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Association between social isolation and depressive symptom onset among older adults: A cross national longitudinal study in England and Japan

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6 **1 Original research**

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9 **2 Title**

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12 **3 Association between social isolation and depressive symptom onset among older adults:**

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15 **4 A cross-national longitudinal study in England and Japan**

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35 **ABSTRACT**

36 **Objective:** Social isolation is a risk factor for depressive symptoms in older age. However,
37 little is known about whether its impact varies depending on country-specific cultural
38 contexts of social relationships, such as friendships or family-based relationships. This
39 study examined the association of social isolation with depressive symptom onset in older
40 adults in England, which values friendship-based relationships, and Japan, where family-
41 based relationships are emphasised.

42 **Design:** Prospective longitudinal study.

43 **Setting:** We utilized data from two ongoing studies: the English Longitudinal Study of
44 Ageing (ELSA) and the Japan Gerontological Evaluation Study (JAGES).

45 **Participants:** Older adults aged ≥ 65 years without depressive symptoms at baseline were
46 followed up regarding depressive symptom onset for two years (2010/11 to 2012/13) for
47 the ELSA and 2.5 years (2010/11 to 2013) for the JAGES.

48 **Primary outcome measure:** Depressive symptoms were assessed with the Center for
49 Epidemiologic Studies Depression Scale for the ELSA and Geriatric Depression Scale
50 for the JAGES. Multivariable logistic regression analysis was performed to evaluate
51 social isolation using multiple parameters (marital status; interaction with children,
52 relatives, and friends; and social participation).

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7 53 **Results:** The data of 3,331 respondents from the ELSA and 33,127 from the JAGES were
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9 54 analysed. Multivariable logistic regression analysis demonstrated that social isolation was
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12 55 significantly associated with depressive symptom onset in both countries. In the ELSA,
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15 56 poor interaction with children marginally affected depressive symptom onset, while in
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18 57 the JAGES, poor interaction with children and no social participation significantly
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21 58 affected depressive symptom onset.
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24 59 **Conclusions:** Despite variations in cultural background, social isolation was associated
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27 60 with depressive symptom onset in both England and Japan. Addressing social isolation
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30 61 to safeguard older adults' mental health must be globally prioritised.
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34 63 **Strengths and limitations of this study**

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37 64 ● This is the first cross-national longitudinal study to examine the association between
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42 65 social isolation and depressive symptom onset in England, which values friendship-
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45 66 based relationships, and Japan, where family-based relationships are emphasised.
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49 67 ● This study included a large sample of over 3,300 people from England and 33,000
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52 68 people from Japan aged 65 years and older.
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55 69 ● A limitation of this study is that we cannot make direct comparisons because of
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58 70 variations in cohort follow-up periods and depressive symptom measurement.
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7 71 ● Another limitation is the substitution of social support for the evaluation of social
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9 72 contact so as to use the same social isolation assessment scale in both countries.
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74 INTRODUCTION

75 With population ageing, there is growing worldwide interest in social issues concerning
76 older adults, including social isolation and the deterioration of physical and mental health.
77 Defined as an objective state where an individual has few close relationships or limited
78 contact within a community,[1] social isolation is recognised as a social determinant of
79 health with relevance to mortality,[2] cardiovascular diseases,[3] dementia,[4] and mental
80 health.[5, 6] Social isolation is a major risk factor for mental health problems in older
81 age. Several systematic reviews have shown that social isolation is associated with
82 depressive symptoms,[5, 6] which, in turn, are correlated with unhealthy behaviours and
83 reduced access to material resources.[7] Depressive symptoms, common in later life, are
84 related to adverse health outcomes such as poor quality of life[8] and functional
85 disability.[9] With the high current global burden of depression expected to increase
86 further by 2030,[10] addressing social isolation is an important gerontological issue for
87 protecting mental health in older adults.

88 The impacts of social isolation on health may vary by country; these differences
89 arise from the culture relating to social networks within and outside the family. A previous
90 cross-national study showed that in the UK, friendship-based social relationships had a
91 significant impact on longevity, whereas in Japan, this impact was associated with family-

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6 92 based social relationships.[11] Another study comparing American and Japanese older
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9 93 adults suggested that the presence of children was associated with depressive symptoms
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12 94 only among the latter.[12] As Japan has retained the traditionally strong influence of
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15 95 family and kinship systems on society[13] and the expected reciprocity between adult
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18 96 children and their parents remains a dominant feature,[14] the emphasis on family-based
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21 97 relationships is stronger than it is in the West.
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24 98 Moreover, the social structure surrounding social isolation varies from country to
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27 99 country. Recognising the impact of social isolation on health and economic loss, the UK
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30 100 established the position of ‘Minister of Loneliness’ in 2018 and is taking a progressive
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33 101 approach to eliminating social isolation.[15] In contrast, Japan, now a super-aged society,
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36 102 is experiencing a rapid increase in the trend of abstaining from marriage and weakening
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39 103 community and neighbourhood relations,[16] leading to a rise in the number of socially
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42 104 isolated people.[17] In Japan, the proportion of people who rarely or never spent time
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45 105 with those close to them was the highest among Organisation for Economic Co-operation
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48 106 and Development countries. In particular, this figure was much higher than in the UK,
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51 107 which has made advances in tackling social isolation (Japan = 15.3%, UK = 5.0%).[18]
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54 108 Owing to differences in the cultural contexts of social relationships and structures, the
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57 109 impact of social isolation on depressive symptoms is expected to vary across countries.
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6 110 As the association between social isolation and depressive symptoms is often
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9 111 described as bidirectional,[19] longitudinal studies are needed to determine causality.
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12 112 However, previous cross-national comparative studies have only employed cross-
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15 113 sectional designs.[12] Therefore, using longitudinal data from both countries, the present
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18 114 study aims to investigate the association of social isolation with depressive symptom
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21 115 onset in England, where the emphasis is on friendship-based relationships, and Japan,
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24 116 which prioritises familial relationships.
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30 118 **METHODS**33 119 **Sample**

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36 120 This longitudinal study was conducted using data from two ongoing prospective cohort
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39 121 studies: the English Longitudinal Study of Ageing (ELSA) and the Japan Gerontological
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42 122 Evaluation Study (JAGES). The ELSA targets independent-living older adults aged ≥ 50 ,
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45 123 while JAGES participants are community-dwelling individuals aged ≥ 65 who are
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48 124 ineligible for long-term healthcare insurance benefits.[20] Details of the ELSA and
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51 125 JAGES can be found elsewhere.[21, 22] For the present analysis, we used the two waves
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54 126 of data that most closely corresponded with the timing of our study: wave 5 (2010/2011)
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57 127 to wave 6 (2012/2013) for the ELSA, and wave 1 (2010/2011) to wave 2 (2013) for the
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6 128 JAGES. We harmonised the data by including older adults aged ≥ 65 , independent in
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9 129 activities of daily living, and without self-reported dementia. Respondents with
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12 130 depressive symptoms at baseline were excluded, and we followed up the onset of
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15 131 depressive symptoms for two years for the ELSA and 2.5 years for the JAGES.
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19 133 **Depressive symptoms**

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24 134 Based on a previous cross-national study,[23] depressive symptoms were measured both
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27 135 at baseline and follow-up using eight items from the Center for Epidemiologic Studies
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30 136 Depression Scale (CES-D) in the ELSA[24] and the Geriatric Depression Scale (GDS-
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33 137 15) in the JAGES.[25] To identify possible depressive cases, the CES-D cut-off was ≥ 4
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36 138 while that for the GDS-15 was ≥ 5 . [24]
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40 140 **Social isolation**

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45 141 Social isolation levels were assessed using the modified Social Isolation Index (SII).[26]
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48 142 The index was computed with respondents given a point if they: (1) were unmarried or
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51 143 living alone, (2) had poor interaction with children (no children or no social support from
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54 144 children), (3) had poor interaction with relatives (no relatives or no social support from
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57 145 relatives), (4) had poor interaction with friends (less than monthly contact or no social
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6 146 support from friends), and (5) had no social participation (no participation in any social
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9 147 or religious groups). The total possible score ranged from 0 to 5, with higher scores
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12 148 indicating greater social isolation. The participants were categorised into the following
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15 149 five groups based on their scores: 0, 1, 2, 3, and 4–5 points. We used the total score and
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18 150 the scores of the five sub-components as predictive variables.
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22 23 24 152 **Covariates**

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27 153 The covariates included age, gender, educational attainment, household equivalised
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30 154 income, present illness, self-rated health, smoking, and drinking. Age was categorised as
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33 155 65–69, 70–74, 75–79, 80–84, and ≥ 85 . Based on the ages of respondents who had
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36 156 completed formal education, the age of final educational attainment was categorised as \leq
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39 157 15 years, 16–18 years, and ≥ 19 years. Household equivalised income was classified into
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42 158 quintiles. Present illness was classified as ‘yes’ or ‘no’ for cancer, heart disease, and
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45 159 stroke. Self-rated health was dichotomised as ‘poor’ and ‘good’. Smoking and drinking
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48 160 were dichotomised as ‘never/past’ and ‘current’.

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52 53 54 162 **Statistical analysis**

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57 163 We analysed the ELSA and JAGES data separately because of differences in research
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6 164 design, especially sampling approaches. A longitudinal weight was applied to account for
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9 165 survey non-response for the ELSA but not the JAGES as its design does not allow it.
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12 166 First, we calculated descriptive statistics. Second, we conducted a multivariate logistic
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15 167 regression analysis to examine the association between SII score and depressive symptom
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18 168 onset and obtained odds ratios (ORs) and 95% confidence intervals (CIs) for depressive
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21 169 symptom onset. Model 1 was not adjusted for covariates while Model 2 was adjusted for
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24 170 all covariates. Additionally, we analysed the association between SII sub-components and
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27 171 depressive symptom onset, adjusted for all covariates.

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30 172 To mitigate potential biases resulting from missing information, we used the
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33 173 multiple imputation approach under the missing at random assumption. We generated 20
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36 174 imputed datasets for the final analysis, which excluded those who met the exclusion
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39 175 criteria and did not respond to the follow-up surveys, using the multiple imputation by
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42 176 chained equations procedure and pooled the results using Rubin's rule.[27]

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45 177 The significance level was set at $p < 0.05$. We used R (Version 3.5.2 for
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48 178 Windows) for all statistical analyses.

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52 53 54 180 **Ethics issues**

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57 181 The ELSA investigators received ethical approval for all waves of the study from the
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6 182 National Health Service Research Ethics Committees under the National Research and
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9 183 Ethics Services (MREC/01/2/91). The JAGES protocols were approved by the Ethics
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12 184 Committee on the Research of Human Subjects at Nihon Fukushi University (10-05).
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17 186 **Patient and public involvement**

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21 187 No patients were involved in the development of the research question, study design, or
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24 188 data interpretation in this study.
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29 30 31 **RESULTS**

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33 191 A total of 3,331 ELSA respondents and 33,127 JAGES respondents were included in the
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36 192 final analysis. Their baseline characteristics are presented in Table 1. The mean age
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39 193 (standard deviation) was 73.6 (6.9) years for the ELSA and 72.4 (5.4) years for the JAGES.
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42 194 Regarding SII scores, the ELSA had the largest number of respondents with 0 and 1 points,
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45 195 while the JAGES had the largest number with 2 and 3 points. In the ELSA, respondents
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48 196 who were older, male, less educated, had a lower income, had heart disease, had poor
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51 197 self-rated health, smoked, did not consume much alcohol, and had higher baseline
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54 198 depressive symptom scores had higher SII scores. A similar trend was observed in the
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57 199 JAGES, but here, those who consumed more alcohol had higher SII scores.
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200 **Table 1. Respondents' baseline characteristics**

	ELSA ^a					JAGES				
	Social Isolation Index score ^b					Social Isolation Index score ^b				
	0	1	2	3	≥ 4	0	1	2	3	≥ 4
	n = 776	n = 906	n = 525	n = 196	n = 47	n = 1402	n = 5981	n = 9723	n = 8735	n = 2176
Age (years), (%)										
65–69	41.0	36.4	29.9	27.6	28.3	38.6	40.5	38.0	37.0	35.8
70–74	26.1	28.3	28.8	29.3	23.6	32.1	32.5	31.6	31.0	30.4
75–79	20.9	17.5	19.3	15.8	20.4	19.2	18.3	19.5	20.3	21.9
80–84	9.1	12.2	12.5	14.5	15.5	8.3	6.7	8.3	9.0	8.8
≥ 85	2.8	5.7	9.5	12.8	12.2	1.9	2.0	2.6	2.7	3.1
Gender, (%)										
Men	50.0	46.1	45.3	51.9	65.8	27.2	35.1	47.0	64.4	66.1
Women	50.0	53.9	54.7	48.1	34.2	72.8	64.9	53.0	35.6	33.9
Educational attainment (years), (%)										
≤ 15	44.1	51.3	52.3	60.9	69.6	42.9	38.1	37.9	38.7	48.6
16–18	35.0	33.8	34.6	27.5	14.1	40.9	40.8	39.3	36.8	31.1
≥ 19	17.8	12.5	11.0	10.3	14.0	15.7	20.4	21.8	23.3	18.5
Missing	3.2	2.4	2.1	1.3	2.3	0.5	0.7	0.9	1.2	1.8
Household equivalised income, (%)										
1st quintile (lowest)	11.4	18.3	23.2	31.2	14.4	7.4	10.9	13.9	15.6	21.3
2nd quintile	21.5	23.7	26.1	24.1	29.6	13.2	13.5	15.0	15.5	16.4
3rd quintile	20.9	21.8	18.9	19.5	27.1	22.5	30.6	30.3	30.6	28.0
4th quintile	21.9	19.9	18.1	16.5	16.6	14.3	13.6	12.7	11.3	9.5
5th quintile (highest)	22.7	15.0	12.7	8.3	12.4	31.5	22.5	19.2	16.8	12.9
Missing	1.5	1.3	0.9	0.4	0.0	11.1	8.9	8.9	10.2	11.9
Cancer, (%)										
No	96.5	95.8	97.1	97.5	96.5	91.0	91.2	90.8	90.1	89.7
Yes	3.4	4.2	2.9	2.5	3.5	3.2	3.1	3.1	3.4	3.7
Missing	0.1	0.0	0.0	0.0	0.0	5.8	5.7	6.1	6.5	6.6
Heart disease, (%)										
No	90.7	86.9	88.4	88.3	77.3	91.0	91.2	90.8	90.1	89.7
Yes	9.3	13.0	11.6	11.7	22.7	3.2	3.1	3.1	3.4	3.7
Missing	0.0	0.1	0.0	0.0	0.0	5.8	5.7	6.1	6.5	6.6
Stroke, (%)										

