

1 **The role of loneliness in the development of depressive symptoms among partnered**
2 **dementia caregivers: Evidence from the English Longitudinal Study of Ageing**

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23 **Keywords:** Loneliness, depression, and dementia care

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Abstract

Background. Depressive symptoms are highly prevalent among partnered dementia caregivers, but the mechanisms are unclear. This study examined the mediating role of loneliness in the association between dementia and other types of care on subsequent depressive symptoms.

Method. Prospective data from partnered caregivers were drawn from the English Longitudinal Study of Ageing. The sample consisted of 4,672 partnered adults aged 50-70 living in England and Wales, followed up between 2006-07 and 2014-15. Caregiving was assessed across waves 3 (2006-07), 4 (2008-09) and 5 (2010-11), loneliness at wave 6 (2012-13), and subsequent depressive symptoms at wave 7 (2014-15). Multivariable logistic regression models were used to assess the association between caregiving for dementia and depressive symptoms compared to caregiving for other illnesses (e.g. diabetes, CHD, cancer, and stroke). Binary mediation analysis was used to estimate the indirect effects of caregiving on depressive symptoms via loneliness.

Results. Care for a partner with dementia was associated with higher odds of depressive symptoms at follow-up compared to those not caring for a partner at all (Odds Ratio (OR)=2.6, 95% Confidence Intervals (CI): 1.4, 5.1). This association was partially mediated by loneliness (34%). Care for a partner with other conditions was also associated with higher odds of depressive symptoms compared to non-caregiving partners (OR=1.7, 95% CI: 1.2, 2.5), but there was no evidence of an indirect pathway via loneliness.

Conclusion. Loneliness represents an important contributor to the relationship between dementia caregiving and subsequent depressive symptoms; therefore, interventions to reduce loneliness among partnered dementia caregivers should be considered. **Keywords:** dementia caregiving, dementia, loneliness, depressive symptoms

47 **Key points**

- 48 ● Partner dementia caregiving was associated with increased odds of depressive symptoms
49 at follow-up.
- 50 ● The relationship between dementia caregiving and depressive symptoms was partially
51 mediated by caregiver loneliness.
- 52 ● These findings highlight the importance of loneliness associated with caring for a partner
53 with dementia on the subsequent mental health of carers, emphasising the need to consider
54 the role of loneliness in interventions aimed to support dementia caregivers.

55

56 **INTRODUCTION**

57 Caring for an individual with dementia has been associated with poor mental health
58 outcomes, but the mechanisms are less understood [1, 2]. Given the increasing number of
59 dementia caregivers globally and potential negative impact on their mental wellbeing [3],
60 identifying modifiable mechanisms that can be targeted through cost-effective interventions is
61 important [4].

62 A meta-analysis of 84 studies found that caregivers were more likely to report depressive
63 symptoms compared to non-caregivers [5]. The incidence of depressive symptoms depends on
64 the characteristics of both the caregiver and recipient [6]. Recipient characteristics such as
65 younger age (i.e. <65 years old compared to ≥ 85), lower education, Hispanic ancestry, higher
66 levels of disability, and the presence of challenging behaviours have all been associated with
67 higher depressive symptoms among caregivers [6]. Being the spouse of a care recipient
68 (especially the wife) is also a risk factor for depression compared to other types of caregiver
69 roles, such as caring for grandchildren [6].

70 Caring for an individual with dementia involves both physical and neurological
71 symptomatology, as well as behavioural and cognitive impairments, which may explain why
72 dementia care incurs a greater burden compared to caring for an individual with only physical
73 (but not neural) impairments [7]. The demands of dementia care could also lead to loneliness
74 among the caregiver, and it is well documented that loneliness is linked with reduced mental
75 wellbeing as well as physical morbidity and increased mortality [8]. A UK-based prevalence
76 study indicated that over two-thirds of dementia caregivers reported feeling lonely [9]. The study
77 found that greater social isolation and caregiver stress were associated with higher loneliness,
78 while caregiver-recipient relationship quality was protective.

79 The relationship between loneliness and depression is well established, but few studies
80 have examined this in relation to dementia caregiving. Loneliness was a strong predictor of
81 depressive symptoms among 242 spousal dementia caregivers in the USA [10], and a cross-
82 sectional study of 49 spousal dementia caregivers found loneliness to explain 49% of the variance
83 depressive symptoms [11]. Caregiver loneliness might increase in parallel with the increasing
84 severity of dementia, which could elevate the risk of adverse mental health among caregivers
85 over time. However, most previous studies have relied on cross-sectional data and have not
86 addressed potential mechanistic relationships between caregiving and depressive symptoms.

87 This study considered whether the higher risk of depressive symptoms among those caring for
88 a partner with dementia (compared to non-caregiving partners) could be explained by loneliness.
89 We tested the following hypotheses:

- 90 1. Individuals providing care for a partner with dementia ('dementia caregiving') would have
91 increased odds of depressive symptoms at follow-up compared to individuals not providing
92 care for their partner (irrespective of partner dementia diagnosis).
- 93 2. Individuals caring for a partner with dementia would report higher levels of loneliness
94 compared to other partnered caregivers.
- 95 3. Loneliness would mediate the relationship between dementia caregiving and subsequent
96 depressive symptoms.

97 **Method**

98 *Design, setting and participants*

99 Data were drawn from the English Longitudinal Study of Ageing (ELSA), an ongoing nationally
100 representative sample of approximately 11,000 individuals aged 50 and over living in England
101 [12]. Participants were initially recruited in 2002-03. Refreshment samples of new participants
102 were recruited in 2006-07, 2008-09, 2010-11, 2012-13, and 2014-15. All waves took place

103 biennially, consisting primarily of self-completed questionnaires and face-to-face interviews.
104 Only waves 3-7 were used in this analysis due to the lack of caregiving data prior to wave 3. We
105 included in our analysis refreshment samples introduced at waves 3 and 4. We selected 10,813
106 individuals who had provided care to their partner between wave 3 (2006-07) and wave 5 (2010-
107 11) and had available data on loneliness at wave 6 (2012-13) and depressive symptoms at wave 7
108 (2014-15). Participants were only eligible if they had a partner.

109 **Measurements**

110 *Caregiving.* Caregiving status was assessed by self-report questions at waves 3, 4, and 5 where
111 participants were asked: “Did you look after anyone in the last week (including your partner or
112 other people in your household)?” Participants responding “No” were classified as ‘non-
113 caregiving partners’. Those responding “Yes” were then asked what their relation to the care
114 recipient was (e.g. partner, child). Those not providing care to a partner were excluded from the
115 final analytic sample. Individuals who provided care for a partner at least once across waves 3, 4,
116 or 5 were classified as a caregiver. Functional impairments were assessed at waves 3, 4 and 5, by
117 asking whether household members required support with Activities of Daily Living (ADLs;
118 bathing or showering, walking across a room, dressing, getting in/out of bed, eating, using the
119 toilet) or Instrumental Activities of Daily Living (IADLs; preparing a hot meal, doing
120 house/garden work, using a map in unknown places, grocery shopping, taking medication,
121 making telephone calls, managing money) [13]. Dementia status was assessed based on self-
122 reported physician-confirmed diagnoses of dementia at waves 3, 4 and 5.

123 Based on this information, we derived a four-level caregiving measure: 0=‘Non-caregiving
124 partners’, the reference category; 1=‘Care for partner with dementia’; 2=‘Care for partner with
125 functional impairments (but no diagnosis of dementia)’; and 3=‘Care for partner with other

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126 conditions'. For mediation analyses, we created binary dummy variables representing each
127 caregiving category.

128 *Depressive symptoms* Self-reported depressive symptoms were assessed at wave 7 (2014/15)
129 using the eight-item version of the Center for Epidemiologic Studies Depression Scale (CES-D)
130 [15], see Table S1. This measure had good internal reliability across waves ($\alpha=0.84$) and
131 comparable psychometric properties to the full 20-item scale [16, 17]. All items were coded as
132 "Yes" or "No". The item addressing loneliness was removed to ensure that this item did not
133 overlap with the mediating effect of loneliness [18]. The remaining seven items were summed
134 and dichotomised, such that participants with scores of ≥ 3 were considered with elevated
135 depressive symptoms) [19-20].

136 *Potential mediator.* Loneliness was measured using the three-item short form of the revised
137 University of California, Los Angeles (UCLA) Loneliness Scale, which has been shown to have
138 acceptable internal reliability ($\alpha=0.78$) [21]. Three questions assessed the frequency that an
139 individual had felt a lack of companionship, left out, or isolated from others over the past week.
140 Answers were scored on a three-point scale ranging from 1 ("Hardly ever or never") to 3
141 ("Often") and summed to create a continuous total score ranging 3-9. Higher scores indicated
142 increased loneliness [22].

