

The U-Shaped Association Between Serum Ferritin Levels and Frailty Risk in Older Adults: A Nationwide Population-Based Study

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Abstract

Background: Ferritin, a key iron storage protein in the body, acts as an essential indicator of iron metabolism and is involved in various health conditions beyond hematologic disorders. Clinical evidence suggests that both elevated and reduced blood ferritin levels correlate with adverse health outcomes.

Objective: To elucidate the role of circulating ferritin as a potential biomarker for frailty, which reflects overall health status and biological age, we investigated the association between serum ferritin concentrations and the frailty index (FI) in a community-dwelling older adults.

Methods: We performed a population-based, cross-sectional analysis using data from the Korea National Health and Nutrition Examination Survey. The study included 6,722 participants aged 65 years and older. A deficit accumulation FI was developed using 36 items covering physical, cognitive, psychological, and social domains. Based on the FI, participants were classified as non-frail (FI \leq 0.15), pre-frail (0.15 < FI \leq 0.25), or frail (FI > 0.25). Serum ferritin levels were measured using an immunoradiometric assay.

Results: When participants were divided into four groups according to serum ferritin concentration quartiles, the FI in both women and men exhibited a U-shaped curve, with the lowest values occurring in the third quartile (Q3). Consequently, differences in FI among the groups were analyzed using Q3 as the reference. In women, the FI was significantly higher in both the lowest quartile (Q1) and the highest quartile (Q4) compared to Q3 ($P < 0.001$ and 0.001 , respectively). Consistently, women in Q1 and Q4 had significantly higher odds ratios for frailty compared to those in Q3, at 2.03 and 1.35 times, respectively ($P < 0.001$ and 0.049 , respectively). Although a similar trend was noted in men, the association between serum ferritin levels and frailty was not as statistically significant as in women.

Conclusions: Our study identified a U-shaped association between serum ferritin concentrations and the FI in a nationally representative cohort. Both low and high ferritin concentrations were associated with an increased risk of frailty, with this relationship being more pronounced in women than in men. This pioneering investigation underscores the potential of serum ferritin, which is widely used in clinical practice, as a predictive biomarker for frailty in older adults.

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Abstract

Background: Ferritin, a key iron storage protein in the body, acts as an essential indicator of iron metabolism and is involved in various health conditions beyond hematologic disorders. Clinical evidence suggests that both elevated and reduced blood ferritin levels correlate with adverse health outcomes. To elucidate the role of circulating ferritin as a potential biomarker for frailty, which reflects overall health status and biological age, we investigated the association between serum ferritin concentrations and the frailty index (FI) in a community-dwelling older adults.

Methods: We performed a population-based, cross-sectional analysis using data from the Korea National Health and Nutrition Examination Survey. The study included 6,722 participants aged 65 years and older. A deficit accumulation FI was developed using 36 items covering physical, cognitive, psychological, and social domains. Based on the FI, participants were classified as non-frail ($FI \leq 0.15$), pre-frail ($0.15 < FI \leq 0.25$), or frail ($FI > 0.25$). Serum ferritin levels were measured using an immunoradiometric assay.

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Conclusion: Our study identified a U-shaped association between serum ferritin concentrations and the FI in a nationally representative cohort. Both low and high ferritin concentrations were associated with an increased risk of frailty, with this relationship being more pronounced in women than in men. This pioneering investigation underscores the potential of serum ferritin, which is widely used in clinical practice, as a predictive biomarker for frailty in older adults.

Keywords: ferritin, frailty index, systemic inflammation, oxidative stress, biomarker

Introduction

Frailty in older adults is a significant geriatric syndrome marked by increased vulnerability to various stressors due to diminished physiological capacity, more accurately reflecting an individual's overall well-being and functional ability than chronological age [1, 2]. The clinical importance of frailty is underscored by its link to adverse health outcomes such as disability, falls, and mortality, necessitating robust assessment tools [2, 3]. While no definitive criterion exists, the "phenotypic frailty" or Fried criteria, focusing mainly on physical aspects, are widely used for their simplicity [4]. However, the "frailty index" developed by Rockwood et al. [5, 6], which includes a broad range of deficits such as social, psychological, and cognitive factors, is regarded as a more comprehensive and superior predictor of key outcomes like hospitalization and death [7, 8]. Recent longitudinal studies have highlighted the frailty index as the most reliable indicator of biological age [9], advocating for its priority use in frailty clinical research. This approach not only enhances the accuracy of frailty assessment but also supports the development of reliable biomarkers, thereby driving advancements in frailty research and promoting more effective interventions to improve quality of life and extend healthy living among the elderly.

Ferritin, a key iron storage protein in the body, serves as a crucial biomarker for iron metabolism and is implicated in a variety of health conditions beyond hematologic disorders.

Elevated circulating ferritin level, indicative of iron overload, increase oxidative stress, leading to tissue damage [10]. Moreover, blood ferritin concentration is recognized as an inflammation marker [11, 12], showing positive correlations with various chronic diseases, including cardiovascular diseases, diabetes, non-alcoholic fatty liver disease, and neurodegenerative disorders [13-16]. Conversely, low ferritin levels can signal poor health due to nutritional deficiencies, including iron deficiency, reduced energy levels, and compromised immune function [17-19]. Given its broad impact on these diverse health issues, ferritin levels provide significant insights into an individual's overall health status. Consequently, ferritin may serve as a valuable blood biomarker for frailty, reflecting physical, social, and mental conditions as well as biological age. Despite this potential, clinical research on the relationship between circulating ferritin concentration and frailty risk remains limited. To address this gap, we aimed to determine the association between serum ferritin concentration and the Rockwood frailty index in a nationally representative sample of community-dwelling older adults.

Methods

Study Population

This cross-sectional study utilized data from the Korea National Health and Nutrition Examination Survey (KNHANES) collected between 2008 and 2012. Since 1998, KNHANES has been conducted regularly to evaluate the health and nutritional status of the Korean population, track health risk factors and chronic disease prevalence, and support health policy and program development in Korea [20]. KNHANES employs a complex, multi-stage probability sampling method to represent the entire non-institutionalized population of Korea. The annual survey employs a three-stage sampling design: initially, primary sample units (PSUs) consisting of 50 to 60 households are selected from census blocks or resident registration addresses. Subsequently, 20-25 households are chosen from each PSU via field surveys. Finally, all individuals aged 1 year and older in the selected households

are surveyed. During the study period, 8,036 individuals aged 65 and older participated in KNHANES. Our analysis included 6,722 participants, after excluding 194 individuals with over 20% missing data on frailty assessment variables and 1,120 individuals lacking ferritin data. (Figure 1). All participants provided informed consent before participating in KNHANES, and personal data were anonymized prior to public release. The study was approved by the Institutional Review Board of Chonnam National University Bitgoeul Hospital, which waived the requirement for additional informed consent (IRB No. CNUBH-2024-013). The study adhered to the Declaration of Helsinki principles.

