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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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1 **Original research**

2 **Title**

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

4 A cross-national longitudinal study in England and Japan

5

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ABSTRACT

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

Design: Prospective longitudinal study.

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

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

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

53 **Results:** The data of 3,331 respondents from the ELSA and 33,127 from the JAGES were

54 analysed. Multivariable logistic regression analysis demonstrated that social isolation was

55 significantly associated with depressive symptom onset in both countries. In the ELSA,

56 poor interaction with children marginally affected depressive symptom onset, while in

57 the JAGES, poor interaction with children and no social participation significantly

58 affected depressive symptom onset.

59 **Conclusions:** Despite variations in cultural background, social isolation was associated

60 with depressive symptom onset in both England and Japan. Addressing social isolation

61 to safeguard older adults' mental health must be globally prioritised.

62

63 **Strengths and limitations of this study**

64 ● This is the first cross-national longitudinal study to examine the association between

65 social isolation and depressive symptom onset in England, which values friendship-

66 based relationships, and Japan, where family-based relationships are emphasised.

67 ● This study included a large sample of over 3,300 people from England and 33,000

68 people from Japan aged 65 years and older.

69 ● A limitation of this study is that we cannot make direct comparisons because of

70 variations in cohort follow-up periods and depressive symptom measurement.

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71 • Another limitation is the substitution of social support for the evaluation of social

72 contact so as to use the same social isolation assessment scale in both countries.

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6

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-

7

92   based social relationships.[11] Another study comparing American and Japanese older

93   adults suggested that the presence of children was associated with depressive symptoms

94   only among the latter.[12] As Japan has retained the traditionally strong influence of

95   family and kinship systems on society[13] and the expected reciprocity between adult

96   children and their parents remains a dominant feature,[14] the emphasis on family-based

97   relationships is stronger than it is in the West.

98   Moreover, the social structure surrounding social isolation varies from country to

99   country. Recognising the impact of social isolation on health and economic loss, the UK

100   established the position of 'Minister of Loneliness' in 2018 and is taking a progressive

101   approach to eliminating social isolation.[15] In contrast, Japan, now a super-aged society,

102   is experiencing a rapid increase in the trend of abstaining from marriage and weakening

103   community and neighbourhood relations,[16] leading to a rise in the number of socially

104   isolated people.[17] In Japan, the proportion of people who rarely or never spent time

105   with those close to them was the highest among Organisation for Economic Co-operation

106   and Development countries. In particular, this figure was much higher than in the UK,

107   which has made advances in tackling social isolation (Japan = 15.3%, UK = 5.0%).[18]

108   Owing to differences in the cultural contexts of social relationships and structures, the

109   impact of social isolation on depressive symptoms is expected to vary across countries.

8

110   As the association between social isolation and depressive symptoms is often

111   described as bidirectional,[19] longitudinal studies are needed to determine causality.

112   However, previous cross-national comparative studies have only employed cross-

113   sectional designs.[12] Therefore, using longitudinal data from both countries, the present

114   study aims to investigate the association of social isolation with depressive symptom

115   onset in England, where the emphasis is on friendship-based relationships, and Japan,

116   which prioritises familial relationships.

117

118   **METHODS**

119   **Sample**

120   This longitudinal study was conducted using data from two ongoing prospective cohort

121   studies: the English Longitudinal Study of Ageing (ELSA) and the Japan Gerontological

122   Evaluation Study (JAGES). The ELSA targets independent-living older adults aged ≥ 50,

123   while JAGES participants are community-dwelling individuals aged ≥ 65 who are

124   ineligible for long-term healthcare insurance benefits.[20] Details of the ELSA and

125   JAGES can be found elsewhere.[21, 22] For the present analysis, we used the two waves

126   of data that most closely corresponded with the timing of our study: wave 5 (2010/2011)

127   to wave 6 (2012/2013) for the ELSA, and wave 1 (2010/2011) to wave 2 (2013) for the

9

128   JAGES. We harmonised the data by including older adults aged ≥ 65, independent in

129   activities of daily living, and without self-reported dementia. Respondents with

130   depressive symptoms at baseline were excluded, and we followed up the onset of

131   depressive symptoms for two years for the ELSA and 2.5 years for the JAGES.

132

Depressive symptoms

134   Based on a previous cross-national study,[23] depressive symptoms were measured both

135   at baseline and follow-up using eight items from the Center for Epidemiologic Studies

136   Depression Scale (CES-D) in the ELSA[24] and the Geriatric Depression Scale (GDS-

137   15) in the JAGES.[25] To identify possible depressive cases, the CES-D cut-off was ≥ 4

138   while that for the GDS-15 was ≥ 5.[24]

139

Social isolation

141   Social isolation levels were assessed using the modified Social Isolation Index (SII).[26]

142   The index was computed with respondents given a point if they: (1) were unmarried or

143   living alone, (2) had poor interaction with children (no children or no social support from

144   children), (3) had poor interaction with relatives (no relatives or no social support from

145   relatives), (4) had poor interaction with friends (less than monthly contact or no social

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146   support from friends), and (5) had no social participation (no participation in any social

147   or religious groups). The total possible score ranged from 0 to 5, with higher scores

148   indicating greater social isolation. The participants were categorised into the following

149   five groups based on their scores: 0, 1, 2, 3, and 4–5 points. We used the total score and

150   the scores of the five sub-components as predictive variables.

151

152   **Covariates**

153   The covariates included age, gender, educational attainment, household equivalised

154   income, present illness, self-rated health, smoking, and drinking. Age was categorised as

155   65–69, 70–74, 75–79, 80–84, and $\geq$ 85. Based on the ages of respondents who had

156   completed formal education, the age of final educational attainment was categorised as $\leq$

157   15 years, 16–18 years, and $\geq$ 19 years. Household equivalised income was classified into

158   quintiles. Present illness was classified as 'yes' or 'no' for cancer, heart disease, and

159   stroke. Self-rated health was dichotomised as 'poor' and 'good'. Smoking and drinking

160   were dichotomised as 'never/past' and 'current'.

