Archives of Gerontology and Geriatrics 136 (2025) 105914

Contents lists available at ScienceDirect

Archives of Gerontology and Geriatrics

journal homepage: www.elsevier.com/locate/archger

Combined association of social isolation and loneliness with frailty onset among independent older adults: A JAGES cohort study

Mamoru Sato [a,b], Manami Hoshi-Harada [b], Kenji Takeuchi [b,c,*], Taro Kusama [b,c], Takaaki Ikeda [b,d], Sakura Kiuchi [b,e], Masashige Saito [f], Naoki Nakaya [a,g], Ken Osaka [b]

[a] Department of Health Behavioral Epidemiology, Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan
[b] Department of International and Community Oral Health, Tohoku University Graduate School of Dentistry, Sendai, Miyagi, Japan
[c] Division of Statistics and Data Science, Liaison Center for Innovative Dentistry, Tohoku University Graduate School of Dentistry, Sendai, Miyagi, Japan
[d] Department of Health Policy Science, Graduate School of Medical Science, Yamagata University, Yamagata, Japan
[e] Department of Dental Public Health, Graduate School of Medical and Dental Sciences, Institute of Science Tokyo, Tokyo, Japan
[f] Faculty of Social Welfare, Nihon Fukushi University, Mihama, Aichi, Japan
[g] Tohoku Medical Megabank Organization, Tohoku University, Sendai, Miyagi, Japan

HIGHLIGHTS

- This study aimed to investigate the interaction of social isolation and loneliness on frailty onset among independent older adults in the Japan Gerontological Evaluation Study.
- The analysis included 8440 participants (mean age: 73.2 [standard deviation, 5.5] years), and 15.1 % of participants experienced frailty onset during the follow-up.
- The “severe isolation” & “severe loneliness” group had the highest risk of frailty onset (RR = 2.09 [95 % CI: 1.60–2.73]) compared to “no isolation” & “not loneliness” group.
- However, there were no significant multiplicative and additive interaction between social isolation and loneliness on frailty onset (multiplicative scale: 0.75 [95 % CI: 0.50–1.11]; RERI: −0.29 [95 % CI: −1.02–0.44]).
- These findings highlight the importance of considering social factors such as interaction with others and loneliness, to prevent frailty.

ARTICLE INFO

Keywords:
Frailty
Social isolation
Loneliness
Interaction effect
Longitudinal study

ABSTRACT

Objectives: Social isolation and loneliness each have negatively affect various health outcomes. No studies have examined the combined association of social isolation and loneliness on frailty onset. This study aimed to investigate both the objective and subjective aspects of isolation by evaluating social isolation and loneliness and to determine their interaction effects on frailty onset.
Methods: This cohort study used data from the 2019 and 2022 Japan Gerontological Evaluation Study. The eligible participants were independent older adults aged ≥65 years without frailty in 2019. The outcome variable was frailty onset in 2022. The exposure variables were social isolation and loneliness in 2019. Risk ratios (RR) and 95 % confidence intervals (CI) were estimated using modified Poisson regression models, with potential confounders as covariates. Moreover, a multiplicative scale and relative excess risk due to interaction (RERI) was used to assess the interaction.
Results: The analysis included 8440 participants (mean age: 73.2 [standard deviation, 5.5] years). During the follow-up, 15.1 % of participants experienced frailty onset. After adjusting for all covariates, the “severe isolation” & “severe loneliness” group had the highest risk of frailty onset (RR = 2.09 [95 % CI: 1.60–2.73]) compared to “no isolation” & “no loneliness” group. However, there were no significant multiplicative and additive interaction between social isolation and loneliness on frailty onset (multiplicative scale: 0.75 [95 % CI: 0.50–1.11]; RERI:0.29 [95 % CI:1.02–0.44]).
Discussion: These findings highlight the importance of considering social factors such as interaction with others and loneliness, to prevent frailty.

* Corresponding author at: Department of International and Community Oral Health, Tohoku University Graduate School of Dentistry, 4-1, Seiryo-machi, Aoba-ku, Sendai, Miyagi, 980-8575, Japan.
E-mail address: kenji.takeuchi.c4@tohoku.ac.jp (K. Takeuchi).

https://doi.org/10.1016/j.archger.2025.105914
Received 9 April 2025; Received in revised form 23 May 2025; Accepted 27 May 2025
Available online 27 May 2025

1. Introduction

Global aging is predicted to result in 1.5 billion people aged 65 years and older by 2050 (United Nations, 2022), highlighting the critical importance of maintaining the health of the aging population, especially, preventing frailty. Frailty, defined as the loss of reserve capacity across multiple physiological systems, increases vulnerability to various stressors and serves as a predictor of all-cause mortality, nursing home admission, hospitalization, functional disability and falls (Fried et al., 2001; Rockwood et al., 1999; Watanabe et al., 2022). Frailty can potentially be reversed to a pre-frail or robust status with appropriate interventions; hence early detection and intervention in crucial (Lee et al., 2014; Trevisan et al., 2017).

Social participation is known to be an effective countermeasure for preventing and intervening against frailty. This involves encouraging interactions with others through hobbies, sports, community events, and employment. Previous studies have shown that among robust older adults, those who participated in social activities had a lower risk of frailty onset than those who did not (Sone et al., 2023; Takeuchi et al., 2023). On the other hand, social isolation and loneliness, which are similar but different concepts from social participation, are also associated with frailty. Previous studies have revealed social isolation associated with several factors related to frailty such as hypertension, type 2 diabetes, inflammatory levels, and blood clotting factors, which are related factors for frailty (Chen et al., 2024; Shankar et al., 2011), and socially isolated individuals have a higher prevalence of frailty and an increased risk of functional disability onset (Kojima, Aoyama & Tanabe, 2022; Nakagomi et al., 2023). Studies have found that loneliness is significantly associated with an increased risk of physical inactivity, depressive symptoms, and frailty onset even when accounting for the reversibility of frailty (Shankar et al., 2011; Zhang et al., 2023; Gale, Westbury & Cooper, 2018; Ge, Yap & Heng, 2022). However, social isolation refers to an objective lack of social participation and interaction with others and loneliness refers to a subjective perception of isolation, which are correlated but distinct (Shankar et al., 2011; Barnes et al., 2022; Kino et al., 2023). Therefore, the effects of social isolation and loneliness on frailty do not merely act independently of each other, but the combination of the two may lead to an interaction effect.