Serum Ferritin Concentration Measurement

Blood samples for serum ferritin measurement were collected from participants aged 10 and older with their consent. After a minimum 8-hour overnight fast, blood samples were drawn from the antecubital vein in the morning. Samples were refrigerated immediately and transported to the Central Testing Institute (Neodin Medical, Inc., Seoul, Korea). The serum ferritin level was determined using an immunoradiometric assay with a 1470 WIZARD gamma-Counter (PerkinElmer, Turku, Finland). The coefficient of variation value was less than 5%.

Frailty-Related Factors Evaluation

Trained nurses measured blood pressure on the right arm using a mercury sphygmomanometer (Baumanometer® Wall Unit 33(0850); W.A. Baum, Copiague, NY, USA) after participants had been seated quietly for at least 5 minutes. Blood pressure was measured three times, and the second and third measurements were averaged. Blood samples were also collected during the survey. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared (kg/m^2). Education level and lifestyle factors were self-reported. Education level was categorized as elementary school or lower, middle school, high school, and college or higher. Smokers were defined

as those who had smoked five or more packs of cigarettes in their lifetime and were currently smoking. Medical conditions were classified based on doctor diagnoses.

Frailty Index

The frailty index was constructed using standard procedures [21] and previous KNHANES-based indices [22, 23]. The index, ranging from 0 (best condition) to 1 (worst condition), comprised 36 items surveyed between 2008 and 2012. These items covered comorbidities (e.g., arthritis, asthma, cancer, cardiovascular disease, diabetes, dyslipidemia, hypertension, stroke), functional abilities (e.g., inactivity, limited exercise capacity, daily living limitations, social activity limitations, self-care inability, chewing difficulty), symptoms (e.g., pain, fatigue, dyspnea, weight loss, depression, anxiety, suicidal ideation, stress), and laboratory values (e.g., blood pressure, heart rate, pulmonary function, BUN, creatinine, cholesterol, triglycerides, HDL cholesterol, fasting glucose, vitamin D, urine protein), as well as smoking status and BMI. (Supplementary Table 1). Participants were classified into non-frail (≤ 0.15), pre-frail (0.15-0.25), and frail (> 0.25) categories based on established criteria [24, 25].

Statistical Analysis

To derive national-level estimates, we employed a complex sample analysis method incorporating assigned weights. The data from annual surveys were pooled, with each year's sample analyzed independently. Results are presented as means with standard errors (SEs) for continuous variables, or as counts with percentages for categorical variables. General linear models were used to compare continuous variables, while categorical variables were analyzed using cross-tabulation methods. Potential confounding factors included age, sex, education, smoking status, diabetes, dyslipidemia, cardiovascular diseases, and BMI. We assessed differences in serum ferritin levels across frailty statuses and variations in the frailty index among serum ferritin quartiles using general linear models.

The relationship between serum ferritin levels and the Rockwood frailty index was examined using linear regression analysis. Multiple logistic regression was utilized to evaluate the risk of frailty across serum ferritin quartiles. A threshold of $P < 0.05$ was set for statistical significance, and all analyses were performed using SPSS software, version 21.0 (IBM Corporation, Armonk, NY, USA).

Results

Baseline Characteristics of Study Participants

Table 1 summarizes the baseline characteristics of 6,722 participants aged 65 years and older. Among the women, 848 (22.0%) were classified as non-frail, 1,441 (37.3%) as pre-frail, and 1,570 (40.7%) as frail, with mean ages of 71.9, 72.1, and 73.0 years, respectively ($P < 0.001$). Among the men, 1,127 (39.4%) were categorized as non-frail, 1,079 (37.7%) as pre-frail, and 657 (22.9%) as frail, with mean ages of 71.0, 71.7, and 72.5 years, respectively ($P < 0.001$). In both men and women, transitioning from non-frail to pre-frail and frail groups was associated with lower levels of education, higher rates of smoking, and increased prevalence of diabetes, dyslipidemia, and cardiovascular diseases (all $P < 0.001$). Additionally, BMI was observed to increase across these groups ($P < 0.001$ in women and $P = 0.006$ in men).

Serum Ferritin Concentrations and Frailty Status

Serum ferritin concentrations by frailty status were analyzed using a general linear model within a complex sample analysis framework (Figure 2). In both women and men, no significant differences in serum ferritin concentrations were observed among the non-frail, pre-frail, and frail groups, irrespective of whether adjustments for confounding variables were made before or after the analysis.

Association Between Serum Ferritin Levels and Frailty Index

Linear regression analyses were conducted to determine the independent relationship between serum

ferritin levels and the Rockwood frailty index (Table 2). In women, higher serum ferritin levels were consistently correlated with a higher frailty index, both before and after adjusting for potential confounders, including age, educational level, smoking status, diabetes, dyslipidemia, cardiovascular diseases, and BMI ($P = 0.005$ to 0.018). However, in men, no statistically significant association between serum ferritin concentration and the frailty index was observed, regardless of the adjustment model used.

Threshold Effect of Serum Ferritin on Frailty Risk

To determine whether there was a threshold effect between serum ferritin concentration and frailty, participants were categorized into four groups according to serum ferritin concentration quartiles (Figure 3). The frailty index in both women and men demonstrated a U-shaped curve, with the lowest values observed in the third quartile (Q3). Therefore, the differences in frailty index among the groups were analyzed using Q3 as the reference. In women, the frailty index was significantly higher in both the lowest quartile (Q1, serum ferritin ≤ 36 ng/mL) and the highest quartile (Q4, serum ferritin > 90 ng/mL) compared to Q3 ($59 < \text{serum ferritin} \leq 90$ ng/mL), regardless of adjustments for confounding variables ($P < 0.001$ to 0.002). In men, the frailty index was initially higher in Q1 (serum ferritin ≤ 52 ng/mL) and Q4 (serum ferritin > 153 ng/mL) compared to Q3 ($89 < \text{serum ferritin} \leq 153$ ng/mL) in the unadjusted model ($P = 0.040$ and 0.030 , respectively). However, after adjusting for potential confounders such as age and BMI, the statistical significance for Q4 disappeared, and a significant increase in frailty index was observed only in the Q1 group ($P = 0.041$).

