



Informal caregiving and mortality—Who is protected and who is not? A prospective cohort study from Japan



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ABSTRACT

Informal caregiving is linked to psychological stress. However, recent studies have suggested a protective association between informal caregiving and mortality among caregivers. We sought to test the association between caregiving and survival in the *Komo-Ise* study, a prospective cohort of community-dwelling residents aged 44–77 years living in two areas in Gunma prefecture, Japan. Caregiving status was assessed in 2000, and 8084 individuals were followed for ten years. All-cause mortality was ascertained from official registers. Using multivariate Cox proportional hazards models, we found no statistically significant overall association between informal caregiving and all-cause mortality for either combined sexes, (HR 0.97, 95% CI 0.79, 1.19), men (HR 0.98, 95% CI 0.76, 1.27), or women (HR 0.95, 95% CI 0.68, 1.34). The propensity score matched model also showed no increased risk of all-cause mortality across all caregivers, male caregivers, and female caregivers. The association with all-cause mortality was not observed regardless of the presence of support for activities of daily living (ADLs)/instrumental activities of daily living (IADLs) or the relationships to the care recipients. In subgroup analyses, informal caregiving was not associated with increased risk of all-cause death across subgroups for combined sexes, men, or women, except for increased mortality among female caregivers in the lowest-income group (HR 1.75, 95% CI 1.03, 3.00). An increase in the risk of mortality was not observed among male caregivers. In conclusion, informal caregiving did not increase mortality as a whole, nor for most subgroups, while some sub-groups such as women in the lower socioeconomic status groups may be vulnerable to the adverse health effects of caregiving.

1. Introduction

The need for caregiving is increasing around the world, in tandem with population aging (Colombo et al., 2011). Despite the establishment of formal care systems (such as long-term care insurance), informal caregiving—provided by family members or friends—continues to play an important role in many countries. Providing care requires caregivers' social, financial, environmental, psychological, and physical resources. Based on the models of the impact of stress on health (McEwen, 1998; Lazarus and Folkman, 1984), if the demand derived from caregiving exceeds the available resources, caregivers will experience high-level stress and physiological dysfunctions. In fact, several epidemiological studies have suggested that informal caregiving causes psychological distress (Oshio, 2015; Pinquart and Sörensen, 2003; Roth et al., 2009). Also, long-hours informal caregiving is reported to increase blood pressure (Capistrant et al., 2012b) and the risk

of cardiovascular disease (CVD) (Capistrant et al., 2012a; Lee et al., 2003; Miyawaki et al., 2017). As physiological mechanisms in the pathway from informal caregiving to adverse health effects, telomere length shortening (O'Donovan et al., 2012), immune dysregulation (Kiecolt-Glaser et al., 2003), inflammation (Gouin et al., 2012), delayed wound healing (Christian et al., 2006), and impaired endothelial function (Mausbach et al., 2010, 2007) have been assumed using comparison of caregivers with volunteer non-caregivers.

Nevertheless, caregiving can have positive impacts on health simultaneously. Emerging population-based studies in the United Kingdom (UK) (O'Reilly et al., 2015, 2008; Ramsay et al., 2013) or the United States (US) (Brown et al., 2009; Fredman et al., 2010; Roth et al., 2013) have reported that informal caregivers have a *lower* risk of death compared to non-caregivers as a whole. In fact, many caregivers report that providing care to loved ones is rewarding and feel a little stress (Roth et al., 2015), even if these observational studies could not

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avoid the bias by a “healthy caregiver effect”, i.e. individuals with a robust constitution are more likely to *enter/remain* in caregiving situations, or alternatively, individuals who become sickened by the burden of caregiving *exit* from their situation. Providing care to family members or friends based on altruism can satisfy and reward caregivers, and is actually suggested to buffer the negative effect of care-related stress and improve health (Beach et al., 2000; Brown et al., 2005; Poulin et al., 2013).

