Doctoral Thesis in Healthy Aging

Association of vascular risk and frailty with cognitive function in older adults: Interaction effect of social contact

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I submit this thesis as the Doctoral thesis in Healthy Aging

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Abstract

Aging population is noticeable in countries around the globe and Korea is a country with especially rapid rate of population aging. Notably, various problems need careful attention in regards to aging, because a number of problems co-occur as an individual ages. Vascular risks, frailty and cognitive decline are a few of the major problems that is being researched in regards to the elderly population. All three health states are known to worsen as a person ages, and furthermore, a number of studies have found that they are related to one another. Additionally, previous studies have shown possibilities of preventing and ameliorating each of the three conditions, thus increasing the importance of studying these issues more carefully. One way that could possibly assist in this regard is the idea of contacting acquaintances more frequently. Because the benefits of social contact in terms of health have been shown through numerous studies, this study aimed to research its benefits as well. Our aims of the study were to study the associations between vascular risks, frailty and cognitive function, and further elucidate the possibility of interaction effect of an individual's social relationships. Using the data from the Korean Frailty and Aging Cohort Study (KFACS), we analyzed associations between each of the variables of interest. Our results indicated a strong association between frailty and cognitive function, but vascular risks were not as strongly associated. Also, even though infrequent social contact was shown to relate to poor cognitive function, this was only true in some cases. Finally, we tried to study the interaction effects of social contact by including interaction terms in our

analyses, but only a few interaction terms remained statistically significant. Although not conclusive, this study does provide valuable insights for future studies, and implementing those findings in future studies could greatly improve the health of elderly population in Korea.

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I. Introduction

A. Background

Around the globe, there have been substantial increase in life expectancy in OECD countries, and among them, Korea has exhibited one of the fastest growth of 20 years from 1970 to 2015 (OECD, 2017). With the rapid aging and low birth rate, elderly population aged 65 years and older in Korea has reached 13.94% in 2017 (Korea, 2017) and naturally, the problems that co-occur with the growing elderly population is of much concern. Deteriorating health status is a common characteristic in the elderly population, and an emphasis on elderly health is spreading throughout numerous studies in Korea. Some of the major issues are vascular risks (Heidenreich et al., 2011; North and Sinclair, 2012), frailty (Tarazona-Santabalbina et al., 2016) and cognitive decline (Hultsch et al., 1993; Tabbarah et al., 2002). These health issues are important, because not only can they lead to adverse outcomes such as mortality, but they are also modifiable as well as reversible. Knowing the possibility of both spectrums, researchers try to understand the underlying mechanisms as well as the relationship between these conditions.

Vascular risks, which relate to factors such as an individual's blood pressure, smoking habits, total cholesterol and HDL cholesterol, have shown associations with depression (Kivimäki et al., 2012), and mortality (Pflederer et al., 2016). Vascular risk is an important issue to consider in the elderly

population because it is known to worsen with increasing age (Heidenreich et al., 2011), and has shown to be modifiable through lifestyle changes in previous studies (Santos-Parker et al., 2014; Ngandu et al., 2015). The possibility of vascular risk modification is important, not only for the purpose of improving vascular health, but also for the sake of reducing the risk of other adverse outcomes, such as cognitive decline. For example, Villeneuve and colleagues (Villeneuve et al., 2009) found an association between vascular risks and executive impairment, and Kaffashian and colleagues (Kaffashian et al., 2011) found an association between vascular risk and cognitive decline, but only in men. Considering these similar, but discrepant findings, researching the relationship between vascular risks and cognition further seems plausible. Also, studying other health conditions related to cognition would bring forth valuable insights concerning the elderly population.

Frailty, which is often defined as a decline in physical reserve and increase in vulnerability to environmental stressors (Campbell and Buchner, 1997; Hamerman, 1999), is being increasingly researched in terms of elderly health (Fried et al., 2001) as well as in association with cognitive function (Aguilar-Navarro et al., 2016). Physical frailty and cognitive decline are often considered as a co-occurring phenomenon with a term "cognitive frailty" (Kelaiditi et al., 2013), but a directional relationship between the two conditions are being studied as well. For instance, compared to non-frail elders, frail elders were more likely to experience incident dementia (Rogers et al., 2017), and cognitive impairment (Fougère et al., 2017). Notably, cognitive functions affected by frailty are similar to those affected by

vascular risks (Langlois et al., 2012). This is an interesting implication, because even though vascular risks and frailty are measured differently, they could share similar physical pathways leading to the decline in same cognitive functions. Also, as vascular risks were shown to be modifiable, the possibility of frailty prevention and reversal was found in previous studies (Chan et al., 2012; Tarazona-Santabalbina et al., 2016). With the evidence to potentially ameliorate vascular risks and frailty, and considering previous findings linking vascular risks and frailty to cognitive function, additional research related to these three factors could significantly enhance the health of the elderly.