However, no studies have assessed isolation from the dual perspectives of social isolation and loneliness or, examined their interaction on frailty onset. Therefore, this study aimed to investigate both the objective and subjective aspects of isolation by evaluating social isolation and loneliness to determine their interaction effects on frailty onset. This study reinforces the importance of considering the social context in the prevention of frailty, including identifying a target population and contributing to the design of complex programs that consider social isolation and loneliness. We hypothesized that social isolation and loneliness have a significant interaction on frailty onset.

2. Methods

2.1. Study design and participants

This three-year follow-up longitudinal study used data from independent older adults aged ≥65 years, obtained from the Japan Gerontological Evaluation Study (JAGES) 2019 and 2022 (Kondo, 2016). Eligible individuals were each distributed one of the eight questionnaire subsets because too many items were included in the whole questionnaire. The baseline survey conducted in 2019 covered 66 municipalities; 39 municipalities were tracked through a follow-up survey conducted in 2022. The exclusion criteria were as follows: 1) functionally dependent at baseline, 2) certified in long-term care, 3) already had frailty status at baseline, 4) invalid age and sex, 5) missing information about social isolation and loneliness, 6) abnormal height and weight (>4 SD at baseline), and 7) lost during follow-up. Based on these exclusion criteria, data from 8440 individuals were analyzed (Fig 1).

2.2. Outcome variable

Frailty was assessed using the Kihon Checklist (KCL) which developed by the Ministry of Health, Labour and Welfare of Japan, and the validity if this scale with the traditional phenotype model used to assess frailty has already been validated (Satake et al., 2016). A key feature of the KCL is its ability to easily assess a wider range of items. The KCL is a self-administered, multiple-choice questionnaire consisting of 25 items across seven domains: activities of daily living (5 items), locomotion (5 items), low nutritional status (2 items), oral function (3items), confinement (2 items), cognitive function (3 items), and depressive mood (5 items). One point was awarded if the participant chose an answer that indicated their daily functions were restricted. The total score ranged from 0 to 25. We used a modified version of the KCL, which has been validated in a Japanese population requiring long-term care or support (Watanabe et al., 2022). In this modified version, the response option "able but I do not" was newly added to the items of instrumental activities of daily living. For details of the questionnaire items, refer to Watanabe et al. (2022). Based on the KCL score, we classified the participants into three groups: "robust" (0–3 points), "pre-frailty" (4–7 points), and "frailty" (≥8 points) (Satake et al., 2016, 2017; Watanabe et al., 2022).

2.3. Exposure variable

We used social isolation and loneliness as exposure variables. Social isolation was evaluated based on the frequency of social contact outside the family, living together or with friends (Saito et al., 2015). Participants were asked the frequency of face-to-face and non-face-to-face contact (e-mails and phone calls) for each of their separated family members, relatives, and friends. Considering that an average month is 4.3 weeks, we classified the possible responses into seven continuous values: almost every day = 21.5, two or three times a week = 10.8, once a week = 4.3, once or twice a month = 1.5, almost none = 0.1 times a month, and none = 0 times a month. The frequency of social contact was assessed by summing the monthly frequencies of both face-to-face and non-face-to-face contacts. Participants were then categorized into three groups based on the average number of social contacts per week: "no isolation" (≥17.2 [>4 times per week]), "moderate isolation" (4.3–17.1 [1–3 times per week]), and "severe isolation" (≤4.2 [less than once per week]) (Noguchi et al., 2024). This approach enables a unified assessment of social contact frequency, regardless of whether the interactions are face-to-face or non-face-to-face. Loneliness was assessed using the three-item Revised University of California, Los Angeles (UCLA) Scale, Japanese version (Saito et al., 2019). This scale includes the following questions: (i) How often do you feel that you lack companionship? (ii) How often do you feel left out? and (iii) How often do you feel isolated from others? The possible responses were as follows; 1 = "hardly ever," 2 = "some of the time," and 3 = "often". The total scores ranged from 3 to 9, with higher scores indicating greater loneliness. We classified participants into three groups: "no loneliness" (3 points), "moderate loneliness" (4–5 points), and "severe loneliness" (≥6 points) (Barnes et al. 2022). Social isolation and loneliness were combined and the participants were categorized into nine groups as follows: 1) "no loneliness" & "no isolation"; 2) "no loneliness" & "moderate isolation"; 3) "no loneliness" & "severe isolation"; 4) "moderate loneliness" & "no isolation"; 5) "moderate loneliness" & "moderate isolation"; 6) "moderate loneliness" & "severe isolation"; 7) "severe loneliness" & "no isolation"; 8) "severe loneliness" & "moderate isolation"; and 9) "severe isolation" & "severe loneliness."

2.4. Covariates

The covariates included age (65–69, 70–74, 75–79, 80–84, or ≥85), sex (male or female), educational attainment (≤ 9, 10–12, or ≥ 13 years), robust-prefrailty status (robust or pre-frailty), smoking status (current, former, or never), alcohol consumption status (current, former, or never), household equivalent income (JPY 〈 2.00, 2.00–2.99, 3.00–3.99, or 〉 4.00 million; USD 1 = JPY 151), number of comorbidities (0, 1, or ≥2 of hypertension, stroke, heart disease, diabetes, respiratory disease, musculoskeletal disorders, and cancer), employment status (current worker or non-worker), and urbanicity. Urbanicity was categorized based on population density into four groups as follows: metropolitan (≥4000), urban (1500–3999), suburban (1000–1499) and rural (≤999) (people/km^2).