143 *Covariates.* Analyses were adjusted for covariates measured at the first non-missing interview
144 between waves 3 and 5. Adjustments were made for gender, age, household wealth, marital
145 status, ethnicity, highest educational qualification, employment status, presence of limiting
146 longstanding illness, and poor self-rated health.

147 To reduce possible confounding, all fully adjusted models were estimated with adjustment for
148 baseline depressive symptoms (CES-D score of ≥ 3 at wave 3; or wave 4, if missing at wave 3).

149 Please see supplementary material for more information on how and why these covariates were
150 chosen/derived.

151 *Statistical analysis*

152 χ^2 and Kruskal-Wallis tests were used to investigate baseline demographic differences
153 between the four caregiving categories, as well as differences in depressive symptoms at follow-
154 up. The association between caregiving and depressive symptoms was assessed using logistic
155 regression models. Three models were estimated (1) unadjusted, (2) adjusted for age, gender,
156 education level, household wealth, marital status, ethnicity, employment status and (3)
157 additionally adjusted for the presence of longstanding limiting illness, self-rated health, and
158 baseline depressive symptoms. All models were estimated in the overall sample and separately
159 for men and women. We reported the Odds Ratios (OR) and 95% Confidence Intervals (CI).

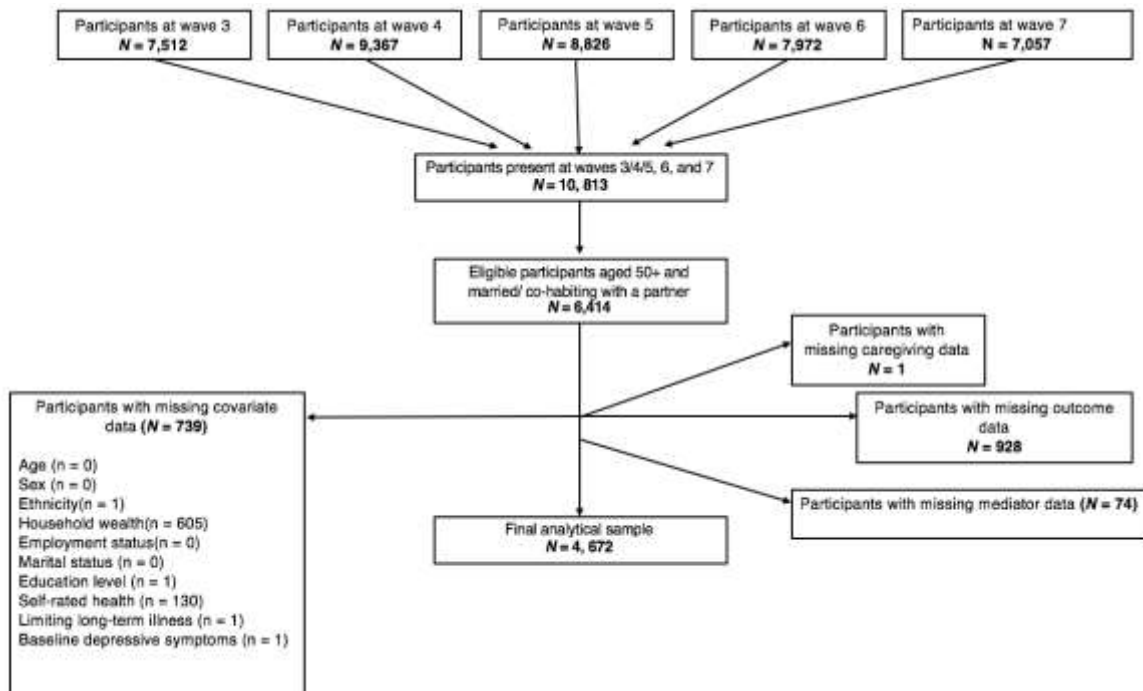
160 Mediation was assessed by fitting a series of linear regression models for continuous variables
161 (loneliness) and logistic regression models for binary variables (depressive symptoms) using the
162 'medeff' statistical package in Stata 14 [23, 24]. Due to differences in sample size across these
163 groups, the sample sizes for assessing mediation vary slightly. The manuscript was written
164 following STROBE guidelines [25], see Table S2.

165 *Sensitivity analyses*

166 To reduce possible confounding, all models were reestimated after excluding participants meeting
167 criteria for clinically significant depressive symptoms at baseline (7-items CES-D score of ≥ 3 at
168 wave 3 or wave 4 if missing at wave 3). A second sensitivity analysis was conducted on the main
169 sample using the 8-item CES-D with a threshold of ≥ 4 at wave 3 or wave 4, if missing at wave 3,
170 instead of the ≥ 3 threshold used in the main analysis

171 **Results**172 *Sample characteristics*

173 The analytical sample included 4,672 participants after removal of those with missing
 174 information on caregiving status ($n=1$), covariates ($n=739$), mediators ($n=74$) or depressive
 175 symptoms ($n=928$) (Figure 1).



176

177 Figure 1. Participant flowchart for the analytical sample

178 Compared to the main sample, excluded participants were older (64.8 vs. 61.9 years),
 179 more likely to be female (59% vs. 51%), similar in terms of non-white ethnicity (4% vs. 3%), had
 180 a higher incidence of longstanding limiting illnesses (37% vs. 26%), were less likely to have
 181 completed any formal education (minimum of O-level award or junior/middle high school
 182 diploma) (67% vs. 80%), were more likely to be in the lowest quintile of household wealth (25%
 183 vs. 8%) and were less likely to be employed (35% vs. 46%).

184 Table 1 presents the demographic characteristics of the analytical sample stratified by
185 caregiving status. Compared to non-caregiving partners, those caring for a partner were more
186 likely to be female than male (59% vs. 51%), older (63.5 vs. 61.8 years), to be in the lowest
187 quintile of household wealth (18% vs. 9%), less likely to be employed (30% vs. 48%) and more
188 likely to report longstanding limiting illnesses (35% vs. 25%). However, non-caregivers at
189 baseline were less likely to report depressive symptoms (9% vs. 13%) and slightly lower levels of
190 loneliness (mean of 3.8 vs. 4.0) compared to caregivers. All differences were statistically
191 significant at $p < 0.005$ except for differences in ethnicity ($p = 0.413$).

192 Dementia caregivers tended to be older (68.0 vs. 61.8 years; $p < 0.001$), female (69% vs.
193 51%; $p < 0.007$) and unemployed (10% vs. 48%; $p < 0.001$), compared to partners not providing
194 any care. The proportion of dementia caregivers reporting depressive symptoms was higher
195 compared to non-caregiving partners (at baseline: 21% vs. 9%; $p < 0.001$; at follow-up: 27% vs.
196 13%; $p < 0.001$) and when compared to those caring for a partner with functional impairments
197 (baseline: 21% vs. 11%; $p = 0.03$; follow-up: 38% vs. 20%; $p < 0.01$). Dementia caregivers were
198 also more likely to report depressive symptoms at follow-up (27% vs. 22%; $p < 0.01$) compared to
199 those caring for a partner with other conditions, but this difference did not reach statistical
200 significance at baseline (21% vs. 13%; $p = 0.09$). Dementia caregivers were more likely to report
201 longstanding limiting illnesses at baseline (44% vs. 25%; $p < 0.005$).