Between these three health states, a possible interacting factor exists, which is an individual's social network. Social network is being increasingly researched in relation to people's health, and was found to be associated with depression (Roh et al., 2015), mortality (Kim et al., 2016), vascular health (Cohen, 1988), frailty (Woo et al., 2005), and cognitive function (Fratiglioni et al., 2004). However, social network is easy to conceptualize, but difficult to contextualize, making it challenging to clearly classify an individual's level of social network. In past studies, researchers have used social support (Woo et al., 2005), social engagement (Bassuk et al., 1999), or social integration (Fratiglioni et al., 2004), which can all be related to a person's social network. Although it is difficult to agree upon a single social network index, social contact appears across various definitions, and this construct is easier to operationalize. In terms of social contact, two things could be considered: the people (e.g. relatives, friends, or neighbors) and the frequency. If a person's social contact can indeed be used as an indicator of a person's social

network, then good social contact will have beneficial effects in terms of people's health. Considering previous studies, it is important to study the role of vascular risk and frailty in terms of cognitive function, as well as the possible interaction effect of social contact.

B. Purpose

The purpose of this study was to find the relationship between vascular risk, frailty and cognitive function. The moderating effect of social contact will also be assessed.

Hypothesis 1: Vascular risk will affect various cognitive functions differently

Hypothesis 2: Frailty will affect various cognitive functions differently

Hypothesis 3: Different social contact types will affect cognitive functions differently

Hypothesis 4: Social contact frequency will have an interaction effect with vascular risk in terms of cognitive function

Hypothesis 5: Social contact frequency will have an interaction effect with frailty in terms of cognitive function

Hypothesis 6: The relationship between vascular risk and cognitive function will differ between frail and non-frail elders