2.5. Statistical analysis

Descriptive analysis was conducted to examine the characteristics of the nine groups of social isolation and loneliness groups. Modified Poisson regression analyses were performed to obtain risk ratios (RR) and 95 % confidence intervals (Cl) for frailty onset. Model 1 was crude. Model 2 was adjusted for sex and age. In addition to the variables adjusted for in Model 2, Model 3 was adjusted for smoking status, alcohol consumption status, household equivalent income, educational attainment, employment status, and urbanicity. Moreover, multiplicative scale and Relative Excess Risk due to Interaction (RERI) were used to assess the interaction. As the sensitivity analyses, complete case analyses were conducted. Sensitivity analyses using the E-value were performed to evaluate the robustness of the findings to potential unmeasured confounding. (VanderWeele et al., 2017). The E-values were calculated from the results of Model 3 in the modified Poisson regression analysis (VanderWeele et al., 2017). The E-value represents the minimum strength of association that an unmeasured confounder would need to have with both the exposure and the outcome to fully account for the observed association (VanderWeele et al., 2017). Missing data were addressed through multiple imputations using multivariate imputations by chained equations (MICE) (White, Royston & Wood. 2011). All statistical analyses were conducted using StataMP17 (StataCorp, College Station, TX, USA), and the significance level was set at alpha = 0.05.

2.6. Ethical issues

Ethical approval for the JAGES 2019 survey was obtained from the Ethics Committee of the National Center for Geriatrics and Gerontology (approval number: 1274–2), Chiba University (approval number: 3442), and the Japan Agency for Gerontological Evaluation study (approval number: 2019–01). Ethical approval for the JAGES 2022 survey was obtained from the Ethics Committee on Research of Human Subjects at the Chiba University Graduate School of Medicine (approval number: M10460) and Tohoku University Graduate School of Dentistry (approval number: 37582).

3. Results

A total of 387320 individuals were targeted at baseline, and 266113 responded (response rate: 68.7 %). Of those, 45934 participants were sent a questionnaire on social isolation and loneliness, and 31857 (69.4 %). After exclusions and follow-up, 8440 participants were included in the final analysis (Fig 1). The mean age of the participants was 73.2 years (standard deviation, 5.5), and 4159 (49.3 %) were men. Table 1 presents the characteristics of the participants at the baseline survey after multiple imputations. Table S1 presents the baseline characteristics divided by social isolation and loneliness. Compared with other groups, the “severe loneliness” & “severe isolation” group was younger, had more men, had more pre-frailty, had lower level of education and income, and were current worker in higher numbers. Additionally, the “no

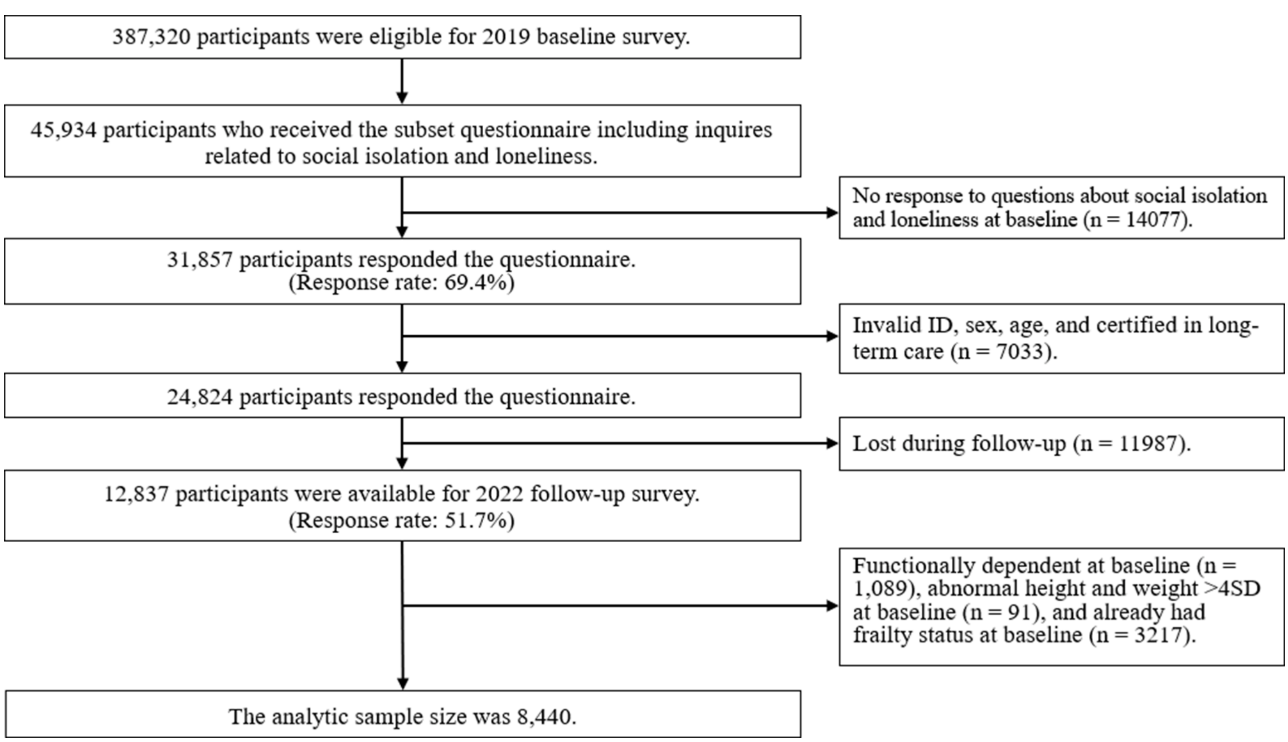

Fig. 1. Flow chart of study participants.

Table 1
Demographic characteristics of the analytic sample with multiple imputation (n= 8440).