202

203 Table 1. Demographic characteristics of the analytic sample (n=4,672)

	Non-caregiving partners (n= 4,251)	Partner caregivers (n= 421)			
		All caregivers (n= 421)	Care for partner with dementia (n = 48) ^a	Care for partner with functional impairments (n = 178)	Other types of partner care (n= 195)
<i>Baseline covariates</i>					
Age (year), mean (SD)	61.8 (7.5)	63.5 (8.0)	68.0 (7.7)	63.6 (8.1)	62.3 (7.7)
Gender (female), n (%)	2,145 (50.5)	248 (58.9)	33 (68.8)	91 (51.1)	124 (63.6)
Ethnicity (White), n (%)	4,131 (97.3)	412 (97.9)	46 (95.8)	176 (88.0)	190 (97.4)
Household wealth, n (%)					
1 st (Lowest)	320 (7.5)	74 (17.6)	9 (18.8)	40 (22.5)	25 (12.8)
2 nd	631 (14.8)	78 (18.5)	9 (18.8)	42 (23.6)	27 (13.9)
3 rd	863 (20.3)	72 (17.1)	8 (16.7)	27 (15.2)	37 (19.0)
4 th	1,079 (25.4)	103 (24.5)	11 (22.9)	38 (21.4)	54 (27.7)
5 th (Highest)	1,358 (31.9)	94 (22.3)	11 (22.9)	31 (17.4)	52 (26.7)
Education level, n (%)					
No qualification (elementary school diploma)	847 (19.9)	100 (23.8)	13 (27.1)	48 (27.0)	39 (20.0)
Up to GCE O-level (middle or junior high school diploma)	1,010 (23.8)	110 (26.1)	10 (20.8)	60 (33.7)	40 (20.5)
Up to A-level/ Equivalent (high school or senior high school diploma)	666 (15.7)	67 (15.9)	13 (27.1)	22 (12.4)	32 (16.4)
Lower than degree	771 (18.1)	68 (16.2)	4 (8.3)	25 (14.0)	39 (20.0)
Degree (university undergraduate certificate)	957 (22.5)	76 (18.1)	8 (16.7)	23 (12.9)	45 (23.1)
Employed, n (%)	2,036 (47.9)	124 (29.5)	5 (10.4)	49 (16.3)	70 (35.9)
Married, n (%)	3,949 (92.9)	399 (94.8)	46 (95.8)	168 (94.4)	185 (94.8)
Self-rated health (1-5), mean (SD)	2.57 (1.0)	2.77 (1.1)	2.83 (1.1)	2.92 (1.2)	2.61 (1.0)
Long-standing limiting illness, n (%)	1,075 (25.3)	148 (35.2)	21 (43.8)	71 (39.9)	56 (28.7)
<i>Mediator</i>					
UCLA Loneliness scale score, mean (SD)	3.93 (1.4)	4.31 (1.6)	5.08 (1.7)	4.43 (1.6)	4.00 (1.4)
<i>Follow-up</i>					

CES-D depressive symptoms scale score (≥ 3), <i>n</i> (%)	556 (13.1)	96 (22.8)	18 (37.5)	36 (20.2)	42 (21.5)
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205 *Note.* *SD* = standard deviation; *n* = sample size

206

207 ***The relationship between caregiving status and subsequent depressive symptoms at follow-up***

208 In the overall sample ($n=4,672$), individuals caring for their partner had higher odds of
 209 developing depressive symptoms compared with those not caring for their partners. This was
 210 especially the case among those providing care to a partner with dementia (Table 2). In
 211 unadjusted analyses, caregiving for a partner with dementia (OR=3.99, 95% CI: 2.21, 7.20),
 212 functional impairments (OR=1.68, 95% CI: 1.16, 2.45), or other conditions (OR=1.82, 95% CI:
 213 1.28, 2.60) was associated with increased levels of depressive symptoms. This relationship was
 214 attenuated after full adjustment and remained statistically significant only for those caring for a
 215 partner with dementia or other conditions. Preliminary analyses found no gender differences
 216 between various types of caregiving within those with depressive symptoms at follow-up ($\chi^2 =$
 217 5.73, $p = 0.13$).

218

219 Table 2. The odds ratios of depressive symptomatology (wave 7) among caregivers (waves 3-5)
 220 in the full analytic sample (N=4,672)

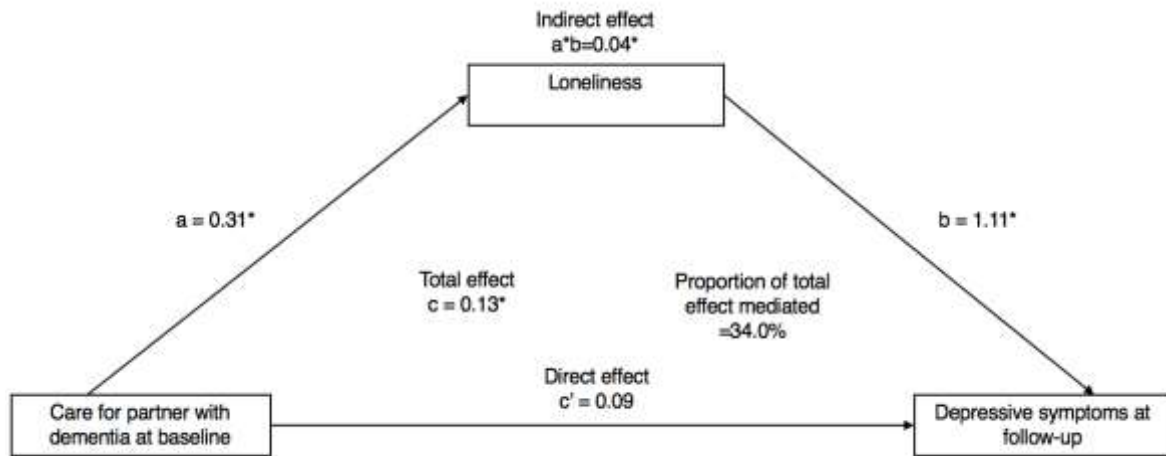
	Full sample (n=4,672)			Males (n=2,279)			Females (n=2,393)		
	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6	Model 7	Model 8	Model 9
	OR (95% CI) ^a	OR (95% CI) ^b	OR (95% CI) ^c	OR (95% CI) ^a	OR (95% CI) ^b	OR (95% CI) ^c	OR (95% CI) ^a	OR (95% CI) ^b	OR (95% CI) ^c
Caregiving group									
<i>Non-caregiving partners</i>	Ref.			Ref.			Ref.		
<i>Care for partner with dementia</i>	3.99** (2.21, 7.20)	2.70** (1.46, 4.98)	2.64** (1.36, 5.10)	4.16* (1.41, 12.28)	3.17* (1.03, 9.72)	2.64 (0.84, 8.29)	3.58** (1.76, 7.26)	2.65* (1.27, 5.53)	3.16** (1.45, 6.90)
<i>Care for partner with functional impairments</i>	1.68* (1.16, 2.45)	1.24 (0.84, 1.82)	1.15 (0.76, 1.75)	1.73 (0.98, 3.07)	1.18 (0.65, 2.15)	1.15 (0.61, 2.17)	1.65 (0.99, 2.72)	1.33 (0.79, 2.23)	1.17 (0.66, 2.06)
<i>Other types of partner care</i>	1.82** (1.28, 2.60)	1.64** (1.14, 2.36)	1.71* (1.16, 2.51)	1.36 (0.69, 2.70)	1.37 (0.68, 2.77)	1.39 (0.66, 2.94)	1.93** (1.26, 2.91)	1.87** (1.21, 2.88)	1.93*** (1.23, 3.05)

221
 222 *Note.* CI: confidence interval; OR = odds ratio
 223 ^a = unadjusted model
 224 ^b = model adjusted for demographic factors (age, marital status, ethnicity, socioeconomic status,
 225 employment and education)
 226 ^c = model adjusted for demographic factors and health-related factors (presence of long-standing
 227 limiting illnesses, self-rated health, and baseline depressive symptoms); each caregiving measure
 228 was tested in a separate model
 229 * = $p < 0.05$, ** = $p < 0.005$, *** = $p < 0.001$

230
 231 ***The mediating role of loneliness (wave 6) on the association between caregiving (waves 3-5)***
 232 ***and depressive symptoms (wave 7)***

233 Caring for a partner with dementia was positively associated with loneliness ($\beta=0.31$, 95% CI:
 234 0.15, 0.47), and loneliness was positively associated with depressive symptoms at follow-up (OR
 235 = 1.11, 95% CI: 0.92, 1.30). Moreover, caring for a partner with dementia was indirectly related

236 to depressive symptoms via loneliness ($\beta=0.04$, Bias corrected (Bc) CI: 0.02, 0.07), which
 237 explained 34% of the total effect.



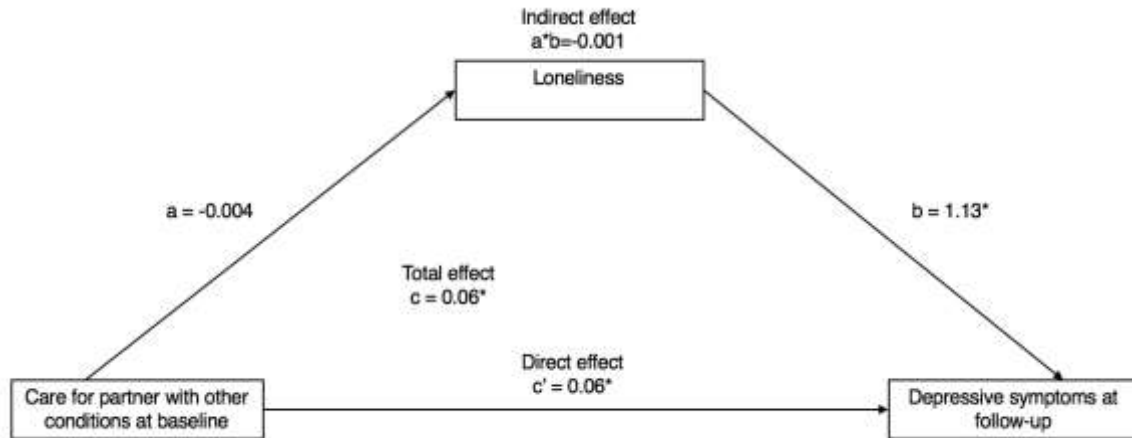
238
 239 Figure 2. Mediation analysis of the association between dementia care (waves 3/4/5) on
 240 depressive symptoms (wave 7) via loneliness (wave 6) (n = 4,229)

241 Note. $*=p<0.05$

242 All models were adjusted for demographics (age, marital status, ethnicity, socioeconomic status,
 243 employment and education) and health-related (presence of longstanding limiting illnesses, self-
 244 rated health, and baseline depressive symptoms) factors. A bias-corrected bootstrap using 1000
 245 iterations was applied to all models. Each caregiving measure was tested in a separate model.