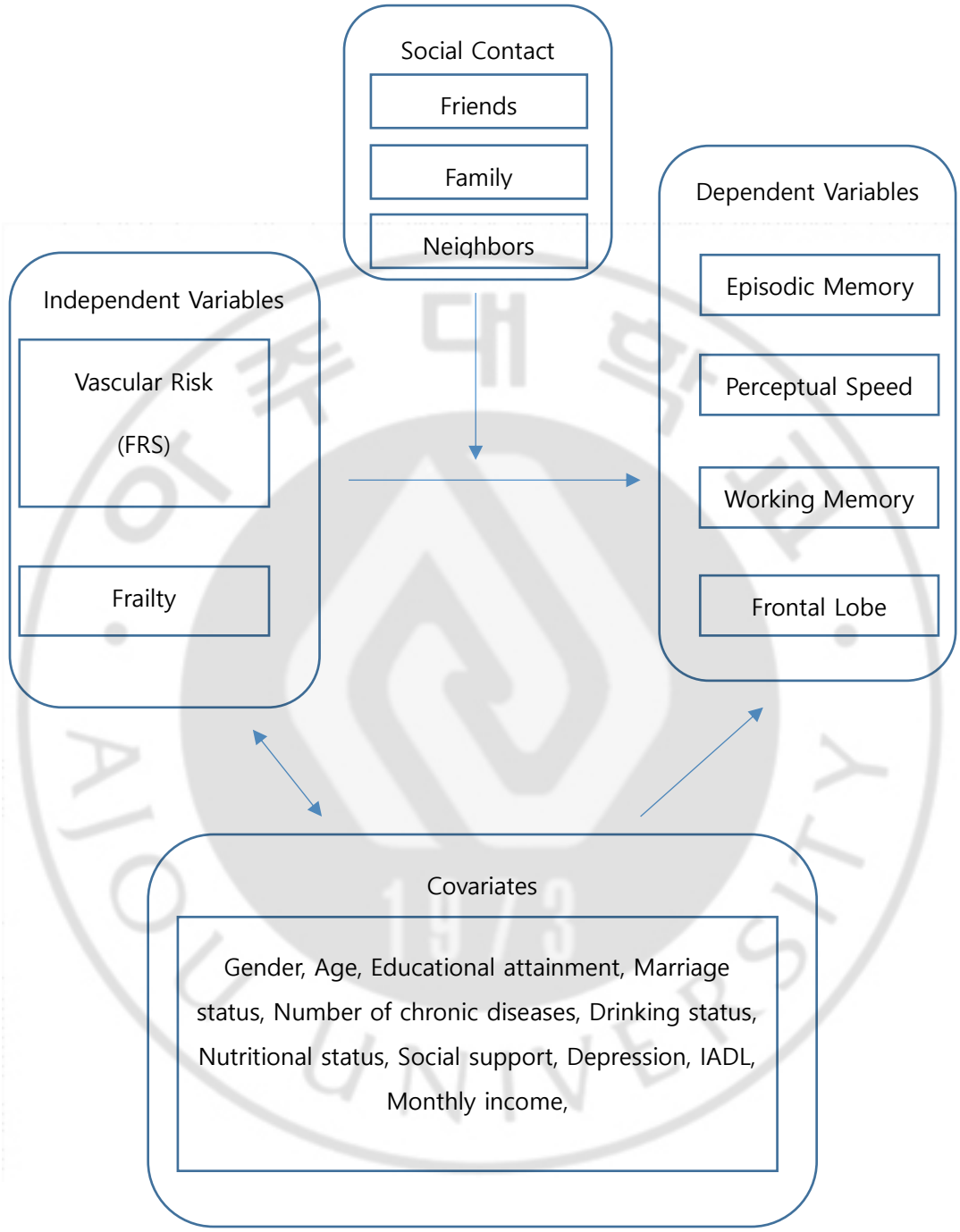

Figure 1. Overall model of the study

C. Theoretical Review

Framingham Cardiovascular Risk Score

Cardiovascular disease is one of the leading causes of deaths worldwide, and it is especially prevalent in the elderly population (Organization, 2015). Studies regarding the risk factors and preventive methods of cardiovascular disease has increased significantly in the past few decades, and the Framingham Heart Study is one of the predecessors in this line of research (Mahmood et al., 2014). This study began with the death of former United States' President Roosevelt, who died due to poorly controlled blood pressure. At the time, the risk factors, symptoms, and the danger of the illness were poorly understood, so the doctors could not do much to alleviate the symptoms. However, learning the seriousness of this condition from President Roosevelt's death, researchers began to design a cohort study. The study was conducted in Framingham, Massachusetts, hence the name Framingham Heart Study. Through decades, researchers have used the data from the study to develop an equation to calculate the cardiovascular risk, and the most recent version of the risk score is composed of age, LDL-cholesterol, HDL-cholesterol, blood pressure, diabetes, smoking status, and is the most widely used cardiovascular risk score worldwide (Wilson et al., 1998).

Despite its popularity, the original Framingham Heart Score should be used with caution, because the score was generated based on a middle-

class population in a specific area. This limits the generalizability of the score, and previous studies have shown overestimation in populations outside of the United States (Pinsky et al., 1985; Liu et al., 2004; Vergnaud et al., 2008; Empana et al., 2011). This overestimation was also apparent in Korea (Ahn et al., 2006), presenting a necessity to adjust the risk score to be used for the Korean population. In order to adjust the Framingham Heart Score for the Korean population, Jee and colleagues (Jee et al., 2014) used the data from the Korean Heart Study and the original Framingham Heart Score. In this study, several models were tested to determine the risk factors enabling acquisition of the most appropriate cardiovascular risk score. In the mid-20^{th} century, people were not able to save a person dying from a vascular problem, but being able to calculate an individual's vascular risk score as precisely as possible informs us about the severity of the condition, and allows us to further act on the problem. Furthermore, as important as it is to control for vascular risks itself, other adverse outcomes, stemming from vascular risks, need to be considered.

Frailty

Frailty is an important public health issue in the aging society around the world, and this has been defined as increased vulnerability to stressors, which lead to higher risk of negative health outcomes (Morley et al., 2013). Frailty is a relatively new concept, and because it could be difficult to consider it as a distinct condition, it is important not to confuse frailty with

vulnerability or disability. In order to clarify frailty, Rodriguez-Mañas et al. (Rodríguez-Mañas et al., 2012) conducted a Delphi survey to gather expert consensus, and ascertained that frailty is a distinct syndrome differing from vulnerability or disability.