In this context, further research on the association between informal caregiving and mortality should be accumulated. It would help answer to the question such as whether further interventions should be considered to mitigate caregiving burden, and if so, to whom. To our knowledge, no previous study has investigated the association between informal caregiving and mortality in Japan. Treatment heterogeneity could arise from differences in the societal or cultural context. For example, in many Confucian cultures (such as Japanese or Chinese society), it is assumed that the family (and in particular, the daughter-in-law) will take care of aging and ailing relatives. Consequently, formal resources (e.g. nursing homes) for assisting informal caregivers may remain under-developed (Bambra, 2007; Liu and Dupre, 2016). We thus sought to investigate the association between informal caregiving and mortality using a community-based cohort in one prefecture in Japan. Also, heterogeneity in the association of caregiving and health should be focused on – viz., some types of individuals may be particularly vulnerable to the adverse effects of caregiving; for example, individuals who lack the financial or emotional resources to alleviate the burden of providing care to others. We hypothesized that the association of informal caregiving with survival would differ by socioeconomic status (SES) or health status, because these factors are linked to the caregiver’s “reserve capacity” to deal with the physical/psychological burden of providing informal care to others.

2. Methods

2.1. Study sample and design

Data are drawn from the *Komo-Ise* study, a prospective cohort established in 1993 among all the inhabitants in *Komochi* village (rural area: population density around 300/km², 0 hospital beds/1000 residents, and 12 nursing home beds per 1000 residents aged 65 or older in 2000, n = 4875) and the downtown of *Isesaki* city (urban area: population density around 2000/km², 13 hospital beds/1000 residents, and 23 nursing home beds per 1000 residents aged 65 or older in 2000, n = 7755), both located in Gunma prefecture, Japan (Iwasaki et al., 2002; Konishi et al., 2015). In 1993, the first questionnaires were distributed by mail, and 11565 residents aged 40–69 years responded (response rate: 91.6%). In 2000, as a follow-up survey, follow-up questionnaires were distributed to the 10898 surviving and uncensored participants who responded in 1993, and a total of 9650 participants responded (response rate: 88.5%). Among these, 9522 (mean age 62.0 years, range 47–77 years) were still living in the study areas as of 1 November 2000, which we set as the start of the observation period. Participants with missing information for at least one of key variables (information of exposure and covariates) were excluded (n = 1438, 15.1% of the participants surviving as of November 2000), and the remaining 8084 participants were analyzed. Participants with missing variables tended to be somewhat older and female compared with those without missing key variables (64.5 vs. 61.6 in mean age and 58.6% vs. 52.1% in the proportion of women).

2.2. Exposures

Caregiving status was assessed in 2000. Informal caregiving was defined as “provid[ing] some type of unpaid, ongoing assistance with activities of daily living (ADLs) or instrumental activities of daily living (IADLs) to a person with a chronic illness or disability (Roth et al.,

2015).” The questionnaires distributed in 2000 asked: “Are you currently providing any support or personal care to disabled relatives or friends?” (Q1) and “How do you support the person(s)?” (Q2) In Q2, respondents were requested to choose from 8 options: 1) “financial support”, 2) “support for shopping or housework”, 3) “travel support”, 4) “arrangement of helper other than respondents”, 5) “support for money management”, 6) “providing personal care (clothing, bathing, grooming activity, etc.)”, 7) “support for medical treatment”, and 8) “others” (multiple answers allowed). Referring to the commonly used ADL and IADL definition (Lawton and Brody, 1969; Mahoney and Barthel, 1965), participants were coded as providing informal care when they answered “yes” to Q1 and chose at least one among 2), 3), 5), 6), or 7) in Q2. Otherwise, we defined participants as not providing informal care.

2.3. Mortality and censoring

Deaths in the cohort were identified through the official register (Japan’s compulsory registration system) of the study areas from November 1, 2000 to October 1, 2010 (study period). Participants who had migrated out of the study areas were contacted by mail, and non-responders were censored.