246 Caring for a partner with other conditions was not significantly associated with loneliness ($\beta=-$
 247 0.004, 95% CI: -0.07, 0.06), and although loneliness was positively related to depressive
 248 symptoms (OR=1.13, 95% CI: 0.94, 1.32), there was no evidence of an indirect effect via
 249 loneliness ($\beta=-0.001$, Bc CI: -0.008, 0.008). Since caring for a partner with functional
 250 impairments was not associated with depressive symptoms after full adjustment (i.e. no 'Total
 251 effect'), this model was not tested for mediation.

252



253
 254 Figure 3. Mediation analysis of the association between ‘care for a partner with other conditions’
 255 (waves 3/4/5) on depressive symptoms (wave 7) via loneliness (wave 6) ($n = 4,446$)

256 Note. $*=p < 0.05$

257 All models were adjusted for demographics (age, marital status, ethnicity, socioeconomic status,
 258 employment and education) and health-related (presence of longstanding limiting illnesses and
 259 self-rated health) factors. A bias-corrected bootstrap with 1000 iterations was applied to all
 260 models (see supplementary materials for details).

261 **Sensitivity analyses**

262 We conducted two sensitivity analyses. Firstly, we excluded all participants who met the
 263 criteria for baseline depressive symptoms ($N=423$), see Tables S3. In the second analysis, we
 264 reestimated all models using the original CES-D scale (with a cut-off of ≥ 4), see Tables S4. The
 265 new results did not substantially alter the strength of the initial associations found between
 266 caregiving types and depressive symptoms at follow-up compared to our main analyses.

267 Moreover, the indirect effect of caregiving on depressive symptoms via loneliness remained
 268 statistically significant among dementia caregivers and non-significant among those in the “other
 269 care” category in both sensitivity analyses (see Figures S1 to S4).

270 **Discussion**

271 We found that caring for a partner with dementia was associated with higher odds of
272 depressive symptoms at follow-up compared to non-caregiving partners and that loneliness
273 significantly mediated this association. A similar association was observed for those caring for
274 other conditions than dementia, but the increased odds of depressive symptoms was lower than
275 for those caring for a partner with dementia. We did not find evidence to suggest loneliness
276 mediates the association between care for a partner with other conditions and subsequent
277 depressive symptoms.

278 Consistent with our first hypothesis, the odds of depressive symptoms were higher among
279 dementia caregivers when compared to non-caregiving partners. This is in line with previous
280 research [5, 6] and may reflect the caregiving burden associated with increased psychological and
281 mental demands, as well as the physical and behavioural challenges that can present in patients
282 with dementia and the strain these can place on the couple [7]. However, we did not find
283 evidence of gender differences in the relationships between caregiving and depressive symptoms,
284 consistent with one other previous study [28]. Caring for individuals with dementia requires
285 ongoing care that may impose withdrawal from paid work, which is another determinant of poor
286 mental health [26, 27]. While some partners may embrace the caregiving role, some report
287 feelings of 'role captivity' which is likely to feed into the development of depressive symptoms
288 [29]. Role captivity refers to a sense of being trapped in a specific social role which limits the
289 individual's freedom. This might partly be responsible for feelings of loneliness and depressive
290 symptomatology.

291 Our findings might support the idea that caring for a partner with both mental and
292 functional impairments (i.e. dementia) is more strenuous than caring for a partner with only
293 functional impairments or physical disability [7]. Although we did not make an active

294 comparison between these groups, this was inferred from the larger odds ratio in the dementia
295 care group compared to the functional impairments group. Notably, caring for a partner with only
296 physical, rather than both mental and physical impairments as in the case of dementia, was not
297 found to be associated with subsequent higher odds of depressive symptoms. This is thought-
298 provoking because it suggests that caring for partners with physical impairments only is not
299 necessarily linked to poorer mental health. It is also possible that greater support is available to
300 carers for partners with only functional impairments, or that those caring for a partner with
301 dementia have less time and opportunities for social support, and therefore more vulnerable to an
302 increased risk of depressive symptoms. Ultimately, it may be that it is the addition of
303 psychological/behavioural impairments that tips the association towards significance.

304 Consistent with our second hypothesis, loneliness was highest among dementia caregivers
305 compared to non-caregiving partners. A possible explanation for this is the shift from partnership
306 to the caregiver-patient role, and thus the loss of a previously meaningful relationship. This is
307 consistent with qualitative findings describing the caregiving experience as one of 'relational
308 deprivation' [30]. The burden of caregiving activities may increase loneliness by reducing the
309 opportunities to engage with a wider social circle [10]. Similarly, the progressive deterioration in
310 cognitive functioning among those with dementia often also results in personality changes, that
311 may precipitate a significant emotional loss in the form of anticipatory grief [31-33]. Both of
312 these factors may contribute to increased loneliness.

313 Consistent with our third hypothesis, we found evidence of indirect effects of dementia
314 caregiving on depressive symptoms via loneliness, highlighting the importance of considering
315 loneliness when supporting such individuals. Interestingly, there was a direct effect of caring for
316 other conditions on depressive symptoms; however, we did not find any indirect effect via
317 loneliness. This suggests that policies and/or therapeutic interventions need to be tailored to the

318 specific needs of the couple. Future research could attempt to uncover what are the specific
319 mediating factors of the 'other care' category.

320 **Strengths and limitations**

321 Our analysis represents a longitudinal investigation of dementia caregivers living in their
322 community and their subsequent level of loneliness and mental health, using a representative
323 sample of the English population. This is a significant benefit since many studies of caregivers
324 are based on the recruitment of participants who have self-identified as distressed caregivers, a
325 factor likely to inflate the findings and reduce ecological validity [34]. We also used a superior
326 design compared to past studies where comparison groups have contained both partnered and un-
327 partnered non-caregivers. Being married or having a partner is usually protective of mental health
328 [35], but previous studies may have underestimated the effect of caregiving on depressive
329 symptoms. Furthermore, we used a prospective longitudinal data that allowed us to test potential
330 causal inferences regarding the impact of partner caregiving on subsequent loneliness and
331 depressive symptoms.

332 However, several potential limitations have been identified. Firstly, caregiving was based
333 on a self-reported measure, and no consideration was given to the intensity of care provided or
334 the duration of the caregiving role (due to sample size limitations). Moreover, our measurement
335 of caregiving did not allow variations in caregiving intensity or transitions in/out of a caregiving
336 role, which previous studies have identified as important for mental health outcomes [36]. By not
337 considering the potential transitions in caring roles may have introduced some bias into our
338 findings. However, we assumed that once an individual becomes a carer for a partner with
339 dementia, their role as caregiver is likely to continue for some time (either until the partner dies,
340 or becomes institutionalised). Furthermore, we assumed that even if caregivers transitioned out of
341 the role between waves 3 and 5, the influence on their mental health would be expected to

342 continue to some degree. This would be in line with the relational deprivation hypothesis, which
343 suggests that it is partly the meaning attributed to the caregiving role (i.e. that it acts as a kind of
344 loss of the partner once known) that mediates depressive symptoms (rather than solely the
345 requirements of the role itself).

346 Secondly, it is also worth noting that although dementia diagnoses were made by a
347 physician, it was still a self-reported physician-based diagnosis reported by either the participant
348 themselves or their carers. This, however, may raise some questions around the reliability of the
349 diagnosis for these analyses, although it is unlikely that such reports will be false positives. In
350 fact, it is estimated that dementia remains undetected in almost 30 to 50% of primary care
351 patients in the UK [37]. Furthermore, it is possible that care-recipients relevant to the “functional
352 impairments” category had dementia during the exposure period but had not yet received a
353 diagnosis by a physician. This may have attenuated differences between each group.