Currently, most widely used frailty index was proposed by Fried et al. from the Cardiovascular Health Study (CHS) and is composed of weight loss, weakness, exhaustion, slowness and low activity (Fried et al., 2001). In their study, they emphasized the importance of including diminished physiological system in the definition of frailty. Figure 2, proposed by Linda Fried and her colleagues (Fried et al., 2001), presents a physiological cycle involved in frailty. Considering the physiology involved in frailty, and previous studies emphasizing the importance of activity and nutrition (Campbell and Buchner, 1997; Paw et al., 1999), CHS frailty index was established.

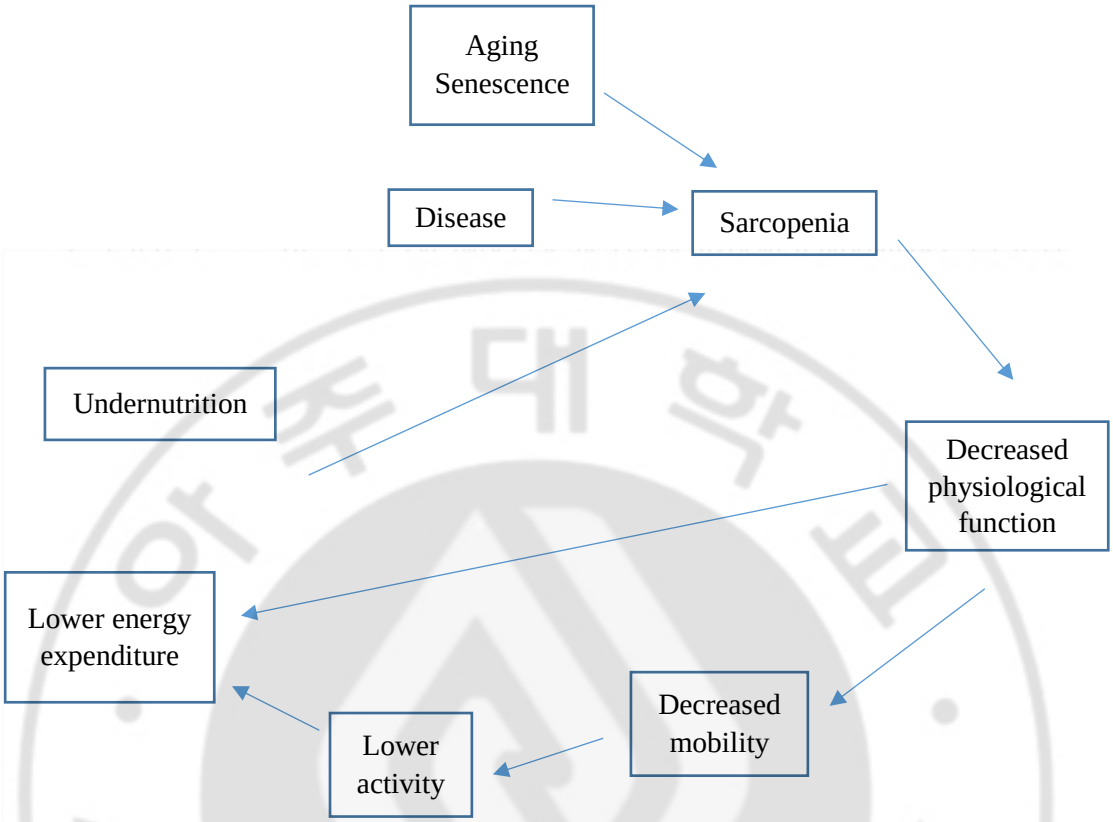

Figure 2. Frailty cycle proposed by Linda Fried and colleagues

CHS Frailty Index

1. Unintentional weight loss of more than 10 pounds within the past year
2. Being in the lowest 20% in gender-, body mass index (BMI)-specific population, for grip strength
3. Self-reported feeling of exhaustion

4. Being in the lowest 20% in gender-, height-specific population, for walking speed

5. Being in the lowest 20% in gender-specific population, for the amount of activity

Of these 5 criteria, scoring 0 meant robust, 1-2 meaning pre-frail, and 3 or more meaning frail.