Characteristics	n	Frailty onset n	Frailty onset %
Age			
65–69	2443	251	10.3
70–74	2756	351	12.7
75–79	2054	362	17.6
80–84	923	218	23.6
≥85	264	96	36.4
Sex			
Male	4159	678	16.3
Female	4281	600	14.0
Education			
≤9 years	1655	351	21.2
≥10 to 12 years	3825	561	14.7
≥13 years	2960	366	12.4
Robust-Pre-frailty			
Robust	5101	310	6.1
Pre-frailty	3339	968	29.0
Smoking Status			
Current	799	128	16.0
Former	2675	466	17.4
Never	4966	684	13.8
Alcohol consumption status			
Current	3867	539	13.9
Former	771	171	22.2
Never	3802	568	14.9
Equivalized household income			
<2.00	3560	634	17.8
≥2.00 to <2.99	2115	320	15.1
≥3.00 to <3.99	1607	189	11.8
≥400	1158	135	11.7
Number of comorbidities			
0	3178	356	11.2
1	3748	574	15.3
≥2	1514	345	22.8
Employment Status			
Current worker	5619	932	16.6
Non-worker	2821	346	12.3
Urbanicity			
Metropolitan	2903	440	15.2
Urban	1329	185	13.9
Suburb	1157	176	15.2
Rural	3051	477	15.6

Each response was the average of 20 imputed datasets.

isolation" & "severe loneliness" group had the highest rate of having two or more comorbidities. Table 2 shows the incidence of frailty onset during follow-up by according to social isolation and loneliness status. The overall frailty onset during the 3-year follow-up period was 15.1 % (n= 1278). The incidence of frailty onset was higher among the "severe loneliness" & "moderate isolation" group (30.4 %) and "severe loneliness" & "severe isolation" group (32.5 %) compared with other groups.

Fig. 2 shows the results of the modified Poisson regression analyses with multiple imputations to investigate the association between social isolation and loneliness status at baseline and frailty onset during follow-up. After adjusting for all covariates in Model 3, the "severe isolation" group had a higher risk of frailty onset than the "no isolation" group (RR = 1.38 [95 % CI: 1.19–1.60]). Additionally, the "severe loneliness" group had a higher risk of frailty onset than the "no loneliness" group (RR = 1.77 [95 % CI: 1.51–2.06]).

Table 3 shows the interaction effects of social isolation and loneliness on frailty onset. After adjusting for all covariates in Model 3, the "severe loneliness" & "severe isolation" group had the highest risk of frailty onset: "severe loneliness" & "severe isolation" group, RR = 2.09 (95 % CI: 1.60–2.73); "severe loneliness" & "moderate isolation" group, RR = 2.00 (95 % CI: 1.57–2.55); "severe loneliness" & "no isolation" group, RR = 1.94 (95 % CI: 1.49–2.52); "moderate loneliness" & "severe isolation" group, RR = 1.60 (95 % CI: 1.28–2.01); "moderate loneliness" & "moderate isolation" group, RR = 1.45 (95 % CI: 1.18–1.78);

Table 2
Frailty onset during follow-up by baseline social isolation and loneliness status with multiple imputation (n= 8440).

	No isolation						Moderate isolation						Severe isolation						All participants	
	No loneliness (n= 3287)		Moderate loneliness (n= 864)		Severe loneliness (n= 283)		No loneliness (n= 1627)		Moderate loneliness (n= 753)		Severe loneliness (n= 294)		No loneliness (n= 660)		Moderate loneliness (n= 460)		Severe loneliness (n= 212)		(n= 8440)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Frailtyonset																				
No	2969	90.3	718	83.1	208	73.8	1411	86.7	610	81.0	204	69.6	545	82.6	354	77.0	143	67.5	7162	84.9
Yes	318	9.7	146	16.9	75	26.2	216	13.3	143	19.0	90	30.4	115	17.4	106	23.0	69	32.5	1278	15.1

Note: Frailty onset was assessed using the Kihon Checklist (cutoff = 8/25 points).
Each response was the average of 20 imputed datasets.

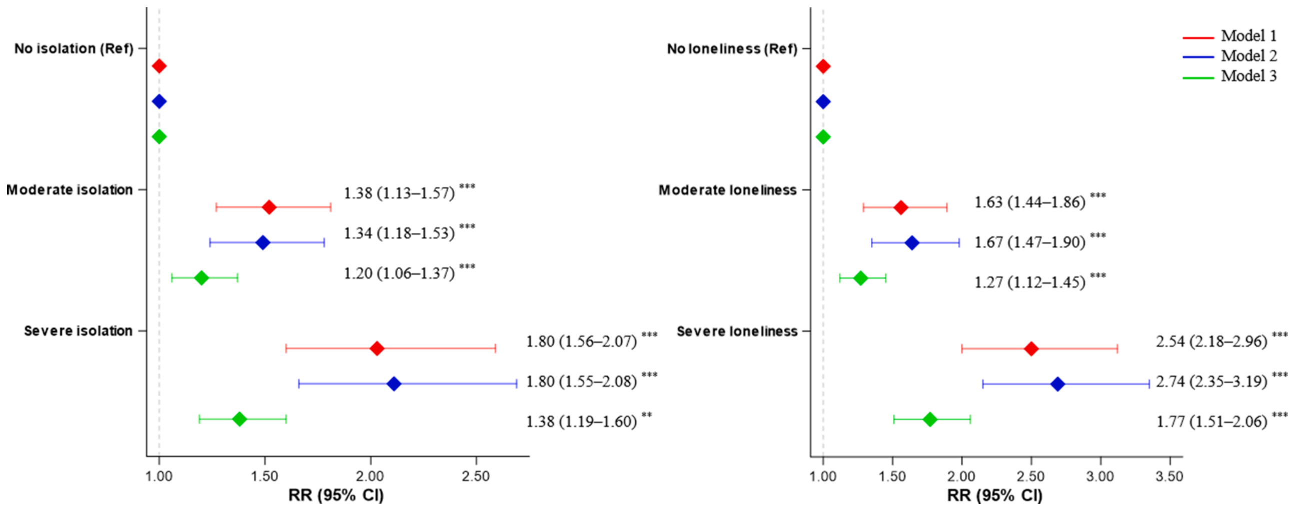

Fig. 2. Modified Poisson regression of social isolation and loneliness for the onset of frailty (n= 8440).
Note: Model 1: unadjusted model; Model 2: adjusted for age, sex; Model 3, adjustment for age, sex, education, robust-pre-frailty status, smoking status, alcohol consumption status, equivalized household income, comorbidities, employment status, urbanicity
*p<.05, **p<.01, ***p<.001
Abbreviation: Ref, reference; RR, risk ratio; CI, confidence interval.