No	96.3	96.1	97	94.4	96.6	93.3	93.6	93.1	92.5	92.2
Yes	3.7	3.8	3.0	5.6	3.4	0.9	0.8	0.8	1.0	1.2
Missing	0	0.1	0.0	0.0	0.0	5.8	5.7	6.1	6.5	6.6
Self-rated health, (%)										
Good	86.4	79.9	78.8	75.4	71.3	92.0	91.7	90.6	90.2	87.2
Poor	13.6	20.1	21.2	24.6	28.7	7.2	7.7	8.6	9.0	12.2
Missing	0.0	0.0	0.0	0.0	0.0	0.8	0.5	0.8	0.8	0.6
Smoking, (%)										
Never/past	95.5	93.1	89.8	82.9	89.4	86.4	86.1	82.9	81.5	78.4
Current	4.5	6.9	10.2	17.1	10.6	6.4	7.4	9.5	11.3	14.2
Missing	0.0	0.0	0.0	0.0	0.0	7.1	6.5	7.5	7.2	7.3
Drinking, (%)										
Never/past	7.5	11.8	14.9	25.8	17.3	65.0	60.0	56.5	50.4	55.0
Current	91.3	87.0	82.9	72.6	73.6	30.2	35.7	38.6	44.7	40.4
Missing	1.3	1.2	2.2	1.6	9.2	4.8	4.3	4.9	4.9	4.6
CES-D score at baseline, (%)										
0	57.2	52.0	45.5	42.2	54.0					
1	27.3	26.2	28.6	31.8	25.5					
2	9.8	13.8	17.1	11.9	15.1					
3	5.7	8.0	8.8	14.2	5.4					
GDS score at baseline, (%)										
0						20.5	30.4	29.0	26.4	24.3
1						25.5	28.4	28.6	26.9	27.0
2						22.5	20.0	19.8	21.5	21.1
3						17.5	13.1	13.5	14.7	15.9
4						14.1	8.1	9.1	10.5	11.7

201 ELSA, English Longitudinal Study of Ageing; JAGES, Japan Gerontological Evaluation
 202 Study; CES-D, Center for Epidemiologic Studies Depression Scale; GDS, Geriatric
 203 Depression Scale

204 ^a ELSA data after sampling weight

205 ^b Missing data: ELSA, n = 468; JAGES, n = 5,110

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7 206 Table 2 presents the description of social isolation and depressive symptom onset.
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9 207 At follow-up, 190 (6.5%) ELSA respondents and 4,456 (13.5%) JAGES respondents
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12 208 exhibited depressive symptom onset. In both studies, higher SII scores were associated
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15 209 with an increased risk of depressive symptom onset. Regarding SII sub-components,
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18 210 ELSA respondents who were unmarried or living alone were more likely to have
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21 211 depressive symptoms, while this was the case with JAGES respondents with no social
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24 212 participation.
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213 **Table 2. Description of social isolation status and depressive symptom onset**

		ELSA ^a		JAGES	
		CES-D score at follow-up		GDS score at follow-up	
		< 4	≥ 4	< 5	≥ 5
		n = 2728	n = 190	n = 28671	n = 4456
Social Isolation Index score,					
(%)					
0		27.5	13.5	4.4	3.0
1		31.2	29.3	18.6	14.3
2		17.9	18.9	29.8	26.3
3		6.5	10.1	26.2	27.5
≥ 4		1.5	2.9	6.1	9.3
Missing		15.4	25.3	14.8	19.7
Social Isolation Index sub-					
components, (%)					
Unmarried or living alone	No	71.9	58.5	88.3	85.2
	Yes	28.1	41.5	10.2	12.7
	Missing	0.0	0.0	1.4	2.1
Poor interaction with children	No	81.8	73.4	26.6	25.0
	Yes	12.5	14.7	71.7	72.9
	Missing	5.7	11.8	1.7	2.1
Poor interaction with relatives	No	76.3	68.1	41.1	38.7
	Yes	17.3	18.6	54.4	56.0
	Missing	6.4	13.4	4.5	5.4
Poor interaction with friends	No	72.2	66.0	37.1	31.2
	Yes	18.4	21.6	58.2	63.8
	Missing	9.4	12.4	4.6	5.0
No social participation	No	61.7	46.3	75.0	63.9
	Yes	28.4	32.5	13.0	20.0
	Missing	10.0	21.2	11.7	16.1

214 ELSA, English Longitudinal Study of Ageing; JAGES, Japan Gerontological Evaluation

215 Study; CES-D, Center for Epidemiologic Studies Depression Scale; GDS, Geriatric

216 Depression Scale

217 ^a ELSA data after sampling weight

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7 218 Table 3 depicts the association between SII scores and depressive symptom onset.
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9 219 Multivariable analysis showed that higher SII scores were associated with a higher risk
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12 220 of depressive symptom onset in both studies after adjusting for all covariates. In the ELSA,
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15 221 the OR of depressive symptom onset was significantly higher from a score \geq one point
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18 222 (OR [95% CI] compared with zero points, one: 1.68 [1.02–2.75], two: 1.77 [1.03–3.05],
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21 223 three: 2.64 [1.37–5.12], \geq four: 4.01 [1.43–11.22], p for trend = 0.015). In the JAGES, as
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24 224 SII scores increased, the OR of depressive symptom onset gradually increased, reaching
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27 225 significance at \geq three points (OR [95% CI] compared with zero points, one: 1.10 [0.89–
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30 226 1.35], two: 1.15 [0.94–1.40], three: 1.28 [1.04–1.56], \geq four: 1.48 [1.18–1.85], p for trend
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33 227 < 0.001). These results showed almost the same tendency as the complete case analysis
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36 228 without multiple imputation (Supplementary Table 1).
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229 **Table 3. Association between social isolation and depressive symptom onset: multivariable logistic regression analysis**

	ELSA		JAGES	
	Crude OR (95% CI)	Adjusted OR (95% CI) ^a	Crude OR (95% CI)	Adjusted OR (95% CI) ^a
Social Isolation Index score				
0	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
1	1.92** (1.19–3.10)	1.68* (1.02–2.75)	1.14 (0.94–1.39)	1.10 (0.89–1.35)
2	2.15** (1.28–3.62)	1.77* (1.03–3.05)	1.32** (1.09–1.60)	1.15 (0.94–1.40)
3	3.19*** (1.73–5.90)	2.64** (1.37–5.12)	1.57*** (1.30–1.90)	1.28* (1.04–1.56)
≥ 4	3.85** (1.46–10.18)	4.01** (1.43–11.22)	2.26*** (1.83–2.79)	1.48*** (1.18–1.85)
	<i>p</i> for trend < 0.001	<i>p</i> for trend = 0.015	<i>p</i> for trend < 0.001	<i>p</i> for trend < 0.001

230 * *p* < 0.05; ** *p* < 0.01; *** *p* < 0.001

231 ELSA, English Longitudinal Study of Ageing; JAGES, Japan Gerontological Evaluation Study; CI, confidence interval; OR, odds ratio

232 ^a Adjusted for age, gender, educational attainment, household equivalised income, present illness (cancer, heart disease, and stroke), self-rated health, smoking, drinking, and depression score at baseline (Center for Epidemiologic Studies Depression Scale for the ELSA and Geriatric Depression Scale for the JAGES).

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6 235 Table 4 presents the impacts of SII sub-components on depressive symptom
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9 236 onset. In the ELSA, sub-components were not significant, although poor interaction with
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12 237 children was marginally significant (OR [95% CI], with ‘none’ as the reference;
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15 238 unmarried or living alone: 1.13 [0.80–1.60], poor interaction with children: 1.55 [1.00–
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18 239 2.41], poor interaction with relatives: 1.24 [0.79–1.94], poor interaction with friends: 1.15
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21 240 [0.77–1.71], no social participation: 1.22 [0.80–1.87]). In the JAGES, poor interaction
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24 241 with children and no social participation were significantly associated with depressive
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27 242 symptom onset after adjusting for all covariates (OR [95% CI], with ‘none’ as the
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30 243 reference; unmarried or living alone: 1.11 [1.00–1.24], poor interaction with children:
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33 244 1.09 [1.01–1.19], poor interaction with relatives: 1.04 [0.96–1.12], poor interaction with
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36 245 friends: 1.03 [0.95–1.11], no social participation: 1.28 [1.17–1.40]). These results were
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39 246 similar to those obtained from the complete case analysis (Supplementary Table 2).
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4 247 **Table 4. Association between sub-components of social isolation and depressive symptom onset: multivariable logistic regression**
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6 248 **analysis**

	ELSA	JAGES
	Adjusted OR (95% CI) ^a	Adjusted OR (95% CI) ^a
Social Isolation Index sub-components (reference: none)		
Unmarried or living alone	1.13 (0.80–1.60)	1.11 [†] (1.00–1.24)
Poor interaction with children	1.55 [†] (1.00–2.41)	1.09* (1.01–1.19)
Poor interaction with relatives	1.24 (0.79–1.94)	1.04 (0.96–1.12)
Poor interaction with friends	1.15 (0.77–1.71)	1.03 (0.95–1.11)
No social participation	1.22 (0.80–1.87)	1.28*** (1.17–1.40)

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20 249 * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; [†] $p < 0.1$
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22 250 ELSA, English Longitudinal Study of Ageing; JAGES, Japan Gerontological Evaluation Study; CI, confidence interval; OR, odds ratio
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24 251 ^a Adjusted for age, gender, educational attainment, equivalent income, present illness (cancer, heart disease, and stroke), self-rated health,
25 252 smoking, drinking, and depression score at baseline (Center for Epidemiologic Studies Depression Scale for the ELSA and Geriatric
26 253 Depression Scale for the JAGES).

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6 254 **DISCUSSION**
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9 255 To the best of our knowledge, this is the first cross-national longitudinal study of the
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12 256 association of social isolation with depressive symptoms among older English and
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15 257 Japanese adults. Social isolation was significantly associated with depressive symptom
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18 258 onset in both countries. Our results support previous longitudinal findings on social
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21 259 relationships and mental health in older adults in England[28] and Japan.[29] Using data
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24 260 frames that were similar with regard to assessment and covariates, we showed that social
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27 261 isolation is a common risk factor for depressive symptoms in England and Japan despite
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30 262 cultural differences such as emphasis on friendships versus familism, respectively. Thus,
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33 263 our results suggest that to safeguard the mental health of older adults, addressing social
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36 264 isolation is a global need.

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39 265 The association between social isolation and depressive symptoms was
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42 266 somewhat stronger in England than in Japan. Although we cannot make direct
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45 267 comparisons because of variations in cohort follow-up periods and depressive symptom
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48 268 measurement, there are several possible reasons for this pattern of findings. The impact
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51 269 of social factors could be different depending on the group and society to which one
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54 270 belongs. This is best understood in the context of the concept of relative deprivation.[30]
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57 271 In other words, higher levels of relative social isolation may induce greater psychological
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6 272 stress. A previous study showed that rich community ties and cohesion were protective
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9 273 factors for health but could have a negative effect on those who were not socially
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12 274 involved.[31] Being isolated in a connected society such as England may represent a more
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15 275 severe condition, which may have a stronger negative impact on mental health.
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18 276 While a previous study showed that friendship-based relationships contributed
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21 277 to longevity in older adults in England, in the present study they were not associated with
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24 278 depressive symptom onset. Another study focused on English older adults indicated the
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27 279 contribution of partner and child support, rather than support from friends, in alleviating
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30 280 depression;[32] thus, relationships with family members might be important for mental
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33 281 health. In the JAGES, poor interaction with children and no social participation were
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36 282 significantly associated with depressive symptom onset. Previous studies on older
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39 283 Japanese adults suggested that interaction with children and social participation were
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42 284 protective factors for mental health problems.[12, 33] Traditionally, Japan has had strong
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45 285 family and kinship ties, and adult children are expected to demonstrate reciprocity with
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48 286 their parents.[14] However, children now tend to live apart from their parents after
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51 287 marriage, and contact is reduced,[34] potentially leading to loneliness in older adults. In
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54 288 such a situation, social participation may improve mental health by establishing a sense
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57 289 of belonging.[33] Our results demonstrate that promoting interaction with children and
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6 290 community participation are essential for safeguarding mental health in older Japanese
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9 291 adults.

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12 292 This study has several strengths. First, it is the first cross-national population-
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15 293 level investigation of the impact of social isolation on depressive symptom onset using a
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18 294 unified data frame. Second, by using two longitudinal datasets, we were able to determine
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21 295 causality in the association between social isolation and depressive symptoms. Third, the
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24 296 use of large-scale data allowed us to detect the effects of relatively rare situations of
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27 297 severe social isolation.

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30 298 However, certain limitations cannot be ignored. First, the measurement of
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33 299 depressive symptoms in the two cohorts was not the same. Therefore, we could not
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36 300 directly compare depressive symptom onset in the two countries. However, these
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39 301 measurements were also used in a previous cross-national comparison study in England
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42 302 and Japan,[23] and we were able to examine the association between social isolation and
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45 303 depressive symptom onset in each country using the same data frame. Second, we
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48 304 substituted social support for the assessment of social contact for some items in order to
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51 305 use the same SII. Therefore, cultural differences in expectations regarding the receipt of
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54 306 social support in both countries might have caused information biases. For instance,
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57 307 expectations regarding social support from relatives could originally have been higher in
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6 308 Japan,[14] leading to overestimation of social isolation levels. Third, there were
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9 309 differences in study design in the data from the two cohorts, such as sampling method
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12 310 and follow-up period. However, we made efforts to harmonise the data: those aged ≤ 64 ,
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15 311 with dementia, and dependent in activities of daily living were excluded from the analysis.
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18 312 Also, the ELSA presents nationally representative population data, while the JAGES does
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21 313 not. However, the JAGES sample is representative of areas from a nationwide ageing
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24 314 study in which about one-fifth of all prefectures (nine out of 47) were enrolled.
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315

316 **CONCLUSION**

317 We examined the association between social isolation and depressive symptom onset
318 among older adults in England and Japan, which have different cultural contexts
319 regarding social relationships, finding a significant association in both countries. Thus,
320 globally, tackling social isolation must be prioritised to safeguard the mental health of
321 older adults. Particularly in Japan, the promotion of interaction with children and social
322 participation could be key factors in addressing social isolation.