Frailty was also shown to be associated with cognition via a systematic review (Panza et al., 2015b), and the findings from a number of studies suggested an association between frailty and vascular dementia (VaD) (Avila-Funes et al., 2012; Gray et al., 2013; Solfrizzi et al., 2013), which could be an indication to the possibility that frailty influences specific cognitive functions more than others. For example, in a study by Langlois et al. (Langlois et al., 2012), frailty was associated with low executive functions and processing speed, but not with memory and verbal reasoning. Notably, these are the cognitive functions often associated with vascular risks, and in the past, studies have found associations between vascular risk and frailty (Afilalo et al., 2009), as well as dementia (O Akinyemi et al., 2013).

Social relationship is also important in terms of a person's health, and in a study by Strawbridge et al. (Strawbridge et al., 1998), socially isolated individuals were more likely to be frail compared to individuals with better social ties. Overall, frailty is an important health status to consider in the elderly population, and it has been shown to be associated with vascular risk, cognitive function, as well as social relationship.

Social Network

Since the late 1900's, studies regarding social network and health outcomes have been conducted (Cohen, 1988; Berkman, 1995). Social network is a psychological concept, and in the past, there were questions to whether or not it was adequate to be included in epidemiological studies. However, throughout the past few decades, it has shown strong associations with various health outcomes (Berkman and Syme, 1979), providing support to the importance of social network in regards to health. In a more psychological point of view, social network can be traced back to attachment, which is known to formulate in infants or toddlers, and a secure attachment could assist in achieving homeostasis (Bowlby, 2008). The attachment theory posits at a human nature, which require connectedness with others. What begins as an attachment to one's guardian develops through life and changes as an individual ages. This change leads to the differences in social circles between different age cohorts, which usually tend to diminish in the elderly population due to factors such as poor health, inadequate resources, or death of the people around them (Arling, 1976). Furthermore, when considering social network in terms of a person's health, it needs to be considered as a multi-level concept.

Social network, proposed by Berkman and colleagues (Berkman et al., 2000), can be divided into 4 levels (e.g., macro, mezzo, micro, pathways). This model is insightful for those researching social network, because it presents a detailed information about the factors, which could affect an individual's social network, at different levels. At the macro level, there are

environmental factors (e.g., culture, socioeconomic factors, or politics) affecting a person's social network (e.g., structure and characteristics), which is then perceived as support, influence or engagement, and finally influences the pathways (e.g., health behavioral, psychological, or physiological) leading to health outcomes. As important as it is to consider each level in order to understand the mechanisms involved in the relationship between social network and health, this paper will focus on the bottom three levels, because the factors at the macro level are not likely to change.

Factors at the mezzo and micro levels are often used interchangeably. For example, previous studies have used terms such as social engagement, which included people's social relationships as well as participation in social activities (Bassuk et al., 1999), social integration (Fratiglioni et al., 2004), and social support (Woo et al., 2005). Different terms were used, but they were all trying to capture the concept of an individual's social network. Also, because the terms could be distinguished at different levels, it is important to clearly define the flow of mechanisms from the mezzo to the pathways level of social network. In this regard, the social network structure could be simplified into a person's social network structure, support provided through this network structure, and how that support ultimately influences health outcomes.

A good way to measure a person's social network at the mezzo level is to consider his/her contact frequency with others. Measuring a person's social contact is much easier than operationalizing social network, and contact frequency has been shown to be beneficial in terms of health outcomes (Chon et al., 2018). In this study, the target as well as the

frequency of contact was important, and although the results of the study do not provide clear causal association between social contact and health, due to its cross-sectional nature, the possibility that support acquired from different targets of contact could be considered. Support received from contact with others can be considered in terms of two models (e.g., main-effect model, buffering model) (Cohen and Wills, 1985).

Main-effect model

According to the main-effect model, social support helps people to feel more secure, and gain a sense of belonging as well as social roles (Cohen and Wills, 1985). Furthermore, the beneficial effects of social support in terms of the main-effect model have been explained with changes in the immune system, which could be affected by emotional variability (Jemmott and Locke, 1984), as well as through positive behavioral change, which could be acquired through an individual's peers (Krantz et al., 1985).