Table 3
Interaction between social isolation and loneliness for the onset of frailty (n= 8440).

Social isolation	Loneliness	Frailty/Total(n)	Model 1 RR (95 %CI)	Model 2 RR (95 %CI)	Model 3 RR (95 %CI)
No isolation	No loneliness	313/3286	Ref	Ref	Ref
	Moderate loneliness	145/866	1.75 (1.43–2.14) ***	1.79 (1.46–2.19) ***	1.35 (1.10–1.65) **
	Severe loneliness	76/282	2.74 (2.12–3.55) ***	3.00 (2.32–3.88) ***	1.94 (1.49–2.52) ***
Moderate isolation	No loneliness	222/1628	1.38 (1.15–1.64) ***	1.33 (1.11–1.59) ***	1.22 (1.02–1.45) ***
	Moderate loneliness	143/757	1.97 (1.61–2.41) ***	1.94 (1.59–2.37) ***	1.45 (1.18–1.78) ***
	Severe loneliness	90/293	3.14 (2.48–3.98) ***	3.21 (2.53–4.08) ***	2.00 (1.57–2.55) ***
Severe isolation	No loneliness	112/657	1.81 (1.46–2.25) ***	1.75 (1.41–2.19) ***	1.44 (1.15–1.79) **
	Moderate loneliness	108/459	2.39 (1.91–2.98) ***	2.46 (1.97–3.09) ***	1.60 (1.28–2.01) ***
	Severe loneliness	68/212	3.38 (2.26–4.40) ***	3.68 (2.82–4.79) ***	2.09 (1.60–2.73) ***
Multiplicative scale (95 % CI) [a]			0.68 (0.46–1.01)	0.70 (0.47–1.04)	0.75 (0.50–1.11)
RERI (95 % CI) [b]			−0.17 (−1.09–0.75)	−0.08 (−1.08–0.92)	−0.29 (−1.02–0.44)

Note: Model 1: unadjusted model; Model 2: adjusted for age, sex; Model 3, adjustment for age, sex, education, robust-pre-frailty status, smoking status, alcohol consumption status, equivalized household income, number of comorbidities, employment status, urbanicity.

[a] The multiplicative scale was calculated using the ratio of "no isolation" & "no loneliness" group to the "severe isolation" & "severe loneliness" group.

[b] The additive scale was calculated from the difference between "no isolation" & "no loneliness" group to "severe isolation" & "severe loneliness" group.

*p<.05, **p<.01, ***p<.001

Abbreviations: Ref reference, RERI relative excess risk due to interaction, RR risk ratio, CI confidence interval.

"moderate loneliness" & "no isolation" group, RR = 1.35 (95 % CI: 1.10–1.65); "no loneliness" & "severe isolation" group, RR = 1.44 (95 % CI: 1.15–1.79); "no loneliness" & "moderate isolation" group, RR = 1.22 (95 % CI: 1.02–1.45). However, there were no significant multiplicative and additive interactions (multiplicative scale = 0.75 [95 % CI: 0.50–1.11]; RERI = −0.29 [95 % CI: −1.02–0.44]). Table S4 shows the results of complete case analysis. The results were consistent with the main results. Table S5 shows the estimated E-values, which ranged 1.74–3.41 for point estimates and 1.16–2.58 for confidence limits across different outcomes.

4. Discussion

This study investigated the associations between social isolation and loneliness on frailty onset among independent older adults in Japan. The results showed that social isolation and loneliness were both associated with frailty onset, with 32 % of those who had severe isolation and severe loneliness experiencing frailty onset at the 3-year follow-up. These results indicate that even self-initiated isolation could be a risk for frailty onset. Those who had both severe isolation and severe loneliness had the highest RR of frailty onset at 2.07; however, there were no multiplicative or additive interaction between social isolation and loneliness on frailty onset.

Our finding regarding the association of social isolation and loneliness with frailty onset is partially supported by previous findings. Frailty individuals have been shown to have higher prevalence of social isolation (Kojima, Aoyama & Tanabe, 2022); however, a longitudinal study revealed no significant association between social isolation and risk of frailty onset (Gale, Westbury & Cooper, 2018; Ge, Yap & Heng, 2022). Conversely, loneliness was associated with an increased risk of frailty onset in a longitudinal study that included individuals with frailty at baseline (Kojima, Taniguchi et al., 2022; Gale, Westbury & Cooper, 2018; Ge, Yap & Heng, 2022; Ye et al., 2024). By contrast, our study showed that both social isolation and loneliness were independently associated with frailty onset, and those who had severe isolation and loneliness had the highest risk of frailty onset. One possible reason for the difference in results regarding social isolation is that those who had frailty at baseline were excluded from the present study, thus eliminating the effect of the reversibility of frailty.

The absence of an interaction suggests that social isolation and loneliness may influence frailty via largely independent pathways. This highlights the need for tailored interventions: individuals who are socially isolated but not lonely may benefit more from increasing opportunities for social participation, whereas those who are lonely despite frequent social contact may require psychological or emotional support. In Japan, all municipalities have implemented community support projects aimed to prevent individuals from needing nursing care (Ministry of Health, Labour & Welfare, 2016), and these programs have reduced the risk of frailty onset, therefore, this widespread community support programs may mitigate interaction effects.