323

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12 328 **AUTHORS' CONTRIBUTIONS**
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15 329 All authors contributed to the conception and design of this study. Data collection was

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18 330 primarily conducted by MS, JA, NC, KO, and KK. Analyses were performed by TN, MS,

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21 331 JA, TT, SK, and TI. TN prepared the initial manuscript and MS, JA, NC, TT, SK, TI, KO,

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23
24 332 and KK significantly contributed to revising it. All authors read and approved the final

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6 362 **DATA SHARING STATEMENT**
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9 363 For the JAGES, all enquiries are to be addressed to the data management committee via
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12 364 e-mail: dataadmin.ml@jages.net. All JAGES datasets have ethical or legal restrictions for
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15 365 public deposition because of the inclusion of sensitive information about the human
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18 366 participants. Regarding the ELSA, data are available in an open-access repository at
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21 367 <http://www.dataarchive.ac.uk/>.
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27 369 **COMPETING INTERESTS STATEMENT**
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36 372 **REFERENCES**
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Supplementary Table 1. Association between social isolation and depressive symptom onset, by complete case analysis

		ELSA		JAGES	
		Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)
Social Isolation Index score	0	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
	1	1.92** (1.19–3.10)	1.56 [†] (0.94–2.60)	1.14 (0.94–1.39)	1.11 (0.87–1.41)
	2	2.15** (1.28–3.62)	1.71 [†] (0.98–2.99)	1.32** (1.09–1.60)	1.20 (0.95–1.51)
	3	3.19*** (1.73–5.90)	2.50** (1.27–4.90)	1.57*** (1.30–1.90)	1.30* (1.03–1.64)
	≥ 4	3.85** (1.46–10.18)	5.17** (1.83–14.66)	2.26*** (1.83–2.79)	1.47** (1.13–1.91)
		<i>p</i> for trend < 0.001	<i>p</i> for trend < 0.001	<i>p</i> for trend < 0.001	<i>p</i> for trend < 0.001
Age (years)	65–69		1.00 (reference)		1.00 (reference)
	70–74		1.37 (0.83–2.25)		1.16** (1.05–1.30)
	75–79		1.24 (0.71–2.14)		1.31*** (1.16–1.48)
	80–84		1.66 [†] (0.92–2.99)		1.60*** (1.37–1.88)
	≥ 85		0.97 (0.45–2.09)		1.79*** (1.39–2.30)
Gender	Male		1.00 (reference)		1.00 (reference)
	Female		1.58* (1.07–2.34)		1.00 (0.90–1.11)
Educational attainment (years)	< 15		1.00 (reference)		1.00 (reference)
	16–18		1.05 (0.68–1.60)		0.81*** (0.74–0.89)
	≥ 19		1.30 (0.70–2.41)		0.68*** (0.60–0.78)
Household equivalised income	1st quintile (lowest)		1.00 (reference)		1.00 (reference)
	2nd quintile		0.70 (0.40–0.21)		0.95 (0.83–1.09)
	3rd quintile		1.11 (0.66–1.87)		0.76*** (0.67–0.87)
	4th quintile		0.82 (0.45–1.50)		0.67*** (0.57–0.79)
	5th quintile (highest)		0.84 (0.42–1.68)		0.65*** (0.56–0.76)

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3	Cancer	No	1.00 (reference)	1.00 (reference)
4		Yes	0.95 (0.32–2.81)	1.16 (0.93–1.43)
5	Heart disease	No	1.00 (reference)	1.00 (reference)
6		Yes	1.13 (0.67–1.92)	1.20 (1.05–1.37)
7	Stroke	No	1.00 (reference)	1.00 (reference)
8		Yes	1.3 (0.56–3.02)	1.18 (0.80–1.73)
9	Self-rated health	Good	1.00 (reference)	1.00 (reference)
10		Poor	1.71* (1.13–2.59)	1.63*** (1.44–1.85)
11	CES-D score at baseline		1.90*** (1.60–2.25)	
12	GDS score at baseline			1.92*** (1.86–1.99)
13	Smoking	Never/past	1.00 (reference)	1.00 (reference)
14		Current	0.76 (0.76–1.56)	1.29*** (1.12–1.48)
15	Drinking	Never/past	1.00 (reference)	1.00 (reference)
16		Current	1.41 (0.81 – 2.44)	1.02 (0.93 – 1.13)

*, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$; †, $p < 0.1$

ELSA, English Longitudinal Study of Ageing; JAGES, Japan Gerontological Evaluation Study; CES-D, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; GDS, Geriatric Depression Scale; OR, odds ratio

Supplementary Table 2. Association between sub-components of social isolation and depressive symptom onset, by complete case analysis

		ELSA		JAGES	
		Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)
Social Isolation Index sub-components (ref; none)					
Unmarried or living alone		1.91*** (1.34–2.72)	1.27 (0.84–1.93)	1.33*** (1.18–1.49)	1.02 (0.88–1.19)
Poor interaction with children		1.08 (0.68–1.74)	1.51 (0.91–2.50)	1.01 (0.98–1.10)	1.13* (1.02–1.25)
Poor interaction with relatives		1.25 (0.83–1.90)	1.33 (0.85–2.08)	1.05 (0.97–1.13)	0.98 (0.90–1.08)
Poor interaction with friends		1.19 (0.78–1.80)	1.21 (0.78–1.87)	1.23 (1.14–1.33)	1.11* (1.01–1.22)
No social participation		1.54* (1.08–2.19)	1.46† (0.98–2.16)	1.70 (1.56–1.86)	1.22*** (1.09–1.36)
Age (years)					
		65–69	1.00 (reference)		1.00 (reference)
		70–74	1.37 (0.83–2.25)		1.17** (1.05–1.30)
		75–79	1.25 (0.72–2.17)		1.31*** (1.16–1.49)
		80–84	1.68† (0.92–3.04)		1.60*** (1.36–1.88)
		≥ 85	1.00 (0.46–2.21)		1.78*** (1.38–2.30)
Gender		Male	1.00 (reference)		1.00 (reference)
		Female	1.59* (1.07–2.37)		1.00 (0.89–1.11)
Educational attainment (years)		< 15	1.00 (reference)		1.00 (reference)
		10–12	1.04 (0.67–1.60)		0.81*** (0.74–0.90)
		≥ 19	1.31 (0.70–2.46)		0.69*** (0.61–0.78)
Household equivalised income		1st quintile (lowest)	1.00 (reference)		1.00 (reference)
		2nd quintile	0.71 (0.41–1.23)		0.95 (0.83–1.09)
		3rd quintile	1.13 (0.67–1.93)		0.76*** (0.67–0.86)
		4th quintile	0.83 (0.45–1.52)		0.67*** (0.57–0.79)
		5th quintile (highest)	0.85 (0.42–1.71)		0.66*** (0.57–0.76)
Cancer		No	1.00 (reference)		1.00 (reference)
		Yes	0.95 (0.32–2.81)		1.15 (0.93–1.43)

Heart disease	No	1.00 (reference)	1.00 (reference)
	Yes	1.16 (0.69–1.96)	1.20** (1.05–1.37)
Stroke	No	1.00 (reference)	1.00 (reference)
	Yes	1.28 (0.55–2.99)	1.18 (0.80–1.73)
Self-rated health	Good	1.00 (reference)	1.00 (reference)
	Poor	1.71* (1.13–2.58)	1.62*** (1.43–1.83)
CES-D score at baseline		1.89*** (1.59–2.25)	1.00 (reference)
GDS score at baseline			1.92*** (1.85–1.99)
Smoking	Never/past	1.00 (reference)	1.00 (reference)
	Current	0.74 (0.36–1.53)	1.29*** (1.13–1.48)
Drinking	Never/past	1.00 (reference)	1.00 (reference)
	Current	1.39 (0.80–2.40)	1.03 (0.93–1.14)

*, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$; †, $p < 0.1$

ELSA, English Longitudinal Study of Ageing; JAGES, Japan Gerontological Evaluation Study; CES-D, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; GDS, Geriatric Depression Scale; OR, odds ratio

STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	1, 3 3-4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6-8
Objectives	3	State specific objectives, including any prespecified hypotheses	8
Methods			
Study design	4	Present key elements of study design early in the paper	8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8-9
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (b) For matched studies, give matching criteria and number of exposed and unexposed	8-9 Not applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	9-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	9-10
Bias	9	Describe any efforts to address potential sources of bias	11
Study size	10	Explain how the study size was arrived at	Not applicable
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9-10
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses	10-11 Not applicable 11 Not applicable Not applicable
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	12-14 Not applicable Not applicable
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	12-14 13-14 9
Outcome data	15*	Report numbers of outcome events or summary measures over time	15-16

1 2 3 4 5 6 7	Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	17-18 Not applicable Not applicable
8 9	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Supplementary 1, 2
10	Discussion			
11	Key results	18	Summarise key results with reference to study objectives	21
12 13 14	Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	23-24
15 16 17 18	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	21-23
19 20	Generalisability	21	Discuss the generalisability (external validity) of the study results	Not applicable
21	Other information			
22 23 24	Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	25-26

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

BMJ Open

Association between social isolation and depression onset among older adults: A cross-national longitudinal study in England and Japan

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Original research

Title

Association between social isolation and depression onset among older adults: A cross-national longitudinal study in England and Japan

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1 **ABSTRACT**

2 **Objective:** Social isolation is a risk factor for depression in older age. However, little is
3 known about whether its impact varies depending on country-specific cultural contexts
4 regarding social relationships. The present study examined the association of social
5 isolation with depression onset among older adults in England, which has taken advanced
6 measures against social isolation, and Japan, a super-aged society with a rapidly
7 increasing number of socially isolated people.

8 **Design:** Prospective longitudinal study.

9 **Setting:** We utilised data from two ongoing studies: the English Longitudinal Study of
10 Ageing (ELSA) and the Japan Gerontological Evaluation Study (JAGES).

11 **Participants:** Older adults aged ≥ 65 years without depression at baseline were followed
12 up regarding depression onset for two years (2010/11 to 2012/13) for the ELSA and 2.5
13 years (2010/11 to 2013) for the JAGES.

14 **Primary outcome measure:** Depression was assessed with the Center for Epidemiologic
15 Studies Depression Scale for the ELSA and Geriatric Depression Scale for the JAGES.
16 Multivariable logistic regression analysis was performed to evaluate social isolation using
17 multiple parameters (marital status; interaction with children, relatives, and friends; and
18 social participation).

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19 **Results:** The data of 3,331 respondents from the ELSA and 33,127 from the JAGES were
20 analysed. Multivariable logistic regression analysis demonstrated that social isolation was
21 significantly associated with depression onset in both countries. In the ELSA, poor
22 interaction with children was marginally associated with depression onset, while in the
23 JAGES, poor interaction with children and no social participation significantly affected
24 depression onset.

25 **Conclusions:** Despite variations in cultural background, social isolation was associated
26 with depression onset in both England and Japan. Addressing social isolation to safeguard
27 older adults' mental health must be globally prioritised.

28 29 **Strengths and limitations of this study**

- 30 ● This is the first cross-national longitudinal study to examine the association between
31 social isolation and depression onset in England, which has taken advanced measures
32 against social isolation, and Japan, a super-aged society with a rapidly increasing
33 number of socially isolated people.
- 34 ● This study included a large sample of over 3,300 people from England and 33,000
35 people from Japan aged 65 years and older.
- 36 ● A limitation of this study is that we cannot make direct comparisons because of

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37 variations in cohort follow-up periods and depression measurement.

38 ● Another limitation is the use of social support for the evaluation of social contact so

39 as to be able to use the same social isolation assessment scale in both countries.

40

For peer review only

41 INTRODUCTION

42 With population ageing, there is growing worldwide interest in social issues concerning
43 older adults, including social isolation and the deterioration of physical and mental health.

44 Defined as an objective state where an individual has few close relationships or limited
45 contact within a community,[1] social isolation is recognised as a social determinant of
46 health with relevance to mortality,[2] cardiovascular diseases,[3] dementia,[4] and mental
47 health.[5, 6] Social isolation is a major risk factor for mental health problems in older
48 age. Several systematic reviews have shown that social isolation is associated with
49 depressive symptoms,[5, 6] which, in turn, are correlated with unhealthy behaviours and
50 reduced access to material resources.[7] Depression, common in later life, is related to
51 adverse health outcomes such as poor quality of life[8] and functional disability.[9] With
52 the high current global burden of depression expected to increase further by 2030,[10]
53 addressing social isolation is an important gerontological issue for protecting mental
54 health in older adults.

55 The impacts of social isolation on health may vary by country; this could be the
56 result of differences in the social environments related to social networks within and
57 outside the family. A recent study of older adults in England and Japan showed that social
58 isolation is a common risk factor for mortality in both countries, with a greater impact in

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6 59 England; the results are discussed in terms of possible differences between societies that
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9 60 are highly connected and those that are not.[11] In the United Kingdom (UK), in
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12 61 recognition of the impact of social isolation on health and economic loss, the position of
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15 62 ‘Minister of Loneliness’ was established in 2018, and the country is taking a progressive
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18 63 approach to the elimination of social isolation.[12] In contrast, Japan, now a super-aged
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21 64 society (more than 21% of the population aged 65 or above),[13] is experiencing a rapid
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24 65 increase in the trend of abstaining from marriage and weakening community and
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27 66 neighbourhood relations,[14] leading to a rise in the number of socially isolated
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30 67 people.[15] In Japan, the proportion of people who rarely or never spend time with those
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33 68 close to them has been reported to be the highest among Organisation for Economic Co-
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36 69 operation and Development countries. In particular, this figure is much higher than in the
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39 70 UK, which has made advances in tackling social isolation (Japan = 15.3%, UK =
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42 71 5.0%).[16] Owing to differences in social structures and the contexts surrounding social
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45 72 isolation, the impact of social isolation on depression is expected to vary across countries.

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48 73 Furthermore, the health effects of social isolation may differ depending on the
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51 74 cultural context of social relationships. In East Asian countries, including Japan, there is
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54 75 a familial norm based on the traditional culture of filial piety,[17] which is often
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57 76 contrasted with individualism in Western countries.[18, 19] Based on this cultural
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6 77 background, Japanese social support networks may be kinship centred, which may be
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9 78 narrower than the types of social networks prevalent in other countries.[20] However,
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12 79 there is a lack of consensus on the health effects of social relationships based on these
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15 80 cultural differences. A previous cross-national study showed that in English men,
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18 81 friendship-based social relationships had a significant impact on longevity, whereas in
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21 82 Japanese men, this impact was associated with family-based social relationships.[21] On
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24 83 the contrary, a study of older adults in the United States (US) and Japan found that while
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27 84 relationships with children were associated with a low level of depression only in Japan,
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30 85 the presence of spouses was important in both countries, but more so in the US.[22]
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33 86 Another comparative study among adults suggested that social contact with friends
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36 87 benefitted women's mental health in the UK but not in Japan.[23] Thus, the family-
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39 88 oriented nature of East Asian societies does not automatically imply the health importance
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42 89 of family-based relationships, and the roles of individual components of social isolation
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45 90 (family, friends, and others) in the mental health of older adults in each country remain
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48 91 controversial.