Buffering model

The buffering model proposes that social support mediates the relationship between stress and adverse health outcomes (Cohen and Wills, 1985). This is important, because stress perceived by an individual tends to exacerbate when he/she does not have the ability to properly cope with that stressor, and according to the buffering hypothesis, social support can help people to better cope with stressors (Cohen and Wills, 1985). Furthermore, previous studies have found that social contact was associated with strengthened resistance to stressors, resulting in positive health outcomes (Berkman and Syme, 1979).

Social support is thought to be an important part in this mechanism (Berkman et al., 2000). Likewise, although social contact itself has been found as a useful contextualization of an individual's social network, how that relationship is perceived needs to be understood to better describe the association between social contact and health outcomes. Previous studies have found beneficial effects of social support through both the main-effect (Miyazaki et al., 2003) and the buffering models (Cohen and Wills, 1985). Therefore, in order to fully understand the relationship between social network and health outcomes, a clear operationalization of the most psychological aspect of an individual is necessary.

Cognitive Function

Cognitive function is known to worsen as people age. However, it is important to note that as some cognitive functions decline with age, some functions remain steady, or even improve with aging. An example of cognitive function that is known to remain steady or in some cases even improve include a person's vocabulary, which tend to improve as a person ages and learns and stores more information. However, reasoning, memory, and processing speed are known to decline with age, and the decline in these abilities differs between persons (Wisdom et al., 2012). These cognitive functions can also be considered in terms of fluid intelligence or crystallized intelligence. Fluid intelligence refers to the ability to solve novel problems and similar to its name, it is an ability for a person to be flexible in different situations. Crystallized intelligence on the other hand relates to the information and ability acquired and embedded in a person's cognitive system. (McGrew, 2009). In general, fluid intelligence is known to decline with aging, whereas crystallized intelligence remains intact. Furthermore, the cognitive functions associated with fluid intelligence are perceptual speed, attention, memory, and executive function (Harada et al., 2013).

Perceptual speed

This cognitive function is associated with the ability to perform

simple tasks with the information gathered through visual stimulus (Ekstrom et al., 1976). This function is well-known to debilitate as a person ages, and in part it is due to the fact that older people find it more difficult to focus on a task with distractions (Salthouse et al., 1995).

Memory

a. Episodic memory:

   This memory function refers specifically to a type of memory that relates to the context in which the information was acquired, and is known to be influenced by neuronal dysfunctions more than other types of memory (Tulving, 2002). Decline in function of this memory type is notable in Alzheimer's disease (AD) (Karantzoulis et al., 2011).

b. Working memory:

   This memory type refers to a temporary memory system, and a person's ability to manipulate that information (Rossi-Arnaud et al., 2012). It is important to distinguish this type of memory from short term memory (STM)

Frontal Lobe

Cognitive functions associated with the frontal lobe region of the brain include attention and executive function (Chayer and Freedman, 2001). Frontal lobe has also shown to be related to an individual's personality, and an interesting case study reported a person, whose personality changed dramatically after a brain injury in the frontal lobe, but no other cognitive impairments were present (Damasio et al., 1994).

These cognitive functions are part of the fluid intelligence, and it is susceptible to change. Aging is a well-known risk factor of cognitive decline, but there are other known risk factors as well, so it is important to research these risk factors further and find possible ameliorating factors. The notion of cognitive reserve has been proposed as a resilience in our brain to buffer against clinical expression of cognitive decline even in the presence of pathological damage (Stern, 2002).

Summary

Vascular risk, frailty and impaired cognitive function are all important health related concerns in the elderly population. Also, a number of previous studies have reported associations between these three factors, and it is important to study more detailed mechanisms involved within these

associations.

II. Methods

Study sample & design

Data were obtained from the Korean Frailty and Aging Cohort Study (KFACS), which gathered its baseline data in 2016 and 2017. Briefly, KFACS conducted a multi-center based sampling in 10 centers in rural and urban regions across Korea. More detailed description is provided in a previous study (Won et al., 2016). The sample consisted of people aged 70-84 years old, selected based on age- and gender-specific strata. An in-person interview and health examinations were performed. All participants provided informed consents. The study was approved by institutional review boards of the participating centers.