2.4. Covariates

The covariates consisted of age (age and squared age), education level, marital status, residential area, income level, job status, and health status (Brown et al., 2009; Fredman et al., 2010; O’Reilly et al., 2015, 2008; Ramsay et al., 2013; Roth et al., 2013). The information was derived from the questionnaires distributed in 2000 except for information on education, which was recorded in 1993. Education level (education years) was categorized into three groups: 9 or less years, 10–15 years, and 16 or more years. Marital status was categorized into “married,” “separated/divorced,” and “never married.” We added a fixed effect for *Isesaki* city (urban), with residence in *Komochi* village (rural) as the reference. We used household equivalized income, calculated as the gross (pre-tax) income divided by square root of the number of household members. The household income was measured in classes (from “0–0.99 million Japanese yen (JPY: 100 JPY = 0.65 British pound, or 1 US dollar)” to “14–14.99 million JPY” plus “15 million JPY or more”). The mid-point of the income class was taken, but the last category was top-coded to 15 million JPY. Four income-level categories were established according to quartiles of calculated equivalent income. Job status was dichotomized (1 = employed, and 0 otherwise). As health status indicators, we used self-reported histories of heart diseases, strokes, or cancers and self-rated health status. Self-rated health status was dichotomized (1 = “Fair” or better, and 0 otherwise), according to the questionnaires in 2000, which asked if self-rated health status was “Very good,” “Good,” “Fair,” or “Bad.”

2.5. Statistical analysis

Baseline characteristics were compared between informal caregivers and non-caregivers. In the main analyses, hazard ratios (HR) and 95% confidence intervals (95% CI) were calculated using Cox’s proportional hazards model for combined sexes and each sex. We ran three models: first, we adjusted only for age and squared age; second, we added residential area, marital status, education level, health status (including baseline diseases), income level and job status as covariates (fully-adjusted model); third, a propensity score (PS) matched model was applied.

The PS matched model was conducted to achieve covariate balance between treatment groups and avoid the problem of off-support inference — i.e. the method focuses on common support regions (in contrast to multivariate adjustment) and does not depend on unreliable extrapolations in regions where the exposed and unexposed individuals

Table 1
Characteristics of the participants as of November 1, 2000 (baseline).

Characteristics	Caregivers	Non-caregivers	P value ^a	
	(n = 1342)	(n = 6742)		
Age, mean (SD)	58.9 (8.0)	62.1 (8.2)	< 0.001	
Sex, %	Male	37.6	50.0	< 0.001
	Female	62.4	50.0	
Residence area, %	Urban	62.3	60.6	0.239
	Rural	37.7	39.4	
Marital status, %	Never	5.9	4.6	0.007
	Separated/ divorced	10.6	13.2	
	Married	83.5	82.3	
Education years, %	16 years or more	13.9	10.9	< 0.001
	10–15 years	54.2	45.9	
	9 years or less	31.9	43.2	
Self-rated health, %	Very good	9.5	11.2	0.160
	Good	44.7	42.7	
	Fair	41.9	42.7	
	Bad	3.9	3.5	
Heart diseases, %	Yes	12.4	12.7	0.720
	No	87.6	87.3	
Strokes, %	Yes	2.2	4.1	0.001
	No	97.8	95.9	
Cancers, %	Yes	4.0	4.0	0.934
	No	96.0	96.0	
Equivalent income, % (Quartiles)	Q1 (lowest)	19.8	22.7	0.100
	Q2	27.3	27.3	
	Q3	25.1	24.2	
	Q4 (highest)	27.8	25.8	
Job status, %	Employed	61.0	57.2	0.010
	Unemployed	39.0	32.8	

Note. SD: Standard deviation. Heart diseases, strokes, and cancers indicate self-reported history. Percentages are calculated within the caregiving category.

^a P values were calculated using *t*-test for age and Pearson's Chi square test for the other discrete variables.

have very different covariate distributions. The PS models were estimated for combined sexes and each sex using logistic regression analyses that adjusted for the possible confounders listed in Table 1 and their quadratic terms. Matching was conducted according to nearest neighbor matching (2:1) with replacement. The caliper widths were set to around 0.2 of the standard deviations of the logit of propensity scores (0.1 for combined sexes, 0.02 for men, and 0.04 for women) (Austin, 2011). The logistic regression models were separately for each sex refined by structured iterative approach to achieve the balance of covariates within matched pairs (Imbens and Rubin, 2015). All the possible covariates were balanced well within the pairs (Appendix A). Individuals who were selected as a control twice or more were appropriately weighted in the analyses. We conducted a PS model approach only for the main analyses.