51 92 As the association between social isolation and depression is often described as
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54 93 bidirectional,[24] longitudinal studies are needed to address temporality. However,
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57 94 previous cross-national comparative studies have only employed cross-sectional
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6 95 designs.[22, 23] Therefore, using longitudinal data from both countries, the present study
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9 96 aims to investigate the association of social isolation with depression onset in England,
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12 97 which has taken advanced measures against social isolation, and Japan, a super-aged
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15 98 society with a rapidly increasing number of socially isolated people.
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100 **METHODS**

101 **Sample**

102 This longitudinal study was conducted using data from two ongoing prospective cohort
103 studies: the English Longitudinal Study of Ageing (ELSA) and the Japan Gerontological
104 Evaluation Study (JAGES). The ELSA targets independent-living older adults aged ≥ 50 ,
105 while JAGES participants are community-dwelling individuals aged ≥ 65 who are
106 ineligible for long-term healthcare insurance benefits.[25] Details of the ELSA and
107 JAGES can be found elsewhere.[26, 27] For the present analysis, we used the two waves
108 of data that most closely corresponded with the timing of our study: wave 5 (2010/2011)
109 to wave 6 (2012/2013) for the ELSA, and wave 1 (2010/2011) to wave 2 (2013) for the
110 JAGES. We harmonised the data by including older adults aged ≥ 65 , independent in
111 activities of daily living, and without self-reported dementia. For analysis, respondents
112 who scored above the cut-off point for depression on each measure in the respective

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6 113 cohort at baseline were excluded, and we followed up the onset of depression for two
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9 114 years for the ELSA and 2.5 years for the JAGES.
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15 116 **Depression**

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18 117 Based on a previous cross-national study,[28] depressive symptoms were measured both
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21 118 at baseline and follow-up using eight items from the Center for Epidemiologic Studies
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24 119 Depression Scale (CES-D) in the ELSA[29] and the Geriatric Depression Scale (GDS-
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27 120 15) in the JAGES.[30] To identify possible depressive cases, the CES-D cut-off was ≥ 4
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30 121 while that for the GDS-15 was ≥ 5 . [31, 32] As previously mentioned, respondents with
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33 122 depression at baseline were excluded, and we observed the onset of depression during
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36 123 follow-up.
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42 125 **Social isolation**

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45 126 Social isolation levels were assessed using a modified version of the Social Isolation
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48 127 Index (SII).[33–35] The index was computed with respondents given a point if they: (1)
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51 128 were unmarried or living alone, (2) had poor interaction with children (did not live with
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54 129 their children or had no one to provide emotional or instrumental social support), (3) had
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57 130 poor interaction with relatives (did not have immediate family members providing
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6 131 emotional or instrumental social support), (4) had poor interaction with friends (less than
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9 132 monthly contact or no friends who could provide emotional or instrumental social
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12 133 support), and (5) had no social participation (no participation in any social or religious
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15 134 groups). The total possible score ranged from 0 to 5, with higher scores indicating greater
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18 135 social isolation. The participants were categorised into the following five groups based
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21 136 on their scores: 0, 1, 2, 3, and 4–5 points. We used the total score and the scores of the
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24 137 five sub-components as predictive variables.
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139 **Covariates**

140 The covariates included age, gender, educational attainment, household equivalised
141 income, present illness, self-rated health, smoking, and drinking. Age was categorised as
142 65–69, 70–74, 75–79, 80–84, and ≥ 85 . Based on the ages of respondents who had
143 completed formal education, the age of final educational attainment was categorised as \leq
144 15 years, 16–18 years, and ≥ 19 years. Household equivalised income was classified into
145 quintiles. Present illness was classified as ‘yes’ or ‘no’ for cancer, heart disease, and
146 stroke. Self-rated health was dichotomised as ‘poor’ and ‘good’. Smoking and drinking
147 were dichotomised as ‘never/past’ and ‘current’.

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149 **Statistical analysis**

150 We analysed the ELSA and JAGES data separately because of differences in research
151 design, especially sampling approaches. A longitudinal weight was applied to account for
152 survey non-response for the ELSA but not the JAGES as its design does not allow it.
153 First, we calculated descriptive statistics. Second, we conducted a multivariable logistic
154 regression analysis to examine the association between SII score and depression onset
155 and obtained odds ratios (ORs) and 95% confidence intervals (CIs) for depression onset.
156 Model 1 was not adjusted for covariates while Model 2 was adjusted for all covariates.
157 Additionally, we analysed the association between SII sub-components and depression
158 onset, adjusted for all covariates.

159 To mitigate potential biases resulting from missing information, we used the
160 multiple imputation approach under the missing at random assumption. We generated 20
161 imputed datasets for the final analysis, which excluded those who met the exclusion
162 criteria and did not respond to the follow-up surveys, using the multiple imputation by
163 chained equations procedure and pooled the results using Rubin's rule.[36]

164 The significance level was set at $p < 0.05$. We used R (Version 3.5.2 for
165 Windows) for all statistical analyses.

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6 167 **Ethical considerations**
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9 168 The ELSA investigators received ethical approval for all waves of the study from the
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12 169 National Health Service Research Ethics Committees under the National Research and
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15 170 Ethics Services (MREC/01/2/91). The JAGES protocols were approved by the Ethics
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18 171 Committee on the Research of Human Subjects at Nihon Fukushi University (10-05).
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24 173 **Patient and public involvement**
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27 174 No patients were involved in the development of the research question, study design, or
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30 175 data interpretation.
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36 177 **RESULTS**
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39 178 A total of 3,331 ELSA respondents and 33,127 JAGES respondents were included in the
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42 179 final analysis. Their baseline characteristics are presented in Table 1. The mean age
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45 180 (standard deviation) was 73.6 (6.9) years for the ELSA and 72.4 (5.4) years for the JAGES.
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48 181 Regarding SII scores, the ELSA had the largest number of respondents with 0 and 1 points,
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51 182 while the JAGES had the largest number with 2 and 3 points. In the ELSA, respondents
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54 183 who were older, male, less educated, had a lower income, had heart disease, had poor
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57 184 self-rated health, smoked, did not consume much alcohol, and had higher baseline
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6 185 depressive symptom scores had higher SII scores. A similar trend was observed in the
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9 186 JAGES, but here, those who consumed more alcohol had higher SII scores.
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187 **Table 1. Respondents' baseline characteristics**

	ELSA ^a					JAGES				
	Social Isolation Index score ^b					Social Isolation Index score ^b				
	0	1	2	3	≥ 4	0	1	2	3	≥ 4
	n = 905	n = 1049	n = 596	n = 216	n = 49	n = 1402	n = 5981	n = 9723	n = 8735	n = 2176
	(27.2%)	(31.5%)	(17.9%)	(6.5%)	(1.5%)	(4.2%)	(18.0%)	(29.4%)	(26.4%)	(6.6%)
Age (years), (%)										
65–69	41.0	36.4	29.9	27.6	28.3	38.6	40.5	38.0	37.0	35.8
70–74	26.1	28.3	28.8	29.3	23.6	32.1	32.5	31.6	31.0	30.4
75–79	20.9	17.5	19.3	15.8	20.4	19.2	18.3	19.5	20.3	21.9
80–84	9.1	12.2	12.5	14.5	15.5	8.3	6.7	8.3	9.0	8.8
≥ 85	2.8	5.7	9.5	12.8	12.2	1.9	2.0	2.6	2.7	3.1
Gender, (%)										
Men	50.0	46.1	45.3	51.9	65.8	27.2	35.1	47.0	64.4	66.1
Women	50.0	53.9	54.7	48.1	34.2	72.8	64.9	53.0	35.6	33.9
Educational attainment (years), (%)										
≤ 15	44.1	51.3	52.3	60.9	69.6	42.9	38.1	37.9	38.7	48.6
16–18	35.0	33.8	34.6	27.5	14.1	40.9	40.8	39.3	36.8	31.1
≥ 19	17.8	12.5	11.0	10.3	14.0	15.7	20.4	21.8	23.3	18.5
Missing	3.2	2.4	2.1	1.3	2.3	0.5	0.7	0.9	1.2	1.8
Household equivalised income, (%)										
1st quintile (lowest)	11.4	18.3	23.2	31.2	14.4	7.4	10.9	13.9	15.6	21.3
2nd quintile	21.5	23.7	26.1	24.1	29.6	13.2	13.5	15.0	15.5	16.4
3rd quintile	20.9	21.8	18.9	19.5	27.1	22.5	30.6	30.3	30.6	28.0
4th quintile	21.9	19.9	18.1	16.5	16.6	14.3	13.6	12.7	11.3	9.5
5th quintile (highest)	22.7	15.0	12.7	8.3	12.4	31.5	22.5	19.2	16.8	12.9
Missing	1.5	1.3	0.9	0.4	0.0	11.1	8.9	8.9	10.2	11.9
Cancer, (%)										
No	96.5	95.8	97.1	97.5	96.5	91.0	91.2	90.8	90.1	89.7
Yes	3.4	4.2	2.9	2.5	3.5	3.2	3.1	3.1	3.4	3.7
Missing	0.1	0.0	0.0	0.0	0.0	5.8	5.7	6.1	6.5	6.6
Heart disease, (%)										
No	90.7	86.9	88.4	88.3	77.3	91.0	91.2	90.8	90.1	89.7
Yes	9.3	13.0	11.6	11.7	22.7	3.2	3.1	3.1	3.4	3.7
Missing	0.0	0.1	0.0	0.0	0.0	5.8	5.7	6.1	6.5	6.6

Stroke, (%)											
No	96.3	96.1	97	94.4	96.6	93.3	93.6	93.1	92.5	92.2	
Yes	3.7	3.8	3.0	5.6	3.4	0.9	0.8	0.8	1.0	1.2	
Missing	0	0.1	0.0	0.0	0.0	5.8	5.7	6.1	6.5	6.6	
Self-rated health, (%)											
Good	86.4	79.9	78.8	75.4	71.3	92.0	91.7	90.6	90.2	87.2	
Poor	13.6	20.1	21.2	24.6	28.7	7.2	7.7	8.6	9.0	12.2	
Missing	0.0	0.0	0.0	0.0	0.0	0.8	0.5	0.8	0.8	0.6	
Smoking, (%)											
Never/past	95.5	93.1	89.8	82.9	89.4	86.4	86.1	82.9	81.5	78.4	
Current	4.5	6.9	10.2	17.1	10.6	6.4	7.4	9.5	11.3	14.2	
Missing	0.0	0.0	0.0	0.0	0.0	7.1	6.5	7.5	7.2	7.3	
Drinking, (%)											
Never/past	7.5	11.8	14.9	25.8	17.3	65.0	60.0	56.5	50.4	55.0	
Current	91.3	87.0	82.9	72.6	73.6	30.2	35.7	38.6	44.7	40.4	
Missing	1.3	1.2	2.2	1.6	9.2	4.8	4.3	4.9	4.9	4.6	
CES-D score at baseline, (%)											
0	57.2	52.0	45.5	42.2	54.0						
1	27.3	26.2	28.6	31.8	25.5						
2	9.8	13.8	17.1	11.9	15.1						
3	5.7	8.0	8.8	14.2	5.4						
GDS score at baseline, (%)											
0						20.5	30.4	29.0	26.4	24.3	
1						25.5	28.4	28.6	26.9	27.0	
2						22.5	20.0	19.8	21.5	21.1	
3						17.5	13.1	13.5	14.7	15.9	
4						14.1	8.1	9.1	10.5	11.7	

188 ELSA, English Longitudinal Study of Ageing; JAGES, Japan Gerontological Evaluation
 189 Study; CES-D, Center for Epidemiologic Studies Depression Scale; GDS, Geriatric
 190 Depression Scale

191 ^a ELSA data after sampling weight

192 ^b Missing data: ELSA, n = 516; JAGES, n = 5,110

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6 193 Table 2 presents the description of social isolation and depression onset. At
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9 194 follow-up, 201 (6.0%) ELSA respondents and 4,456 (13.5%) JAGES respondents
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12 195 exhibited depression onset. In both studies, higher SII scores were associated with an
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15 196 increased risk of depression onset. Regarding SII sub-components, ELSA respondents
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18 197 who were unmarried or living alone were more likely to have depression, while this was
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21 198 the case with JAGES respondents with no social participation.
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199 **Table 2. Description of social isolation status and depression onset**

		ELSA ^a		JAGES	
		CES-D score at follow-up		GDS score at follow-up	
		< 4	≥ 4	< 5	≥ 5
		n = 3130 (94.0%)	n = 201 (6.0%)	n = 28671 (86.5%)	n = 4456 (13.5%)
Social Isolation Index score, (%)					
0		27.5	13.5	4.4	3.0
1		31.2	29.3	18.6	14.3
2		17.9	18.9	29.8	26.3
3		6.5	10.1	26.2	27.5
≥ 4		1.5	2.9	6.1	9.3
Missing		15.4	25.3	14.8	19.7
Social Isolation Index sub-components, (%)					
Unmarried or living alone	No	71.9	58.5	88.3	85.2
	Yes	28.1	41.5	10.2	12.7
	Missing	0.0	0.0	1.4	2.1
Poor interaction with children	No	81.8	73.4	26.6	25.0
	Yes	12.5	14.7	71.7	72.9
	Missing	5.7	11.8	1.7	2.1
Poor interaction with relatives	No	76.3	68.1	41.1	38.7
	Yes	17.3	18.6	54.4	56.0
	Missing	6.4	13.4	4.5	5.4
Poor interaction with friends	No	72.2	66.0	37.1	31.2
	Yes	18.4	21.6	58.2	63.8
	Missing	9.4	12.4	4.6	5.0
No social participation	No	61.7	46.3	75.0	63.9
	Yes	28.4	32.5	13.0	20.0
	Missing	10.0	21.2	11.7	16.1

200 ELSA, English Longitudinal Study of Ageing; JAGES, Japan Gerontological Evaluation
 201 Study; CES-D, Center for Epidemiologic Studies Depression Scale; GDS, Geriatric
 202 Depression Scale

203 ^a ELSA data after sampling weight

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6 204 Table 3 depicts the association between SII scores and depression onset.
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9 205 Multivariable analysis showed that higher SII scores were associated with a higher risk
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12 206 of depression onset in both studies after adjusting for all covariates. In the ELSA, the OR
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15 207 of depression onset was significantly higher from a score \geq one point (OR [95% CI]
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18 208 compared with zero points, one: 1.68 [1.02–2.75], two: 1.77 [1.03–3.05], three: 2.64
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21 209 [1.37–5.12], \geq four: 4.01 [1.43–11.22], p for trend = 0.015). In the JAGES, as SII scores
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24 210 increased, the OR of depression onset gradually increased, reaching significance at \geq
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27 211 three points (OR [95% CI] compared with zero points, one: 1.10 [0.89–1.35], two: 1.15
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30 212 [0.94–1.40], three: 1.28 [1.04–1.56], \geq four: 1.48 [1.18–1.85], p for trend < 0.001). These
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33 213 results showed almost the same tendency as the complete case analysis without multiple
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36 214 imputation (Supplementary Table 1).
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215 **Table 3. Association between social isolation and depression onset: multivariable logistic regression analysis**

	ELSA		JAGES	
	Crude OR (95% CI)	Adjusted OR (95% CI) ^a	Crude OR (95% CI)	Adjusted OR (95% CI) ^a
Social Isolation Index score				
0	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
1	1.92** (1.19–3.10)	1.68* (1.02–2.75)	1.14 (0.94–1.39)	1.10 (0.89–1.35)
2	2.15** (1.28–3.62)	1.77* (1.03–3.05)	1.32** (1.09–1.60)	1.15 (0.94–1.40)
3	3.19*** (1.73–5.90)	2.64** (1.37–5.12)	1.57*** (1.30–1.90)	1.28* (1.04–1.56)
≥ 4	3.85** (1.46–10.18)	4.01** (1.43–11.22)	2.26*** (1.83–2.79)	1.48*** (1.18–1.85)
	<i>p</i> for trend < 0.001	<i>p</i> for trend = 0.015	<i>p</i> for trend < 0.001	<i>p</i> for trend < 0.001

