods**

1. **Covariate assessment**

Intracranial volume was defined as the sum of total brain volume and cerebrospinal fluid (CSF) was used as a proxy for head size. Smoking habits were categorized as never, former or current smoker. Alcohol consumption in gram per day was categorized as none (no alcoholic drinks), moderate (≤1 drink/day) or heavy (>1 drink/day). Body height and weight were measured during the research visit and used to calculate body mass index (BMI in kg/m2). We calculated a multimorbidity score, based on the Healthy Aging Score’s chronic disease domain, which was previously developed in the Rotterdam Study and is described in detail elsewhere.(Jaspers *et al.*, 2017) In brief, chronic diseases were included in this score based on their burden and chronicity and multimorbidity was classified into three categories: low (no chronic diseases), moderate (one chronic disease) and high (more than one chronic disease). In the current study we included cancer, coronary heart disease, heart failure, stroke and Parkinson’s Disease. We did not have data on chronic obstructive pulmonary disease, chronic kidney disease and diabetes mellitus type 2 for the entire study sample and therefore did not included these in the score. CES-D score at time of the MRI was included as depressive symptoms are associated with brain structure and may be associated with social health at a later time point.(Schmaal *et al.*, 2017) Ethnicity was determined using genotype data and ancestral groups were defined as European, Asian, African or mixed (individuals with less than 50% genetic material from any ancestry).

1. **Linear mixed models: random effects structure**

In the random effects structure, we tested for random linear slopes and covariance matrices. Best model fit was achieved with random intercepts and random linear slopes for all linear mixed models, except for *Giving/receiving help during coronavirus infection* (best fit with random intercept only). The linear mixed model (LMM) for *Feeling connected to others* was modeled with a symmetrical covariance matrix, all other LMMs used a diagonal covariance matrix. In the generalized estimating equations model, we applied a first-order autoregressive correlation matrix.

**Supplemental references**

**Jaspers, L.*, et al.*** (2017). Development of a Healthy Aging Score in the Population-Based Rotterdam Study: Evaluating Age and Sex Differences. *J Am Med Dir Assoc*, 18, 276 e271-276 e277.

**Schmaal, L.*, et al.*** (2017). Cortical abnormalities in adults and adolescents with major depression based on brain scans from 20 cohorts worldwide in the ENIGMA Major Depressive Disorder Working Group. *Molecular Psychiatry*, 22, 900-909.

**Supplementary Table 1. Physical distancing measures in the Netherlands**

|  |  |  |
| --- | --- | --- |
| **Date** |  | **Regulation** |
| 12 March 2020 |  | * Stay home with symptoms (symptoms of a cold, coughing, fever, sore throat).
* Avoid physical contact with others.
* Work from home as much as possible.
* Universities: offer education online.
* Events with more than 100 persons are cancelled.
* Frail persons: avoid large groups and public transport.
 |
| 15 March 2020 |  | * Keep 1.5 meter distance if possible.
* Schools (primary, secondary and higher education) close.
* Daycares close (exception for children of essential workers).
* All cafés and restaurants, sports and fitness clubs, saunas, sex clubs and coffee shops close.
 |
| 18 March 2020 |  | Borders close for non-essential travel from outside EU |
| 19 March 2020 |  | Nursing homes and small scale housing will be closed for visitors and others not required for essential care.  |
| 23 March 2020 |  | **Intelligent lockdown*** Stay home as much as possible.
* Going outside is allowed, but not in a group.
* Only go outside for groceries, to care for others or for work if you cannot work from home.
* Keep 1.5 meters distance and avoid social activities and groups of people.
* Maximum of three visitors at home allowed, distance needs to be kept.
* If one person in the household has fever, everyone must stay home.
* All events are forbidden until June 1. Exception for funerals and church weddings (maximum of 30 persons allowed).
* Shops and public measures must ensure 1.5 meters distance between visitors.
* Hairdressers, beauticians and other contact professions close. Physiotherapists provide telemedicine as much as possible.
 |
| 11 May 2020 |  | **First restrictions are eased*** Visitor regulation in care homes is tested.
* Outdoor exercise in groups with 1.5 meter distance is allowed.
* Outdoor youth activities (13-18 year olds) with 1.5 meter distance are allowed.
* Contact professions can start again.
* Libraries open.
* Primary education and daycares open with limited group sizes.
* Special education in primary education opens.
 |
| 1 June 2020 |  | **Restrictions are eased for second time*** Outdoor group gathering is allowed with 1.5 meter distance.
* Outdoor exercise without distance for 13-18-year-olds.
* Restaurants open: max 30 visitors indoors, unlimited visitors outdoors.
* Cultural institutions open with 1.5 meter distance with ticket sales and medical check. Maximum number of visitors depends on building structure.
* Public transport: face mask obligatory from 13 years and older. Non-essential travel and travel during rush hour is discouraged.
* Everyone with symptoms can be tested.
* Secondary (special) education opens with 1.5 meter distance.
 |
| 8 June 2020 |  | * Primary education and daycares open 100%.
 |
| 15 June 2020 |  | * Higher education can start exams, practical lessons and guidance of vulnerable students.
* Music schools and art centers open.
* Visitor regulations for nursing homes are eased.
* Testing is allowed with mild symptoms, including loss of sense of smell or taste.
* Travel to 16 countries within EU/Schengen Zone is allowed.
 |
| 1 July 2020 |  | **Restrictions are eased for third time*** Movie theaters, restaurants, cultural institutions, organized social gatherings are allowed with maximum 100 visitors indoors.
* All cafés and restaurants, sports and fitness clubs, saunas, casinos open.
* Keeping 1.5 meters distance without a maximum number of visitors in indoor and outdoor public places where visitors move through (e.g. libraries, shops, museums).
* Outdoor public places: maximum of 250 visitors with assigned seating, medical check and reservation.
* No requirement for 1.5 meters distance for children up to age of 12 with each other and adults. Children up to 18 do not need to keep distance from other children, but do keep distance to adults.
* Travel entry ban is eased.
* 1.5 distance needs to be kept at all times, with exceptions for e.g. people within the same household, caretakers and patients, contact professions.
 |