The risk of frailty according to serum ferritin quartile groups was assessed using logistic regression analyses (Figure 4). In women, compared to Q3 in the unadjusted model, Q1 and Q4 showed significantly higher odds ratios for frailty, at 1.83 and 1.50 times, respectively ($P < 0.001$ and 0.006 , respectively). This statistical significance persisted even after multivariable adjustment

for various confounding variables ($P < 0.001$ and 0.049 , respectively). In men, the unadjusted model also showed 1.39-fold and 1.41-fold higher odds ratios for frailty in Q1 and Q4 compared to Q3 (both $P = 0.042$). However, after adjusting for variables such as age and BMI, no significant differences were observed among the four quartile groups.

Discussion

Circulating ferritin, a marker traditionally used to assess iron storage, has been increasingly linked to various disease states, especially in geriatric populations. This large-scale study, involving community-dwelling older adults aged 65 and above, reveals a U-shaped relationship between serum ferritin concentrations and the frailty index in women. Specifically, women in the lowest and highest serum ferritin quartiles exhibited a significantly higher risk of frailty. Although a similar trend was observed in men, the association between serum ferritin levels and frailty attenuated after adjusting for confounding variables. This pioneering investigation into the general population underscores the potential of serum ferritin, which is widely used in clinical practice, as a predictive biomarker for frailty in older adults.

Both the phenotype model and the cumulative deficit model are utilized to define frailty [2]; however, the Rockwood frailty index, which offers a thorough evaluation of an individual's health status and is expressed as a continuous variable, demonstrates superior sensitivity in detecting changes in the health status of older adults and predicting health outcomes compared to the dichotomous classification of the Fried criteria based on five physical criteria [4-6]. This index not only captures a wide array of health deficits but also incorporates their cumulative impact, offering a more holistic view of a person's health condition [4-8]. The KNHANES provides an extensive dataset required to calculate the Rockwood frailty index. This comprehensive data, collected with high reliability and representing the national population, includes detailed information on various health parameters, lifestyle factors, and clinical measures [20]. Consequently, KNHANES is

uniquely positioned as an optimal cohort for conducting frailty research, leveraging big data to enhance the precision and applicability of health assessments in geriatric populations.

Frailty, marked by muscle weakness, decreased energy, lower levels of physical activity, and reduced resilience, is gaining recognition as a critical clinical issue in rapidly aging societies [1]. As a result, there is growing interest in discovering potential biomarkers for the early identification of those at high risk of developing frailty [26]. Although numerous clinical studies have explored the association between circulating ferritin levels and various chronic diseases that may predispose individuals to frailty, research directly examining its impact on frailty itself remains limited. Our literature review identified only two studies addressing the connection between blood ferritin and frailty; however, these studies utilized the Edmonton Frailty Scale [27] and the Fried criteria [28], respectively, which may not comprehensively capture the broad spectrum of frailty, including overall health and functional capacity. To address this gap, our study is the first to leverage extensive national datasets, generating a comprehensive frailty index that encompasses medical, functional, and psychosocial deficits related to aging to explore the link between ferritin and frailty. This approach provides robust clinical evidence supporting the potential role of ferritin as a biomarker for frailty development.

High serum ferritin, indicative of iron overload, contributes to the development of frailty through multiple, intertwined pathophysiological mechanisms. Firstly, iron overload can catalyze the formation of reactive oxygen species (ROS), leading to oxidative stress and cellular damage, particularly affecting mitochondrial function [10]. This oxidative stress accelerates cellular aging and impairs muscle function, contributing to sarcopenia—a key component of frailty [29]. Additionally, excess iron can cause chronic inflammation by activating pro-inflammatory pathways [11, 12], which further exacerbates muscle wasting and reduces physical resilience. Iron-induced inflammation can also impair the immune response [12], increasing susceptibility to infections and reducing overall physiological robustness. Moreover, iron deposits in organs such as the heart and

liver can lead to organ dysfunction [30, 31], thereby compromising the body's ability to respond to stressors. Finally, iron overload may disrupt endocrine functions, particularly those regulating metabolism and muscle maintenance, thus exacerbating physical decline [30, 32]. Collectively, these processes undermine the physiological reserves and adaptability of elderly individuals, promoting the onset and progression of frailty.

On the other hand, low serum ferritin levels, indicative of iron deficiency, are also associated with an increased risk of frailty through distinct but equally impactful mechanisms. Iron is crucial for various physiological functions, including oxygen transport, DNA synthesis, and mitochondrial energy production [33]. Iron deficiency leads to anemia, resulting in reduced oxygen delivery to tissues and diminished physical endurance [19], which can contribute to muscle weakness and fatigue—core components of frailty. Furthermore, insufficient iron impairs mitochondrial function and reduces ATP production [34], leading to decreased muscle strength and physical performance. Iron is also essential for proper immune function; deficiency can lead to compromised immunity, increasing vulnerability to infections and further exacerbating frailty [17]. Additionally, iron plays a role in neurotransmitter synthesis and cognitive function, and deficiency may contribute to cognitive decline and reduced coordination [35], both of which are critical in maintaining physical independence. Therefore, both iron overload and deficiency disrupt key physiological processes, each promoting frailty through different but interrelated pathways.

The particularly interesting findings of our study including women and men aged 65 years and older, the U-shaped association between blood ferritin concentration and frailty was more pronounced in women than in men, likely due to gender-specific physiological and biological factors. Postmenopausal women, who constituted a significant portion of our female cohort, experience changes in iron metabolism that can lead to increased iron accumulation, heightening the risk of iron overload [36]. Conversely, women are also more prone to iron deficiency due to a history of lower baseline iron stores and higher lifetime iron demands. Additionally, the loss of estrogen's protective

effects post-menopause can exacerbate oxidative stress and inflammation [37], which are key contributors to frailty. Women also tend to have a higher prevalence of conditions like osteoporosis and sarcopenia [38], which can be worsened by both iron deficiency and overload, thereby increasing their vulnerability to frailty. Social and behavioral factors, including differences in diet and health-seeking behavior, may further influence iron status [39] and its impact on frailty more significantly in women. Thus, these combined factors likely explain the more pronounced U-shaped association between blood ferritin levels and frailty observed in women in our study.

Our study's primary strength is the use of complex sample analysis methods with weighted adjustments, which allows for the estimation of national-level statistics, thereby enhancing the generalizability of our findings. Moreover, the large sample size enabled us to adjust for various confounding factors, increasing the statistical rigor of our results. However, there are several limitations to consider when interpreting our data. A major limitation is the cross-sectional design, which does not allow for establishing a causal link between serum ferritin levels and frailty. Additionally, the KNHANES dataset lacks measurements of systemic inflammation and oxidative stress, preventing us from determining if the increased frailty risk associated with high or low ferritin levels is directly due to these factors. Another limitation is the reliance on self-reported data, which may introduce recall and social desirability biases. Finally, as our study focused exclusively on a Korean population, the findings may not be applicable to other demographic groups, particularly Caucasians.