161

162   **Statistical analysis**

163   We analysed the ELSA and JAGES data separately because of differences in research

164   design, especially sampling approaches. A longitudinal weight was applied to account for

165   survey non-response for the ELSA but not the JAGES as its design does not allow it.

166   First, we calculated descriptive statistics. Second, we conducted a multivariate logistic

167   regression analysis to examine the association between SII score and depressive symptom

168   onset and obtained odds ratios (ORs) and 95% confidence intervals (CIs) for depressive

169   symptom onset. Model 1 was not adjusted for covariates while Model 2 was adjusted for

170   all covariates. Additionally, we analysed the association between SII sub-components and

171   depressive symptom onset, adjusted for all covariates.

172   To mitigate potential biases resulting from missing information, we used the

173   multiple imputation approach under the missing at random assumption. We generated 20

174   imputed datasets for the final analysis, which excluded those who met the exclusion

175   criteria and did not respond to the follow-up surveys, using the multiple imputation by

176   chained equations procedure and pooled the results using Rubin's rule.[27]

177   The significance level was set at $p < 0.05$. We used R (Version 3.5.2 for

178   Windows) for all statistical analyses.

179

180   **Ethics issues**

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

12

182   National Health Service Research Ethics Committees under the National Research and

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

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

185

186   **Patient and public involvement**

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

188   data interpretation in this study.

189

190   **RESULTS**

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

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

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

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

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

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

197   self-rated health, smoked, did not consume much alcohol, and had higher baseline

198   depressive symptom scores had higher SII scores. A similar trend was observed in the

199   JAGES, but here, those who consumed more alcohol had higher SII scores.

13

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

15

206   Table 2 presents the description of social isolation and depressive symptom onset.

207   At follow-up, 190 (6.5%) ELSA respondents and 4,456 (13.5%) JAGES respondents

208   exhibited depressive symptom onset. In both studies, higher SII scores were associated

209   with an increased risk of depressive symptom onset. Regarding SII sub-components,

210   ELSA respondents who were unmarried or living alone were more likely to have

211   depressive symptoms, while this was the case with JAGES respondents with no social

212   participation.

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

17

218   Table 3 depicts the association between SII scores and depressive symptom onset.

219   Multivariable analysis showed that higher SII scores were associated with a higher risk

220   of depressive symptom onset in both studies after adjusting for all covariates. In the ELSA,

221   the OR of depressive symptom onset was significantly higher from a score ≥ one point

222   (OR [95% CI] compared with zero points, one: 1.68 [1.02–2.75], two: 1.77 [1.03–3.05],

223   three: 2.64 [1.37–5.12], ≥ four: 4.01 [1.43–11.22], p for trend = 0.015). In the JAGES, as

224   SII scores increased, the OR of depressive symptom onset gradually increased, reaching

225   significance at ≥ three points (OR [95% CI] compared with zero points, one: 1.10 [0.89–

226   1.35], two: 1.15 [0.94–1.40], three: 1.28 [1.04–1.56], ≥ four: 1.48 [1.18–1.85], p for trend

227   < 0.001). These results showed almost the same tendency as the complete case analysis

228   without multiple imputation (Supplementary Table 1).

18

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)
	p for trend < 0.001	p for trend = 0.015	p for trend < 0.001	p 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-

233 rated health, smoking, drinking, and depression score at baseline (Center for Epidemiologic Studies Depression Scale for the ELSA and

234 Geriatric Depression Scale for the JAGES).

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235   Table 4 presents the impacts of SII sub-components on depressive symptom

236   onset. In the ELSA, sub-components were not significant, although poor interaction with

237   children was marginally significant (OR [95% CI], with 'none' as the reference;

238   unmarried or living alone: 1.13 [0.80–1.60], poor interaction with children: 1.55 [1.00–

239   2.41], poor interaction with relatives: 1.24 [0.79–1.94], poor interaction with friends: 1.15

240   [0.77–1.71], no social participation: 1.22 [0.80–1.87]). In the JAGES, poor interaction

241   with children and no social participation were significantly associated with depressive

242   symptom onset after adjusting for all covariates (OR [95% CI], with 'none' as the

243   reference; unmarried or living alone: 1.11 [1.00–1.24], poor interaction with children:

244   1.09 [1.01–1.19], poor interaction with relatives: 1.04 [0.96–1.12], poor interaction with

245   friends: 1.03 [0.95–1.11], no social participation: 1.28 [1.17–1.40]). These results were

246   similar to those obtained from the complete case analysis (Supplementary Table 2).

20

247 **Table 4. Association between sub-components of social isolation and depressive symptom onset: multivariable logistic regression**
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)

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

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

251 [a] Adjusted for age, gender, educational attainment, equivalent income, present illness (cancer, heart disease, and stroke), self-rated health,

252 smoking, drinking, and depression score at baseline (Center for Epidemiologic Studies Depression Scale for the ELSA and Geriatric

253 Depression Scale for the JAGES).

21

254 **DISCUSSION**

255 To the best of our knowledge, this is the first cross-national longitudinal study of the

256 association of social isolation with depressive symptoms among older English and

257 Japanese adults. Social isolation was significantly associated with depressive symptom

258 onset in both countries. Our results support previous longitudinal findings on social

259 relationships and mental health in older adults in England[28] and Japan.[29] Using data

260 frames that were similar with regard to assessment and covariates, we showed that social

261 isolation is a common risk factor for depressive symptoms in England and Japan despite

262 cultural differences such as emphasis on friendships versus familism, respectively. Thus,

263 our results suggest that to safeguard the mental health of older adults, addressing social

264 isolation is a global need.

265　　The association between social isolation and depressive symptoms was

266 somewhat stronger in England than in Japan. Although we cannot make direct

267 comparisons because of variations in cohort follow-up periods and depressive symptom

268 measurement, there are several possible reasons for this pattern of findings. The impact

269 of social factors could be different depending on the group and society to which one

270 belongs. This is best understood in the context of the concept of relative deprivation.[30]

271 In other words, higher levels of relative social isolation may induce greater psychological

272   stress. A previous study showed that rich community ties and cohesion were protective

273   factors for health but could have a negative effect on those who were not socially

274   involved.[31] Being isolated in a connected society such as England may represent a more

275   severe condition, which may have a stronger negative impact on mental health.