**Supplementary Table 2. Associations of determinants with rate of change of perceived social isolation and loneliness trajectories**

Mean diff. denotes mean difference in social health marker over time per determinant (interaction of determinant\*time). Basic models are age- and sex-adjusted. Mutually adjusted models are mutually adjusted for all determinants presented.

\* Brain health analyses were performed in a subset of 1,720 participants. Models were adjusted for age, sex, ethnicity, time difference between scan and COVID-19 baseline, education level, employment status, household size, marital status, prior loneliness, clinically relevant depressive symptoms at scan, smoking at scan, alcohol consumption at scan, BMI at scan, multimorbidity at scan. Total brain volume, gray matter and white matter volume were additionally adjusted for intracranial volume. Brain health models were not mutually adjusted.

Statistically significant associations after multiple testing correction in bold (p<0.0032).

|  |  |  |  |
| --- | --- | --- | --- |
|  | Perceived social isolation |  | UCLA Loneliness Scale |
|  | Basic model, |  | Mutually adjusted, |  | Basic model, |  | Mutually adjusted, |
|  | Mean diff. (95%CI) |  | Mean diff. (95%CI) |  | Mean diff. (95%CI) |  | Mean diff. (95%CI) |
| **Sociodemographic** |  |  |  |  |  |  |  |
| Time\*Age (centered) | 0.002 (0.000; 0.003) |  | 0.002 (-0.001; 0.004) |  | 0.000 (0.000; 0.001) |  | 0.001 (0.000; 0.003) |
| Time\*Sex (female) | 0.025 (-0.009; 0.058) |  | 0.021 (-0.015; 0.055) |  | -0.012 (-0.029; 0.004) |  | -0.006 (-0.023; 0.012) |
| *Employment (reference: employed)* |
| Time\*On sick leave | 0.001 (-0.156; 0.157) |  | -0.003 (-0.160; 0.154) |  | -0.029 (-0.108; 0.050) |  | -0.020 (-0.099; 0.060) |
| Time\*Unemployed | -0.054 (-0.155; 0.047) |  | -0.047 (-0.148; 0.055) |  | -0.035 (-0.086; 0.015) |  | -0.026 (-0.077; 0.025) |
| Time\*Retired | 0.047 (0.011; 0.083) |  | 0.031 (-0.026; 0.088) |  | 0.001 (-0.017; 0.019) |  | -0.012 (-0.041; 0.017) |
| Time\*Other | **0.126 (0.044; 0.209)** |  | 0.120 (0.035; 0.205) |  | -0.005 (-0.046; 0.037) |  | 0.001 (-0.041; 0.044) |
| *Education (reference: primary education)* |
| Time\*Lower-intermediate | 0.021(-0.058; 0.100) |  | 0.031 (-0.048; 0.110) |  | 0.014 (-0.026; 0.053) |  | 0.011 (-0.028; 0.051) |
| Time\*Intermediate-higher | 0.012 (-0.067; 0.092) |  | 0.034 (-0.045; 0.114) |  | 0.021 (-0.019; 0.061) |  | 0.018 (-0.022; 0.058) |
