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Association Between Central Sensitization Symptoms and Cold Hypersensitivity Severity in Older Adults: A Cross-Sectional Analysis from the Otassha Study

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Research Article

Keywords: Central sensitization, Cold hypersensitivity, Hie, Severity, Community-dwelling older adults, Cross-sectional study

Posted Date: April 23rd, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9163241/v1

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Additional Declarations: No competing interests reported.

Version of Record: A version of this preprint was published at BMC Geriatrics on September 4th, 2026.
See the published version at https://doi.org/10.1186/s12877-026-08248-2.

Abstract

Introduction: Cold hypersensitivity (Hie) is a common complaint among older adults in East Asia and has traditionally been attributed to peripheral circulatory dysfunction. However, emerging evidence suggests that central sensitization (CS) may also contribute. This study examined the association between central sensitization symptoms and the severity of cold hypersensitivity in community-dwelling older adults.

Methods: We analyzed cross-sectional data from 586 adults aged 65–84 years participating in the 2024 Otassha Study in Tokyo, Japan. Cold hypersensitivity was assessed using a validated 10-item questionnaire and categorized into four levels (negative, mild, moderate, severe). Central sensitization symptoms were measured using the Japanese version of the Central Sensitization Inventory (CSI). The primary analysis consisted of multinomial logistic regression examining the association between CSI total score (per 10-point increase) and cold hypersensitivity severity, adjusting for age, sex, smoking status, alcohol consumption, and physical activity. Exploratory analyses examined associations between individual CSI items and cold hypersensitivity with false discovery rate correction.

Results: Among the 586 participants, 396 (67.6%) were classified as having cold hypersensitivity. In adjusted multinomial logistic regression analyses, higher CSI total scores were significantly associated with increasing severity of cold hypersensitivity. Each 10-point increase in CSI score was associated with higher odds of mild (AOR 1.70, 95% CI 1.35–2.15), moderate (AOR 2.35, 95% CI 1.78–3.09), and severe cold hypersensitivity (AOR 4.33, 95% CI 2.29–8.19), compared with participants without cold hypersensitivity, indicating a graded association. In exploratory analyses, low energy, jaw pain, and headaches remained significantly associated after correction for multiple comparisons.

Conclusion: In this cross-sectional study of older adults, greater central sensitization symptom burden was associated with increasing severity of cold hypersensitivity. These findings suggest that cold hypersensitivity may reflect neurophysiological processes related to central sensitization. Longitudinal studies are needed to clarify temporal relationships.

Introduction

Cold hypersensitivity, or "Hie" in Japanese, is commonly reported among older populations, particularly postmenopausal women[1]. Traditionally viewed as a peripheral circulatory issue or constitutional trait, its chronic presentation and overlap with symptoms found in fibromyalgia and chronic fatigue syndrome suggest the possibility of central nervous system involvement[2,3]. Cold hypersensitivity is not a phenomenon limited to Japan; in Korea, a similar concept has been referred to as cold hypersensitivity in the hands and feet[4]. Cold hypersensitivity refers to a sensation of coldness, but it is not limited to the perception caused solely by low temperatures as defined in Western medicine[5]. Rather, it encompasses a broader range of discomforts that can lead to various complaints and significantly impair patients' quality of life. While the concept of cold hypersensitivity is unfamiliar to most Westerners[5], it is one of the most common symptoms in Japan. In our previous study, we conducted an epidemiological analysis

of this condition, which had been considered unique to Japan, and developed a questionnaire that was published in an international journal[6]. In this study, cold hypersensitivity was found to be associated with somatic symptoms, autonomic dysfunction, and depressive symptoms, suggesting a potential link to central nervus system[6].

In recent years, the concept of central sensitization has been attracting attention[7]. Central sensitization (CS) is characterized by amplified neural signalling within the central nervous system, leading to hypersensitivity to various stimuli[8]. Although central sensitization significantly influences pain sensitivity, its underlying mechanisms and contributing factors are still not fully elucidated. Central sensitization may be related to many conditions. In our previous research, we found that central sensitization is associated with multiple physical symptoms, depression, and anxiety[9]. CS is defined as an aggravating factor for somatic symptom disorder in the Diagnostic statistical manual of mental disorder 5 text revision (DSM-5 TR)[10]. Furthermore, we found that it is associated with smoking among women, a lifestyle habit[11]. CS has been reported to be associated with chronic pain, psychiatric disorders, and even medically unexplained symptoms[12,13].