276   While a previous study showed that friendship-based relationships contributed

277   to longevity in older adults in England, in the present study they were not associated with

278   depressive symptom onset. Another study focused on English older adults indicated the

279   contribution of partner and child support, rather than support from friends, in alleviating

280   depression;[32] thus, relationships with family members might be important for mental

281   health. In the JAGES, poor interaction with children and no social participation were

282   significantly associated with depressive symptom onset. Previous studies on older

283   Japanese adults suggested that interaction with children and social participation were

284   protective factors for mental health problems.[12, 33] Traditionally, Japan has had strong

285   family and kinship ties, and adult children are expected to demonstrate reciprocity with

286   their parents.[14] However, children now tend to live apart from their parents after

287   marriage, and contact is reduced,[34] potentially leading to loneliness in older adults. In

288   such a situation, social participation may improve mental health by establishing a sense

289   of belonging.[33] Our results demonstrate that promoting interaction with children and

290   community participation are essential for safeguarding mental health in older Japanese

291   adults.

292   This study has several strengths. First, it is the first cross-national population-

293   level investigation of the impact of social isolation on depressive symptom onset using a

294   unified data frame. Second, by using two longitudinal datasets, we were able to determine

295   causality in the association between social isolation and depressive symptoms. Third, the

296   use of large-scale data allowed us to detect the effects of relatively rare situations of

297   severe social isolation.

298   However, certain limitations cannot be ignored. First, the measurement of

299   depressive symptoms in the two cohorts was not the same. Therefore, we could not

300   directly compare depressive symptom onset in the two countries. However, these

301   measurements were also used in a previous cross-national comparison study in England

302   and Japan,[23] and we were able to examine the association between social isolation and

303   depressive symptom onset in each country using the same data frame. Second, we

304   substituted social support for the assessment of social contact for some items in order to

305   use the same SII. Therefore, cultural differences in expectations regarding the receipt of

306   social support in both countries might have caused information biases. For instance,

307   expectations regarding social support from relatives could originally have been higher in

24

308 Japan,[14] leading to overestimation of social isolation levels. Third, there were

309 differences in study design in the data from the two cohorts, such as sampling method

310 and follow-up period. However, we made efforts to harmonise the data: those aged ≤ 64,

311 with dementia, and dependent in activities of daily living were excluded from the analysis.

312 Also, the ELSA presents nationally representative population data, while the JAGES does

313 not. However, the JAGES sample is representative of areas from a nationwide ageing

314 study in which about one-fifth of all prefectures (nine out of 47) were enrolled.

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

324 **ACKNOWLEDGEMENTS**

325 We wish to express our deepest gratitude to the members in the Japan Gerontological

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

327

AUTHORS' CONTRIBUTIONS

329 All authors contributed to the conception and design of this study. Data collection was

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

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

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

333 manuscript.

334

FUNDING STATEMENT

27

362 **DATA SHARING STATEMENT**

363 For the JAGES, all enquiries are to be addressed to the data management committee via

364 e-mail: dataadmin.ml@jages.net. All JAGES datasets have ethical or legal restrictions for

365 public deposition because of the inclusion of sensitive information about the human

366 participants. Regarding the ELSA, data are available in an open-access repository at

367 http://www. dataarchive.ac.uk/.

368

369 **COMPETING INTERESTS STATEMENT**

370 The authors declare no conflict of interest.

371

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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)
		p for trend < 0.001	*p* for trend < 0.001	*p* for trend < 0.001	*p* 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)

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 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	1, 3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	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	8-9
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	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	10-11
		(*b*) Describe any methods used to examine subgroups and interactions	Not applicable
		(*c*) Explain how missing data were addressed	11
		(*d*) If applicable, explain how loss to follow-up was addressed	Not applicable
		(*e*) Describe any sensitivity analyses	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	12-14
		(b) Give reasons for non-participation at each stage	Not applicable
		(c) Consider use of a flow diagram	Not applicable
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	12-14
		(b) Indicate number of participants with missing data for each variable of interest	13-14
		(c) Summarise follow-up time (eg, average and total amount)	9
Outcome data	15*	Report numbers of outcome events or summary measures over time	15-16

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	17-18
		(*b*) Report category boundaries when continuous variables were categorized	Not applicable
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Supplementary 1, 2

Discussion

Key results	18	Summarise key results with reference to study objectives	21
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
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
Generalisability	21	Discuss the generalisability (external validity) of the study results	Not applicable

Other information

| 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.

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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).

4

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

5

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

6

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

7

59   England; the results are discussed in terms of possible differences between societies that

60   are highly connected and those that are not.[11] In the United Kingdom (UK), in

61   recognition of the impact of social isolation on health and economic loss, the position of

62   'Minister of Loneliness' was established in 2018, and the country is taking a progressive

63   approach to the elimination of social isolation.[12] In contrast, Japan, now a super-aged

64   society (more than 21% of the population aged 65 or above),[13] is experiencing a rapid

65   increase in the trend of abstaining from marriage and weakening community and

66   neighbourhood relations,[14] leading to a rise in the number of socially isolated

67   people.[15] In Japan, the proportion of people who rarely or never spend time with those

68   close to them has been reported to be the highest among Organisation for Economic Co-

69   operation and Development countries. In particular, this figure is much higher than in the

70   UK, which has made advances in tackling social isolation (Japan = 15.3%, UK =

71   5.0%).[16] Owing to differences in social structures and the contexts surrounding social

72   isolation, the impact of social isolation on depression is expected to vary across countries.