In conclusion, our study identified a U-shaped association between serum ferritin concentrations and the frailty index in a nationally representative cohort of older adults aged 65 and above. Both low and high ferritin concentrations were linked to an increased risk of frailty, with this relationship being more pronounced in women than in men. Future research is needed to investigate whether interventions aimed at maintaining ferritin concentrations within an optimal range can mitigate frailty, which reflects biological aging.

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The authors of this manuscript certify that they comply with the ethical guidelines for authorship and publishing in the *JMIR Aging*.

Conflict of Interest

Hee-Won Jung cofounded Dyphi Inc, a startup company developing sensor technologies for human movement and robotics. Min-gu Kang, Il-Young Jang, Ji Yeon Baek, Yunju Jo, Dongryeol Ryu, and Beom-Jun Kim declare that they have no conflict of interest.

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Table 1. Baseline characteristics of the study participants according to frailty status

Variables	Women (N=3,859)				Men (N=2,863)			
	Non-frail (N=848)	Pre-frail (N=1,441)	Frail (N=1,570)	P value	Non-frail (N=1,127)	Pre-frail (N=1,079)	Frail (N=657)	P value
Age (years), mean (SE)	71.9 (0.2)	72.1 (0.2)	73.0 (0.2)	<0.001	71.0 (0.2)	71.7 (0.2)	72.5 (0.2)	<0.001
Level of education, %				<0.001				<0.001
1st	80.0%	84.3%	90.0%		41.4%	47.9%	62.7%	
2nd	8.3%	7.7%	6.1%		17.3%	20.4%	15.5%	
3rd	9.0%	6.6%	3.2%		22.2%	20.6%	16.1%	
4th	2.7%	1.4%	0.7%		19.1%	11.2%	5.7%	
Smoking, n (%)	21 (2.7%)	43 (3.0%)	110 (7.6%)	<0.001	193 (18.4%)	310 (30.0%)	227 (36.8%)	<0.001
Diabetes, n (%)	70 (8.4%)	259 (19.7%)	444 (31.1%)	<0.001	137 (11.3%)	258 (24.7%)	207 (32.9%)	<0.001
Dyslipidemia, n (%)	124 (15.4%)	335 (23.4%)	453 (30.8%)	<0.001	85 (7.6%)	143 (13.4%)	120 (19.3%)	<0.001
Cardiovascular disease (MI, angina), n (%)	14 (1.4%)	66 (4.1%)	151 (9.7%)	<0.001	50 (4.0%)	84 (7.6%)	89 (13.9%)	<0.001
BMI (kg/m ²), mean (SE)	23.2 (0.1)	24.2 (0.1)	24.9 (0.1)	<0.001	23.0 (0.1)	23.4 (0.1)	23.3 (0.2)	0.006

Continuous and categorical variables were compared using general linear model and crosstabs

analyses in a complex sample analysis method, respectively. Bold numbers indicate statistically significant values. SE, standard error; BMI, body mass index.

Table 2. Multiple linear regression analysis to determine whether serum ferritin level is independently associated with frailty index

Adjustment	Dependent variable: frailty index		
	β	SE	P value
Women			
Unadjusted	0.000079	0.000030	0.009
Age and BMI	0.000070	0.000025	0.005
Multivariable	0.000059	0.000025	0.018
Men			
Unadjusted	0.000008	0.000014	0.557
Age and BMI	0.000007	0.000012	0.543
Multivariable	-0.000002	0.000008	0.817

General linear model analysis was performed with frailty index as a dependent variable, and with serum ferritin level (ng/mL) as an independent variable. Multivariable adjustment model includes age, level of education, smoking, diabetes, dyslipidemia, cardiovascular diseases, and body mass index as confounding factors. Bold numbers indicate statistically significant values. β , regression coefficient; SE, standard error; BMI, body mass index.

Legends for Figures

Figure 1. Flow diagram of the study participants.

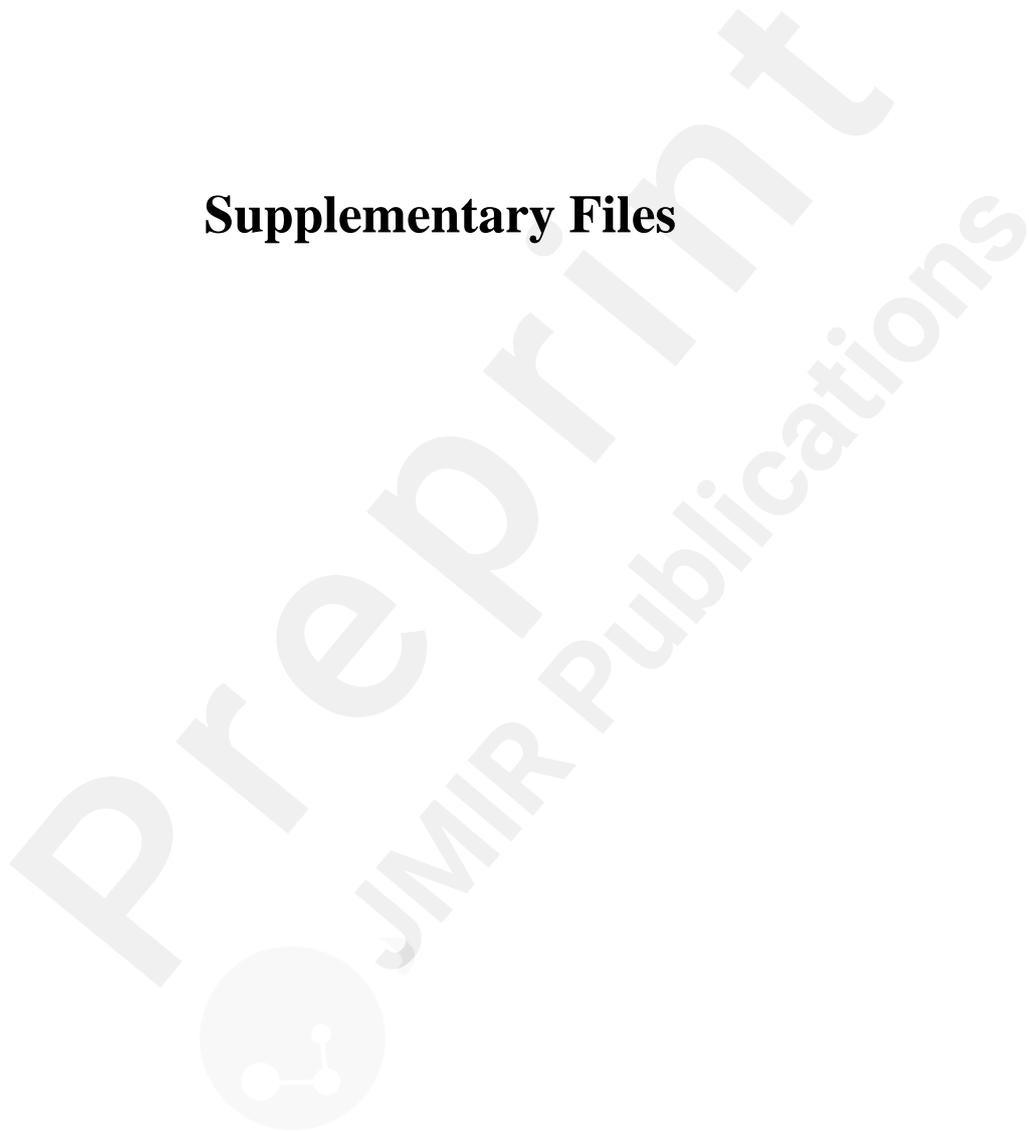
Figure 2. Differences in serum ferritin levels according to the frailty status in women (A) and men (B). The estimated means with 95% confidence intervals were generated and compared using general linear model analysis in a complex sample analysis method. Multivariable adjusted model: adjusted for age, level of education, smoking, diabetes, dyslipidemia, cardiovascular diseases, and body mass index.