Considering these circumstances, we hypothesized that central sensitization may be associated with cold hypersensitivity, which can be conceptualized as a manifestation of heightened sensitivity to cold. To the best of our knowledge, no previous studies have directly examined the association between central sensitization and cold hypersensitivity. To date, no population-based epidemiological studies have directly examined the relationship between cold hypersensitivity and central sensitization symptoms in older adults. Therefore, this study aimed to examine the association between central sensitization symptoms and cold hypersensitivity among community-dwelling older adults. We hypothesized that higher central sensitization symptom burden would be associated with greater severity of cold hypersensitivity. The primary outcome was cold hypersensitivity severity (negative, mild, moderate, severe), and the primary analysis consisted of a multinomial logistic regression examining the association between CSI total score (per 10-point increase) and cold hypersensitivity severity. Secondary exploratory analyses examined associations with individual CSI items.

Materials and Methods

Design

This cross-sectional analysis was conducted in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement for observational studies[14,15].

Setting

We used data collected from September 26 to October 6, 2024, as part of the ongoing Otassha Study, a longitudinal health survey of community-dwelling older adults in Japan that began in 2011. The study

site was Itabashi Ward, a suburban district of Tokyo functioning as a typical commuter area, where in April 2025, adults aged 65 years or older comprised 22.6% of the total population.

Participants

Invitation letters were sent to all residents aged 65–84 years listed in the Basic Resident Register, excluding those living in institutions and individuals who had participated in previous surveys conducted by our institute. Follow-up assessments were conducted annually, and newly eligible residents were invited upon reaching 65 years of age. A flow diagram (Fig. 1) summarizing the participant selection and exclusion process was added in accordance with STROBE recommendations[14,15]. In the 2024 wave, 586 residents participated in the annual health examinations and provided written informed consent. The research was approved by the Ethics Committee of the Tokyo Metropolitan Institute of Gerontology (protocol code R22-034) and conducted in accordance with the Declaration of Helsinki.

Evaluation of Central Sensitization

CS was assessed using the Japanese adaptation of the Central Sensitization Inventory (CSI), a validated questionnaire developed to measure the presence and severity of symptoms associated with CS syndrome[18]. The Japanese version has undergone cross-cultural adaptation and psychometric testing to confirm its reliability and suitability for use among Japanese individuals[19]. The CSI consists of 25 items that evaluate the frequency of CS-related symptoms, each scored on a 5-point Likert scale from “never” (0) to “always” (4). Higher total scores reflect a greater likelihood of having conditions linked to CS.

Evaluation of Cold hypersensitivity

Cold hypersensitivity was assessed using the Cold Hypersensitivity Questionnaire that we had previously developed in our earlier studies[6]. This questionnaire consists of five sections: I. Assessment of the degree of cold hypersensitivity using a Visual Analogue Scale, II. Assessment of the frequency of cold hypersensitivity, III. Assessment of quality of life related to cold hypersensitivity, IV. Identification of affected body sites, and V. Evaluation of cold hypersensitivity using questionnaire items. In the present study, section V was used. This section comprises 10 questions, each rated on a five-point Likert scale. The minimum possible score is 10 and the maximum is 50, with a score of 20 or higher, indicating the presence of cold hypersensitivity[6]. According to the definition of the questionnaire, mild cold hypersensitivity was defined as a score of 20 or higher, moderate as 30 or higher, and severe as 40 or higher[6].

Evaluation of other possible lifestyle related variables

In this study on central sensitization and cold hypersensitivity, we also examined lifestyle habits as potential contributing factors. Specifically, smoking, alcohol consumption and physical activity were selected because these behaviors are known to influence health-related decision-making and are highly

responsive to both individual- and group-level interventions[20]. The level of physical activity was assessed using the International Physical Activity Questionnaire (IPAQ) Short Form[21].

Regarding alcohol use, participants were first asked whether they drank alcohol in the past week (yes/no). Smoking status was classified into two groups: current smokers (including those who had smoked at least 100 cigarettes in their lifetime) and non-smokers. For physical activity, participants were asked whether they had engaged in exercise lasting at least 10 minutes at a time during the previous week. If so, they were further asked about the type, frequency, and duration of such activities. Activity intensity was divided into three levels—vigorous, moderate, and walking—based on the subjective evaluation of average weekly activity intensity using the IPAQ Short Form[21]. Examples of vigorous activity included carrying heavy loads, uphill cycling, jogging, or playing singles tennis. Moderate activity encompassed carrying light loads, playing tag with children, swimming slowly, doubles tennis, or playing golf without a cart. Walking activity referred to walking for more than 10 minutes, either as exercise or as a leisure activity.