Two further analyses were conducted. First, to explore the heterogeneity by the details of informal caregiving, the exposure was subdivided into several caregiving types as follows: 1) supporting ADL and supporting IADL and 2) caring a spouse, caring parents, caring parents-in-law, and caring others. The same person was allowed to be assigned to each category multiple times. The mortality HR was calculated using the fully adjusted model for each category with the non-caregivers as the reference. Supporting ADL was identified when the participants answered “yes” to Q1 and chose 6) in Q2, and supporting IADL was identified when the participants answered “yes” to Q1 and chose at least one among 2), 3), 5), or 7) in Q2. Second, stratified analyses were conducted by equalized income levels (the quartile 1 to 4), education levels (less than 9 and 10 or more years), and self-rated health (Fair or better/Bad) using the fully adjusted model. Robust standard errors were estimated. 2-tailed *P* values below 0.05 were interpreted as statistically significant. Following Vittinghoff and McCulloch (2007), the estimators derived from the analyses that had fewer than 5 events per variable

were not shown because such estimators were too likely to be biased. The proportional hazards assumption was evaluated graphically and via Schoenfeld test; there was no violation of the assumption for each model. We conducted all analyses using Stata version 14 (StataCorp., 2015).

2.6. Sensitivity analysis

Instead of excluding the participants with missing key variables, the analyses in the main text were repeated after incomplete variables were imputed under fully conditional specification using multiple imputation by chained equations assuming a missing at random mechanism (Van Buuren et al., 2006). The imputation model was specified on an exposure, covariates, and outcomes. Twenty datasets were generated and the results were pooled using Rubin's rules (Donald B. Rubin, 2008).

3. Results

Of 8084 analytic participants, 1342 (16.6%) provided informal care for dependent persons as of 2000. Table 1 reports the characteristics of participants according to caregiving status. Compared with non-caregivers, informal caregivers tended to be younger, more likely to be female, more educated, more likely to be employed, and less likely to have a history of stroke.

Fig. 1 displays the descriptive survival curves for the caregivers and the non-caregivers calculated by the PS model. During the study period, 105 (7.8%) of the 1342 caregivers died (65 men of the 504 male caregivers and 40 women of the 838 female caregivers), while 760 (11.3%) of 6742 non-caregivers died (513 men of the 3368 male caregivers and 247 women of the 3374 female caregivers). Only 31 individuals (0.4%) dropped out.

Table 2 shows the association between informal caregiving and mortality. Caregivers tended to show a lower *crude* all-cause mortality than non-caregivers, but had comparable levels of age-adjusted mortality. In the fully-adjusted model, Cox's proportional hazards analysis did not show a statistically significant overall association between informal caregiving and all-cause mortality for combined sexes (HR 0.97, 95% CI 0.79, 1.19), men (HR 0.98, 95% CI 0.76, 1.27), or women (HR 0.95, 95% CI 0.68, 1.34), either. In the PS matched model, after dropping 5280 individuals for the model of combined sex, 2976 individuals for the model of men, and 2765 individuals for the model of women due to inability to match, we found similar results as the multivariable-adjusted model. Analyses of the overall sample (men and women combined) including a sex × caregiving interaction term were also conducted; the interaction term for all-cause mortality was statistically insignificant (the HR of the interaction term was 1.02, and 95% CI was 0.67–1.57).

In Table 3, the exposure was subdivided into several caregiving types. Supporting ADL or IADL was not significantly associated with all-cause mortality for combined sexes, women, or men, either. Also, across the relationships to the care recipients, informal caregiving was not associated with all-cause mortality for combined sexes, women, or men.

We next present the results of the subgroup analyses stratified by SES, health status, and marital/job status in Table 4. Informal caregiving was significantly associated with an increased risk of all-cause death only in the lowest-income group for combined sexes (HR 1.53, 95% CI 1.06, 2.21) and for females (HR 1.75, 95% CI 1.03, 3.00). On the other hand, for males, there was no significant association between informal caregiving and increased mortality among all of the displayed subgroups; rather informal caregivers in the highest income group had a lower risk of all-cause death than their peers (HR 0.38, 95% CI 0.15, 0.96). The joint hypothesis that all the coefficients of caregiving × income-level interaction terms took one was tested using the overall sample; it was statistically rejected (*p* = 0.035).