216 * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

217 ELSA, English Longitudinal Study of Ageing; JAGES, Japan Gerontological Evaluation Study; CI, confidence interval; OR, odds ratio

218 ^a Adjusted for age, gender, educational attainment, household equivalised income, present illness (cancer, heart disease, and stroke), self-rated health, smoking, drinking, and depression score at baseline (Center for Epidemiologic Studies Depression Scale for the ELSA and Geriatric Depression Scale for the JAGES).
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6 221 Table 4 presents the associations of SII sub-components with depression onset.
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9 222 In the ELSA, sub-components were not significant, although poor interaction with
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12 223 children was marginally significant (OR [95% CI], with ‘none’ as the reference;
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15 224 unmarried or living alone: 1.13 [0.80–1.60], poor interaction with children: 1.55 [1.00–
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18 225 2.41], poor interaction with relatives: 1.24 [0.79–1.94], poor interaction with friends: 1.15
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21 226 [0.77–1.71], no social participation: 1.22 [0.80–1.87]). In the JAGES, poor interaction
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24 227 with children and no social participation were significantly associated with depression
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27 228 onset after adjusting for all covariates (OR [95% CI], with ‘none’ as the reference;
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30 229 unmarried or living alone: 1.11 [1.00–1.24], poor interaction with children: 1.09 [1.01–
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33 230 1.19], poor interaction with relatives: 1.04 [0.96–1.12], poor interaction with friends: 1.03
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36 231 [0.95–1.11], no social participation: 1.28 [1.17–1.40]). These results were similar to those
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39 232 obtained from the complete case analysis (Supplementary Table 2).
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233 **Table 4. Association between sub-components of social isolation and depression onset: multivariable logistic regression analysis**

	ELSA	JAGES
	Adjusted OR (95% CI) ^a	Adjusted OR (95% CI) ^a
Social Isolation Index sub-components (reference: none)		
Unmarried or living alone	1.13 (0.80–1.60)	1.11 [†] (1.00–1.24)
Poor interaction with children	1.55 [†] (1.00–2.41)	1.09* (1.01–1.19)
Poor interaction with relatives	1.24 (0.79–1.94)	1.04 (0.96–1.12)
Poor interaction with friends	1.15 (0.77–1.71)	1.03 (0.95–1.11)
No social participation	1.22 (0.80–1.87)	1.28*** (1.17–1.40)

234 * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; [†] $p < 0.1$

235 ELSA, English Longitudinal Study of Ageing; JAGES, Japan Gerontological Evaluation Study; CI, confidence interval; OR, odds ratio

236 ^a Adjusted for age, gender, educational attainment, equivalent income, present illness (cancer, heart disease, and stroke), self-rated health,
 237 smoking, drinking, and depression score at baseline (Center for Epidemiologic Studies Depression Scale for the ELSA and Geriatric
 238 Depression Scale for the JAGES).

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6 239 **DISCUSSION**
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9 240 To the best of our knowledge, this is the first cross-national longitudinal study of the
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12 241 association of social isolation with depression among older English and Japanese adults.
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15 242 Social isolation was significantly associated with depression onset in both countries. Our
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18 243 results support previous longitudinal findings on social relationships and mental health in
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21 244 older adults in England[37] and Japan.[38] Using data frames that were similar with
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24 245 regard to assessment and covariates, we showed that social isolation is a common risk
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27 246 factor for depression in England and Japan despite country-specific cultural differences
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30 247 regarding social relationships. Thus, our results suggest that to safeguard the mental
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33 248 health of older adults, addressing social isolation is a global need.
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36 249 The association between social isolation and depression was somewhat stronger
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39 250 in England than in Japan. These results are similar to a previous report concerning
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42 251 mortality among older adults in England and Japan.[11] Although we cannot make direct
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45 252 comparisons because of variations in cohort follow-up periods and depression
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48 253 measurement, there are several possible reasons for this pattern of findings. The impact
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51 254 of social factors could be different depending on the group and society to which one
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54 255 belongs. This is best understood in the context of the concept of relative deprivation.[39]
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57 256 In other words, higher levels of relative social isolation may induce greater psychological
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6 257 stress. A previous study showed that rich community ties and cohesion were protective
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9 258 factors for health but could have a negative effect on those who were not socially
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12 259 involved.[40] Being isolated in a connected society such as the UK may represent a more
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15 260 severe condition, with a stronger negative impact on mental health.

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18 261 Our results showed that poor interaction with children was significant with
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21 262 regard to depression onset in Japan. In England, while the association was marginal, of
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24 263 the components of social isolation, poor interaction with children had the greatest effect.
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27 264 The lack of interaction with children could have an adverse effect on the mental health of
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30 265 older adults in both countries. Previous studies in England[41] and Japan[22] have
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33 266 reported that social support from children can contribute to alleviating depression, and
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36 267 our results point in the same direction. Older adults without children can be considered a
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39 268 vulnerable group, because adult children, in particular, are often the main source of
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42 269 positive social support for older parents.[42] Older parents have certain expectations with
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45 270 regard to receiving support from their children, and situations wherein these expectations
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48 271 are not met may lead to depressive mood.[43] On the contrary, a previous study reported
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51 272 no association between the presence of children and depression among older adults in the
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54 273 US.[22] Owing to strong spousal relationships in the US, the effect of the presence of
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57 274 children might be relatively small. Thus, our study confirmed the adverse effects of poor
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6 275 interaction with children common to England and Japan, but international generalizability
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9 276 can only be established based on further research considering the cultural background of
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12 277 family relationships in individual countries.
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15 278 Although traditionally Japan is a country where adult children are expected to
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18 279 demonstrate reciprocity with their parents owing to the strong family and kinship-based
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21 280 cultural background,[44] in this study, the effect of interaction with children on
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24 281 depression was relatively modest. In recent years, with trends such as adult children
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27 282 commonly living apart from their parents after marriage[45] and the development of
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30 283 public long-term care services for the ageing population,[46] Japan's family system has
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33 284 not remained as traditional as before. Therefore, interaction with children may not be as
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36 285 essential to the health of older adults as before. However, despite these cultural transitions,
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39 286 we believe that interaction with children has some value with regard to preventing
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42 287 depression in old age in Japan.
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45 288 Social participation was a strong protective factor for depression onset in Japan,
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48 289 whereas there was no association in England, although the OR was somewhat greater.
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51 290 Several previous studies have reported that social participation helps prevent depression
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54 291 onset.[37, 47–49] Our results pertaining to Japan support these reports. On the contrary,
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57 292 the protective effects of social participation on mental health have been shown to vary
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6 293 depending on the type of organisation an individual is involved with,[48] the individual's
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9 294 attitude towards participation,[48] and the duration[37] and frequency[49] of
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12 295 participation. Regarding the present study, in the English context, the role of social
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15 296 participation in depression prevention might have been unidentifiable because of
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18 297 differences in the effects of these participation contexts. We only took into account social
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21 298 participation, without delving into specific types. Thus, the context of effective social
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24 299 participation, such as type, duration, and role in the organisation in both countries,
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27 300 requires further investigation. Despite these challenges, our findings suggest that in Japan,
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30 301 social isolation prevention measures based on the promotion of social participation could
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33 302 be beneficial for safeguarding the mental health of older adults.

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36 303 This study has several strengths. First, it is the first cross-national population-
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39 304 level investigation of the association of social isolation with depression onset using a
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42 305 unified data frame. Second, by using two longitudinal datasets, we were able to examine
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45 306 the prospective association between social isolation and depression. Third, the use of
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48 307 large-scale data allowed us to detect the effects of relatively rare situations of severe
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51 308 social isolation.

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54 309 However, certain limitations cannot be ignored. First, the measurement of
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57 310 depression in the two cohorts was not the same. Therefore, we could not directly compare
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6 311 depression onset in the two countries. However, these measurements were also used in a
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9 312 previous cross-national comparison study in England and Japan,[28] and we were able to
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12 313 examine the association between social isolation and depression onset in both countries
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15 314 using the same data frame. Second, we used social support for the assessment of social
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18 315 contact for some items in order to be able to use the same SII. Therefore, cultural
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21 316 differences in expectations regarding the receipt of social support in both countries might
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24 317 have caused information biases. For instance, expectations regarding social support from
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27 318 relatives could originally have been higher in Japan,[44] leading to overestimation of
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30 319 social isolation levels. Third, regarding the items of the SII, the questions and their
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33 320 response options in the ELSA and JAGES were not exactly the same, nor were they
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36 321 strictly authorised through procedures such as reverse translation and confirming
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39 322 reliability and validity. However, we believe it is certainly meaningful to evaluate social
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42 323 isolation using the same framework. Finally, there were differences in study design in the
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45 324 data from the two cohorts, such as sampling method and follow-up period. We, therefore,
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48 325 made efforts to harmonise the data: those aged ≤ 64 , with dementia, and dependent in
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51 326 activities of daily living were excluded from the analysis. Moreover, the ELSA presents
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54 327 nationally representative population data, while the JAGES does not. However, the
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57 328 JAGES sample is representative of areas from a nationwide ageing study in which about
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329 one-fifth of all prefectures (nine out of 47) were enrolled. Even so, unlike the ELSA,
330 analysis in the JAGES does not use sampling weights, which may lead to selection bias.

331

332 **CONCLUSION**

333 We examined the association between social isolation and depression onset among older
334 adults in England and Japan, which have different cultural contexts regarding social
335 relationships, finding a significant association in both countries. Thus, globally, tackling
336 social isolation must be prioritised to safeguard the mental health of older adults.
337 Particularly in Japan, the promotion of interaction with children and social participation
338 could be key factors in addressing social isolation.

339

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342 Evaluation Study. We would also like to thank everyone who participated in the surveys.

343

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345 All authors contributed to the conception and design of this study. Data collection was
346 primarily conducted by MS, JA, NC, KO, and KK. Analyses were performed by TN, MS,

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6 347 JA, TT, SK, and TI. TN prepared the initial manuscript and MS, JA, NC, TT, SK, TI, KO,
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9 348 and KK significantly contributed to revising it. All authors read and approved the final
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12 349 manuscript.

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39 376 design, data collection and analysis, decision to publish or preparation of the manuscript.
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45 378 **DATA SHARING STATEMENT**

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48 379 For the JAGES, all enquiries are to be addressed to the data management committee via
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51 380 e-mail: dataadmin.ml@jages.net. All JAGES datasets have ethical or legal restrictions for
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54 381 public deposition because of the inclusion of sensitive information about the human
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57 382 participants. Regarding the ELSA, data are available in an open-access repository at
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6 383 <http://www.dataarchive.ac.uk/>.

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12 385 **COMPETING INTERESTS STATEMENT**

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15 386 The authors declare no conflict of interest.

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21 388 **REFERENCES**

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Supplementary Table 1. Association between social isolation and depression onset, by complete case analysis

		ELSA		JAGES	
		Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)
Social Isolation Index score	0	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
	1	1.92** (1.19–3.10)	1.56 [†] (0.94–2.60)	1.14 (0.94–1.39)	1.11 (0.87–1.41)
	2	2.15** (1.28–3.62)	1.71 [†] (0.98–2.99)	1.32** (1.09–1.60)	1.20 (0.95–1.51)
	3	3.19*** (1.73–5.90)	2.50** (1.27–4.90)	1.57*** (1.30–1.90)	1.30* (1.03–1.64)
	≥ 4	3.85** (1.46–10.18)	5.17** (1.83–14.66)	2.26*** (1.83–2.79)	1.47** (1.13–1.91)
		<i>p</i> for trend < 0.001	<i>p</i> for trend < 0.001	<i>p</i> for trend < 0.001	<i>p</i> for trend < 0.001
Age (years)	65–69		1.00 (reference)		1.00 (reference)
	70–74		1.37 (0.83–2.25)		1.16** (1.05–1.30)
	75–79		1.24 (0.71–2.14)		1.31*** (1.16–1.48)
	80–84		1.66 [†] (0.92–2.99)		1.60*** (1.37–1.88)
	≥ 85		0.97 (0.45–2.09)		1.79*** (1.39–2.30)
Gender	Male		1.00 (reference)		1.00 (reference)
	Female		1.58* (1.07–2.34)		1.00 (0.90–1.11)
Educational attainment (years)	< 15		1.00 (reference)		1.00 (reference)
	16–18		1.05 (0.68–1.60)		0.81*** (0.74–0.89)
	≥ 19		1.30 (0.70–2.41)		0.68*** (0.60–0.78)
Household equivalised income	1st quintile (lowest)		1.00 (reference)		1.00 (reference)
	2nd quintile		0.70 (0.40–0.21)		0.95 (0.83–1.09)
	3rd quintile		1.11 (0.66–1.87)		0.76*** (0.67–0.87)
	4th quintile		0.82 (0.45–1.50)		0.67*** (0.57–0.79)
	5th quintile (highest)		0.84 (0.42–1.68)		0.65*** (0.56–0.76)

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Cancer	No	1.00 (reference)	1.00 (reference)
	Yes	0.95 (0.32–2.81)	1.16 (0.93–1.43)
Heart disease	No	1.00 (reference)	1.00 (reference)
	Yes	1.13 (0.67–1.92)	1.20 (1.05–1.37)
Stroke	No	1.00 (reference)	1.00 (reference)
	Yes	1.3 (0.56–3.02)	1.18 (0.80–1.73)
Self-rated health	Good	1.00 (reference)	1.00 (reference)
	Poor	1.71* (1.13–2.59)	1.63*** (1.44–1.85)
CES-D score at baseline		1.90*** (1.60–2.25)	
GDS score at baseline			1.92*** (1.86–1.99)
Smoking	Never/past	1.00 (reference)	1.00 (reference)
	Current	0.76 (0.76–1.56)	1.29*** (1.12–1.48)
Drinking	Never/past	1.00 (reference)	1.00 (reference)
	Current	1.41 (0.81 – 2.44)	1.02 (0.93 – 1.13)

*, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$; †, $p < 0.1$

ELSA, English Longitudinal Study of Ageing; JAGES, Japan Gerontological Evaluation Study; CES-D, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; GDS, Geriatric Depression Scale; OR, odds ratio

Supplementary Table 2. Association between sub-components of social isolation and depression onset, by complete case analysis