73   Furthermore, the health effects of social isolation may differ depending on the

74   cultural context of social relationships. In East Asian countries, including Japan, there is

75   a familial norm based on the traditional culture of filial piety,[17] which is often

76   contrasted with individualism in Western countries.[18, 19] Based on this cultural

8

77 background, Japanese social support networks may be kinship centred, which may be

78 narrower than the types of social networks prevalent in other countries.[20] However,

79 there is a lack of consensus on the health effects of social relationships based on these

80 cultural differences. A previous cross-national study showed that in English men,

81 friendship-based social relationships had a significant impact on longevity, whereas in

82 Japanese men, this impact was associated with family-based social relationships.[21] On

83 the contrary, a study of older adults in the United States (US) and Japan found that while

84 relationships with children were associated with a low level of depression only in Japan,

85 the presence of spouses was important in both countries, but more so in the US.[22]

86 Another comparative study among adults suggested that social contact with friends

87 benefitted women's mental health in the UK but not in Japan.[23] Thus, the family-

88 oriented nature of East Asian societies does not automatically imply the health importance

89 of family-based relationships, and the roles of individual components of social isolation

90 (family, friends, and others) in the mental health of older adults in each country remain

91 controversial.

92   As the association between social isolation and depression is often described as

93 bidirectional,[24] longitudinal studies are needed to address temporality. However,

94 previous cross-national comparative studies have only employed cross-sectional

9

95   designs.[22, 23] Therefore, using longitudinal data from both countries, the present study

96   aims to investigate the association of social isolation with depression onset in England,

97   which has taken advanced measures against social isolation, and Japan, a super-aged

98   society with a rapidly increasing number of socially isolated people.

99

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

10

113   cohort at baseline were excluded, and we followed up the onset of depression for two

114   years for the ELSA and 2.5 years for the JAGES.

115

116   **Depression**

117   Based on a previous cross-national study,[28] depressive symptoms were measured both

118   at baseline and follow-up using eight items from the Center for Epidemiologic Studies

119   Depression Scale (CES-D) in the ELSA[29] and the Geriatric Depression Scale (GDS-

120   15) in the JAGES.[30] To identify possible depressive cases, the CES-D cut-off was ≥ 4

121   while that for the GDS-15 was ≥ 5.[31, 32] As previously mentioned, respondents with

122   depression at baseline were excluded, and we observed the onset of depression during

123   follow-up.

124

125   **Social isolation**

126   Social isolation levels were assessed using a modified version of the Social Isolation

127   Index (SII).[33–35] The index was computed with respondents given a point if they: (1)

128   were unmarried or living alone, (2) had poor interaction with children (did not live with

129   their children or had no one to provide emotional or instrumental social support), (3) had

130   poor interaction with relatives (did not have immediate family members providing

131 emotional or instrumental social support), (4) had poor interaction with friends (less than

132 monthly contact or no friends who could provide emotional or instrumental social

133 support), and (5) had no social participation (no participation in any social or religious

134 groups). The total possible score ranged from 0 to 5, with higher scores indicating greater

135 social isolation. The participants were categorised into the following five groups based

136 on their scores: 0, 1, 2, 3, and 4–5 points. We used the total score and the scores of the

137 five sub-components as predictive variables.

138

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 $\geq$ 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 $\geq$ 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'.

148

12

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.

166

167 **Ethical considerations**

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

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

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

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

172

173 **Patient and public involvement**

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

175 data interpretation.

176

177 **RESULTS**

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

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

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

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

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

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

184 self-rated health, smoked, did not consume much alcohol, and had higher baseline

14

185   depressive symptom scores had higher SII scores. A similar trend was observed in the

186   JAGES, but here, those who consumed more alcohol had higher SII scores.

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

16

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

193   Table 2 presents the description of social isolation and depression onset. At

194   follow-up, 201 (6.0%) ELSA respondents and 4,456 (13.5%) JAGES respondents

195   exhibited depression onset. In both studies, higher SII scores were associated with an

196   increased risk of depression onset. Regarding SII sub-components, ELSA respondents

197   who were unmarried or living alone were more likely to have depression, while this was

198   the case with JAGES respondents with no social participation.

18

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	n = 201	n = 28671	n = 4456
		(94.0%)	(6.0%)	(86.5%)	(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

204   Table 3 depicts the association between SII scores and depression onset.

205   Multivariable analysis showed that higher SII scores were associated with a higher risk

206   of depression onset in both studies after adjusting for all covariates. In the ELSA, the OR

207   of depression onset was significantly higher from a score ≥ one point (OR [95% CI]

208   compared with zero points, one: 1.68 [1.02–2.75], two: 1.77 [1.03–3.05], three: 2.64

209   [1.37–5.12], ≥ four: 4.01 [1.43–11.22], p for trend = 0.015). In the JAGES, as SII scores

210   increased, the OR of depression onset gradually increased, reaching significance at ≥

211   three points (OR [95% CI] compared with zero points, one: 1.10 [0.89–1.35], two: 1.15

212   [0.94–1.40], three: 1.28 [1.04–1.56], ≥ four: 1.48 [1.18–1.85], p for trend < 0.001). These

213   results showed almost the same tendency as the complete case analysis without multiple

214   imputation (Supplementary Table 1).

20

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)
	p for trend < 0.001	p for trend = 0.015	p for trend < 0.001	p for trend < 0.001

[*] $p < 0.05$; [**] $p < 0.01$; [***] $p < 0.001$

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

[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).

221   Table 4 presents the associations of SII sub-components with depression onset.

222 In the ELSA, sub-components were not significant, although poor interaction with

223 children was marginally significant (OR [95% CI], with 'none' as the reference;

224 unmarried or living alone: 1.13 [0.80–1.60], poor interaction with children: 1.55 [1.00–

225 2.41], poor interaction with relatives: 1.24 [0.79–1.94], poor interaction with friends: 1.15

226 [0.77–1.71], no social participation: 1.22 [0.80–1.87]). In the JAGES, poor interaction

227 with children and no social participation were significantly associated with depression

228 onset after adjusting for all covariates (OR [95% CI], with 'none' as the reference;

229 unmarried or living alone: 1.11 [1.00–1.24], poor interaction with children: 1.09 [1.01–

230 1.19], poor interaction with relatives: 1.04 [0.96–1.12], poor interaction with friends: 1.03

231 [0.95–1.11], no social participation: 1.28 [1.17–1.40]). These results were similar to those

232 obtained from the complete case analysis (Supplementary Table 2).

22

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).

239   **DISCUSSION**

240   To the best of our knowledge, this is the first cross-national longitudinal study of the

241   association of social isolation with depression among older English and Japanese adults.