After the analyses were repeated using the dataset whose missing data was imputed by the multiple imputation (Appendix B), the point

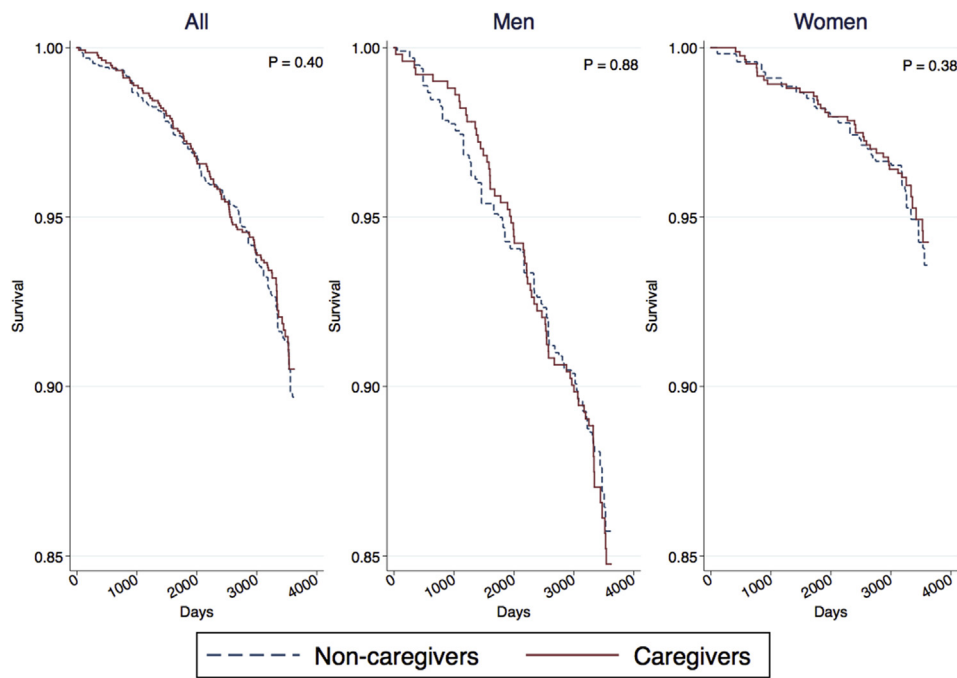


Fig. 1. Survival curves (all-cause mortality) of caregivers (solid line) and propensity-matched non-caregivers (dashed line) for combined sexes and each sex from the Komo-Ise Study over the 10 years of follow-up, 2000–2010.

estimates and statistical significance did not essentially change except for the association between informal caregiving and decreased mortality in the highest income group for males, suggesting that missing data had minimal impact on our conclusions (Table A2 and A3).

4. Discussion

In this community-based cohort of informal caregivers in Japan, we found no overall association between informal caregiving and all-cause mortality. This conclusion was robust to performing a propensity-score matching analysis which attempted to carefully achieve covariate balance across treatment groups. Also, the association with all-cause mortality was not observed regardless of the presence of ADL/IADL or the relationships to the care recipients. These findings were in contrast to the previous studies that suggested protective effects of caregiving on mortality as a whole and among most subgroups in the UK (O’Reilly et al., 2015, 2008; Ramsay et al., 2013) or the US (Brown et al., 2009; Fredman et al., 2010; Roth et al., 2013).

In general, the net effect of informal caregiving on health should be

considered as a balance between the positive effects and the negative effects of informal caregiving (Roth et al., 2015). Based on the model of the impact of stress on physiological/psychological health (McEwen, 1998; Richard S. Lazarus and Folkman, 1984), informal caregiving will cause declined health when its psychological/physical burden exceeds the reserve capacity of available internal and external resources (Roth et al., 2015), while some investigations in the context of altruism and health have noted that providing help to others itself is associated with positive health outcome such as decreased depression and lower morbidity (Beach et al., 2000; Brown et al., 2005) and can buffer/exceed the negative effect of stress involved with caregiving on mortality (Poulin et al., 2013). In this framework, the direction of the association between informal caregiving and health outcomes would depend on the kind of the outcomes and the targeted population. For example, the negative effects of informal caregiving on psychological health, especially depressive state, have been reported in a lot of literature (Oshio, 2015; Pinquart and Sörensen, 2003; Roth et al., 2009). Meanwhile, the epidemiological studies found the increased risk of incident CVD among long-hours caregivers compared to non-caregivers (Capistrant et al.,

Table 2
Association between informal caregiving and all-cause mortality.