Sample size and missing data

Although no formal a priori sample size calculation was conducted, the present study utilized all available participants from the 2024 wave of the Otassha Study. Participants had no missing values for key variables such as cold hypersensitivity or CSI scores. Therefore, all available data were included in the analyses, and no imputation procedures were necessary.

Statistical analysis

All analyses were conducted using Stata version 19 (StataCorp, College Station, TX, USA). Continuous variables are presented as means with standard deviations (SD), and categorical variables as frequencies and percentages. No statistical significance testing was performed for comparisons of baseline characteristics, in accordance with recommendations for observational studies[14,15].

Primary analysis

The primary outcome was cold hypersensitivity severity, categorized into four levels (negative, mild, moderate, and severe). The primary exposure was the CSI total score, modeled per 10-point increase. Multinomial logistic regression analyses were performed with the “negative” group as the reference category. Crude models (Model 1) and multivariable-adjusted models (Model 2) were constructed. Model 2 adjusted for age (60s, 70s, ≥ 80 years), sex, smoking status, alcohol consumption, and physical activity intensity. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated.

Exploratory analysis

To further characterize symptom-specific associations, logistic regression analyses were performed using each of the 25 individual CSI items as exposures and cold hypersensitivity (yes/no) as the

outcome. Because multiple comparisons were performed, we controlled for false discovery using the Benjamini–Hochberg false discovery rate (FDR) procedure. Adjusted q values are reported, and these analyses are interpreted as exploratory. A two-sided p value < 0.05 was considered statistically significant for primary analyses.

Results

A total of 586 community-dwelling older adults (mean age 73.9 ± 6.6 years; 365 women and 221 men) were included in the analysis. Among them, 396 participants (67.6%) met the criteria for cold hypersensitivity, while 190 (32.4%) were classified as non–cold hypersensitivity (Table 1). Participants with cold hypersensitivity were more likely to be women and had higher mean CSI scores compared with those without cold hypersensitivity. The mean CSI score was 17.4 (SD 10.3) in the cold hypersensitivity group and 11.8 (SD 9.2) in the non–cold hypersensitivity group.

Table 1
Basic characteristics of the participant

	Total	**Cold hypersensitivity**	
	(n = 586)	**positive**	**negative**
		(n = 396)	**(n = 190)**
Age, mean (S.D.)	73.9 (6.6)	74.2 (6.6)	73.3 (6.5)
Women/Men, number	365/221	280/116	85/105
Smoking history, n (%)			
Current smokers	34 (5.8)	21 (10.1)	13 (3.4)
Past or non-smokers	552 (94.2)	177 (89.9)	375 (96.6)
Drinking history, n (%)			
Regular drinkers	297 (50.7)	103 (54.2)	194 (49.0)
Past or non-drinkers	289 (49.3)	87 (45.8)	202 (51.0)
Physical activity intensity, n (%)*			
Walking	563 (96.1)	379 (95.8)	184 (96.8)
Moderate	264 (45.1)	171 (43.2)	93 (48.9)
Vigorous	107 (18.3)	63 (15.9)	44 (23.2)
CSI score, mean (S.D.)	15.6 (10.3)	17.4 (10.3)	11.8 (9.2)

Cold hypersensitivity includes all participants with mild symptoms. S.D. means standard deviation.
*Physical activity intensity was classified into light, moderate, and vigorous categories, with overlap allowed.

Table 2. Adjusted multinomial logistic regression analysis of cold hypersensitivity severity (n = 586)

Cold hypersensitivity (ref: negative)	n	AOR (95% CI) for CSI score (per 10-point increase)	p value
Mild	243	1.70 (1.35–2.15)	< 0.01
Moderate	137	2.35 (1.78–3.09)	< 0.01
Severe	16	4.33 (2.29–8.19)*	< 0.01

Adjusted for age (60s, 70s, ≥ 80 years), sex, smoking status, alcohol consumption, and physical activity. Physical activity was categorized into mutually exclusive intensity groups (vigorous, moderate, and light activity [including none]). Estimates for severe cold hypersensitivity should be interpreted with caution because of the small sample size.