354 Thirdly, we had no means of knowing whether caregivers were receiving psychological
355 support and the number of individuals with dementia was small, both of which could have
356 affected the results. Similarly, excluding participants with missing data could have diluted the
357 reported effect sizes. For example, based on their characteristics (see results section), excluded
358 participants might be more at risk of depressive symptoms compared to those without missing
359 data. While the reasons for attrition among ELSA participants have been previously explored, it
360 is unclear whether the caregiving role had any influence on this attrition, and what the impact on
361 the results was [36].

362 Fourthly, to maximise the use of available data, our measurement of caregiving captured
363 caring roles at either wave 3, 4, or 5. We took this approach because if an individual entered a
364 caregiving role at waves 4 or 5, we wanted to avoid classifying them as “Not caring” based on
365 wave 3 alone. As discussed above, a caregiving role at any single wave may still be associated

366 with subsequent depressive symptoms. This measurement of caregiving across multiple waves
367 introduced a further limitation whereby for a small minority (less than 5% of the analytical
368 sample) caregiving status and covariates were measured at different waves. However, for most of
369 our covariates with the exception of age, we did not expect a real change over time.

370 Finally, although we found evidence of an indirect effect of dementia caregiving on
371 depressive symptoms via loneliness, it was unclear whether it was due to the caregiving itself or
372 the death of the care-recipient, for example. Having said that, the specific causes of loneliness are
373 likely to vary between individuals, and this would be explored as part of any therapeutic
374 intervention.

375

376 **Conclusion**

377 Our findings indicate that partner dementia caregiving is indirectly associated with
378 depressive symptoms via feelings of loneliness. The mental health of dementia caregivers is
379 arguably an essential psychiatric priority, given that it could seriously influence the quality of
380 care provided to their partner and thus impact the rate of care-recipient institutionalisation [34,
381 39].

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393 **Sponsor's role**

394 The views expressed are those of the authors and not of the funding agencies.

395 **Conflicts of interest**

396 On behalf of all co-authors, we have no conflict of interest to declare.

397 **Authors' notes:**

398 DC dedicates this work to her mum, who was a spousal dementia carer.

399 **Data Availability Statement**

400 The ELSA data containing the individual items and the derived scores have been made available
401 via UK Data Service (<http://www.esds.ac.uk/longitudinal/access/elsa>), and the study number is
402 5050 (<http://doi.org/10.5255/UKDA-SN-8502-2>).

403

404 **References**

- 405 [1] Sallim AB, Sayampanathan AA, Cuttilan A, Ho R. Prevalence of mental health disorders
406 among caregivers of patients with Alzheimer's disease. *J Am Med Dir Assoc.* 2015; 16: 1034-
407 41. <https://doi.org/10.1016/j.jamda.2015.09.007>
- 408 [2] Sørensen S, Conwell Y. Issues in dementia caregiving: Effects on mental and physical
409 health, intervention strategies, and research needs. *Am J Geriatr Psychiatry.* 2013;19: 491-6.
410 <https://doi.org/10.1097/JGP.0b013e31821c0e6e>
- 411 [3] Alzheimer's Association. Alzheimer's Disease Facts and Figures. *Alzheimer's Dement.*
412 2017; 13: 325-73. <https://doi.org/10.1002/alz.12068>
- 413 [4] Hoff A. Current and Future Challenges of Family Care in the UK: future of an ageing
414 population. [https://www.gov.uk/government/publications/future-of-ageing-family-care-in-the-](https://www.gov.uk/government/publications/future-of-ageing-family-care-in-the-uk)
415 [uk](https://www.gov.uk/government/publications/future-of-ageing-family-care-in-the-uk); 2015 [accessed 18 January 2020]
- 416 [5] Pinquart M, Sørensen S. Differences between caregivers and noncaregivers in
417 psychological health and physical health: a meta-analysis. *Psychol Aging.* 2003; 18: 250-67.
418 <https://doi.org/10.1037/0882-7974.18.2.250>
- 419 [6] Covinsky KE, Newcomer R, Fox P, et al. Patient and caregiver characteristics associated
420 with depression in caregivers of patients with dementia. *J Gen Intern Med.* 2003; 18: 1006-14.
421 <https://doi.org/10.1111/j.1525-1497.2003.30103.x>
- 422 [7] Ory MG, Hoffman RR, Yee JL, Tennstedt S, Schulz R. Prevalence and impact of
423 caregiving: a detailed comparison between dementia and nondementia caregivers.
424 *Gerontologist.* 1999; 39: 177-85. <https://doi.org/10.1093/geront/39.2.177>

Accepted manuscript: Authors' Copy

- 425 [8] Hawkey LC, Cacioppo JT. Loneliness matters: a theoretical and empirical review of
426 consequences and mechanisms. *Ann Behav Med.* 2010; 40: 218-27.
427 <https://doi.org/10.1007/s12160-010-9210-8>
- 428 [9] Victor CR, Rippon I, Quinn C, Nelis SM, Martyr A, Hart N et al. The prevalence and
429 predictors of loneliness in caregivers of people with dementia: findings from the IDEAL
430 programme. *Aging Ment Health.* 2020; 1-7. <https://doi.org/10.1080/13607863.2020.1753014>
- 431 [10] Beeson RA, Horton-Deutsch S, Farran C, Neundorfer M. Loneliness and depression in
432 caregivers of persons with Alzheimer's disease or related disorders. *Issues Ment Health N.*
433 2000; 21: 779-806. <https://doi.org/10.1080/016128400750044279>
- 434 [11] Beeson RA. Loneliness and depression in spousal caregivers of those with Alzheimer's
435 disease versus non-caregiving spouses. *Arch Psychiatr Nurs.* 2003; 17: 135-43.
436 [https://doi.org/10.1016/S0883-9417\(03\)00057-8](https://doi.org/10.1016/S0883-9417(03)00057-8)
- 437 [12] Steptoe A, Breeze E, Banks J, Nazroo J. Cohort Profile: The English Longitudinal Study
438 of Ageing. *Int J Epidemiol.* 2013; 42: 1640-8. <https://doi.org/10.1093/ije/dys168>
- 439 [13] Torres JL, Lima-Costa MF, Marmot M, de Oliveira C. Wealth and disability in later life:
440 The English Longitudinal Study of Ageing (ELSA). *PLoS One.* 2016; 11: e0166825.
441 <https://doi.org/10.1371/journal.pone.0166825>
- 442 [14] Bradford A, Kunik ME, Schulz P, Williams SP, Singh H. Missed and delayed diagnosis
443 of dementia in primary care: prevalence and contributing factors. *Alzheimer Dis Assoc*
444 *Disord.* 2009; 23: 306-14. <https://doi.org/10.1097/WAD.0b013e3181a6bebc>
- 445 [15] Radloff L. The CES-D scale: A self-report depression scale for research in the general
446 population. *Appl Psychol Meas.* 1977; 1: 385-401.
447 <https://doi.org/10.1177/014662167700100306>

Accepted manuscript: Authors' Copy

- 448 [16] Rafnsson SB, Shankar A, Steptoe A. Informal caregiving transitions, subjective well-
449 being and depressed mood: Findings from the English Longitudinal Study of Ageing. *Aging*
450 *Ment Health*. 2017; 21: 104-12. <https://doi.org/10.1080/13607863.2015.1088510>
- 451 [17] Turvey CL, Wallace RB, Herzog R. A revised CES-D measure of depressive symptoms
452 and a DSM-based measure of major depressive episodes in the elderly. *Int Psychogeriatr*.
453 1999; 11: 139-48. <https://doi.org/10.1017/s1041610299005694>
- 454 [18] Cacioppo JT, Hawkley LC, Thisted RA. Perceived social isolation makes me sad: 5-year
455 cross-lagged analyses of loneliness and depressive symptomatology in the Chicago Health,
456 Aging, and Social Relations Study. *Psychol Aging*. 2010; 25: 453-63.
457 <https://doi.org/10.1037/a0017216>
- 458 [19] Daly M. The relationship of C-reactive protein to obesity-related depressive symptoms: a
459 longitudinal study. *Obesity (Silver Spring)*. 2013 Feb;21(2):248-50. doi: 10.1002/oby.20051.
460 PMID: 23404927.
- 461 [20] White J, Zaninotto P, Walters K, Kivimäki M, Demakakos P, Biddulph J, Kumari M, De
462 Oliveira C, Gallacher J, Batty GD. Duration of depressive symptoms and mortality risk: the
463 English Longitudinal Study of Ageing (ELSA). *Br J Psychiatry*. 2016 Apr;208(4):337-42.
464 doi: 10.1192/bjp.bp.114.155333. Epub 2016 Jan 21. PMID: 26795425; PMCID:
465 PMC4816969.
- 466 [21] Hughes ME, Waite LJ, Hawkley LC, Cacioppo JT. A Short Scale for Measuring
467 Loneliness in Large Surveys: Results From Two Population-Based Studies. *Res Aging*. 2004;
468 26: 655-72. <https://doi.org/10.1177/0164027504268574>
- 469 [22] Shankar A, Hamer M, McMunn A, Steptoe A. Social isolation and loneliness:
470 relationships with cognitive function during 4 years of follow-up in the English Longitudinal