| Time\*Higher-university | 0.058 (-0.022; 0.138) |  | 0.089 (-0.008; 0.171) |  | 0.039 (-0.001; 0.061) |  | 0.036 (-0.005; 0.076) |
| Time\*Pets (owns a pet) | 0.038 (0.003; 0.073) |  | **0.057 (0.020; 0.094)** |  | 0.003 (-0.015; 0.021) |  | 0.008 (-0.011; 0.026) |
| **Social health** |  |  |  |  |  |  |  |
| Time\*Prior loneliness | 0.003 (-0.047; 0.052) |  | -0.016 (-0.069; 0.037) |  | -0.012 (-0.036; 0.013) |  | 0.002 (-0.024; 0.029) |
| Time\*Housemates (yes) | -0.041 (-0.079; -0.004) |  | -0.034 (-0.086; 0.017) |  | 0.018 (-0.001; 0.037) |  | 0.028 (0.002; 0.053) |
| *Marital status (reference: Partner/married)* |
| Time\*Never married | 0.025 (-0.049; 0.100) |  | 0.008 (-0.073; 0.089) |  | -0.007 (-0.044; 0.031) |  | 0.015 (-0.026; 0.056) |
| Time\*Widowed/divorced | 0.010 (-0.036; 0.055) |  | -0.024 (-0.082; 0.033) |  | -0.009 (-0.031; 0.014) |  | 0.013 (-0.016; 0.042) |
| **Mental and cognitive health** |  |  |  |  |  |  |  |
| Time\*CES-D ≥ 16 | 0.026 (-0.019; 0.071) |  | 0.021 (-0.027; 0.068) |  | -0.028 (-0.051; -0.006) |  | -0.024 (-0.047; 0.000) |
| Time\*MMSE score | -0.005 (-0.015; 0.006) |  | -0.004 (-0.015; 0.007) |  | 0.003 (-0.002; 0.008) |  | 0.002 (-0.004; 0.007) |
| **Brain health** |  |  |  |  |  |  |  |
| Time\*Total brain volume |  |  | 0.003 (-0.026; 0.032) |  |  |  | -0.003 (-0.017; 0.012) |
| Time\*Intracranial volume |  |  | 0.009 (-0.020; 0.038) |  |  |  | 0.000 (-0.014; 0.014) |
| Time\*Gray matter volume |  |  | 0.001 (-0.027; 0.030) |  |  |  | -0.007 (-0.021; 0.007) |
| Time\*White matter volume |  |  | 0.004 (-0.025; 0.032) |  |  |  | 0.002 (-0.012; 0.016) |

**Supplementary Table 3. Associations of determinants with rate of change of social connectedness trajectories**

Mean diff. denotes mean difference in social connectedness over time per determinant (interaction of determinant\*time). Basic models are age- and sex-adjusted. Mutually adjusted models are mutually adjusted for all determinants presented.

\* Brain health analyses were performed in a subset of 1,720 participants. Models were adjusted for age, sex, ethnicity, time difference between scan and COVID-19 baseline, education level, employment status, household size, marital status, prior loneliness, clinically relevant depressive symptoms at scan, smoking at scan, alcohol consumption at scan, BMI at scan, multimorbidity at scan. Total brain volume, gray matter and white matter volume were additionally adjusted for intracranial volume. Brain health models were not mutually adjusted.