Primary analysis

In multinomial logistic regression analyses (Table 2), higher CSI total scores were significantly associated with increasing severity of cold hypersensitivity. In the multivariable-adjusted model, each 10-point increase in CSI score was associated with higher odds of mild cold hypersensitivity (AOR 1.70, 95% CI 1.35–2.15), moderate cold hypersensitivity (AOR 2.35, 95% CI 1.78–3.09), and severe cold hypersensitivity (AOR 4.33, 95% CI 2.29–8.19), compared with participants without cold hypersensitivity. A monotonic increase in effect size was observed across severity categories, indicating a graded association between central sensitization symptom burden and cold hypersensitivity severity. Estimates for severe cold hypersensitivity should be interpreted with caution because of the small number of participants in this category (n = 16).

Exploratory analysis

To further characterize symptom-specific associations, logistic regression analyses were performed using individual CSI items as exposures (Table 3). Several items showed significant associations with cold hypersensitivity in crude and adjusted models. After controlling for multiple comparisons using the false discovery rate procedure, low energy (AOR 2.01, 95% CI 1.54–2.63), jaw pain (AOR 1.91, 95% CI 1.17–3.14), and headaches (AOR 1.88, 95% CI 1.36–2.60) remained statistically significant. These item-level findings should be interpreted as exploratory.

Table 3. Association between each CSI item and cold hypersensitivity (n = 586)

	Cold hypersensitivity				
	Model 1 (crude)		Model 2 (adjusted)		FDR-adjusted
	OR (95% CI)	p value	AOR (95% CI)	p value	q value
Unrefreshed sleep	1.24 (1.04-1.49)	0.02	1.36 (1.12-1.66)	<0.01	<0.01
Muscle stiffness and aches	1.50 (1.24-1.82)	<0.01	1.50 (1.23-1.84)	<0.01	<0.01
Anxiety attacks	1.37 (0.91-2.06)	0.14	1.36 (0.89-2.10)	0.16	0.17
Teeth grinding/clenching	1.57 (1.24-2.00)	<0.01	1.61 (1.26-2.07)	<0.01	<0.01
Bowel issues	1.35 (1.12-1.62)	<0.01	1.42 (1.17-1.73)	<0.01	<0.01
Difficulty with daily activities	1.32 (0.81-2.16)	0.27	1.22 (0.74-2.01)	0.43	0.43
Light sensitivity	1.40 (1.12-1.74)	<0.01	1.36 (1.08-1.70)	0.01	0.01
Physical fatigue	1.62 (1.31-1.99)	<0.01	1.62 (1.31-2.01)	<0.01	<0.01
Widespread pain	1.54 (1.19-1.99)	<0.01	1.49 (1.14-1.94)	<0.01	<0.01
Headaches	1.91 (1.39-2.63)	<0.01	1.88 (1.36-2.60)	<0.01	<0.01
Bladder discomfort or burning	1.15 (0.91-1.46)	0.25	1.30 (1.01-1.68)	0.04	0.05
Poor sleep quality	1.36 (1.14-1.63)	<0.01	1.39 (1.16-1.67)	<0.01	<0.01
Concentration difficulty	1.39 (1.11-1.75)	<0.01	1.41 (1.11-1.77)	<0.01	<0.01
Skin issues	1.28 (1.07-1.53)	<0.01	1.32 (1.10-1.58)	<0.01	<0.01
Symptoms worsening with stress	1.52 (1.15-2.02)	<0.01	1.53 (1.14-2.06)	<0.01	<0.01
Depressed mood	1.29 (1.01-1.63)	0.04	1.34 (1.04-1.72)	0.02	0.03
Low energy	1.94 (1.50-2.51)	<0.01	2.01 (1.54-2.63)	<0.01	<0.01
Neck and shoulder tension	1.68 (1.38-2.05)	<0.01	1.60 (1.31-1.97)	<0.01	<0.01
Jaw pain	2.02 (1.23-3.33)	<0.01	1.91 (1.17-3.14)	<0.01	<0.01
Sensitivity to smells	1.53 (1.16-2.03)	<0.01	1.46 (1.09-1.95)	0.01	0.01
Frequent urination	1.12 (0.96-1.31)	0.16	1.23 (1.04-1.46)	0.02	0.02
Restless legs at night	1.30 (1.01-1.67)	0.04	1.33 (1.02-1.74)	0.04	0.04
Memory difficulty	1.40 (1.13-1.75)	<0.01	1.49 (1.19-1.87)	<0.01	<0.01
Childhood trauma	1.58 (1.08-2.31)	0.02	1.72 (1.16-2.56)	<0.01	<0.01
Pelvic pain	1.44 (1.15-1.79)	<0.01	1.41 (1.12-1.76)	<0.01	<0.01

Model 2: Adjusted for age (60s, 70s, ≥ 80 years), sex, smoking status, alcohol consumption, and physical activity categorized into mutually exclusive intensity groups (vigorous, moderate, and light activity [including none]). The q values were calculated using the Benjamini–Hochberg false discovery rate (FDR) procedure based on the p values from Model 2.