Accepted manuscript: Authors' Copy

- 471 Study of Ageing. *Psychosom Med.* 2013; 75: 161-70.
472 <https://doi.org/10.1097/PSY.0b013e31827f09cd>
- 473 [23] Hicks R, Tingley D. Causal mediation analysis. *The Stata Journal.* 2011; 11: 605–19.
- 474 [24] StataCorp. 2014. *Statistic Software: Release 7.0.* College Station, TX: Stata Corporation.
- 475 [25] von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP;
476 STROBE Initiative. The Strengthening the Reporting of Observational Studies in
477 Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet.*
478 2007 Oct 20;370(9596):1453-7. PMID: 18064739
- 479 [26] Sefcik J, Petrovsky D, McPhillips MV, Hodgson N, Gitlin L. Financial strain among
480 dementia informal caregivers. *Innov Aging.* 2018; 2: 76.
481 <https://doi.org/10.1093/geroni/igy023.290>
- 482 [27] Quinn C, Clare L, Woods RT. The impact of motivations and meanings on the wellbeing
483 of caregivers of people with dementia: a systematic review. *Int Psychogeriatr.* 2019; 22: 43-
484 55. <https://doi.org/10.1017/S1041610209990810>
- 485 [28] Pöysti MM, Laakkonen ML, Strandberg T, et al. Gender differences in dementia spousal
486 caregiving. *Int J Alzheimers Dis.* 2012; 162960. <https://doi:10.1155/2012/162960>
- 487 [29] Givens JL, Mezzacappa C, Heeren T, Yaffe K, Fredman L. Depressive symptoms among
488 dementia caregivers: role of mediating factors. *Am J Geriatr Psychiatry.* 2014; 22: 481-88.
489 <https://doi.org/10.1016/j.jagp.2012.08.010>
- 490 [30] Vasileiou K, Barnett J, Barreto M, Vines J, Atkinson M, Lawson S, Wilson M.
491 Experiences of Loneliness Associated with Being an Informal Caregiver: A Qualitative
492 Investigation. *Front Psychol.* 2017; 8: 585. <https://doi:10.3389/fpsyg.2017.00585>

Accepted manuscript: Authors' Copy

- 493 [31] Robins Wahlin TB, Byrne GJ. Personality changes in Alzheimer's disease: a systematic
494 review. *Int J Geriatr Psychiatry*. 2011; 26: 1019-29. <https://doi.org/10.1002/gps.2655>
- 495 [32] Hazan C, Shaver PR. Romantic love conceptualised as an attachment process. *J Pers and*
496 *Soc Psychol*. 1987; 52: 511-524. <https://doi.org/10.1037/0022-3514.52.3.511>
- 497 [33] Blandin K, Pepin R. Dementia grief: A theoretical model of a unique grief experience.
498 *Dementia (London)*. 2015; 16: 67-78. <https://doi.org/10.1177/1471301215581081>
- 499 [34] Ask H, Langballe E, Holmen J, Selbæk G, Saltvedt I, Tambs K. Mental health and
500 wellbeing in spouses of persons with dementia: the Nord-Trøndelag health study. *BMC*
501 *Public Health*. 2014; 14: 1-12. <https://doi.org/10.1186/1471-2458-14-413>
- 502 [35] Akhtar-Danesh N, Landeen J. Relation between depression and sociodemographic
503 factors. *Int J Ment Health Syst*. 2007; 1: 4. <https://doi:10.1186/1752-4458-1-4>
- 504 [36] Seltzer MM, Li WL. The dynamics of caregiving: transitions during a three-year
505 prospective study. *The Gerontol Soc Amer*. 2000; 40: 165-78.
506 <https://doi.org/10.1093/geront/40.2.165>
- 507 [37] Connolly A, Gaehl E, Martin H, Morris J, Purandare N. Underdiagnosis of dementia in
508 primary care: variations in the observed prevalence and comparisons to the expected
509 prevalence. *Aging Ment Health* 2011;15:978–84.
- 510 [38] Banks J, Muriel A, Smith JP. Attrition and health in ageing studies: Evidence from
511 ELSA and HRS. *Longit Life Course Stud*. 2011; 2: 24376472.
512 <https://doi:10.14301/llcs.v2i2.115>
- 513 [39] Coehlo DP, Hooker K, Bowman S. Institutional placement of persons with dementia:
514 what predicts occurrence and timing? *J Fam Nurs*. 2007; 13: 253-77.
515 <https://doi.org/10.1177/1074840707300947>

516 **Supplementary material**

517 **Justification of covariates**

518 Our analyses were adjusted for baseline covariates selected based on theory and previous
519 findings. These were derived by using their first non-missing value between waves 3 and 5. All
520 analyses were adjusted for age, ethnicity, sex, socioeconomic status, education, employment,
521 marital status, self-rated health and longstanding limiting illness since they are associated with the
522 mediator and/or outcome [1-3]. Socioeconomic status was measured based on quintiles of
523 household wealth, and wealth was measured as net wealth (sum of personal savings, investments,
524 physical wealth and housing wealth after removal of the mortgage) minus financial debt [4].
525 Marital status and self-reported employment status were dichotomised. Formal education was
526 classified into five groups (none; up to O level; A level/equivalent; higher than A level, but lower
527 than a degree; university degree or higher).

528 Self-rated health was used as a proxy for health status assessed by asking participants to
529 rate their general health on a 5-point scale ranging from poor to excellent [5]. Participants were
530 classified as having a longstanding limiting illness if they reported the presence of any illness that
531 limited their daily activities. The self-reported limiting longstanding illness reflects the extent to
532 which participants feel their daily activities are limited by the presence of illness. This was
533 assessed with two questions: (1) 'Do you have any longstanding illness, disability or infirmity?
534 By longstanding I mean anything that has troubled you over a period of time or that is likely to
535 affect you over a period of time.' Those who responded yes were asked: (2) 'Does this illness or
536 disability limit your activities in any way?' Affirmation of a longstanding illness and any form of
537 limitation classified the participant as having a limiting longstanding illness. The presence of
538 limiting longstanding limiting illness was coded in our analyses as no, versus yes and limiting.
539 Analyses were also adjusted for baseline depressive symptoms in order to ensure that the

540 measured outcome was indeed the effect of caregiving rather than the presence of pre-existing
541 symptoms of depression.

542

543 **References**

544 [1] Akhtar-Danesh N, Landeen J. Relation between depression and sociodemographic factors. *Int*
545 *J Ment Health Syst.* 2007; 1: 4. <https://doi:10.1186/1752-4458-1-4>

546

547 [2] Victor C, Scambler S, Bowling A, Bond J. The prevalence of, and risk factors for, loneliness
548 in later life: a survey of older people in Great Britain. *Ageing Soc.* 2005; 25: 357-375.
549 <https://doi:10.1017/S0144686X04003332>

550

551 [3] Skarupski KA, de Leon CFM, Bienias JL, Barnes LL, Everson-Rose SA, Wilson RS, et al.
552 Black-white differences in depressive symptoms among older adults over time. *J Gerontol B*
553 *Psychol Sci Soc Sci.* 2005; 60: 136-142. <https://doi:10.1093/geronb/60.3.p136>

554

555 [4] Steptoe A, Breeze E, Banks J, Nazroo J. Cohort Profile: The English Longitudinal Study of
556 Ageing. *Int J Epidemiol.* 2013; 42: 1640-8. <https://doi.org/10.1093/ije/dys168>

557

558 [5] Moriconi PA, Nadeau L. A Cross-Sectional Study of Self-Rated Health among Older Adults:
559 Association with Drinking Profiles and Other Determinants of Health. *Curr Gerontol Geriatr Res.*
560 2015; 2015: 352947. <https://doi:10.1155/2015/352947>

561

562 **Supplementary Tables and figures**

563 Supplementary Table S1. The 8-item version of the Center of Epidemiological Studies-
 564 Depression Scale (Radloff, 1975)

The 8-items of the Center of Epidemiological Studies-Depression Scale		Score
1	Whether felt depressed much of the time during the past week	yes/no - 1/0
2	Whatever felt everything they did during the past week was an effort	yes/no - 1/0
3	Whatever felt their sleep was restless during the past week	yes/no - 1/0
4	Whatever was happy much of the time during the past week	yes/no - 0/1
5	Whatever felt lonely much of the time during the past week	yes/no - 1/0
6	Whatever enjoyed life much of the time during the past week	yes/no - 0/1
7	Whatever felt sad much of the time during the past week	yes/no - 1/0
8	Whatever could not get going much of the time during the past week	yes/no - 1/0

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566 Supplementary Table S2. STROBE Statement—Checklist of items that should be included in
 567 reports of cohort studies
 568

Item Number		Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(a) Give the eligibility criteria and the sources and methods of selection of participants. Describe methods of follow-up
		(b) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
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
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative	11	Explain how quantitative variables were handled in the analyses. If

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variables		applicable, describe which groupings were chosen and why
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding
		(b) Describe any methods used to examine subgroups and interactions
		(c) Explain how missing data were addressed
		(d) If applicable, explain how loss to follow-up was addressed
		(e) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) Summarise follow-up time (e.g. average and total amount)
Outcome data	15*	Report numbers of outcome events or summary measures over time
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g. 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(b) Report category boundaries when continuous variables were categorized
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—e.g. analyses of subgroups and interactions, and sensitivity analyses

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Discussion		
Key results	18	Summarise key results with reference to study objectives
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
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
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

569

570 *Give information separately for exposed and unexposed groups.