Figure 3. Differences in frailty index according to serum ferritin quartiles in women (A) and men (B). The estimated means with 95% confidence intervals were generated and compared using general linear model analysis in a complex sample analysis method. Multivariable adjusted model: adjusted for age, level of education, smoking, diabetes, dyslipidemia, cardiovascular diseases, and body mass index. Asterisk indicates statistically significant difference from the Q3. Q, quartile. Ferritin quartiles in women: Q1 = serum ferritin ≤ 36 (ng/mL), Q2 = $36 < \text{serum ferritin} \leq 59$, Q3 = $59 < \text{serum ferritin} \leq 90$, Q4 = serum ferritin > 90 . Ferritin quartiles in men: Q1 = serum ferritin ≤ 52 (ng/mL), Q2 = $52 < \text{serum ferritin} \leq 89$, Q3 = $89 < \text{serum ferritin} \leq 153$, Q4 = serum ferritin > 153 .

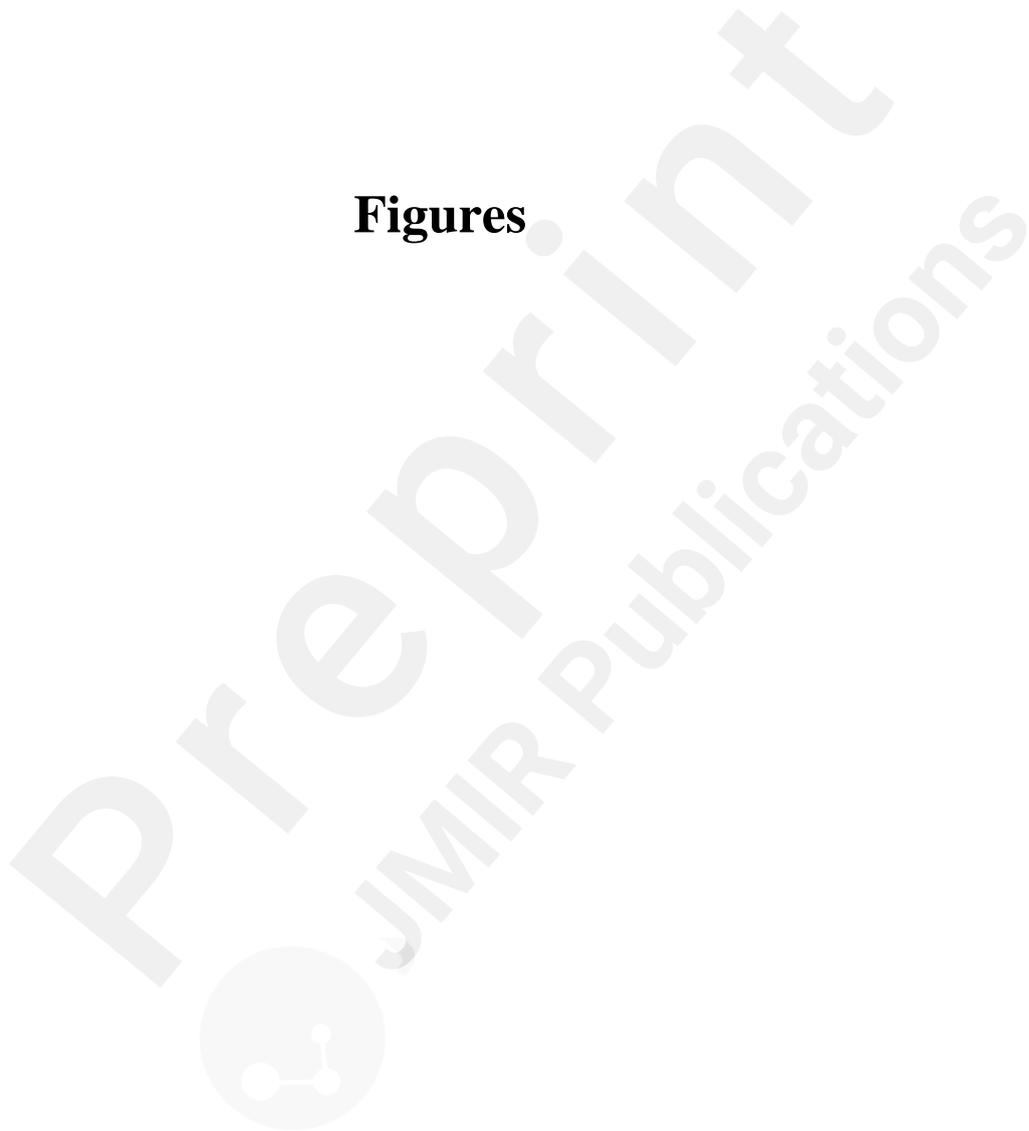
Figure 4. Logistic regression analyses to determine the odds ratios for pre-frail and frail status

according to serum ferritin quartiles in women (A) and men (B). Multivariable adjusted model: adjusted for age, level of education, smoking, diabetes, dyslipidemia, cardiovascular diseases, and body mass index. OR, odds ratio; CI, confidence interval; Q, quartile. Ferritin quartiles in women: Q1 = serum ferritin ≤ 36 (ng/mL), Q2 = $36 < \text{serum ferritin} \leq 59$, Q3 = $59 < \text{serum ferritin} \leq 90$, Q4 = serum ferritin > 90 . Ferritin quartiles in men: Q1 = serum ferritin ≤ 52 (ng/mL), Q2 = $52 < \text{serum ferritin} \leq 89$, Q3 = $89 < \text{serum ferritin} \leq 153$, Q4 = serum ferritin > 153 .