242   Social isolation was significantly associated with depression onset in both countries. Our

243   results support previous longitudinal findings on social relationships and mental health in

244   older adults in England[37] and Japan.[38] Using data frames that were similar with

245   regard to assessment and covariates, we showed that social isolation is a common risk

246   factor for depression in England and Japan despite country-specific cultural differences

247   regarding social relationships. Thus, our results suggest that to safeguard the mental

248   health of older adults, addressing social isolation is a global need.

249   The association between social isolation and depression was somewhat stronger

250   in England than in Japan. These results are similar to a previous report concerning

251   mortality among older adults in England and Japan.[11] Although we cannot make direct

252   comparisons because of variations in cohort follow-up periods and depression

253   measurement, there are several possible reasons for this pattern of findings. The impact

254   of social factors could be different depending on the group and society to which one

255   belongs. This is best understood in the context of the concept of relative deprivation.[39]

256   In other words, higher levels of relative social isolation may induce greater psychological

24

257   stress. A previous study showed that rich community ties and cohesion were protective

258   factors for health but could have a negative effect on those who were not socially

259   involved.[40] Being isolated in a connected society such as the UK may represent a more

260   severe condition, with a stronger negative impact on mental health.

261   Our results showed that poor interaction with children was significant with

262   regard to depression onset in Japan. In England, while the association was marginal, of

263   the components of social isolation, poor interaction with children had the greatest effect.

264   The lack of interaction with children could have an adverse effect on the mental health of

265   older adults in both countries. Previous studies in England[41] and Japan[22] have

266   reported that social support from children can contribute to alleviating depression, and

267   our results point in the same direction. Older adults without children can be considered a

268   vulnerable group, because adult children, in particular, are often the main source of

269   positive social support for older parents.[42] Older parents have certain expectations with

270   regard to receiving support from their children, and situations wherein these expectations

271   are not met may lead to depressive mood.[43] On the contrary, a previous study reported

272   no association between the presence of children and depression among older adults in the

273   US.[22] Owing to strong spousal relationships in the US, the effect of the presence of

274   children might be relatively small. Thus, our study confirmed the adverse effects of poor

25

275   interaction with children common to England and Japan, but international generalizability

276   can only be established based on further research considering the cultural background of

277   family relationships in individual countries.

278   Although traditionally Japan is a country where adult children are expected to

279   demonstrate reciprocity with their parents owing to the strong family and kinship-based

280   cultural background,[44] in this study, the effect of interaction with children on

281   depression was relatively modest. In recent years, with trends such as adult children

282   commonly living apart from their parents after marriage[45] and the development of

283   public long-term care services for the ageing population,[46] Japan's family system has

284   not remained as traditional as before. Therefore, interaction with children may not be as

285   essential to the health of older adults as before. However, despite these cultural transitions,

286   we believe that interaction with children has some value with regard to preventing

287   depression in old age in Japan.

288   Social participation was a strong protective factor for depression onset in Japan,

289   whereas there was no association in England, although the OR was somewhat greater.

290   Several previous studies have reported that social participation helps prevent depression

291   onset.[37, 47–49] Our results pertaining to Japan support these reports. On the contrary,

292   the protective effects of social participation on mental health have been shown to vary

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293   depending on the type of organisation an individual is involved with,[48] the individual's

294   attitude towards participation,[48] and the duration[37] and frequency[49] of

295   participation. Regarding the present study, in the English context, the role of social

296   participation in depression prevention might have been unidentifiable because of

297   differences in the effects of these participation contexts. We only took into account social

298   participation, without delving into specific types. Thus, the context of effective social

299   participation, such as type, duration, and role in the organisation in both countries,

300   requires further investigation. Despite these challenges, our findings suggest that in Japan,

301   social isolation prevention measures based on the promotion of social participation could

302   be beneficial for safeguarding the mental health of older adults.

303   This study has several strengths. First, it is the first cross-national population-

304   level investigation of the association of social isolation with depression onset using a

305   unified data frame. Second, by using two longitudinal datasets, we were able to examine

306   the prospective association between social isolation and depression. Third, the use of

307   large-scale data allowed us to detect the effects of relatively rare situations of severe

308   social isolation.

309   However, certain limitations cannot be ignored. First, the measurement of

310   depression in the two cohorts was not the same. Therefore, we could not directly compare

311 depression onset in the two countries. However, these measurements were also used in a

312 previous cross-national comparison study in England and Japan,[28] and we were able to

313 examine the association between social isolation and depression onset in both countries

314 using the same data frame. Second, we used social support for the assessment of social

315 contact for some items in order to be able to use the same SII. Therefore, cultural

316 differences in expectations regarding the receipt of social support in both countries might

317 have caused information biases. For instance, expectations regarding social support from

318 relatives could originally have been higher in Japan,[44] leading to overestimation of

319 social isolation levels. Third, regarding the items of the SII, the questions and their

320 response options in the ELSA and JAGES were not exactly the same, nor were they

321 strictly authorised through procedures such as reverse translation and confirming

322 reliability and validity. However, we believe it is certainly meaningful to evaluate social

323 isolation using the same framework. Finally, there were differences in study design in the

324 data from the two cohorts, such as sampling method and follow-up period. We, therefore,

325 made efforts to harmonise the data: those aged ≤ 64, with dementia, and dependent in

326 activities of daily living were excluded from the analysis. Moreover, the ELSA presents

327 nationally representative population data, while the JAGES does not. However, the

328 JAGES sample is representative of areas from a nationwide ageing study in which about

28

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

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

343

AUTHORS' CONTRIBUTIONS

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

348 and KK significantly contributed to revising it. All authors read and approved the final

349 manuscript.

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378 **DATA SHARING STATEMENT**

379 For the JAGES, all enquiries are to be addressed to the data management committee via

380 e-mail: dataadmin.ml@jages.net. All JAGES datasets have ethical or legal restrictions for

381 public deposition because of the inclusion of sensitive information about the human

382 participants. Regarding the ELSA, data are available in an open-access repository at

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383   http://www. dataarchive.ac.uk/.