	Caregiving	Death	Person-years	Crude mortality ^a	Hazard ratio (95% confidence intervals)		
					Age-adjusted	Fully-adjusted	PS Matching ^b
All ^c	No	760	60612	12.5	ref	ref	ref
	Yes	105	12233	8.6	0.97 (0.79, 1.19)	0.97 (0.79, 1.19)	0.92 (0.76, 1.11)
Men	No	513	29762	17.2	ref	ref	ref
	Yes	65	4514	14.4	1.02 (0.79, 1.31)	0.98 (0.76, 1.27)	1.02 (0.80, 1.30)
Women	No	247	30850	8.0	ref	ref	ref
	Yes	40	7719	5.2	0.92 (0.65, 1.28)	0.95 (0.68, 1.34)	0.87 (0.64, 1.18)

Note. PS matching: Propensity score matching. In the age-adjusted model, we adjusted for age and quadratic age, and in the fully adjusted model, we additively included residential area, marital status, education level, health status (including baseline diseases), income level and job status as covariates.

^a Per 1000 person-years.

^b The numbers of the sample finally analyzed were 922 matched non-caregivers and 1342 caregivers for the model of combined sexes; 392 matched non-caregivers and 504 for caregivers for the model of men; and 611 matched non-caregivers and 836 caregivers for the model of women. The samples that were selected as a control twice or more were appropriately weighted in the analyses.

^c The model of combined sexes, where sex was adjusted for.

Table 3
Association between the types of caregiving and all-cause mortality.

	All ^a		Men		Women	
	N	HR (95% CI)	N	HR (95% CI)	N	HR (95% CI)
Non-caregivers	6742	ref	3368	ref	3374	ref
Caregivers	1342	0.97 (0.79, 1.19) ^b	504	0.98 (0.76, 1.27) ^b	838	0.95 (0.68, 1.34) ^b
Contents of care ^c						
Supporting IADL	1305	0.95 (0.75, 1.19)	494	0.98 (0.75, 1.29)	811	0.88 (0.58, 1.35)
Supporting ADL	305	1.03 (0.66, 1.63)	72	1.06 (0.56, 2.01)	233	1.06 (0.53, 2.12)
Relationship to care recipients ^c						
Caring a spouse	350	0.75 (0.53, 1.05)	120	0.79 (0.52, 1.20)	230	0.68 (0.37, 1.22)
Caring parents	517	0.98 (0.67, 1.42)	243	1.04 (0.68, 1.59)	274	0.83 (0.39, 1.79)
Caring parents-in-law	292	1.12 (0.65, 1.91)	54	1.11 (0.49, 2.52)	238	1.15 (0.55, 2.43)
Caring others	296	1.27 (0.88, 1.83)	89	1.25 (0.75, 2.09)	207	1.27 (0.74, 2.17)

Note. HR: hazard ratio. 95% CI: 95% confidence interval. We applied the fully-adjusted model (with adjustment for age, residential area, marital status, education level, health status (including baseline diseases), income level and job status).

^a The model of combined sexes, where sex was adjusted for.

^b These values are reshown (see Table 2).

^c The sum of the number of participants in each category was not equal to the number of the caregivers, respectively, because the same person could be counted twice or more (i.e. a caregiver might provide both ADL and IADL supports).

2012a; Lee et al., 2003; Miyawaki et al., 2017), but no overall association between informal caregiving (regardless of caregiving hours) and incident CVD (Buyck et al., 2013; Miyawaki et al., 2017). Furthermore, the physiological effect of informal caregiving has been inconclusive; some research that compared informal caregivers with volunteers who did not provide care supports the association between caregiving strain and biological dysregulation, including inflammation, hyper-coagulation, cellular aging, and immune dysfunction (Gouin et al., 2012; Kiecolt-Glaser et al., 2003; Mausbach et al., 2010, 2007; O'Donovan et al., 2012), but the other population-based studies failed to find the overall association between informal caregiving and increased inflammation biomarkers (Kang and Marks, 2014; Shivpuri et al., 2012), neuroendocrine and immune dysfunction (Provinciali et al., 2004), or metabolic dysfunction (Kang and Marks, 2014), as well as increased allostatic load (Dich et al., 2015; Kang and Marks, 2014). The series of studies that did not demonstrate the effect of informal caregiving on increased mortality (Brown et al., 2009; Fredman et al., 2010; O'Reilly et al., 2015, 2008; Ramsay et al., 2013; Roth et al., 2013), including our study, suggest that the positive effects of informal caregiving would buffer and complement the negative effects of informal caregiving, at least regarding all-cause mortality as an outcome.