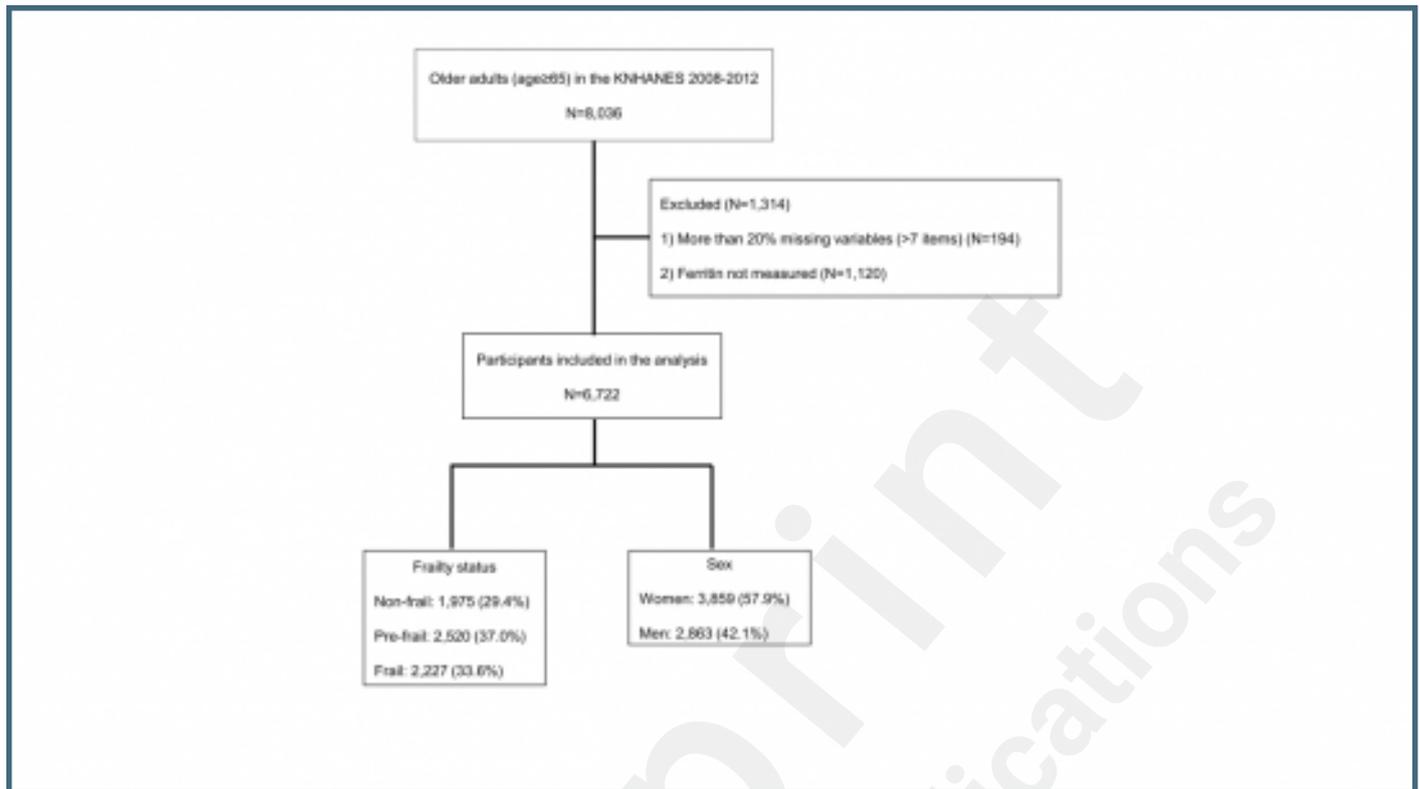
Supplementary Files



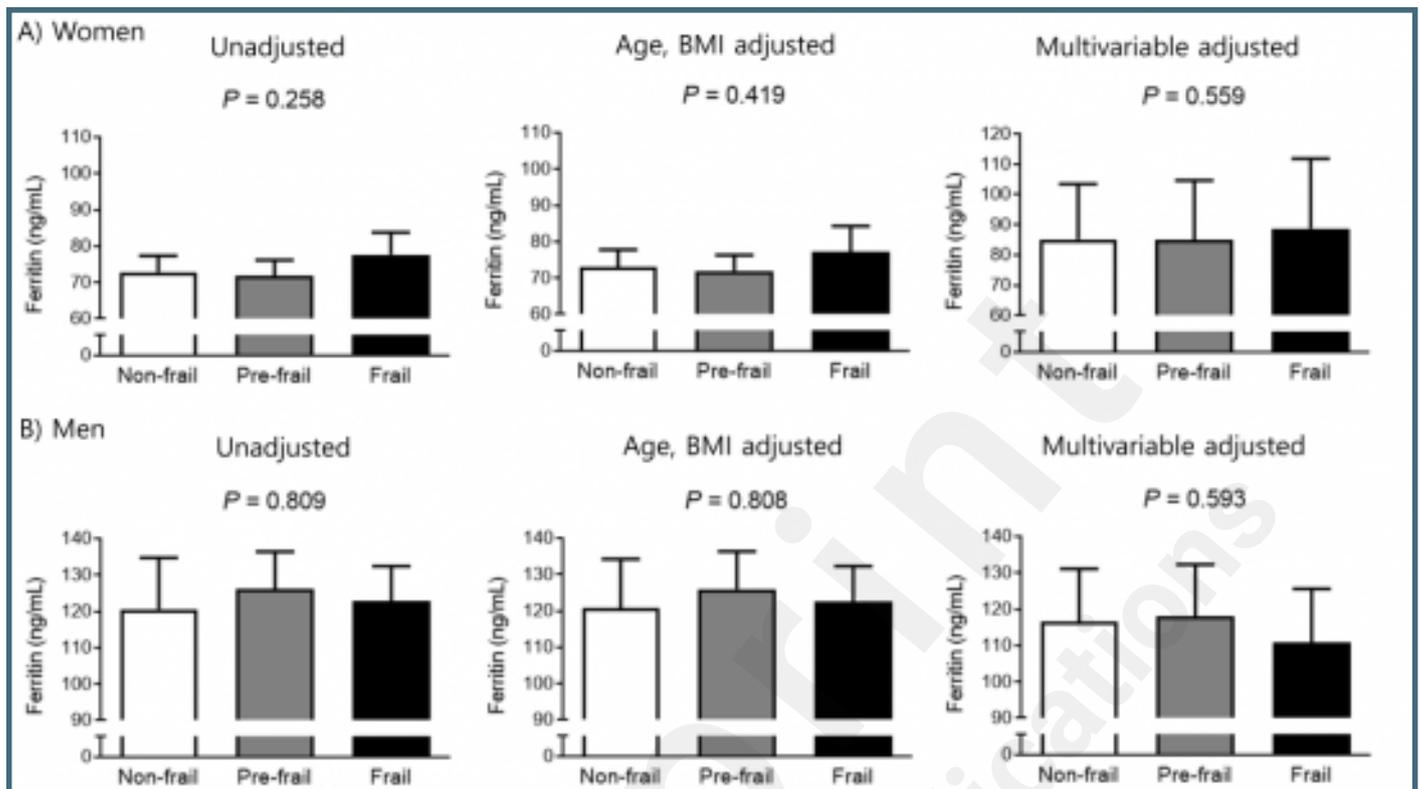