		ELSA		JAGES	
		Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)
Social Isolation Index sub-components (ref; none)					
Unmarried or living alone		1.91*** (1.34–2.72)	1.27 (0.84–1.93)	1.33*** (1.18–1.49)	1.02 (0.88–1.19)
Poor interaction with children		1.08 (0.68–1.74)	1.51 (0.91–2.50)	1.01 (0.98–1.10)	1.13* (1.02–1.25)
Poor interaction with relatives		1.25 (0.83–1.90)	1.33 (0.85–2.08)	1.05 (0.97–1.13)	0.98 (0.90–1.08)
Poor interaction with friends		1.19 (0.78–1.80)	1.21 (0.78–1.87)	1.23 (1.14–1.33)	1.11* (1.01–1.22)
No social participation		1.54* (1.08–2.19)	1.46† (0.98–2.16)	1.70 (1.56–1.86)	1.22*** (1.09–1.36)
Age (years)					
		65–69	1.00 (reference)		1.00 (reference)
		70–74	1.37 (0.83–2.25)		1.17** (1.05–1.30)
		75–79	1.25 (0.72–2.17)		1.31*** (1.16–1.49)
		80–84	1.68† (0.92–3.04)		1.60*** (1.36–1.88)
		≥ 85	1.00 (0.46–2.21)		1.78*** (1.38–2.30)
Gender		Male	1.00 (reference)		1.00 (reference)
		Female	1.59* (1.07–2.37)		1.00 (0.89–1.11)
Educational attainment (years)		< 15	1.00 (reference)		1.00 (reference)
		10–12	1.04 (0.67–1.60)		0.81*** (0.74–0.90)
		≥ 19	1.31 (0.70–2.46)		0.69*** (0.61–0.78)
Household equivalised income		1st quintile (lowest)	1.00 (reference)		1.00 (reference)
		2nd quintile	0.71 (0.41–1.23)		0.95 (0.83–1.09)
		3rd quintile	1.13 (0.67–1.93)		0.76*** (0.67–0.86)
		4th quintile	0.83 (0.45–1.52)		0.67*** (0.57–0.79)
		5th quintile (highest)	0.85 (0.42–1.71)		0.66*** (0.57–0.76)
Cancer		No	1.00 (reference)		1.00 (reference)
		Yes	0.95 (0.32–2.81)		1.15 (0.93–1.43)

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Heart disease	No	1.00 (reference)	1.00 (reference)
	Yes	1.16 (0.69–1.96)	1.20** (1.05–1.37)
Stroke	No	1.00 (reference)	1.00 (reference)
	Yes	1.28 (0.55–2.99)	1.18 (0.80–1.73)
Self-rated health	Good	1.00 (reference)	1.00 (reference)
	Poor	1.71* (1.13–2.58)	1.62*** (1.43–1.83)
CES-D score at baseline		1.89*** (1.59–2.25)	1.00 (reference)
GDS score at baseline			1.92*** (1.85–1.99)
Smoking	Never/past	1.00 (reference)	1.00 (reference)
	Current	0.74 (0.36–1.53)	1.29*** (1.13–1.48)
Drinking	Never/past	1.00 (reference)	1.00 (reference)
	Current	1.39 (0.80–2.40)	1.03 (0.93–1.14)

*, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$; †, $p < 0.1$
 ELSA, English Longitudinal Study of Ageing; JAGES, Japan Gerontological Evaluation Study; CES-D, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; GDS, Geriatric Depression Scale; OR, odds ratio

STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	1, 3 3-4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6-9
Objectives	3	State specific objectives, including any prespecified hypotheses	9
Methods			
Study design	4	Present key elements of study design early in the paper	9
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	9-10
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (b) For matched studies, give matching criteria and number of exposed and unexposed	9-10 Not applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	10-11
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	10-11
Bias	9	Describe any efforts to address potential sources of bias	12
Study size	10	Explain how the study size was arrived at	Not applicable
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	10-11
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses	11-12 Not applicable 12 Not applicable Not applicable
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	13 Not applicable Not applicable
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	13-14 15-16 10
Outcome data	15*	Report numbers of outcome events or summary measures over time	17-18

1 2 3 4 5 6 7	Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	19-21 Not applicable Not applicable
8 9	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Supplementary 1, 2
10	Discussion			
11	Key results	18	Summarise key results with reference to study objectives	23
12 13 14	Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	26-28
15 16 17 18	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	23-26
19 20	Generalisability	21	Discuss the generalisability (external validity) of the study results	24-25
21	Other information			
22 23 24	Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	29-30

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

BMJ Open

Association between social isolation and depression onset among older adults: A cross-national longitudinal study in England and Japan

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Original research

Title

Association between social isolation and depression onset among older adults: A cross-national longitudinal study in England and Japan

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51 **Word count:** 3,216 words

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6 **1 ABSTRACT**
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9 **2 Objective:** Social isolation is a risk factor for depression in older age. However, little is
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12 **3** known regarding whether its impact varies depending on country-specific cultural
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15 **4** contexts regarding social relationships. The present study examined the association of
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18 **5** social isolation with depression onset among older adults in England, which has taken
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21 **6** advanced measures against social isolation, and Japan, a super-aged society with a rapidly
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24 **7** increasing number of socially isolated people.
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27 **8 Design:** Prospective longitudinal study.
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30 **9 Setting:** We utilised data from two ongoing studies: the English Longitudinal Study of
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33 **10** Ageing (ELSA) and the Japan Gerontological Evaluation Study (JAGES).
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36 **11 Participants:** Older adults aged ≥ 65 years without depression at baseline were followed
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39 **12** up regarding depression onset for two years (2010/11 to 2012/13) for the ELSA and 2.5
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42 **13** years (2010/11 to 2013) for the JAGES.
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45 **14 Primary outcome measure:** Depression was assessed with the Center for Epidemiologic
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48 **15** Studies Depression Scale for the ELSA and Geriatric Depression Scale for the JAGES.
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51 **16** Multivariable logistic regression analysis was performed to evaluate social isolation using
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54 **17** multiple parameters (marital status; interaction with children, relatives, and friends; and
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57 **18** social participation).
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7 19 **Results:** The data of 3,331 respondents from the ELSA and 33,127 from the JAGES were
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9 20 analysed. Multivariable logistic regression analysis demonstrated that social isolation was
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12 21 significantly associated with depression onset in both countries. In the ELSA, poor
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15 22 interaction with children was marginally associated with depression onset, while in the
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18 23 JAGES, poor interaction with children and no social participation significantly affected
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21 24 depression onset.

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24 25 **Conclusions:** Despite variations in cultural background, social isolation was associated
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27 26 with depression onset in both England and Japan. Addressing social isolation to safeguard
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30 27 older adults' mental health must be globally prioritised.

31 32 33 28 34 35 36 29 **Strengths and limitations of this study**

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39 30 ● This is the first cross-national longitudinal study to examine the association between
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42 31 social isolation and depression onset in England, which has taken advanced measures
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45 32 against social isolation, and Japan, a super-aged society with a rapidly increasing
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48 33 number of socially isolated people.
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51 34 ● This study included a large sample of over 3,300 individuals from England and
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54 35 33,000 individuals from Japan aged 65 years and older.
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57 36 ● A limitation of this study is that we cannot make direct comparisons because of
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6 37 variations in cohort follow-up periods and depression measurement.
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9 38 ● Another limitation is the use of social support for the evaluation of social contact so
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12 39 as to permit the use of the same social isolation assessment scale in both countries.
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For peer review only

40 INTRODUCTION

41 With population ageing, there is growing worldwide interest in social issues concerning
42 older adults, including social isolation and the deterioration of physical and mental health.

43 Defined as an objective state in where an individual has few close relationships or limited
44 contact within a community,[1] social isolation is recognised as a social determinant of
45 health with relevance to mortality,[2] cardiovascular diseases,[3] dementia,[4] and mental
46 health.[5, 6] Social isolation is a major risk factor for mental health problems in older
47 age. Several systematic reviews have demonstrated that social isolation is associated with
48 depressive symptoms,[5, 6] which, in turn, are correlated with unhealthy behaviours and
49 reduced access to material resources.[7] Depression, common in later life, is related to
50 adverse health outcomes such as poor quality of life[8] and functional disability.[9] With
51 the high current global burden of depression expected to increase further by 2030,[10]
52 addressing social isolation is an important gerontological issue for protecting mental
53 health among older adults.

54 The impacts of social isolation on health may vary by country; this could be the
55 result of differences in the social environments related to social networks within and
56 outside the family. A recent study of older adults in England and Japan showed that social
57 isolation is a common risk factor for mortality in both countries, with a greater impact

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6 58 observed in England; the results are discussed in terms of possible differences between
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9 59 societies that are highly connected and those that are not.[11] In the United Kingdom
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12 60 (UK), in recognition of the impact of social isolation on health and economic loss, the
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15 61 position of ‘Minister of Loneliness’ was established in 2018, and the country is taking a
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18 62 progressive approach to the elimination of social isolation.[12] In contrast, Japan, now a
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21 63 super-aged society (more than 21% of the population aged 65 or above),[13] is
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24 64 experiencing a rapidly increasing trend in the number of never-married persons and
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27 65 weakening community and neighbourhood relations,[14] leading to a rise in the number
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30 66 of socially isolated individuals.[15] In Japan, the proportion of people who rarely or never
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33 67 spend time with those close to them has been reported to be the highest among
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36 68 Organisation for Economic Co-operation and Development countries. In particular, this
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39 69 figure is much higher than in the UK, which has made advances in tackling social
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42 70 isolation (Japan = 15.3%, UK = 5.0%).[16] Owing to differences in social structures and
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45 71 the contexts surrounding social isolation, the impact of social isolation on depression is
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48 72 expected to vary across countries.

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51 73 Furthermore, the health effects of social isolation may differ depending on the
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54 74 cultural context of social relationships. In East Asian countries, including Japan, there is
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57 75 a familial norm based on the traditional culture of filial piety,[17] which is often
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6 76 contrasted with individualism in Western countries.[18, 19] Based on this cultural
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9 77 background, Japanese social support networks may be kinship centred, which may be
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12 78 narrower than the types of social networks prevalent in other countries.[20] However,
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15 79 there is a lack of consensus on the health effects of social relationships based on these
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18 80 cultural differences. A previous cross-national study showed that among English men,
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21 81 friendship-based social relationships had a significant impact on longevity, whereas
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24 82 among Japanese men, this impact was associated with family-based social
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27 83 relationships.[21] In contrast, a study of older adults in the United States (US) and Japan
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30 84 demonstrated that while relationships with children were associated with a low level of
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33 85 depression only in Japan, the presence of spouses was important in both countries, but
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36 86 more so in the US.[22] Another comparative study among adults suggested that social
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39 87 contact with friends benefitted women's mental health in the UK but not in Japan.[23]
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42 88 Thus, the family-oriented nature of East Asian societies does not automatically imply the
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45 89 health importance of family-based relationships, and the roles of individual components
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48 90 of social isolation (family, friends, and others) in the mental health of older adults in each
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51 91 country remain controversial.

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54 92 As the association between social isolation and depression is often described as
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57 93 bidirectional,[24] longitudinal studies are needed to address temporality. However,
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6 94 previous cross-national comparative studies have employed only cross-sectional
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9 95 designs.[22, 23] Therefore, using longitudinal data from both countries, the present study
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12 96 aims to investigate the association of social isolation with depression onset in England,
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15 97 which has taken advanced measures against social isolation, and Japan, a super-aged
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18 98 society with a rapidly increasing number of socially isolated people.
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24 100 **METHODS**

27 101 **Sample**

30 102 This longitudinal study was conducted using data from two ongoing prospective cohort
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33 103 studies: the English Longitudinal Study of Ageing (ELSA) and the Japan Gerontological
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36 104 Evaluation Study (JAGES). The ELSA targets independent-living older adults aged ≥ 50 ,
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39 105 while JAGES participants are community-dwelling individuals aged ≥ 65 who are
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42 106 ineligible for long-term healthcare insurance benefits.[25] Details of the ELSA and
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45 107 JAGES can be found elsewhere.[26, 27] For the present analysis, we used the two waves
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48 108 of data that most closely corresponded with the timing of our study: wave 5 (2010/2011)
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51 109 to wave 6 (2012/2013) for the ELSA, and wave 1 (2010/2011) to wave 2 (2013) for the
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54 110 JAGES. We harmonised the data by including older adults aged ≥ 65 , independent in
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57 111 activities of daily living, and without self-reported dementia. For analysis, respondents
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6 112 who scored above the cut-off point for depression on each measure in the respective
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9 113 cohort at baseline were excluded and we followed up the onset of depression for two years
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12 114 for the ELSA and 2.5 years for the JAGES.
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18 116 **Depression**

21 117 Based on a previous cross-national study,[28] depressive symptoms were measured both
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24 118 at baseline and follow-up using eight items from the Center for Epidemiologic Studies
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27 119 Depression Scale (CES-D) in the ELSA[29] and the Geriatric Depression Scale (GDS-
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30 120 15) in the JAGES.[30] To identify possible depressive cases, the CES-D cut-off was ≥ 4
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33 121 while that for the GDS-15 was ≥ 5 . [31, 32] As previously mentioned, respondents with
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36 122 depression at baseline were excluded and we observed the onset of depression during
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39 123 follow-up.
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45 125 **Social isolation**

48 126 Social isolation levels were assessed using a modified version of the Social Isolation
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51 127 Index (SII).[33–35] The index was computed with respondents given a point if they: (1)
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54 128 were unmarried or living alone, (2) had poor interaction with children (did not live with
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57 129 their children or had no one to provide emotional or instrumental social support), (3) had
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6 130 poor interaction with relatives (did not have immediate family members providing
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9 131 emotional or instrumental social support), (4) had poor interaction with friends (less than
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12 132 monthly contact or no friends who could provide emotional or instrumental social
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15 133 support), and (5) had no social participation (no participation in any social or religious
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18 134 groups). The total possible score ranged from 0 to 5, with higher scores indicating greater
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21 135 social isolation. The participants were categorised into the following five groups based
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24 136 on their scores: 0, 1, 2, 3, and 4–5 points. We used the total score and the scores of the
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27 137 five sub-components as predictive variables.
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32 33 139 **Covariates**

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36 140 The covariates included age, gender, educational attainment, household equivalised
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39 141 income, present illness, self-rated health, smoking, and drinking. Age was categorised as
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42 142 65–69, 70–74, 75–79, 80–84, and ≥ 85 . Based on the ages of respondents who had
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45 143 completed formal education, the age of final educational attainment was categorised as \leq
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48 144 15 years, 16–18 years, and ≥ 19 years. Household equivalised income was classified into
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51 145 quintiles. Present illness was classified as ‘yes’ or ‘no’ for cancer, heart disease, and
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54 146 stroke. Self-rated health was dichotomised as ‘poor’ and ‘good’. Smoking and drinking
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57 147 were dichotomised as ‘never/past’ and ‘current’.
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149 **Statistical analysis**

150 We analysed the ELSA and JAGES data separately because of differences in research
151 design, especially sampling approaches. A longitudinal weight was applied to account for
152 survey non-response for the ELSA but not the JAGES as its design does not allow it.
153 First, we calculated descriptive statistics. Second, we conducted a multivariable logistic
154 regression analysis to examine the association between SII score and depression onset
155 and obtained odds ratios (ORs) and 95% confidence intervals (CIs) for depression onset.
156 Model 1 was not adjusted for covariates while Model 2 was adjusted for all covariates.
157 Additionally, we analysed the association between SII sub-components and depression
158 onset, adjusted for all covariates.