There are several possible explanations for the association of social isolation and loneliness with frailty. Social isolation, the objective aspects of reduced opportunities to interact with others, has been associated with hypertension, type 2 diabetes, increased inflammatory levels, and altered blood clotting factors, all of which are risk factors for cardiovascular disease (Chen et al., 2024; Shankar et al., 2011). Additionally, events such as the death of a close relative, one of the factors in social isolation, has been reported to induce physical inactivity (Driggers et al., 2024). In contrast, loneliness, the subjective aspect of isolation, has been reported to be associated with physical inactivity and depressive symptoms (Shankar et al., 2011; Zhang et al., 2023). These findings suggest that social isolation is associated with physical health components, such as multimorbidity, while loneliness is more closely related to psychological factors, such as depression, both of which may increase the risk of frailty onset. Whereas previous studies have focused on physical activity and protein intake as preventive measures against frailty (Imai et al., 2014; Yuki et al., 2019), the present study demonstrates that social isolation and loneliness are associated with a higher risk of frailty. This finding underscores the importance of considering social factors in the prevention of frailty. Furthermore, it contributes to the identification of target populations and the design of complex programs that consider both social isolation and loneliness for frailty prevention. Notably, social isolation and loneliness do not always overlap; some individuals may feel lonely despite sufficient social contact, while others may not feel lonely even when socially isolated. Our results suggest that loneliness has a stronger impact on frailty onset than social isolation. Therefore, psychological interventions, such as cognitive bias modification, may be particularly effective for individuals who are not socially isolated but experience severe loneliness (Riddleston L et al., 2023). Conversely, even self-initiated isolation can increase frailty risk, highlighting the need for support that addresses both objective and subjective aspects of social relationships. A previous study reported that socially isolated and lonely individuals had poor social support and a higher risk of psychological distress, but also had a desire for further social participation (Menec et al., 2020). Therefore, in addition to nutrition and exercise, community-based frailty prevention programs should evaluate social factors such as connections with others and loneliness and encourage connections among community-dwelling older adults.

This study has several strengths. First, it is the first study to clarify the associations between social isolation and loneliness on frailty onset in the Japanese context. Second, it evaluated isolation from both subjective and objective perspectives and examined their additive interaction effects. Third, by excluding individuals who had frailty at baseline, a more accurate estimation of the impact of social isolation and loneliness on frailty onset without the reversibility of frailty was possible. However, this study also has several limitations. First, the use of self-reported questionnaire data may have introduced a measurement bias, leading to underestimation. Nevertheless, the scales used for social isolation, and frailty (KCL) are well-established and validated (Saito et al., 2015; Satake et al., 2016; Watanabe et al., 2022) and are commonly employed in surveys of older adults (Kino et al., 2023; Nakagomi et al., 2023; Takeuchi et al., 2023). Although the questionnaire for loneliness (the Japanese version of the three-item Revised UCLA Loneliness Scale) is a subjective self-report measure, it has been validated against the original full-length scale and is commonly employed in population-based surveys (Kino et al., 2023; Russell et al., 1980; Saito et al., 2019). Therefore, the influence of the measurement bias can be considered small. Second, as the municipalities participating in the JAGES survey were not selected randomly, they may include health-conscious populations; thus, the generalizability of these findings is limited. These results were also likely influenced by community support projects in place in all Japanese municipalities; hence, they have limited generalizability to residents in other countries where such projects are not in place. Third, selection bias may have affected the results of this study because of the use of a subset of the questionnaire and the follow-up rate was not high. Table S2 presents the baseline characteristics before MICE, and Table S3 shows the baseline characteristics of the participants lost during follow-up. The analytic sample included fewer individuals aged 85 years or older and those with slightly higher educational attainment. Compared to participants who remained in the study, those lost to follow-up were less likely to be in the “no isolation” and “no loneliness” groups and included a slightly higher proportions of individuals aged over 80 years. Therefore, the loss to follow-up may have led to an underestimation of the impact of social isolation and loneliness on frailty onset. Fourth, we were unable to account for the specific content of community support projects in each municipality. Although all municipalities in Japan are mandated to implement community support projects, the extent to which these projects include measures to prevent social isolation and loneliness varies across municipalities (Ministry of Health, Labour & Welfare, 2016). Therefore, the nature of the projects implemented in each municipality may partially explain the social isolation and loneliness experienced by residents. Future research should consider the characteristics of community support projects at the municipal level. Finally, the effect of residual confounding was not eliminated even after adjusting for nine covariates, including socioeconomic status and other potential confounders reported in previous studies. While residual confounding due to unmeasured variables cannot be denied, the E-values suggest that its influence is relatively small. Although chronic conditions have been reported to affect frailty onset, this study only adjusted for the presence or sequelae of comorbidities (Fried et al., 2001). This limitation arose because the questionnaire used in this study could not track new onset of chronic diseases such as hypertension and diabetes, which may increase the risk of frailty (Fried et al., 2001). Future studies with careful adjustment for these factors are warranted.

5. Conclusion

This 3-year follow-up cohort study identified associations between social isolation and loneliness on frailty onset among independent older adults in Japan. Importantly, after considering the potential confounders, both social isolation and loneliness were associated with an increased risk of frailty onset, although no multiplicative or additive interactions were observed. These findings underscore the importance of considering social factors in frailty prevention. Efforts should focus on maintaining social connections and mitigating feelings of loneliness to reduce the risk of frailty in older adults.

Funding

This work was supported by the Japan Gerontological Evaluation Study (JAGES). This study was supported by Grant-in-Aid for Scientific Research (19K02200, 20H00557, 20H03954, 20K02176, 20K10540, 20K13721, 20K19534, 21H00792, 21H03196, 21K02001, 21K10323, 21K11108, 21K17302, 21K17308, 21K17322, 22H00934, 22H03299, 22J00662, 22J01409, 22K01434, 22K04450, 22K10564, 22K11101, 22K13558, 22K17265, 22K17364, 22K17409, 23K16320, 23H00449, 23H03117, 23K19793, 23K21500) from Japan Society for the Promotion of Science (JSPS), Health Labour Sciences Research Grants (19FA1012, 19FA2001, 21FA1012, 22FA2001, 22FA1010, 22FG2001), Research Institute of Science and Technology for Society (JPMJOP1831) from the Japan Science and Technology (JST), a grant from Japan Health Promotion & Fitness Foundation, TMDU priority research areas grant and National Research Institute for Earth Science and Disaster Resilience. The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the respective funding organizations.