Figures



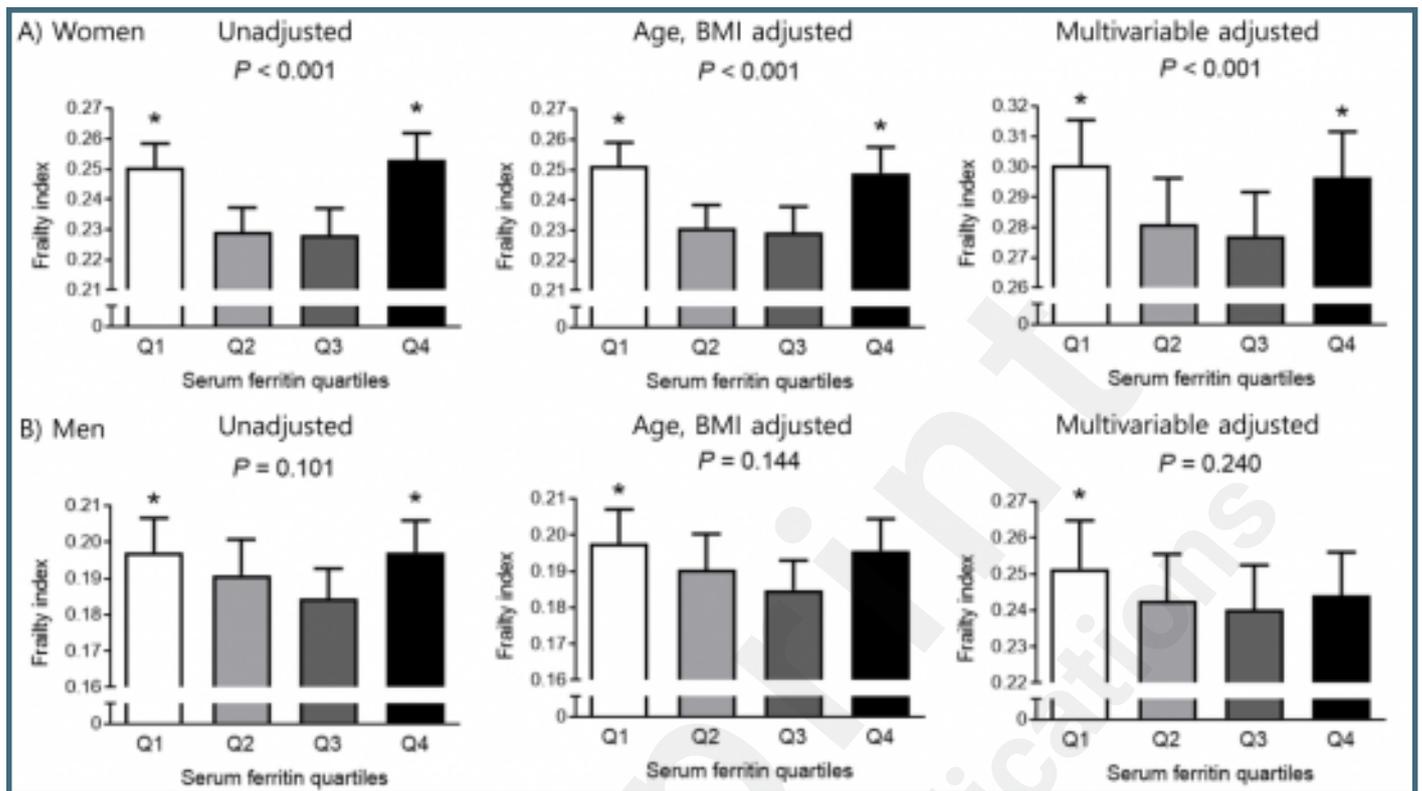
Flow diagram of the study participants.