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385   **COMPETING INTERESTS STATEMENT**

386   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)
		p for trend < 0.001	p for trend < 0.001	p for trend < 0.001	p 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)

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)

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	1, 3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	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	9-10
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	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	11-12
		(*b*) Describe any methods used to examine subgroups and interactions	Not applicable
		(*c*) Explain how missing data were addressed	12
		(*d*) If applicable, explain how loss to follow-up was addressed	Not applicable
		(*e*) Describe any sensitivity analyses	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	13
		(b) Give reasons for non-participation at each stage	Not applicable
		(c) Consider use of a flow diagram	Not applicable
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	13-14
		(b) Indicate number of participants with missing data for each variable of interest	15-16
		(c) Summarise follow-up time (eg, average and total amount)	10
Outcome data	15*	Report numbers of outcome events or summary measures over time	17-18

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	19-21
		(*b*) Report category boundaries when continuous variables were categorized	Not applicable
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Supplementary 1, 2
Discussion			
Key results	18	Summarise key results with reference to study objectives	23
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
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
Generalisability	21	Discuss the generalisability (external validity) of the study results	24-25
Other information			
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.

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1

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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3

1   **ABSTRACT**

2   **Objective:** Social isolation is a risk factor for depression in older age. However, little is

3   known regarding whether its impact varies depending on country-specific cultural

4   contexts regarding social relationships. The present study examined the association of

5   social isolation with depression onset among older adults in England, which has taken

6   advanced 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).

4

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 individuals from England and

35   33,000 individuals from Japan aged 65 years and older.

36   ● A limitation of this study is that we cannot make direct comparisons because of

5

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 permit the use of the same social isolation assessment scale in both countries.

6

INTRODUCTION

With population ageing, there is growing worldwide interest in social issues concerning

older adults, including social isolation and the deterioration of physical and mental health.

Defined as an objective state in where an individual has few close relationships or limited

contact within a community,[1] social isolation is recognised as a social determinant of

health with relevance to mortality,[2] cardiovascular diseases,[3] dementia,[4] and mental

health.[5, 6] Social isolation is a major risk factor for mental health problems in older

age. Several systematic reviews have demonstrated that social isolation is associated with

depressive symptoms,[5, 6] which, in turn, are correlated with unhealthy behaviours and

reduced access to material resources.[7] Depression, common in later life, is related to

adverse health outcomes such as poor quality of life[8] and functional disability.[9] With

the high current global burden of depression expected to increase further by 2030,[10]

addressing social isolation is an important gerontological issue for protecting mental

health among older adults.

The impacts of social isolation on health may vary by country; this could be the

result of differences in the social environments related to social networks within and

outside the family. A recent study of older adults in England and Japan showed that social

isolation is a common risk factor for mortality in both countries, with a greater impact

58 observed in England; the results are discussed in terms of possible differences between

59 societies that are highly connected and those that are not.[11] In the United Kingdom

60 (UK), in recognition of the impact of social isolation on health and economic loss, the

61 position of 'Minister of Loneliness' was established in 2018, and the country is taking a

62 progressive approach to the elimination of social isolation.[12] In contrast, Japan, now a

63 super-aged society (more than 21% of the population aged 65 or above),[13] is

64 experiencing a rapidly increasing trend in the number of never-married persons and

65 weakening community and neighbourhood relations,[14] leading to a rise in the number

66 of socially isolated individuals.[15] In Japan, the proportion of people who rarely or never

67 spend time with those close to them has been reported to be the highest among

68 Organisation for Economic Co-operation and Development countries. In particular, this

69 figure is much higher than in the UK, which has made advances in tackling social

70 isolation (Japan = 15.3%, UK = 5.0%).[16] Owing to differences in social structures and

71 the contexts surrounding social isolation, the impact of social isolation on depression is

72 expected to vary across countries.

73   Furthermore, the health effects of social isolation may differ depending on the

74 cultural context of social relationships. In East Asian countries, including Japan, there is

75 a familial norm based on the traditional culture of filial piety,[17] which is often

8

76   contrasted with individualism in Western countries.[18, 19] Based on this cultural

77   background, Japanese social support networks may be kinship centred, which may be

78   narrower than the types of social networks prevalent in other countries.[20] However,

79   there is a lack of consensus on the health effects of social relationships based on these

80   cultural differences. A previous cross-national study showed that among English men,

81   friendship-based social relationships had a significant impact on longevity, whereas

82   among Japanese men, this impact was associated with family-based social

83   relationships.[21] In contrast, a study of older adults in the United States (US) and Japan

84   demonstrated that while relationships with children were associated with a low level of

85   depression only in Japan, the presence of spouses was important in both countries, but

86   more so in the US.[22] Another comparative study among adults suggested that social

87   contact with friends benefitted women's mental health in the UK but not in Japan.[23]

88   Thus, the family-oriented nature of East Asian societies does not automatically imply the

89   health importance of family-based relationships, and the roles of individual components

90   of social isolation (family, friends, and others) in the mental health of older adults in each

91   country remain controversial.

92   As the association between social isolation and depression is often described as

93   bidirectional,[24] longitudinal studies are needed to address temporality. However,

94   previous cross-national comparative studies have employed only cross-sectional

95   designs.[22, 23] Therefore, using longitudinal data from both countries, the present study

96   aims to investigate the association of social isolation with depression onset in England,

97   which has taken advanced measures against social isolation, and Japan, a super-aged

98   society with a rapidly increasing number of socially isolated people.

99

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

10

112   who scored above the cut-off point for depression on each measure in the respective

113   cohort at baseline were excluded and we followed up the onset of depression for two years

114   for the ELSA and 2.5 years for the JAGES.

115

116   **Depression**

117   Based on a previous cross-national study,[28] depressive symptoms were measured both

118   at baseline and follow-up using eight items from the Center for Epidemiologic Studies

119   Depression Scale (CES-D) in the ELSA[29] and the Geriatric Depression Scale (GDS-

120   15) in the JAGES.[30] To identify possible depressive cases, the CES-D cut-off was ≥ 4

121   while that for the GDS-15 was ≥ 5.[31, 32] As previously mentioned, respondents with

122   depression at baseline were excluded and we observed the onset of depression during

123   follow-up.