Statistically significant associations after multiple testing correction in bold (p<0.0032).

|  |  |  |  |
| --- | --- | --- | --- |
|  | Feeling connected to others |  | Giving/receiving help during COVID-19 infection |
|  | Basic model, |  | Mutually adjusted, |  | Basic model, |  | Mutually adjusted, |
|  | Mean diff. (95%CI) |  | Mean diff. (95%CI) |  | Mean diff. (95%CI) |  | Mean diff. (95%CI) |
| **Sociodemographic** |  |  |  |  |  |  |  |
| Time\*Age | 0.000 (-0.001; 0.000) |  | 0.000 (-0.001; 0.001) |  | 0.000 (-0.001; 0.001) |  | 0.000 (-0.001; 0.001) |
| Time\*Sex (female) | -0.002 (-0.015; 0.012) |  | 0.004 (-0.018; 0.011) |  | 0.011 (-0.002; 0.024) |  | 0.010 (-0.004; 0.024) |
| *Employment (reference: employed)* |
| Time\*On sick leave | 0.017 (-0.047; 0.082) |  | 0.018 (-0.047; 0.082) |  | 0.006 (-0.056; 0.068) |  | -0.001 (-0.063; 0.062) |
| Time\*Unemployed | 0.055 (0.014; 0.097) |  | 0.059 (0.018; 0.101) |  | -0.010 (-0.049; 0.030) |  | -0.012 (-0.052; 0.028) |
| Time\*Retired | -0.001 (-0.016; 0.014) |  | 0.006 (-0.017; 0.030) |  | -0.001 (-0.015; 0.013) |  | 0.002 (-0.021; 0.024) |
| Time\*Other | 0.039 (0.005; 0.072) |  | 0.042 (0.008; 0.077) |  | 0.014 (-0.018; 0.046) |  | 0.009 (-0.024; 0.043) |
| *Education (reference: primary education)* |
| Time\*Lower-intermediate | 0.018 (-0.014; 0.050) |  | 0.022 (-0.010; 0.054) |  | -0.007 (-0.038; 0.024) |  | -0.003 (-0.035; 0.028) |
| Time\*Intermediate-higher | 0.028 (-0.004; 0.060) |  | 0.033 (0.001; 0.066) |  | -0.005 (-0.036; 0.026) |  | 0.000 (-0.031; 0.032) |
| Time\*Higher-university | 0.032 (0.000; 0.064) |  | 0.039 (0.006; 0.072) |  | -0.012 (-0.043; 0.019) |  | -0.004 (-0.036; 0.028) |
| Time\*Pets (owns a pet) | 0.007 (-0.008; 0.021) |  | 0.007 (-0.009; 0.022) |  | 0.000 (-0.014; 0.014) |  | -0.002 (-0.016; 0.013) |
| **Social health** |  |  |  |  |  |  |  |
| Time\*Prior loneliness | 0.013 (-0.008; 0.033) |  | 0.007 (-0.015; 0.028) |  | -0.002 (-0.022; 0.017) |  | -0.010 (-0.031; 0.011) |
| Time\*Housemates (yes) | -0.006 (-0.022; 0.009) |  | -0.009 (-0.030; 0.012) |  | 0.001 (-0.014; 0.016) |  | 0.012 (-0.009; 0.032) |
| *Marital status (reference: Partner/married)* |
| Time\*Never married | 0.018 (-0.013; 0.048) |  | 0.008 (-0.025; 0.041) |  | 0.001 (-0.028; 0.030) |  | 0.006 (-0.026; 0.038) |
| Time\*Widowed/divorced | 0.001 (-0.017; 0.020) |  | -0.005 (-0.029; 0.018) |  | 0.012 (-0.006; 0.030) |  | 0.018 (-0.005; 0.040) |
| **Mental and cognitive health** |  |  |  |  |  |  |  |
| Time\*CES-D ≥ 16 | 0.011 (-0.007; 0.029) |  | 0.006 (-0.014; 0.025) |  | 0.011 (-0.007; 0.028) |  | 0.009 (-0.009; 0.028) |
| Time\*MMSE score | -0.002 (-0.006; 0.003) |  | -0.002 (-0.007; 0.002) |  | -0.005 (-0.009; 0.000) |  | -0.005 (-0.009; 0.000) |
| **Brain health\*** |  |  |  |  |  |  |  |
| Time\*Total brain volume |  |  | 0.014 (0.002; 0.026) |  |  |  | 0.015 (0.003; 0.026) |
| Time\*Intracranial volume |  |  | 0.012 (0.000; 0.024) |  |  |  | **0.017 (0.006; 0.029)** |
| Time\*Gray matter volume |  |  | 0.013 (0.002; 0.025) |  |  |  | 0.008 (-0.003; 0.019) |
| Time\*White matter volume |  |  | 0.010 (-0.002; 0.022) |  |  |  | 0.016 (0.005; 0.028) |

**Supplementary Table 4. Associations of determinants with rate of change of loneliness trajectories (CES-D)**

OR denotes odds ratio for loneliness over time per determinant (interaction of determinant\*time). Basic models are age- and sex-adjusted. Mutually adjusted models are mutually adjusted for all determinants presented.