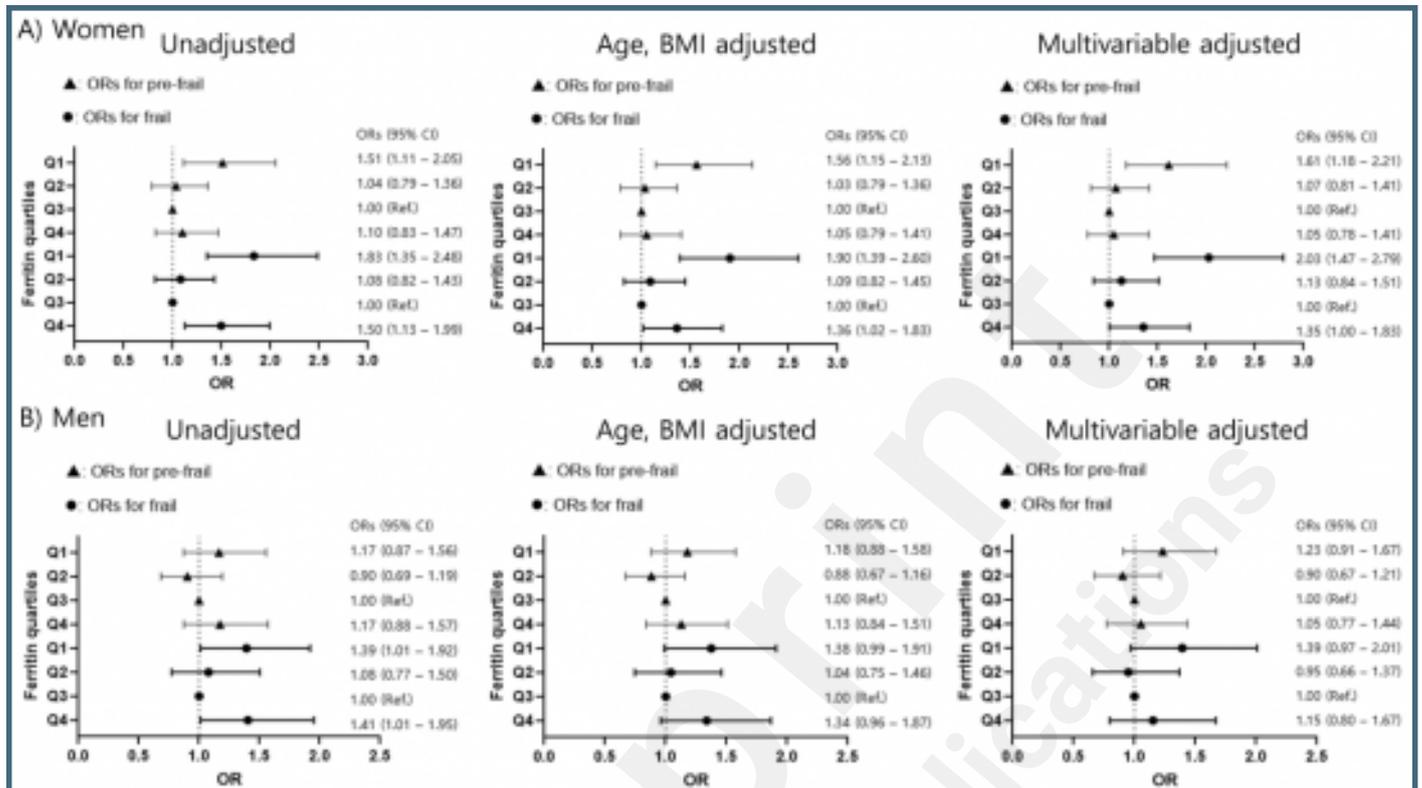
Differences in serum ferritin levels according to the frailty status in women (A) and men (B).



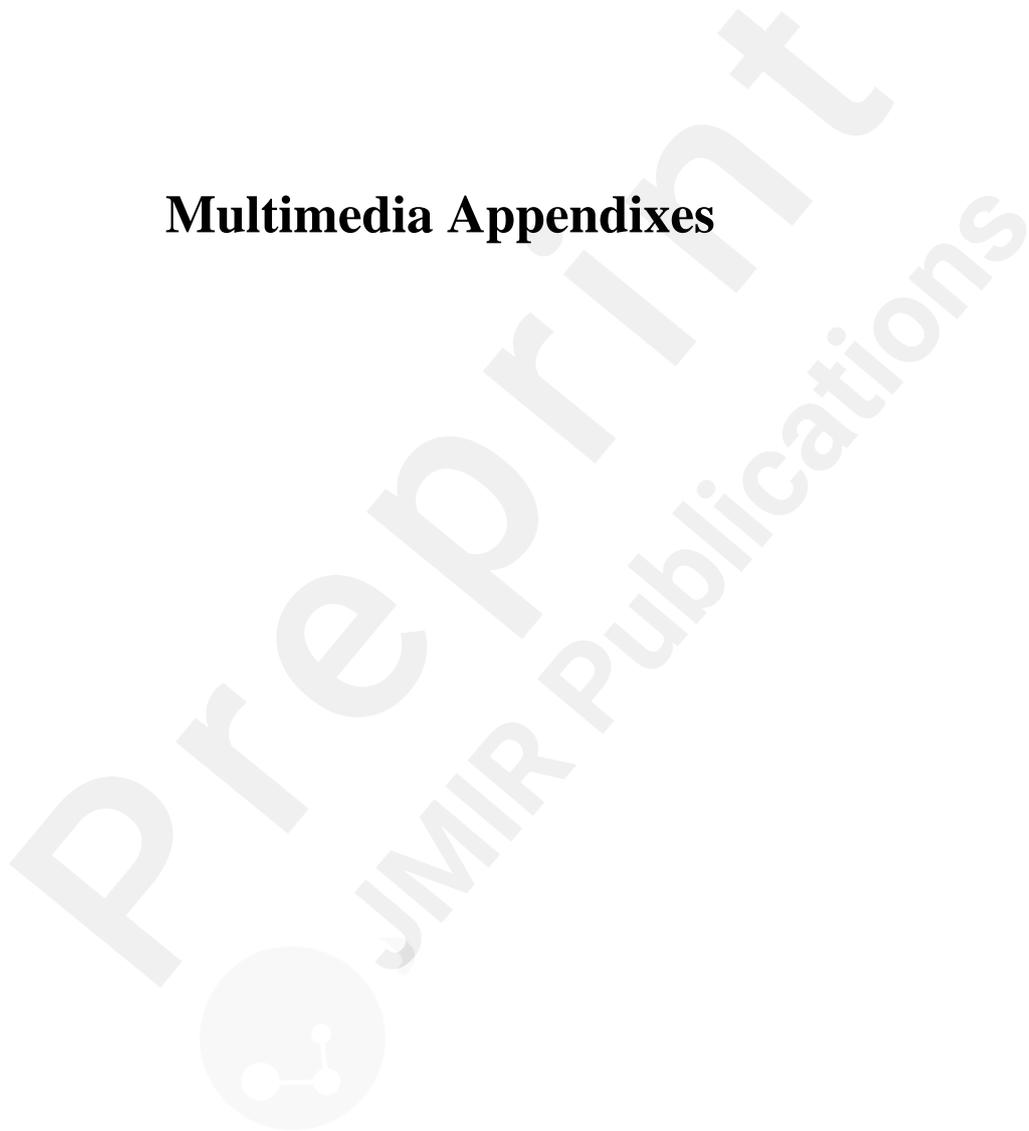
Differences in frailty index according to serum ferritin quartiles in women (A) and men (B).



Logistic regression analyses to determine the odds ratios for pre-frail and frail status according to serum ferritin quartiles in women (A) and men (B).



Multimedia Appendixes



Variables included in the frailty index.

URL: <http://asset.jmir.pub/assets/ed136b8e62c775a78e95b079e1f04f77.docx>