159 To mitigate potential biases resulting from missing information, we used the
160 multiple imputation approach under the missing at random assumption. We generated 20
161 imputed datasets for the final analysis, which excluded those who met the exclusion
162 criteria and did not respond to the follow-up surveys, using the multiple imputation by
163 chained equations procedure and pooled the results using Rubin's rule.[36]

164 The significance level was set at $p < 0.05$. We used R (Version 3.5.2 for
165 Windows) for all statistical analyses.

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10 167 **Ethical considerations**

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12 168 The ELSA investigators received ethical approval for all waves of the study from the

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15 169 National Health Service Research Ethics Committees under the National Research and

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18 170 Ethics Services (MREC/01/2/91). The JAGES protocols were approved by the Ethics

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21 171 Committee on the Research of Human Subjects at Nihon Fukushi University (10-05).

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27 173 **Patient and public involvement**

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30 174 No patients were involved in the development of the research question, study design, or

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33 175 data interpretation.

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39 177 **RESULTS**

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42 178 A total of 3,331 ELSA respondents and 33,127 JAGES respondents were included in the

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45 179 final analysis. Their baseline characteristics are presented in Table 1. The mean age

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48 180 (standard deviation) was 73.6 (6.9) years for the ELSA and 72.4 (5.4) years for the JAGES.

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51 181 Regarding SII scores, the ELSA had the largest number of respondents with 0 and 1 points,

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54 182 while the JAGES had the largest number with 2 and 3 points. In the ELSA, respondents

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57 183 who were older, male, less educated, had a lower income, had heart disease, had poor

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6 184 self-rated health, smoked, consumed little alcohol, and had higher baseline depressive
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9 185 symptom scores and higher SII scores. A similar trend was observed in the JAGES, but
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12 186 here, those who consumed more alcohol had higher SII scores.
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187 **Table 1. Respondents' baseline characteristics**

	ELSA ^a					JAGES				
	Social Isolation Index score ^b					Social Isolation Index score ^b				
	0	1	2	3	≥ 4	0	1	2	3	≥ 4
	n = 905	n = 1049	n = 596	n = 216	n = 49	n = 1402	n = 5981	n = 9723	n = 8735	n = 2176
	(27.2%)	(31.5%)	(17.9%)	(6.5%)	(1.5%)	(4.2%)	(18.0%)	(29.4%)	(26.4%)	(6.6%)
Age (years), (%)										
65–69	41.0	36.4	29.9	27.6	28.3	38.6	40.5	38.0	37.0	35.8
70–74	26.1	28.3	28.8	29.3	23.6	32.1	32.5	31.6	31.0	30.4
75–79	20.9	17.5	19.3	15.8	20.4	19.2	18.3	19.5	20.3	21.9
80–84	9.1	12.2	12.5	14.5	15.5	8.3	6.7	8.3	9.0	8.8
≥ 85	2.8	5.7	9.5	12.8	12.2	1.9	2.0	2.6	2.7	3.1
Gender, (%)										
Men	50.0	46.1	45.3	51.9	65.8	27.2	35.1	47.0	64.4	66.1
Women	50.0	53.9	54.7	48.1	34.2	72.8	64.9	53.0	35.6	33.9
Educational attainment (years), (%)										
≤ 15	44.1	51.3	52.3	60.9	69.6	42.9	38.1	37.9	38.7	48.6
16–18	35.0	33.8	34.6	27.5	14.1	40.9	40.8	39.3	36.8	31.1
≥ 19	17.8	12.5	11.0	10.3	14.0	15.7	20.4	21.8	23.3	18.5
Missing	3.2	2.4	2.1	1.3	2.3	0.5	0.7	0.9	1.2	1.8
Household equivalised income, (%)										
1st quintile (lowest)	11.4	18.3	23.2	31.2	14.4	7.4	10.9	13.9	15.6	21.3
2nd quintile	21.5	23.7	26.1	24.1	29.6	13.2	13.5	15.0	15.5	16.4
3rd quintile	20.9	21.8	18.9	19.5	27.1	22.5	30.6	30.3	30.6	28.0
4th quintile	21.9	19.9	18.1	16.5	16.6	14.3	13.6	12.7	11.3	9.5
5th quintile (highest)	22.7	15.0	12.7	8.3	12.4	31.5	22.5	19.2	16.8	12.9
Missing	1.5	1.3	0.9	0.4	0.0	11.1	8.9	8.9	10.2	11.9
Cancer, (%)										
No	96.5	95.8	97.1	97.5	96.5	91.0	91.2	90.8	90.1	89.7
Yes	3.4	4.2	2.9	2.5	3.5	3.2	3.1	3.1	3.4	3.7
Missing	0.1	0.0	0.0	0.0	0.0	5.8	5.7	6.1	6.5	6.6
Heart disease, (%)										
No	90.7	86.9	88.4	88.3	77.3	91.0	91.2	90.8	90.1	89.7
Yes	9.3	13.0	11.6	11.7	22.7	3.2	3.1	3.1	3.4	3.7
Missing	0.0	0.1	0.0	0.0	0.0	5.8	5.7	6.1	6.5	6.6

Stroke, (%)											
No	96.3	96.1	97	94.4	96.6	93.3	93.6	93.1	92.5	92.2	
Yes	3.7	3.8	3.0	5.6	3.4	0.9	0.8	0.8	1.0	1.2	
Missing	0	0.1	0.0	0.0	0.0	5.8	5.7	6.1	6.5	6.6	
Self-rated health, (%)											
Good	86.4	79.9	78.8	75.4	71.3	92.0	91.7	90.6	90.2	87.2	
Poor	13.6	20.1	21.2	24.6	28.7	7.2	7.7	8.6	9.0	12.2	
Missing	0.0	0.0	0.0	0.0	0.0	0.8	0.5	0.8	0.8	0.6	
Smoking, (%)											
Never/past	95.5	93.1	89.8	82.9	89.4	86.4	86.1	82.9	81.5	78.4	
Current	4.5	6.9	10.2	17.1	10.6	6.4	7.4	9.5	11.3	14.2	
Missing	0.0	0.0	0.0	0.0	0.0	7.1	6.5	7.5	7.2	7.3	
Drinking, (%)											
Never/past	7.5	11.8	14.9	25.8	17.3	65.0	60.0	56.5	50.4	55.0	
Current	91.3	87.0	82.9	72.6	73.6	30.2	35.7	38.6	44.7	40.4	
Missing	1.3	1.2	2.2	1.6	9.2	4.8	4.3	4.9	4.9	4.6	
CES-D score at baseline, (%)											
0	57.2	52.0	45.5	42.2	54.0						
1	27.3	26.2	28.6	31.8	25.5						
2	9.8	13.8	17.1	11.9	15.1						
3	5.7	8.0	8.8	14.2	5.4						
GDS score at baseline, (%)											
0						20.5	30.4	29.0	26.4	24.3	
1						25.5	28.4	28.6	26.9	27.0	
2						22.5	20.0	19.8	21.5	21.1	
3						17.5	13.1	13.5	14.7	15.9	
4						14.1	8.1	9.1	10.5	11.7	

188 ELSA, English Longitudinal Study of Ageing; JAGES, Japan Gerontological Evaluation
 189 Study; CES-D, Center for Epidemiologic Studies Depression Scale; GDS, Geriatric
 190 Depression Scale

191 ^a ELSA data after sampling weight

192 ^b Missing data: ELSA, n = 516; JAGES, n = 5,110

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6 193 Table 2 presents the description of social isolation and depression onset. At
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9 194 follow-up, 201 (6.0%) ELSA respondents and 4,456 (13.5%) JAGES respondents
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12 195 exhibited depression onset. In both studies, higher SII scores were associated with an
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15 196 increased risk of depression onset. Regarding SII sub-components, ELSA respondents
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18 197 who were unmarried or living alone were more likely to have depression, while this was
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21 198 the case with JAGES respondents with no social participation.
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199 **Table 2. Description of social isolation status and depression onset**

		ELSA ^a		JAGES	
		CES-D score at follow-up		GDS score at follow-up	
		< 4	≥ 4	< 5	≥ 5
		n = 3130 (94.0%)	n = 201 (6.0%)	n = 28671 (86.5%)	n = 4456 (13.5%)
Social Isolation Index score, (%)					
0		27.5	13.5	4.4	3.0
1		31.2	29.3	18.6	14.3
2		17.9	18.9	29.8	26.3
3		6.5	10.1	26.2	27.5
≥ 4		1.5	2.9	6.1	9.3
Missing		15.4	25.3	14.8	19.7
Social Isolation Index sub-components, (%)					
Unmarried or living alone	No	71.9	58.5	88.3	85.2
	Yes	28.1	41.5	10.2	12.7
	Missing	0.0	0.0	1.4	2.1
Poor interaction with children	No	81.8	73.4	26.6	25.0
	Yes	12.5	14.7	71.7	72.9
	Missing	5.7	11.8	1.7	2.1
Poor interaction with relatives	No	76.3	68.1	41.1	38.7
	Yes	17.3	18.6	54.4	56.0
	Missing	6.4	13.4	4.5	5.4
Poor interaction with friends	No	72.2	66.0	37.1	31.2
	Yes	18.4	21.6	58.2	63.8
	Missing	9.4	12.4	4.6	5.0
No social participation	No	61.7	46.3	75.0	63.9
	Yes	28.4	32.5	13.0	20.0
	Missing	10.0	21.2	11.7	16.1

200 ELSA, English Longitudinal Study of Ageing; JAGES, Japan Gerontological Evaluation
 201 Study; CES-D, Center for Epidemiologic Studies Depression Scale; GDS, Geriatric
 202 Depression Scale

203 ^a ELSA data after sampling weight

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6 204 Table 3 depicts the association between SII scores and depression onset.
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9 205 Multivariable analysis showed that higher SII scores were associated with a higher risk
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12 206 of depression onset in both studies after adjusting for all covariates. In the ELSA, the OR
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15 207 of depression onset was significantly higher from a score \geq one point (OR [95% CI]
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18 208 compared with zero points, one: 1.68 [1.02–2.75], two: 1.77 [1.03–3.05], three: 2.64
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21 209 [1.37–5.12], \geq four: 4.01 [1.43–11.22], p for trend = 0.015). In the JAGES, as SII scores
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24 210 increased, the OR of depression onset gradually increased, reaching significance at \geq
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27 211 three points (OR [95% CI] compared with zero points, one: 1.10 [0.89–1.35], two: 1.15
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30 212 [0.94–1.40], three: 1.28 [1.04–1.56], \geq four: 1.48 [1.18–1.85], p for trend $<$ 0.001). These
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33 213 results showed almost the same tendency as the complete case analysis without multiple
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36 214 imputation (Supplementary Table 1).
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215 **Table 3. Association between social isolation and depression onset: multivariable logistic regression analysis**

	ELSA		JAGES	
	Crude OR (95% CI)	Adjusted OR (95% CI) ^a	Crude OR (95% CI)	Adjusted OR (95% CI) ^a
Social Isolation Index score				
0	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
1	1.92** (1.19–3.10)	1.68* (1.02–2.75)	1.14 (0.94–1.39)	1.10 (0.89–1.35)
2	2.15** (1.28–3.62)	1.77* (1.03–3.05)	1.32** (1.09–1.60)	1.15 (0.94–1.40)
3	3.19*** (1.73–5.90)	2.64** (1.37–5.12)	1.57*** (1.30–1.90)	1.28* (1.04–1.56)
≥ 4	3.85** (1.46–10.18)	4.01** (1.43–11.22)	2.26*** (1.83–2.79)	1.48*** (1.18–1.85)
	<i>p</i> for trend < 0.001	<i>p</i> for trend = 0.015	<i>p</i> for trend < 0.001	<i>p</i> for trend < 0.001

216 * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

217 ELSA, English Longitudinal Study of Ageing; JAGES, Japan Gerontological Evaluation Study; CI, confidence interval; OR, odds ratio

218 ^a Adjusted for age, gender, educational attainment, household equivalised income, present illness (cancer, heart disease, and stroke), self-rated health, smoking, drinking, and depression score at baseline (Center for Epidemiologic Studies Depression Scale for the ELSA and Geriatric Depression Scale for the JAGES).
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6 221 Table 4 presents the associations of SII sub-components with depression onset.
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9 222 In the ELSA, sub-components were not significant, although poor interaction with
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12 223 children was marginally significant (OR [95% CI], with ‘none’ as the reference;
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15 224 unmarried or living alone: 1.13 [0.80–1.60], poor interaction with children: 1.55 [1.00–
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18 225 2.41], poor interaction with relatives: 1.24 [0.79–1.94], poor interaction with friends: 1.15
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21 226 [0.77–1.71], no social participation: 1.22 [0.80–1.87]). In the JAGES, poor interaction
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24 227 with children and no social participation were significantly associated with depression
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27 228 onset after adjusting for all covariates (OR [95% CI], with ‘none’ as the reference;
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30 229 unmarried or living alone: 1.11 [1.00–1.24], poor interaction with children: 1.09 [1.01–
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33 230 1.19], poor interaction with relatives: 1.04 [0.96–1.12], poor interaction with friends: 1.03
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36 231 [0.95–1.11], no social participation: 1.28 [1.17–1.40]). These results were similar to those
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39 232 obtained from the complete case analysis (Supplementary Table 2).
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233 **Table 4. Association between sub-components of social isolation and depression onset: multivariable logistic regression analysis**

	ELSA	JAGES
	Adjusted OR (95% CI) ^a	Adjusted OR (95% CI) ^a
Social Isolation Index sub-components (reference: none)		
Unmarried or living alone	1.13 (0.80–1.60)	1.11 [†] (1.00–1.24)
Poor interaction with children	1.55 [†] (1.00–2.41)	1.09* (1.01–1.19)
Poor interaction with relatives	1.24 (0.79–1.94)	1.04 (0.96–1.12)
Poor interaction with friends	1.15 (0.77–1.71)	1.03 (0.95–1.11)
No social participation	1.22 (0.80–1.87)	1.28*** (1.17–1.40)

234 * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; [†] $p < 0.1$

235 ELSA, English Longitudinal Study of Ageing; JAGES, Japan Gerontological Evaluation Study; CI, confidence interval; OR, odds ratio

236 ^a Adjusted for age, gender, educational attainment, equivalent income, present illness (cancer, heart disease, and stroke), self-rated health,
237 smoking, drinking, and depression score at baseline (Center for Epidemiologic Studies Depression Scale for the ELSA and Geriatric
238 Depression Scale for the JAGES).