Meanwhile, our overall results failed to find a statistically

significant protective effect of caregiving on survival, and the overall point estimate of HR was close to one, which was inconsistent to the previous studies (Brown et al., 2009; Fredman et al., 2010; O'Reilly et al., 2015, 2008; Ramsay et al., 2013; Roth et al., 2013). One explanation of this difference may be the shortage in long-term care resources available to caregivers in Japan that might add to the caregiver's burden. Formal care services provided by long-term care workers have been available (with 10% coinsurance rate) through the national Long-Term Care Insurance since April 2000 (seven months before the start of the observation period of this study) in Japan. Even nowadays, however, the number of long-term care workers and nurses working in institutions per 1000 persons over 65 years in Japan is far lower than in the US (11 vs. 33 for care workers and 3 vs. 59 nurses in 2015, respectively), possibly due to the aging work force and the reluctance of the Japanese government to allow the entry of more nursing home workers from the rest of Asia (Tabuchi, 2011). Nursing home beds are fewer compared to the UK and the US (24 in Japan vs. 36 in the UK and 49 in the US per 1000 persons over 65 years) (Organisation for Economic Co-operation and Development, 2017). Consequently, Japan faces a long waiting list for the public nursing homes (Ministry of Health Labour and Welfare Japan, 2017). Also supports for caregivers (e.g. respite care and counseling) are underfinanced compared to the

Table 4
Association between informal caregiving and all-cause mortality: subgroup analyses.

		Hazard ratio (95% confidence intervals) ^a					
		All ^b		Men		Women	
Income level	Q1 (lowest)	1.53*	(1.06, 2.21)	1.33	(0.80, 2.21)	1.75*	(1.03, 3.00)
	Q2	1	(0.71, 1.40)	1.17	(0.78, 1.74)	0.78	(0.41, 1.49)
	Q3	0.81	(0.52, 1.28)	1.00	(0.60, 1.67)	- ^c	- ^c
	Q4 (highest)	0.54	(0.29, 1.02)	0.38*	(0.15, 0.96)	- ^c	- ^c
Education	–9 years	1.05	(0.78, 1.41)	0.89	(0.60, 1.33)	1.28	(0.83, 1.97)
	10 + years	0.90	(0.67, 1.21)	1.02	(0.73, 1.44)	0.67	(0.38, 1.17)
Self-rated health	Bad	0.61	(0.28, 1.32)	- ^c	- ^c	- ^c	- ^c
	Fair or better	1.03	(0.84, 1.27)	1.09	(0.84, 1.42)	0.94	(0.65, 1.35)
Marital status	Unmarried	1.12	(0.70, 1.79)	1.04	(0.51, 2.15)	1.16	(0.62, 2.19)
	Married	0.91	(0.72, 1.15)	0.96	(0.72, 1.26)	0.84	(0.55, 1.28)
Job status	Unemployed	1.04	(0.80, 1.36)	1.03	(0.73, 1.46)	1.06	(0.71, 1.58)
	Employed	0.85	(0.60, 1.19)	0.94	(0.64, 1.39)	- ^c	- ^c

Note. We applied the fully-adjusted model (with adjustment for age, sex, residential area, marital status, education level, health status (including baseline diseases), income level and job status, except for the variable by which the sample was stratified).

^{*}, p < 0.05.

^a The hazard ratios among those providing informal care referring to those not providing informal care were shown for each subgroup.

^b The model of combined sexes, where sex was adjusted for.

^c The estimators were not shown because the numbers of events per variable in these models were under 5.

UK and the US (Colombo et al., 2011). Given these facts, there is a heavy caregiver burden especially on those who are unable to afford private long-term care resources (e.g. the low-income group).