CRediT authorship contribution statement

Mamoru Sato: Writing – review & editing, Writing – original draft, Visualization, Validation, Project administration, Methodology, Formal analysis, Conceptualization. **Manami Hoshi-Harada:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Formal analysis, Conceptualization. **Kenji Takeuchi:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Formal analysis, Conceptualization. **Taro Kusama:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Formal analysis, Conceptualization. **Takaaki Ikeda:** Writing – review & editing, Supervision, Software, Project administration, Methodology, Formal analysis, Conceptualization. **Sakura Kiuchi:** Writing – review & editing, Supervision, Software, Methodology, Conceptualization. **Masashige Saito:** Writing – review & editing, Supervision, Resources, Investigation, Funding acquisition, Conceptualization. **Naoki Nakaya:** Writing – review & editing, Conceptualization. **Ken Osaka:** Writing – review & editing, Project administration, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

S. Mamoru was supported by JST SPRING, Grant Number JPMJSP2114.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.archger.2025.105914.

References

Barnes, T. L., Ahuja, M., MacLeod, S., Tkatch, R., Albright, L., Schaeffer, J. A., & Yeh, C. S. (2022a). Loneliness, social isolation, and all-cause mortality in a large sample of older adults. *Journal of Aging and Health, 34*(6–8), 883–892.

Barnes, T. L., MacLeod, S., Tkatch, R., Ahuja, M., Albright, L., Schaeffer, J. A., & Yeh, C. S. (2022b). Cumulative effect of loneliness and social isolation on health outcomes among older adults. *Aging & Mental Health, 26*(7), 1327–1334. https://doi.org/10.1080/13607863.2021.1940096

Chen, Y., Xue, H., Ai, S., Liu, Y., Nie, Y., Ai, Q. H., Zhang, J., & Liang, Y. Y. (2024). Trajectories of social isolation and loneliness and the risk of incident type 2 diabetes mellitus across genetic risk score. *Diabetes & Metabolism, 50*(3), Article 101526. https://doi.org/10.1016/j.diabet.2024.101526

Driggers, A., Kennedy, R. E., Williams, B. R., Brown, C. J., & Buys, D. R. (2024). Changes in life-space mobility with loss of relatives and friends among older adults: Results from the UAB Study of Aging. *The Gerontologist, 64*(4), gnad116. https://doi.org/10.1093/geront/gnad116

Fried, L. P., Tangen, C. M., Walston, J., Newman, A. B., Hirsch, C., Gottdiener, J., Seeman, T., Tracy, R., Kop, W. J., Burke, G., McBurnie, M. A., & Cardiovascular Health Study Collaborative Research Group. (2001). Frailty in older adults: Evidence for a phenotype. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences, 56*(3), M146–M156. https://doi.org/10.1093/gerona/56.3.m146

Gale, C. R., Westbury, L., & Cooper, C. (2018). Social isolation and loneliness as risk factors for the progression of frailty: The English Longitudinal Study of Ageing. *Age and Ageing, 47*(3), 392–397. https://doi.org/10.1093/ageing/afx188

Ge, L., Yap, C. W., & Heng, B. H. (2022). Associations of social isolation, social participation, and loneliness with frailty in older adults in Singapore: A panel data analysis. *BMC Geriatrics, 22*(1), 26. https://doi.org/10.1186/s12877-021-02745-2

Imai, E., Tsubota-Utsugi, M., Kikuya, M., Satoh, M., Inoue, R., Hosaka, M., Metoki, H., Fukushima, N., Kurimoto, A., Hirose, T., Asayama, K., Imai, Y., & Ohkubo, T. (2014). Animal protein intake is associated with higher-level functional capacity in elderly adults: The Ohasama study. *Journal of the American Geriatrics Society, 62*(3), 426–434. https://doi.org/10.1111/jgs.12690

Kino, S., Stickley, A., Arakawa, Y., Saito, M., Saito, T., & Kondo, N. (2023). Social isolation, loneliness, and their correlates in older Japanese adults. *Psychogeriatrics: The Official Journal of the Japanese Psychogeriatric Society, 23*(3), 475–486. https://doi.org/10.1111/psyg.12957

Kojima, G., Aoyama, R., & Tanabe, M. (2022). Associations between social isolation and physical frailty in older adults: A systematic review and meta-analysis. *Journal of the American Medical Directors Association, 23*(11), e3–e6. https://doi.org/10.1016/j.jamda.2022.06.012

Kojima, G., Taniguchi, Y., Aoyama, R., & Tanabe, M. (2022). Associations between loneliness and physical frailty in community-dwelling older adults: A systematic review and meta-analysis. *Ageing Research Reviews, 81*, Article 101705. https://doi.org/10.1016/j.arr.2022.101705

Kondo, K. (2016). Progress in aging epidemiology in Japan: The JAGES project. *Journal of Epidemiology, 26*(7), 331–336. https://doi.org/10.2188/jea.JE20160093

Lee, J. S., Auyeung, T. W., Leung, J., Kwok, T., & Woo, J. (2014). Transitions in frailty states among community-living older adults and their associated factors. *Journal of the American Medical Directors Association, 15*(4), 281–286. https://doi.org/10.1016/j.jamda.2013.12.002

Menec, V. H., Newall, N. E., Mackenzie, C. S., Shooshtari, S., & Nowicki, S. (2020). Examining social isolation and loneliness in combination in relation to social support and psychological distress using Canadian Longitudinal Study of Aging (CLSA) data. *PloS One, 15*(3), Article e0230673. https://doi.org/10.1371/journal.pone.0230673

Ministry of Health, Labour and Welfare. (2016). Long-term care, health and welfare services for the elderly. Retrieved from https://www.mhlw.go.jp/english/policy/care-welfare/care-welfare-elderly/index.html Accessed February 3, 2025.