571 **Note:** An Explanation and Elaboration article discusses each checklist item and gives a methodological
572 background and published examples of transparent reporting. The STROBE checklist is best used in
573 conjunction with this article (freely available on the Web sites of PLoS Medicine at

574 <http://www.plosmedicine.org/>, Annals of Internal Medicine <http://www.annals.org/>, and Epidemiology at

575 <http://www.epidem.com/>). Information on the STROBE Initiative is available at [576 \[statement.org\]\(http://www.strobe-statement.org\).](http://www.strobe-</p></div><div data-bbox=)

577

578 **Sensitivity Analyses**

579
580 The association between dementia care and loneliness remained statistically significant
581 after exclusion of those with baseline depressive symptoms ($\beta=0.36$, 95% CI: 0.18, 0.53), and
582 using the higher CES-D cut-off score ($\beta=0.31$, 95% CI: 0.15, 0.47) (figures S1 and S2).
583 Similarly, the association between loneliness and depressive symptoms remained significant in
584 both analyses (after exclusion of those with baseline depressive symptoms: OR = 1.20, 95% CI:
585 0.99, 1.42; using higher CES-D cut-off score: OR = 1.46, 95% CI: 1.22, 1.69), as did the indirect
586 effect of dementia care on the development of depressive symptoms via loneliness (after
587 exclusion of those with baseline depressive symptoms: $\beta=0.05$, Bias corrected (Bc) CI: 0.02,
588 0.09; using higher CES-D cut-off score: $\beta=0.04$, Bias corrected (Bc) CI: 0.02, 0.07). The
589 proportion of the total effect mediated by loneliness among these caregivers remained at 34%
590 after excluding those with baseline depressive symptoms but increased to 46% when using the
591 higher CES-D cut-off score.

592 The association between caring for a partner with other conditions and loneliness
593 remained statistically non-significant after exclusion of those with baseline depressive symptoms
594 ($\beta=0.001$, 95% CI: -0.08, 0.05), and using the higher CES-D cut-off score ($\beta=-0.004$, 95% CI: -
595 0.066, 0.057) (figures S3 and S4). Similarly, the association between loneliness and depressive
596 symptoms remained significant in both analyses (after exclusion of those with baseline
597 depressive symptoms: OR = 1.24, 95% CI: 1.02, 1.46; using higher CES-D cut-off score: OR =
598 1.42, 95% CI: 1.21, 1.64), as did the indirect effect of dementia care on the development of
599 depressive symptoms via loneliness (after exclusion of those with baseline depressive symptoms:
600 $\beta=-0.002$, Bias corrected (Bc) CI: -0.102, 0.007; using higher CES-D cut-off score: $\beta=-0.001$,
601 Bias corrected (Bc) CI: -0.007, 0.006).

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603 Supplementary Table S3. Logistic regression models of depressive symptomatology (wave 7) on
 604 caregiving (waves 3/4/5) after exclusion of those with baseline depressive symptoms
 605

	Full sample (n=4,249)			Males (n=2,123)			Females (n=2,126)		
	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6	Model 7	Model 8	Model 9
	OR (95% CI) ^a	OR (95% CI) ^b	OR (95% CI) ^c	OR (95% CI) ^a	OR (95% CI) ^b	OR (95% CI) ^c	OR (95% CI) ^a	OR (95% CI) ^b	OR (95% CI) ^c
Caregiving group									
Non-caregiving partners	Ref.			Ref.			Ref.		
Care for partner with dementia	4.57*** (2.32, 9.00)	3.10** (1.54, 6.23)	3.32** (1.61, 6.85)	8.79*** (2.66, 29.12)	6.00** (1.74, 20.72)	4.88* (1.38, 17.22)	3.14* (1.36, 7.25)	2.46* (1.03, 5.86)	2.92* (1.21, 7.09)
Care for partner with functional impairments	1.80* (1.17, 2.75)	1.40 (0.91, 2.18)	1.23 (0.78, 1.94)	2.14* (1.18, 3.88)	1.44 (0.78, 2.68)	1.25 (0.65, 2.41)	1.54 (0.83, 2.83)	1.39 (0.74, 2.60)	1.20 (0.62, 2.31)
Other types of partner care	1.97** (1.32, 2.95)	1.77* (1.17, 2.67)	1.86** (1.21, 2.84)	1.27 (0.57, 2.83)	1.26 (0.56, 2.84)	1.30 (0.57, 3.01)	2.24** (1.39, 3.60)	2.20** (1.35, 3.60)	2.30** (1.39, 3.81)

606
 607 *Note.* CI: confidence interval; OR = odds ratio.

608 ^a = unadjusted model

609 ^b = model adjusted for demographic factors (age, marital status, ethnicity, socioeconomic
 610 status, employment and education)

611 ^c = model adjusted for demographic factors and health-related factors (presence of long-standing
 612 limiting illnesses, and self-rated health); each caregiving measure was tested in a separate model

613 * $p < 0.05$, ** $p < 0.005$, *** $p < 0.001$

614

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615 Supplementary material Table S4. Logistic regression models of depressive symptomatology
 616 (wave 7) on caregiving (waves 3/4/5) using the original CES-D scale

	Full sample (n=4,672)			Males (n=2,279)			Females (n=2,393)		
	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6	Model 7	Model 8	Model 9
	OR (95% CI) ^a	OR (95% CI) ^b	OR (95% CI) ^c	OR (95% CI) ^a	OR (95% CI) ^b	OR (95% CI) ^c	OR (95% CI) ^a	OR (95% CI) ^b	OR (95% CI) ^c
Caregiving group									
<i>Non-caregiving partners</i>	<i>Ref.</i>			<i>Ref.</i>			<i>Ref.</i>		
<i>Care for partner with dementia</i>	3.87*** (2.03, 7.39)	2.52* (1.29, 4.95)	2.46* (1.19, 5.06)	5.19* (1.63, 16.50)	4.05* (1.21, 13.49)	3.00 (0.87, 10.35)	3.06* (1.41, 6.67)	2.21 (0.98, 4.99)	2.49* (1.03, 6.02)
<i>Care for partner with functional impairments</i>	2.11*** (1.41, 3.17)	1.54* (1.01, 2.35)	1.50 (0.95, 2.36)	2.28* (1.21, 4.30)	1.59 (0.82, 3.08)	1.64 (0.82, 3.26)	2.01* (1.12, 3.43)	1.57 (0.90, 2.73)	1.42 (0.78, 2.60)
<i>Other types of partner care</i>	1.68* (1.10, 2.55)	1.45 (0.94, 2.24)	1.52 (0.96, 2.40)	1.56 (0.70, 3.47)	1.57 (0.69, 3.56)	1.62 (0.68, 3.88)	1.57 (0.96, 2.58)	1.51 (0.90, 2.51)	1.55 (0.91, 2.65)

617 *Note.* CI: confidence interval; OR = odds ratio.