Discussion

In this cross-sectional study of community-dwelling older adults, we found that higher central sensitization symptom burden was associated with increasing severity of cold hypersensitivity. In multinomial logistic regression analyses, CSI total scores showed a graded association across severity categories, with a monotonic increase in adjusted odds ratios from mild to severe cold hypersensitivity. These findings suggest that central sensitization symptoms may be systematically related to the clinical spectrum of cold hypersensitivity.

The present results extend prior research in several important ways. Cold hypersensitivity has traditionally been regarded as a culturally specific phenomenon, particularly in East Asian contexts such as Japan and Korea[1,2,4,22], and has often been attributed to peripheral circulatory dysfunction or constitutional traits[5]. However, the graded association observed in this study suggests that cold hypersensitivity may also reflect broader neurophysiological mechanisms involving central nervous system sensitization[8,12]. This interpretation is consistent with previous studies linking central sensitization to chronic pain conditions, fibromyalgia, chronic fatigue syndrome, and somatic symptom disorders[3,12,23]. Our findings therefore support the possibility that cold hypersensitivity may share underlying mechanisms with central sensitivity syndromes[3,12].

Importantly, the association between CSI scores and cold hypersensitivity persisted after adjustment for age, sex, smoking status, alcohol consumption, and physical activity. Although cold hypersensitivity was more prevalent among women[1,2,4,22], the observed relationship was not fully explained by sex differences. This suggests that central sensitization may contribute to cold hypersensitivity beyond demographic and lifestyle-related factors. Prior research has also demonstrated associations between central sensitization and smoking[11,29], as well as depression and anxiety[9], further supporting the multifactorial nature of central sensitization–related symptom clusters.

In exploratory item-level analyses, several CSI symptoms—including low energy, jaw pain, and headaches—remained significantly associated after correction for multiple comparisons. Low energy and headaches are commonly reported features of central sensitization syndromes[3,12,23], while jaw pain is frequently linked to temporomandibular disorders, another condition in which central sensitization has been implicated[12]. These overlapping symptom domains further support the view that cold hypersensitivity may be situated within a broader central sensitivity spectrum[3]. Nevertheless, these item-level findings should be interpreted cautiously, as they were exploratory in nature.

Several mechanisms may underlie the observed associations. First, amplification of sensory processing within the central nervous system may enhance the perception of cold stimuli, even in the absence of objectively low temperatures[8,24]. Second, autonomic nervous system dysregulation may contribute to altered thermoregulation and co-occurring symptoms such as fatigue and headaches[25,26]. Third, hormonal and sex-related biological factors may modulate pain processing and vascular responses, potentially influencing both central sensitization and cold hypersensitivity[27,28]. These hypotheses warrant further investigation in longitudinal and mechanistic studies.

The relatively high prevalence of cold hypersensitivity in this population (67.6%) should be interpreted in light of the questionnaire cutoff (≥ 20), which was designed to capture mild symptoms in community settings[6]. In older adults, heightened somatic awareness and symptom reporting may also contribute to higher observed prevalence. Because the prevalence of the outcome was high, odds ratios may overestimate the magnitude of association compared with prevalence ratios.

Several limitations should be acknowledged. First, the cross-sectional design precludes conclusions regarding temporal direction or causality. Whether central sensitization predisposes individuals to cold hypersensitivity, or whether persistent cold hypersensitivity contributes to central sensitization over time, remains unclear. Second, both constructs were assessed using self-report questionnaires[6,18,19], which may be subject to reporting bias. Objective physiological measures such as skin temperature, peripheral blood flow, or autonomic markers were not available. Third, we did not adjust for potential confounders such as body mass index, chronic medical conditions, anemia, sleep disturbance, or depressive and anxiety symptoms[9], and residual confounding cannot be excluded. Finally, the study population consisted of urban, community-dwelling older adults in Japan, which may limit generalizability to other age groups or cultural contexts.