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6 239 **DISCUSSION**
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9 240 To the best of our knowledge, this is the first cross-national longitudinal study of the
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12 241 association of social isolation with depression among older English and Japanese adults.
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15 242 Social isolation was significantly associated with depression onset in both countries. Our
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18 243 results support previous longitudinal findings on social relationships and mental health
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21 244 among older adults in England[37] and Japan.[38] Using data frames that were similar
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24 245 with regard to assessment and covariates, we demonstrated that social isolation is a
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27 246 common risk factor for depression in England and Japan, despite country-specific cultural
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30 247 differences regarding social relationships. Thus, our results suggest that to safeguard the
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33 248 mental health of older adults, addressing social isolation is a global need.
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36 249 The association between social isolation and depression was somewhat stronger
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39 250 in England than in Japan. These results are similar to a previous report concerning
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42 251 mortality among older adults in England and Japan.[11] Although we cannot make direct
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45 252 comparisons due to variations in cohort follow-up periods and depression measurement,
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48 253 there are several possible reasons for this pattern of findings. The impact of social factors
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51 254 could differ depending on the group and society to which one belongs. This is best
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54 255 understood in the context of the concept of relative deprivation.[39] In other words, higher
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57 256 levels of relative social isolation may induce greater psychological stress. A previous
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6 257 study showed that rich community ties and cohesion were protective factors for health
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9 258 but could have a negative effect on those who were not socially involved.[40] Being
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12 259 isolated in a connected society such as the UK may represent a more severe condition,
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15 260 with a stronger negative impact on mental health.
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18 261 Our results revealed that poor interaction with children was significant with
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21 262 regard to depression onset in Japan. In England, while the association was marginal, of
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24 263 the components of social isolation, poor interaction with children had the greatest effect.
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27 264 The lack of interaction with children could have an adverse effect on the mental health of
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30 265 older adults in both countries. Previous studies in England[41] and Japan[22] have
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33 266 reported that social support from children can contribute to alleviating depression, and
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36 267 our results point in the same direction. Older adults without children can be considered a
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39 268 vulnerable group, because adult children, in particular, are often the main source of
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42 269 positive social support for older parents.[42] Older parents have certain expectations with
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45 270 regard to receiving support from their children, and situations wherein these expectations
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48 271 are not met may lead to depressive mood.[43] However, a previous study reported no
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51 272 association between the presence of children and depression among older adults in the
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54 273 US.[22] Owing to strong spousal relationships in the US, the effect of the presence of
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57 274 children might be relatively small. Thus, our study confirmed the adverse effects of poor
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6 275 interaction with children common to England and Japan, but international generalizability
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9 276 can only be established based on further research considering the cultural background of
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12 277 family relationships in individual countries.
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15 278 Although traditionally Japan is a country in which adult children are expected to
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18 279 demonstrate reciprocity with their parents based on the strong family and kinship-based
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21 280 cultural background,[44] in this study, the effect of interaction with children on
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24 281 depression was relatively modest. In recent years, with trends such as adult children
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27 282 commonly living apart from their parents after marriage[45] and the development of
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30 283 public long-term care services for the ageing population,[46] Japan's family system has
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33 284 become less traditional. Therefore, interaction with children may not be as essential to
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36 285 the health of older adults as before. However, despite these cultural transitions, we believe
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39 286 that interaction with children has some value with regard to preventing depression in old
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42 287 age in Japan.
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45 288 Social participation was a strong protective factor for depression onset in Japan,
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48 289 whereas there was no association in England, although the OR was somewhat greater.
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51 290 Several previous studies have reported that social participation helps prevent depression
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54 291 onset.[37, 47–49] Our results pertaining to Japan support these reports. However, the
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57 292 protective effects of social participation on mental health vary depending on the type of
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6 293 organisation with which an individual is involved,[48] the individual's attitude towards
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9 294 participation,[48] and the duration[37] and frequency[49] of participation. Regarding the
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12 295 present study, in the English context, the role of social participation in depression
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15 296 prevention might have been unidentifiable due to differences in the effects of these
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18 297 participation contexts. We took into account only social participation, without delving
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21 298 into specific types. Thus, the context of effective social participation, such as type,
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24 299 duration, and role in the organisation in both countries, requires further investigation.
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27 300 Despite these challenges, our findings suggest that in Japan, social isolation prevention
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30 301 measures based on the promotion of social participation could be beneficial for
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33 302 safeguarding the mental health of older adults.

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36 303 This study has several strengths. First, it is the first cross-national population-
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39 304 level investigation of the association of social isolation with depression onset using a
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42 305 unified data frame. Second, by using two longitudinal datasets, we were able to examine
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45 306 the prospective association between social isolation and depression. Third, the use of
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48 307 large-scale data allowed us to detect the effects of relatively rare situations of severe
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51 308 social isolation.

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54 309 However, certain limitations cannot be ignored. First, the measurement of
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57 310 depression in the two cohorts was not the same. Therefore, we could not directly compare
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6 311 depression onset in the two countries. However, these measurements were also used in a
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9 312 previous cross-national comparison study in England and Japan,[28] and we were able to
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12 313 examine the association between social isolation and depression onset in both countries
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15 314 using the same data frame. Second, we used social support for the assessment of social
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18 315 contact for some items in order to be able to use the same SII. Therefore, cultural
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21 316 differences in expectations regarding the receipt of social support in both countries might
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24 317 have caused information biases. For instance, expectations regarding social support from
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27 318 relatives could originally have been higher in Japan,[44] leading to overestimation of
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30 319 social isolation levels. Third, regarding the items of the SII, the questions and their
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33 320 response options in the ELSA and JAGES were not exactly the same, nor were they
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36 321 strictly authorised through procedures such as reverse translation and confirming
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39 322 reliability and validity. However, we believe it is certainly meaningful to evaluate social
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42 323 isolation using the same framework. Finally, there were differences in study design in the
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45 324 data from the two cohorts, such as sampling method and follow-up period. We, therefore,
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48 325 made efforts to harmonise the data: those aged ≤ 64 , with dementia, and dependent in
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51 326 activities of daily living were excluded from the analysis. Moreover, the ELSA presents
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54 327 nationally representative population data, while the JAGES does not. However, the
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57 328 JAGES sample is representative of areas from a nationwide ageing study in which
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6 329 approximately one-fifth of all prefectures (nine out of 47) were enrolled. Even so, unlike
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9 330 the ELSA, analysis in the JAGES does not use sampling weights, which may lead to
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12 331 selection bias.
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18 333 **CONCLUSION**

21 334 We examined the association between social isolation and depression onset among older
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24 335 adults in England and Japan, who experience different cultural contexts regarding social
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27 336 relationships, and found a significant association in both countries; we also observed that
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30 337 in England, poor interaction with children was marginally associated, and in Japan, poor
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33 338 interaction and lack of social participation were significantly associated with depression.
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36 339 Tackling social isolation must be prioritised to safeguard the mental health of older adults
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39 340 worldwide. Particularly in Japan, the promotion of interaction with children and social
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42 341 participation could be key factors in addressing social isolation.
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6 347 **AUTHORS' CONTRIBUTIONS**
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9 348 All authors contributed to the conception and design of this study. Data collection was
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12 349 primarily conducted by MS, JA, NC, KO, and KK. Analyses were performed by TN, MS,
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15 350 JA, TT, SK, and TI. TN prepared the initial manuscript and MS, JA, NC, TT, SK, TI, KO,
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18 351 and KK significantly contributed to revising it. All authors read and approved the final
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48 379 design, data collection and analysis, decision to publish or preparation of the manuscript.
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54 381 **DATA SHARING STATEMENT**

57 382 For the JAGES, all enquiries are to be addressed to the data management committee via
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6 383 e-mail: dataadmin.ml@jages.net. All JAGES datasets have ethical or legal restrictions for
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9 384 public deposition because of the inclusion of sensitive information about the human
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12 385 participants. Regarding the ELSA, data are available in an open-access repository at
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15 386 [http://www. dataarchive.ac.uk/](http://www.dataarchive.ac.uk/).

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21 388 **COMPETING INTERESTS STATEMENT**

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24 389 The authors declare no conflict of interest.

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Supplementary Table 1. Association between social isolation and depression onset, by complete case analysis

		ELSA		JAGES	
		Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)
Social Isolation Index score	0	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
	1	1.92** (1.19–3.10)	1.56 [†] (0.94–2.60)	1.14 (0.94–1.39)	1.11 (0.87–1.41)
	2	2.15** (1.28–3.62)	1.71 [†] (0.98–2.99)	1.32** (1.09–1.60)	1.20 (0.95–1.51)
	3	3.19*** (1.73–5.90)	2.50** (1.27–4.90)	1.57*** (1.30–1.90)	1.30* (1.03–1.64)
	≥ 4	3.85** (1.46–10.18)	5.17** (1.83–14.66)	2.26*** (1.83–2.79)	1.47** (1.13–1.91)
		<i>p</i> for trend < 0.001	<i>p</i> for trend < 0.001	<i>p</i> for trend < 0.001	<i>p</i> for trend < 0.001
Age (years)	65–69		1.00 (reference)		1.00 (reference)
	70–74		1.37 (0.83–2.25)		1.16** (1.05–1.30)
	75–79		1.24 (0.71–2.14)		1.31*** (1.16–1.48)
	80–84		1.66 [†] (0.92–2.99)		1.60*** (1.37–1.88)
	≥ 85		0.97 (0.45–2.09)		1.79*** (1.39–2.30)
Gender	Male		1.00 (reference)		1.00 (reference)
	Female		1.58* (1.07–2.34)		1.00 (0.90–1.11)
Educational attainment (years)	< 15		1.00 (reference)		1.00 (reference)
	16–18		1.05 (0.68–1.60)		0.81*** (0.74–0.89)
	≥ 19		1.30 (0.70–2.41)		0.68*** (0.60–0.78)
Household equivalised income	1st quintile (lowest)		1.00 (reference)		1.00 (reference)
	2nd quintile		0.70 (0.40–0.21)		0.95 (0.83–1.09)
	3rd quintile		1.11 (0.66–1.87)		0.76*** (0.67–0.87)
	4th quintile		0.82 (0.45–1.50)		0.67*** (0.57–0.79)
	5th quintile (highest)		0.84 (0.42–1.68)		0.65*** (0.56–0.76)

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Cancer	No	1.00 (reference)	1.00 (reference)
	Yes	0.95 (0.32–2.81)	1.16 (0.93–1.43)
Heart disease	No	1.00 (reference)	1.00 (reference)
	Yes	1.13 (0.67–1.92)	1.20 (1.05–1.37)
Stroke	No	1.00 (reference)	1.00 (reference)
	Yes	1.3 (0.56–3.02)	1.18 (0.80–1.73)
Self-rated health	Good	1.00 (reference)	1.00 (reference)
	Poor	1.71* (1.13–2.59)	1.63*** (1.44–1.85)
CES-D score at baseline		1.90*** (1.60–2.25)	
GDS score at baseline			1.92*** (1.86–1.99)
Smoking	Never/past	1.00 (reference)	1.00 (reference)
	Current	0.76 (0.76–1.56)	1.29*** (1.12–1.48)
Drinking	Never/past	1.00 (reference)	1.00 (reference)
	Current	1.41 (0.81 – 2.44)	1.02 (0.93 – 1.13)

*, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$; †, $p < 0.1$

ELSA, English Longitudinal Study of Ageing; JAGES, Japan Gerontological Evaluation Study; CES-D, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; GDS, Geriatric Depression Scale; OR, odds ratio

Supplementary Table 2. Association between sub-components of social isolation and depression onset, by complete case analysis

		ELSA		JAGES	
		Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)
Social Isolation Index sub-components (ref; none)					
Unmarried or living alone		1.91*** (1.34–2.72)	1.27 (0.84–1.93)	1.33*** (1.18–1.49)	1.02 (0.88–1.19)
Poor interaction with children		1.08 (0.68–1.74)	1.51 (0.91–2.50)	1.01 (0.98–1.10)	1.13* (1.02–1.25)
Poor interaction with relatives		1.25 (0.83–1.90)	1.33 (0.85–2.08)	1.05 (0.97–1.13)	0.98 (0.90–1.08)
Poor interaction with friends		1.19 (0.78–1.80)	1.21 (0.78–1.87)	1.23 (1.14–1.33)	1.11* (1.01–1.22)
No social participation		1.54* (1.08–2.19)	1.46† (0.98–2.16)	1.70 (1.56–1.86)	1.22*** (1.09–1.36)
Age (years)					
		65–69	1.00 (reference)		1.00 (reference)
		70–74	1.37 (0.83–2.25)		1.17** (1.05–1.30)
		75–79	1.25 (0.72–2.17)		1.31*** (1.16–1.49)
		80–84	1.68† (0.92–3.04)		1.60*** (1.36–1.88)
		≥ 85	1.00 (0.46–2.21)		1.78*** (1.38–2.30)
Gender		Male	1.00 (reference)		1.00 (reference)
		Female	1.59* (1.07–2.37)		1.00 (0.89–1.11)
Educational attainment (years)		< 15	1.00 (reference)		1.00 (reference)
		10–12	1.04 (0.67–1.60)		0.81*** (0.74–0.90)
		≥ 19	1.31 (0.70–2.46)		0.69*** (0.61–0.78)
Household equivalised income		1st quintile (lowest)	1.00 (reference)		1.00 (reference)
		2nd quintile	0.71 (0.41–1.23)		0.95 (0.83–1.09)
		3rd quintile	1.13 (0.67–1.93)		0.76*** (0.67–0.86)
		4th quintile	0.83 (0.45–1.52)		0.67*** (0.57–0.79)
		5th quintile (highest)	0.85 (0.42–1.71)		0.66*** (0.57–0.76)
Cancer		No	1.00 (reference)		1.00 (reference)
		Yes	0.95 (0.32–2.81)		1.15 (0.93–1.43)

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Heart disease	No	1.00 (reference)	1.00 (reference)
	Yes	1.16 (0.69–1.96)	1.20** (1.05–1.37)
Stroke	No	1.00 (reference)	1.00 (reference)
	Yes	1.28 (0.55–2.99)	1.18 (0.80–1.73)
Self-rated health	Good	1.00 (reference)	1.00 (reference)
	Poor	1.71* (1.13–2.58)	1.62*** (1.43–1.83)
CES-D score at baseline		1.89*** (1.59–2.25)	1.00 (reference)
GDS score at baseline			1.92*** (1.85–1.99)
Smoking	Never/past	1.00 (reference)	1.00 (reference)
	Current	0.74 (0.36–1.53)	1.29*** (1.13–1.48)
Drinking	Never/past	1.00 (reference)	1.00 (reference)
	Current	1.39 (0.80–2.40)	1.03 (0.93–1.14)

*, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$; †, $p < 0.1$
 ELSA, English Longitudinal Study of Ageing; JAGES, Japan Gerontological Evaluation Study; CES-D, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; GDS, Geriatric Depression Scale; OR, odds ratio

STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	1, 3 3-4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6-9
Objectives	3	State specific objectives, including any prespecified hypotheses	9
Methods			
Study design	4	Present key elements of study design early in the paper	9
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	9-10
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (b) For matched studies, give matching criteria and number of exposed and unexposed	9-10 Not applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	10-11
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	10-11
Bias	9	Describe any efforts to address potential sources of bias	12
Study size	10	Explain how the study size was arrived at	Not applicable
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	10-11
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses	11-12 Not applicable 12 Not applicable Not applicable
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	13 Not applicable Not applicable
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	13-14 15-16 10
Outcome data	15*	Report numbers of outcome events or summary measures over time	17-18