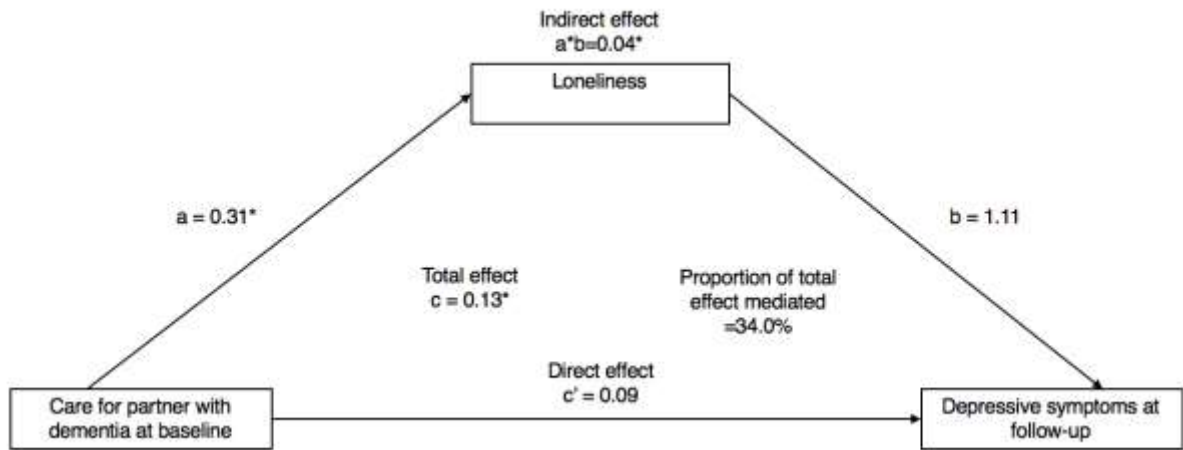
618 ^a = unadjusted model

619 ^b = model adjusted for demographic factors (age, marital status, ethnicity, socioeconomic status,
 620 employment and education)

621 ^c = model adjusted for demographic factors and health-related factors (presence of longstanding
 622 limiting illnesses, self-rated health, and baseline depressive symptoms); each caregiving measure
 623 was tested in a separate model.

624 * $p < 0.05$, ** $p < 0.005$, *** $p < 0.001$

625



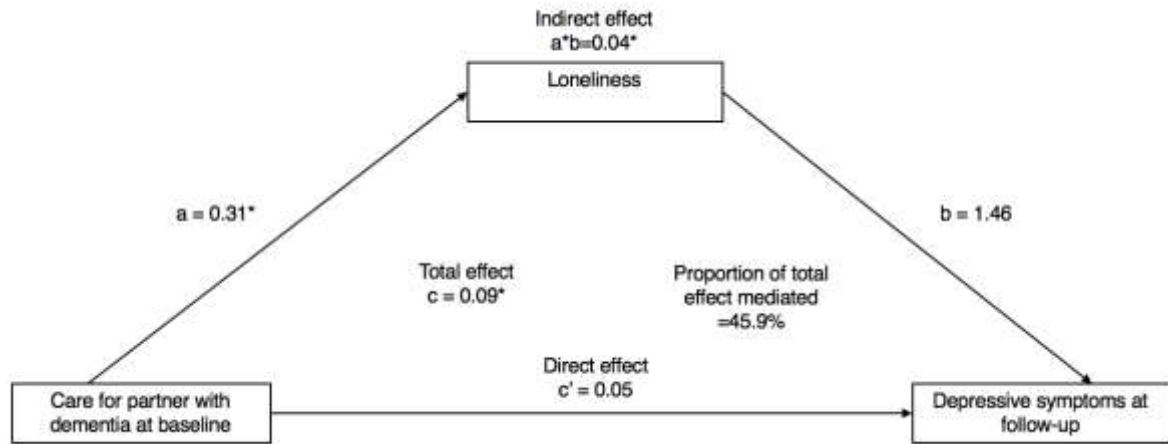
626

627 Figure S1. Mediation analysis of the association between dementia care (waves 3/4/5) on
 628 depressive symptoms (wave 7) via loneliness (wave 6) after exclusion of those with baseline
 629 depressive symptoms (n = 3, 921).

630 Note. *= $p < 0.05$

631 All models were adjusted for demographics (age, marital status, ethnicity, socioeconomic status,
 632 employment and education) and health-related (presence of longstanding limiting illnesses, and
 633 self-rated health) factors. A bias-corrected bootstrap using 1000 iterations was applied to all
 634 models. Each caregiving measure was tested in a separate model.

635

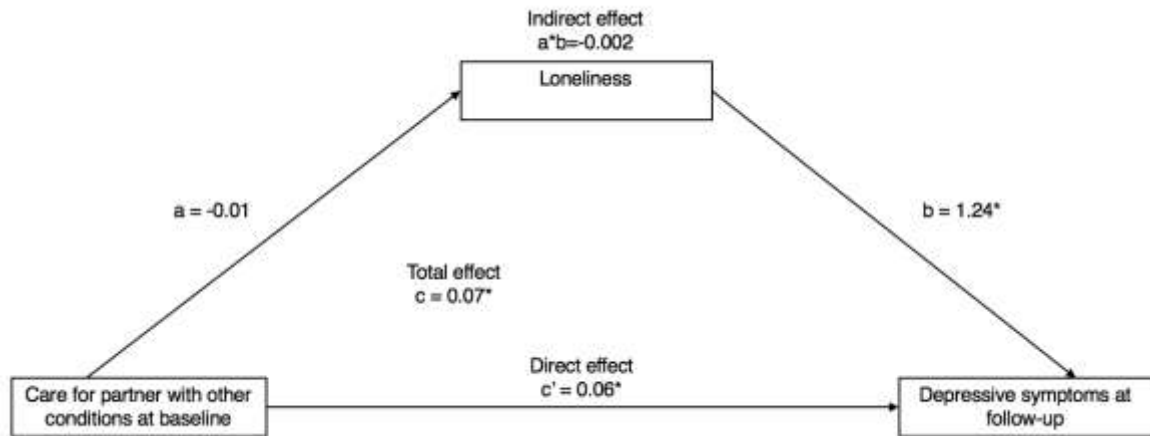


636
637 Figure S2. Mediation analysis of the association between dementia care (waves 3/4/5) on
638 depressive symptoms (wave 7) via loneliness (wave 6), using original CES-D scale (waves 3/4/5)
639 (n = 4,229)

640 Note. $*=p<0.05$

641 All models were adjusted for demographics (age, marital status, ethnicity, socioeconomic status,
642 employment and education) and health-related (presence of longstanding limiting illnesses and
643 self-rated health) factors. A bias-corrected bootstrap using 1000 iterations was applied to all
644 models.

645

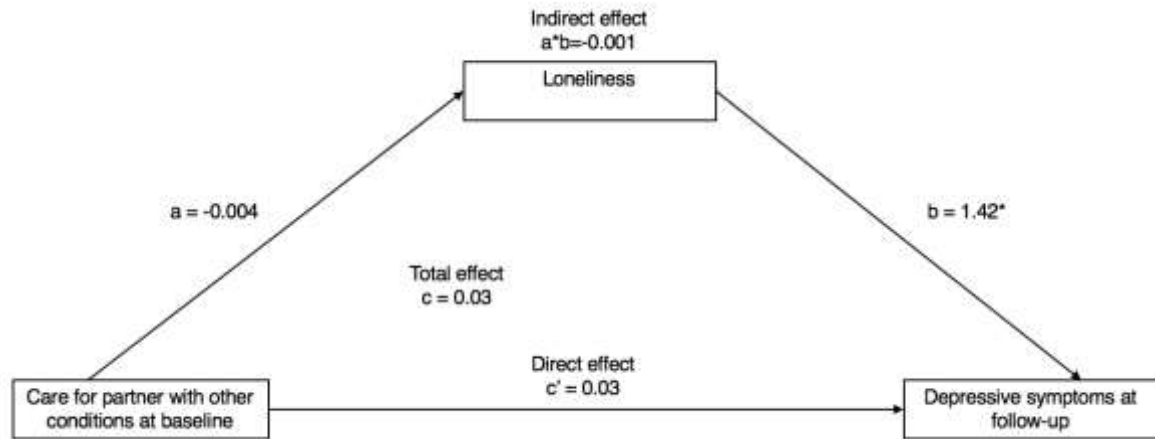


646
647 Figure S3. Mediation analysis of the association between ‘care for a partner with other
648 conditions’ (waves 3/4/5) on depressive symptoms (wave 7) via loneliness (wave 6) (n = 4,052)
649 after excluding those with baseline depressive symptoms (waves 3/4/5)

650 Note. $*=p<0.05$

651 All models were adjusted for demographics (age, marital status, ethnicity, socioeconomic status,
652 employment and education) and health-related (presence of longstanding limiting illnesses and
653 self-rated health) factors. A bias-corrected bootstrap with 1000 iterations was applied to all
654 models.

655



656

657 Figure S4. Mediation analysis of the association between ‘care for a partner with other
658 conditions’ (waves 3/4/5) on depressive symptoms (wave 7) via loneliness (wave 6) ($n = 4,446$)
659 using original CES-D scale (waves 3/4/5)

660 *Note.* $*=p<0.05$

661 All models were adjusted for demographics (age, marital status, ethnicity, socioeconomic status,
662 employment and education) and health-related (presence of longstanding limiting illnesses, self-
663 rated health, and baseline depression) factors. A bias-corrected bootstrap with 1000 iterations was
664 applied to all models.