Nakagomi, A., Tsuji, T., Saito, M., Ide, K., Kondo, K., & Shiba, K. (2023). Social isolation and subsequent health and well-being in older adults: A longitudinal outcome-wide analysis. *Social Science & Medicine (1982), 327*, Article 115937. https://doi.org/10.1016/j.socscimed.2023.115937

Noguchi, T., Ikeda, T., Kanai, T., Saito, M., Kondo, K., & Saito, T. (2024). Association of social isolation and loneliness with chronic low back pain among older adults: A cross-sectional study from Japan gerontological Evaluation study (JAGES). *Journal of Epidemiology, 34*(6), 270–277. https://doi.org/10.2188/jea.JE20230127

Riddleston, L., Bangura, E., Gibson, O., Qualter, P., & Lau, J. Y. F. (2023). Developing an interpretation bias modification training task for alleviating loneliness in young people. *Behaviour Research and Therapy, 168*, Article 104380. https://doi.org/10.1016/j.brat.2023.104380

Rockwood, K., Stadnyk, K., MacKnight, C., McDowell, I., Hébert, R., & Hogan, D. B. (1999). A brief clinical instrument to classify frailty in elderly people. *Lancet (London, England), 353*(9148), 205–206. https://doi.org/10.1016/S0140-6736(98)04402-X

Russell, D., Peplau, L. A., & Cutrona, C. E. (1980). The revised UCLA Loneliness Scale: Concurrent and discriminant validity evidence. *Journal of Personality and Social Psychology, 39*(3), 472–480. https://doi.org/10.1037//0022-3514.39.3.472

Saito, M., Kondo, K., Ojima, T., Hirai, H., & Group, J. A. G. E. S. (2015). Criteria for social isolation based on associations with health indicators among older people: A 10-year follow-up of the gerontological evaluation study. *Japanese Journal of Public Health, 62*(3), 95–105. https://doi.org/10.11236/jph.62.3_95

Saito, T., Cable, N., Aida, J., Shirai, K., Saito, M., & Kondo, K. (2019). Validation study on a Japanese version of the three-item UCLA Loneliness Scale among community-dwelling older adults. *Geriatrics & Gerontology International, 19*(10), 1068–1069. https://doi.org/10.1111/ggi.13758

Satake, S., Senda, K., Hong, Y. J., Miura, H., Endo, H., Sakurai, T., Kondo, I., & Toba, K. (2016). Validity of the Kihon Checklist for assessing frailty status. *Geriatrics & Gerontology International, 16*(6), 709–715. https://doi.org/10.1111/ggi.12543

Satake, S., Shimokata, H., Senda, K., Kondo, I., & Toba, K. (2017). Validity of total Kihon checklist score for predicting the incidence of 3-year dependency and mortality in a community-dwelling older population. *Journal of the American Medical Directors Association, 18*(6), 552.e1–552.e6. https://doi.org/10.1016/j.jamda.2017.03.013

Shankar, A., McMunn, A., Banks, J., & Steptoe, A. (2011). Loneliness, social isolation, and behavioral and biological health indicators in older adults. *Health Psychology: Official Journal of the Division of Health Psychology, American Psychological Association, 30*(4), 377–385. https://doi.org/10.1037/a0022826

Sone, T., Nakaya, N., Sugawara, Y., Matsuyama, S., & Tsuji, I. (2023). Effect of social participation on the association between frailty and disability. *Archives of Gerontology and Geriatrics, 110*, Article 104989. https://doi.org/10.1016/j.archger.2023.104989

Takeuchi, H., Ide, K., Hayashi, T., Abe, N., Nakagomi, A., & Kondo, K. (2023). Association between social participation and frailty among older adults: A longitudinal study from Japan Gerontological Evaluation Study. *Japanese Journal of Public Health, 70*(9), 529–543. https://doi.org/10.11236/jph.22-088

Trevisan, C., Veronese, N., Maggi, S., Baggio, G., Toffanello, E. D., Zambon, S., Sartori, L., Musacchio, E., Perissinotto, E., Crepaldi, G., Manzato, E., & Sergi, G. (2017). Factors influencing transitions between frailty states in elderly adults: The Progetto Veneto Anziani Longitudinal Study. *Journal of the American Geriatrics Society, 65*(1), 179–184. https://doi.org/10.1111/jgs.14515

United Nations. (2022). World population prospects 2022. Retrieved from https://www.un.org/en/global-issues/ageing Accessed November 21, 2024.

VanderWeele, T. J., & Ding, P. (2017). Sensitivity analysis in observational research: Introducing the E-value. *Annals of Internal Medicine, 167*(4), 268–274. https://doi.org/10.7326/M16-2607

Watanabe, R., Tsuji, T., Ide, K., Noguchi, T., Yasuoka, M., Kamiji, K., Satake, S., Kondo, K., & Kojima, M. (2022). Predictive validity of the modified Kihon Checklist for the incidence of functional disability among older people: A 3-year cohort study from the JAGES. *Geriatrics & Gerontology International, 22*(8), 667–674. https://doi.org/10.1111/ggi.14439

White, I. R., Royston, P., & Wood, A. M. (2011). Multiple imputation using chained equations: Issues and guidance for practice. *Statistics in Medicine, 30*(4), 377–399. https://doi.org/10.1002/sim.4067

Ye, L., Bally, E., Korenhof, S. A., Fierloos, I., Alhambra Borrás, T., Clough, G., Raat, H., & van Grieken, A. (2024). The association between loneliness and frailty among community-dwelling older adults in five European countries: A longitudinal study. *Age and Ageing, 53*(10), afae210. https://doi.org/10.1093/ageing/afae210

Yuki, A., Otsuka, R., Tange, C., Nishita, Y., Tomida, M., Ando, F., Shimokata, H., & Arai, H. (2019). Daily physical activity predicts frailty development among community-dwelling older Japanese adults. *Journal of the American Medical Directors Association, 20*(8), 1032–1036. https://doi.org/10.1016/j.jamda.2019.01.001

Zhang, Y., Kuang, J., Xin, Z., Fang, J., Song, R., Yang, Y., Song, P., Wang, Y., & Wang, J. (2023). Loneliness, social isolation, depression and anxiety among the elderly in Shanghai: Findings from a longitudinal study. *Archives of Gerontology and Geriatrics, 110*, Article 104980. https://doi.org/10.1016/j.archger.2023.104980