When we examined sub-groups of informal caregivers, informal caregiving was not associated with increased mortality for most sub-groups. This finding was also consistent to the previous studies (O'Reilly et al., 2015; Roth et al., 2013). However, in this study, low-income caregivers appeared to have an increased risk of all-cause mortality especially among women. To explore what cause-specific mortality was driving this excess risk, the analyses were repeated for two kinds of cause-specific mortality as outcomes: cancer mortality (C00-C97 and D00-D48) and CVD mortality (I00-I99), based on the cause of death recorded in the official register using the International Classification of Diseases 10th edition (World Health Organization, 2016), because cancer and CVD death accounted for 28.5% and 23.5% of all-cause deaths in 2016 in the whole of Japan, respectively (Ministry of Health Labour and Welfare Japan, 2016). Table A4 in Appendix C shows the increased CVD mortality among low-income caregivers for both sexes (HR 2.39, 95% CI 1.23, 4.68). This finding was in contrast with protective associations of caregiving for both all-cause mortality and CVD mortality found by O'Reilly et al. (2015), suggesting that the excess risk of all-cause death among the lowest-income group in our study might be explained by increased CVD mortality. The HRs of all-cause mortality became smaller by gradation as the income-level became higher. These findings might underpin the idea that the positive effects and the negative effects of informal caregiving on survival compete with each other. In the low-income households, informal caregiving would be less likely to be voluntary compared to their peers, because they tend not to have sufficient available resources such as information, finances, support from the other family members, and formal care. Thus, caregivers in the low-income group would experience higher levels of stress (Saito et al., 2018), so that the positive experience of informal caregiving could not buffer it, and they might result in health decline. The higher HR among women might be associated with a strong tradition of family responsibility (familism) for providing care rests with middle-aged adult children (especially daughters-in-law as shown in Table 3) in Confucian cultures such as Japanese society (Bambra, 2007; Liu and Dupre, 2016). In fact, it is reported that the feeling of obligation from familism can have an adverse effect on mental or subjective physical health overall, overwhelming the positive health effect of familial support (Sayegh and Knight, 2011). This traditional arrangement is represented by the higher proportion of elderly persons who cohabit with their children compared to the West (Cabinet Office, Government of Japan, 2015), and has posed an increasing burden on women who are forced to juggle caregiving responsibilities with their paid/unpaid work roles and bringing up their own children. Consequently, Japanese women perform a far higher percentage of household unpaid work compared to Western women (Organisation for Economic Co-operation and Development, 2018).

The strengths of the present study were 1) the precise definition of informal caregiving, 2) using the official resident registration file to identify death, 3) the quite low rate of loss of follow-up, and 4) the relatively long follow-up period. However, some limitations should be noted. First, the generalizability of the results is limited. The participants of this study were community-dwelling middle-aged or older adults in one prefecture of Japan and not representative of the general population in Japan. For example, the access to formal care resources in the rural area of this study was limited compared to the average level in Japan (e.g., 12 vs. 24 nursing home beds per 1000 residents aged 65 or older). Second, caution may be needed in interpreting our findings, especially for subgroups, because a limited number of sample population and events due to stratification could lead to relatively wide confidence intervals. Third, the factors that could modify the effect of informal caregiving on mortality are not considered in our study: for instance, the information on care recipients (comorbidity and cognitive function) and hours spent on care. It is known that caregivers of persons

with dementia experience chronic stressors, which may more frequently cause depression, CVD, and ultimately death (Ory et al., 1999). Hours spent on care is also associated with caregivers burden (Kim et al., 2012), and long hours of care exacerbate psychological stress induced by caregiving (Oshio, 2015). Thus, information of caregiving hours might have helped understand the mechanism of the difference in the effects of informal caregiving on mortality across subgroups.

5. Conclusions

In our study, informal caregiving was not associated with increased/decreased all-cause mortality as a whole, nor for most subgroups. On the other hand, informal caregiving was associated with increased mortality in the low-SES groups uniquely for females in Japan. This implies that the impact of informal caregiving on mortality may differ by societal contexts. Our findings indicate that, in general, informal caregivers should not be considered to have a risk of health deterioration, though policy-makers and care providers may need to pay attention to some vulnerable caregivers and ensure their access to formal care.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.socscimed.2019.01.034>.

Declarations of interest

None.

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