\* Brain health analyses were performed in a subset of 1,720 participants. Models were adjusted for age, sex, ethnicity, time difference between scan and COVID-19 baseline, education level, employment status, household size, marital status, prior loneliness, clinically relevant depressive symptoms at scan, smoking at scan, alcohol consumption at scan, BMI at scan, multimorbidity at scan. Total brain volume, gray matter and white matter volume were additionally adjusted for intracranial volume. Brain health models were not mutually adjusted.

Statistically significant associations after multiple testing correction in bold (p<0.0032).

|  |  |  |
| --- | --- | --- |
|  |  | Loneliness (CES-D) |
|  |  | Basic model, |  | Mutually adjusted, |
|  |  | OR (95%CI) |  | OR (95%CI) |
| **Sociodemographic** |  |  |  |  |
| Time\*Age |  | 1.00 (1.00; 1.00) |  | 1.00 (1.00; 1.00) |
| Time\*Sex (female) |  | 0.98 (0.94; 1.02) |  | 0.97 (0.93; 1.02) |
| *Employment (reference: employed)* |  |  |  |  |
| Time\*On sick leave |  | 0.92 (0.77; 1.10) |  | 0.88 (0.73; 1.07) |
| Time\*Unemployed |  | 1.04 (0.93; 1.17) |  | 1.06 (0.93; 1.22) |
| Time\*Retired |  | 1.00 (0.95; 1.04) |  | 0.99 (0.91; 1.07) |
| Time\*Other |  | 0.97 (0.88; 1.06) |  | 0.99 (0.88; 1.10) |
| *Education (reference: primary education)* |  |  |  |  |
| Time\*Lower-intermediate |  | 0.98 (0.90; 1.08) |  | 0.99 (0.88; 1.10) |
| Time\*Intermediate-higher |  | 0.98 (0.89; 1.07) |  | 0.99 (0.89; 1.11) |
| Time\*Higher-university |  | 0.99 (0.90; 1.09) |  | 1.01 (0.90; 1.13) |
| Time\*Pets (owns a pet) |  | 1.02 (0.97; 1.06) |  | 1.02 (0.97; 1.07) |
| **Social health** |  |  |  |  |
| Time\*Prior loneliness |  | 1.00 (0.95; 1.06) |  | 1.01 (0.94; 1.08) |
| Time\*Housemates (yes) |  | 1.05 (1.00; 1.09) |  | 1.09 (1.02; 1.17) |
| *Marital status (reference: Partner/married)* |  |  |  |  |
| Time\*Never married |  | 0.96 (0.88; 1.04) |  | 1.01 (0.91; 1.13) |
| Time\*Widowed/divorced |  | 0.97 (0.93; 1.02) |  | 1.04 (0.96; 1.12) |
| **Mental and cognitive health** |  |  |  |  |
| Time\*CES-D ≥ 16 |  | 0.96 (0.91; 1.01) |  | 0.94 (0.89; 1.00) |
| Time\*MMSE score |  | 0.99 (0.98; 1.01) |  | 0.99 (0.98; 1.01) |
| **Brain health** |  |  |  |  |
| Time\*Total brain volume |  |  |  | 0.97 (0.94; 1.00) |
| Time\*Intracranial volume |  |  |  | 0.99 (0.96; 1.02) |
| Time\*Gray matter volume |  |  |  | 0.98 (0.95; 1.01) |
| Time\*White matter volume |  |  |  | 0.97 (0.94; 1.00) |

**Supplementary Figure 1. Flow chart of the study population**

Received COVID-19 baseline questionnaire

N=8,732

Social data incomplete N=1,222

* *UCLA score*
* *CESD loneliness*
* *social connectedness*
* *social isolation scale*

rs\_cohort and sex missing, N=2

Filled out Q1

N=6,241

**Follow-up questionnaires**

Complete social data Q2, N=3,784

Complete social data Q3, N=3,157

Complete social data Q1

N=5,017

Underwent brain MRI 2010-2017

N=2,047

Missing segmentation data or data of insufficient quality, N=276

Prevalent dementia diagnosis during time of scan, N=12

Cortical brain infarcts on MRI scan, N=39

Sample without cortical infarcts

N=1,732

Sample with structural imaging data, N=1,771

Study sample for imaging analyses, N=1,720