From a clinical perspective, these findings suggest that older adults who report cold hypersensitivity may also experience a higher burden of central sensitization–related symptoms. While causal inferences cannot be drawn, clinicians may consider assessing broader symptom patterns when encountering patients with persistent cold hypersensitivity.

In conclusion, this study demonstrated a graded association between central sensitization symptoms and cold hypersensitivity severity in community-dwelling older adults. The findings support the view that cold hypersensitivity may not be solely a peripheral or culturally specific phenomenon[5], but may also reflect neurophysiological processes related to central sensitization[8,12]. Future longitudinal studies are needed to clarify temporal relationships and to determine whether interventions targeting central sensitization–related mechanisms may influence cold hypersensitivity.

Declarations

Acknowledgements

We thank the individuals who participated in this study.

Funding

This work was supported by the Health and Labour Sciences Research Grant (Grant No. 23FC105) from the Ministry of Health, Labour and Welfare, Japan, titled “Multicentre integrated epidemiological study aiming to elucidate the role of central sensitization in intractable diseases with various symptoms and to promote quality of life and public awareness.”

Declaration of conflicting interests

The authors declare that they have no conflicts of interest.

Author contributions

TT: Formal analysis, Methodology, Writing – original draft. TS: Investigation, Resources, Writing –review & editing. KH: Investigation, Resources, Writing –review & editing. KI: Investigation, Writing – review & editing. SO: Data curation, Investigation, Methodology, Project administration, Resources, Validation, Writing – review & editing. HH: Investigation, Resources, Writing – review & editing. YF: Investigation, Writing – review & editing. HK: Investigation, Resources, Writing – review & editing. HS: Investigation, Resources, Writing – review & editing. MH: Conceptualization, Data curation, Funding acquisition, Project administration, Resources, Supervision, Writing – review & editing.

Data availability statement

The data underlying this article will be shared upon reasonable request from the corresponding authors.

Ethical approval

This study was approved by the Ethics Committee of the Tokyo Metropolitan Institute of Gerontology (protocol codes: R22-034). All participants provided written informed consent to participate in this study.

Clinical trial number: not applicable.

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Figures

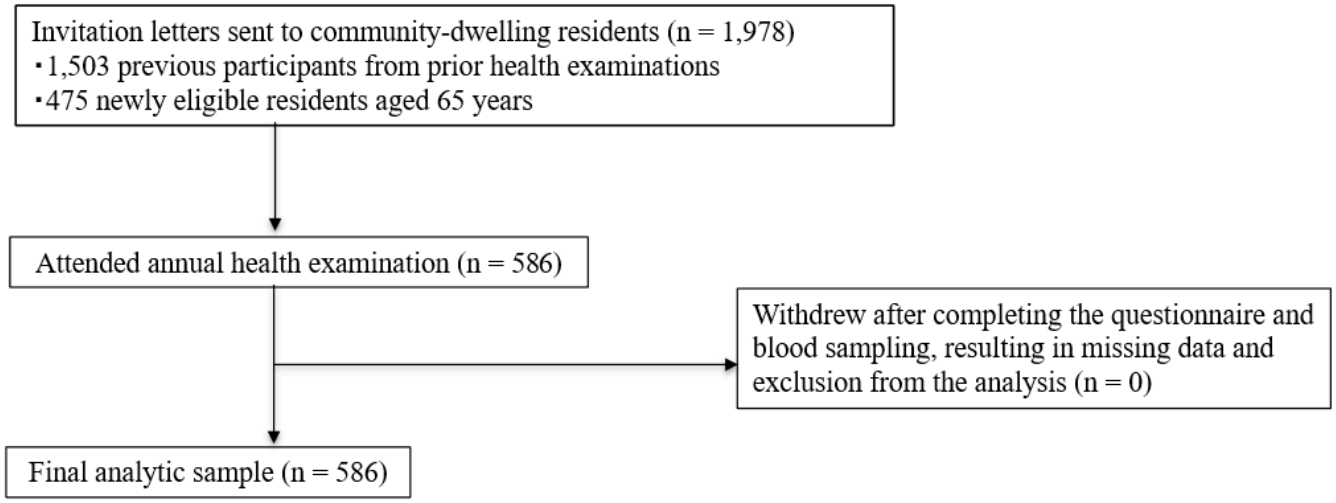


Figure 1. Flowchart of participant recruitment and inclusion in the 2024 Otassha Study

Figure 1

See image above for figure legend.