124

125   **Social isolation**

126   Social isolation levels were assessed using a modified version of the Social Isolation

127   Index (SII).[33–35] The index was computed with respondents given a point if they: (1)

128   were unmarried or living alone, (2) had poor interaction with children (did not live with

129   their children or had no one to provide emotional or instrumental social support), (3) had

130 poor interaction with relatives (did not have immediate family members providing

131 emotional or instrumental social support), (4) had poor interaction with friends (less than

132 monthly contact or no friends who could provide emotional or instrumental social

133 support), and (5) had no social participation (no participation in any social or religious

134 groups). The total possible score ranged from 0 to 5, with higher scores indicating greater

135 social isolation. The participants were categorised into the following five groups based

136 on their scores: 0, 1, 2, 3, and 4–5 points. We used the total score and the scores of the

137 five sub-components as predictive variables.

138

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 ≤

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'.

12

148

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.

166

Ethical considerations

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

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

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

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

172

Patient and public involvement

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

175 data interpretation.

176

RESULTS

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

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

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

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

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

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

14

184   self-rated health, smoked, consumed little alcohol, and had higher baseline depressive

185   symptom scores and higher SII scores. A similar trend was observed in the JAGES, but

186   here, those who consumed more alcohol had higher SII scores.

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

16

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

17

193   Table 2 presents the description of social isolation and depression onset. At

194   follow-up, 201 (6.0%) ELSA respondents and 4,456 (13.5%) JAGES respondents

195   exhibited depression onset. In both studies, higher SII scores were associated with an

196   increased risk of depression onset. Regarding SII sub-components, ELSA respondents

197   who were unmarried or living alone were more likely to have depression, while this was

198   the case with JAGES respondents with no social participation.

18

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	n = 201	n = 28671	n = 4456
		(94.0%)	(6.0%)	(86.5%)	(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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204   Table 3 depicts the association between SII scores and depression onset.

205 Multivariable analysis showed that higher SII scores were associated with a higher risk

206 of depression onset in both studies after adjusting for all covariates. In the ELSA, the OR

207 of depression onset was significantly higher from a score ≥ one point (OR [95% CI]

208 compared with zero points, one: 1.68 [1.02–2.75], two: 1.77 [1.03–3.05], three: 2.64

209 [1.37–5.12], ≥ four: 4.01 [1.43–11.22], p for trend = 0.015). In the JAGES, as SII scores

210 increased, the OR of depression onset gradually increased, reaching significance at ≥

211 three points (OR [95% CI] compared with zero points, one: 1.10 [0.89–1.35], two: 1.15

212 [0.94–1.40], three: 1.28 [1.04–1.56], ≥ four: 1.48 [1.18–1.85], p for trend < 0.001). These

213 results showed almost the same tendency as the complete case analysis without multiple

214 imputation (Supplementary Table 1).

20

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)
	p for trend < 0.001	p for trend = 0.015	p for trend < 0.001	p for trend < 0.001

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

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

[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).

221   Table 4 presents the associations of SII sub-components with depression onset.

222 In the ELSA, sub-components were not significant, although poor interaction with

223 children was marginally significant (OR [95% CI], with 'none' as the reference;

224 unmarried or living alone: 1.13 [0.80–1.60], poor interaction with children: 1.55 [1.00–

225 2.41], poor interaction with relatives: 1.24 [0.79–1.94], poor interaction with friends: 1.15

226 [0.77–1.71], no social participation: 1.22 [0.80–1.87]). In the JAGES, poor interaction

227 with children and no social participation were significantly associated with depression

228 onset after adjusting for all covariates (OR [95% CI], with 'none' as the reference;

229 unmarried or living alone: 1.11 [1.00–1.24], poor interaction with children: 1.09 [1.01–

230 1.19], poor interaction with relatives: 1.04 [0.96–1.12], poor interaction with friends: 1.03

231 [0.95–1.11], no social participation: 1.28 [1.17–1.40]). These results were similar to those

232 obtained from the complete case analysis (Supplementary Table 2).

22

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).

DISCUSSION

To the best of our knowledge, this is the first cross-national longitudinal study of the

association of social isolation with depression among older English and Japanese adults.

Social isolation was significantly associated with depression onset in both countries. Our

results support previous longitudinal findings on social relationships and mental health

among older adults in England[37] and Japan.[38] Using data frames that were similar

with regard to assessment and covariates, we demonstrated that social isolation is a

common risk factor for depression in England and Japan, despite country-specific cultural

differences regarding social relationships. Thus, our results suggest that to safeguard the

mental health of older adults, addressing social isolation is a global need.

The association between social isolation and depression was somewhat stronger

in England than in Japan. These results are similar to a previous report concerning

mortality among older adults in England and Japan.[11] Although we cannot make direct

comparisons due to variations in cohort follow-up periods and depression measurement,

there are several possible reasons for this pattern of findings. The impact of social factors

could differ depending on the group and society to which one belongs. This is best

understood in the context of the concept of relative deprivation.[39] In other words, higher

levels of relative social isolation may induce greater psychological stress. A previous

24

257   study showed that rich community ties and cohesion were protective factors for health

258   but could have a negative effect on those who were not socially involved.[40] Being

259   isolated in a connected society such as the UK may represent a more severe condition,

260   with a stronger negative impact on mental health.

261   Our results revealed that poor interaction with children was significant with

262   regard to depression onset in Japan. In England, while the association was marginal, of

263   the components of social isolation, poor interaction with children had the greatest effect.

264   The lack of interaction with children could have an adverse effect on the mental health of

265   older adults in both countries. Previous studies in England[41] and Japan[22] have

266   reported that social support from children can contribute to alleviating depression, and

267   our results point in the same direction. Older adults without children can be considered a

268   vulnerable group, because adult children, in particular, are often the main source of

269   positive social support for older parents.[42] Older parents have certain expectations with

270   regard to receiving support from their children, and situations wherein these expectations

271   are not met may lead to depressive mood.[43] However, a previous study reported no

272   association between the presence of children and depression among older adults in the

273   US.[22] Owing to strong spousal relationships in the US, the effect of the presence of

274   children might be relatively small. Thus, our study confirmed the adverse effects of poor

25

275   interaction with children common to England and Japan, but international generalizability

276   can only be established based on further research considering the cultural background of

277   family relationships in individual countries.

278   Although traditionally Japan is a country in which adult children are expected to

279   demonstrate reciprocity with their parents based on the strong family and kinship-based

280   cultural background,[44] in this study, the effect of interaction with children on

281   depression was relatively modest. In recent years, with trends such as adult children

282   commonly living apart from their parents after marriage[45] and the development of

283   public long-term care services for the ageing population,[46] Japan's family system has

284   become less traditional. Therefore, interaction with children may not be as essential to

285   the health of older adults as before. However, despite these cultural transitions, we believe

286   that interaction with children has some value with regard to preventing depression in old

287   age in Japan.

288   Social participation was a strong protective factor for depression onset in Japan,

289   whereas there was no association in England, although the OR was somewhat greater.

290   Several previous studies have reported that social participation helps prevent depression

291   onset.[37, 47–49] Our results pertaining to Japan support these reports. However, the

292   protective effects of social participation on mental health vary depending on the type of

26

293   organisation with which an individual is involved,[48] the individual's attitude towards

294   participation,[48] and the duration[37] and frequency[49] of participation. Regarding the

295   present study, in the English context, the role of social participation in depression

296   prevention might have been unidentifiable due to differences in the effects of these

297   participation contexts. We took into account only social participation, without delving

298   into specific types. Thus, the context of effective social participation, such as type,

299   duration, and role in the organisation in both countries, requires further investigation.

300   Despite these challenges, our findings suggest that in Japan, social isolation prevention

301   measures based on the promotion of social participation could be beneficial for

302   safeguarding the mental health of older adults.

303   This study has several strengths. First, it is the first cross-national population-

304   level investigation of the association of social isolation with depression onset using a

305   unified data frame. Second, by using two longitudinal datasets, we were able to examine

306   the prospective association between social isolation and depression. Third, the use of

307   large-scale data allowed us to detect the effects of relatively rare situations of severe

308   social isolation.

309   However, certain limitations cannot be ignored. First, the measurement of

310   depression in the two cohorts was not the same. Therefore, we could not directly compare

311 depression onset in the two countries. However, these measurements were also used in a

312 previous cross-national comparison study in England and Japan,[28] and we were able to

313 examine the association between social isolation and depression onset in both countries

314 using the same data frame. Second, we used social support for the assessment of social

315 contact for some items in order to be able to use the same SII. Therefore, cultural

316 differences in expectations regarding the receipt of social support in both countries might

317 have caused information biases. For instance, expectations regarding social support from

318 relatives could originally have been higher in Japan,[44] leading to overestimation of

319 social isolation levels. Third, regarding the items of the SII, the questions and their

320 response options in the ELSA and JAGES were not exactly the same, nor were they

321 strictly authorised through procedures such as reverse translation and confirming

322 reliability and validity. However, we believe it is certainly meaningful to evaluate social

323 isolation using the same framework. Finally, there were differences in study design in the

324 data from the two cohorts, such as sampling method and follow-up period. We, therefore,

325 made efforts to harmonise the data: those aged $\leq$ 64, with dementia, and dependent in

326 activities of daily living were excluded from the analysis. Moreover, the ELSA presents

327 nationally representative population data, while the JAGES does not. However, the

328 JAGES sample is representative of areas from a nationwide ageing study in which

28

329 approximately one-fifth of all prefectures (nine out of 47) were enrolled. Even so, unlike

330 the ELSA, analysis in the JAGES does not use sampling weights, which may lead to

331 selection bias.

332

333 **CONCLUSION**

334 We examined the association between social isolation and depression onset among older

335 adults in England and Japan, who experience different cultural contexts regarding social

336 relationships, and found a significant association in both countries; we also observed that

337 in England, poor interaction with children was marginally associated, and in Japan, poor

338 interaction and lack of social participation were significantly associated with depression.

339 Tackling social isolation must be prioritised to safeguard the mental health of older adults

340 worldwide. Particularly in Japan, the promotion of interaction with children and social

341 participation could be key factors in addressing social isolation.

342

343 **ACKNOWLEDGEMENTS**

346

29

347   **AUTHORS' CONTRIBUTIONS**

348   All authors contributed to the conception and design of this study. Data collection was

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

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

351   and KK significantly contributed to revising it. All authors read and approved the final

352   manuscript.

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DATA SHARING STATEMENT

382   For the JAGES, all enquiries are to be addressed to the data management committee via

383 e-mail: dataadmin.ml@jages.net. All JAGES datasets have ethical or legal restrictions for

384 public deposition because of the inclusion of sensitive information about the human

385 participants. Regarding the ELSA, data are available in an open-access repository at

386 http://www. dataarchive.ac.uk/.

387

388 **COMPETING INTERESTS STATEMENT**

389 The authors declare no conflict of interest.

390

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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)
		p for trend < 0.001	p for trend < 0.001	p for trend < 0.001	p 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)

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)

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	1, 3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	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	9-10
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	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	11-12
		(*b*) Describe any methods used to examine subgroups and interactions	Not applicable
		(*c*) Explain how missing data were addressed	12
		(*d*) If applicable, explain how loss to follow-up was addressed	Not applicable
		(*e*) Describe any sensitivity analyses	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	13
		(b) Give reasons for non-participation at each stage	Not applicable
		(c) Consider use of a flow diagram	Not applicable
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	13-14
		(b) Indicate number of participants with missing data for each variable of interest	15-16
		(c) Summarise follow-up time (eg, average and total amount)	10
Outcome data	15*	Report numbers of outcome events or summary measures over time	17-18

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	19-21
		(*b*) Report category boundaries when continuous variables were categorized	Not applicable
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Supplementary 1, 2

Discussion

Key results	18	Summarise key results with reference to study objectives	23
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
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
Generalisability	21	Discuss the generalisability (external validity) of the study results	24-25

Other information

| 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.