Inclusion & Exclusion Criteria

Participants of KFACS were included in the study. Of the 3,014 baseline cohort, those who reported "yes" to being diagnosed to dementia or scored 2 standard deviations below the mean MMSE-KC score, adjusted for age, education, and gender, were excluded from the study. These participants were excluded, because their cognitive functions could be too impaired, which could lead to biased results. Participants with missing values on the main variables of interest were also excluded from the study. In the final analysis, 2,538 participants remained (Figure 3).

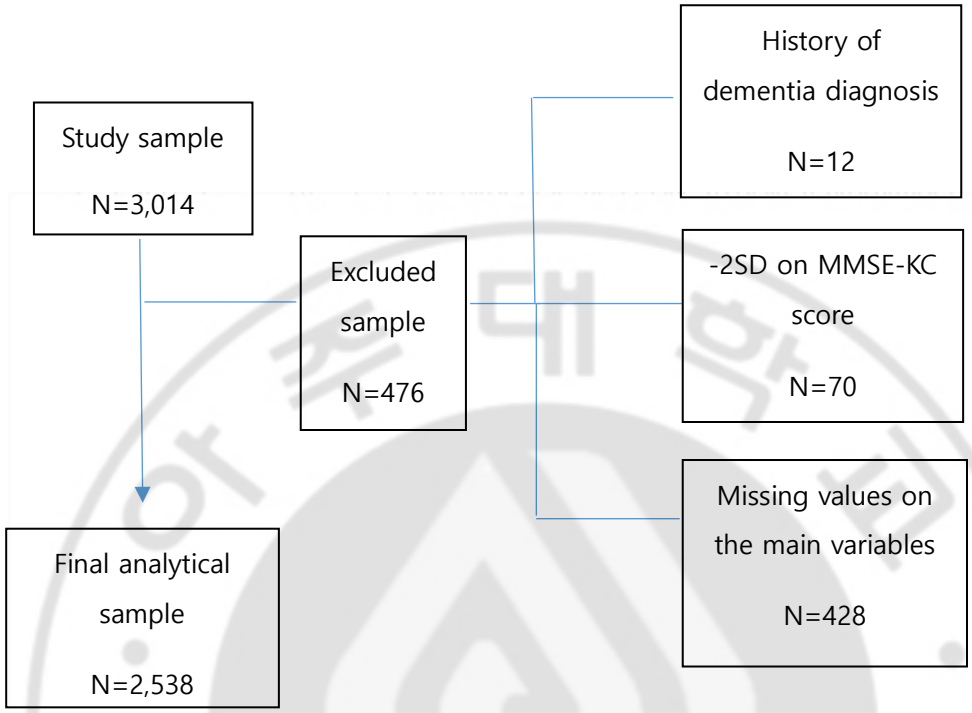

Figure 3. Diagram of participant inclusion/exclusion

Independent variables

The independent variables were the frailty status, Framingham Risk Score (FRS) and social contact frequency.

FRAMINGHAM RISK SCORE (FRS)

Korean version of the Framingham Risk Score, developed by Jee et al. (Jee et al., 2014), was used. The variables used in the equation were as follows: AGE=age, AGESQ=square of age, HTN2= 120≤sbp<140 or 80≤dbp<90, HTN3=140≤sbp<160 or 90≤dbp<100, HTN4=160≤sbp or 100≤dbp, TC2=160≤Total cholesterol (in mg/dl)<200, TC3=200≤Total cholesterol (in mg/dl)<240, TC4=240≤Total cholesterol (in mg/dl)<280, TC5=280≤Total cholesterol (in mg/dl), HDL2=35≤HDL-cholesterol (in mg/dl)<45, HDL3=45≤HDL-cholesterol (in mg/dl)<50, HDL4=50≤HDL-cholesterol (in mg/dl)<60, HDL5=60≤HDL-cholesterol (in mg/dl), EXSMOK=ex-smoker, CUSMOK=current smoker, DM=diabetes.

Male:

FRS=0.13759*(AGE-45.7991)-0.0006964*(AGESQ-2186.58)+ 0.24130*(HTN2-0.40678)+ 0.54176*(HTN3-0.18005)+ 0.79091*(HTN4-0.06823)+ 0.30303*(TC2-0.43540)+ 0.72508*(TC3-0.31439)+ 1.02770*(TC4-0.08486)+ 1.51018*(TC5-0.01387)-0.41580*(HDL2-0.31063)-0.59809*(HDL3-0.22692)-0.80256*(HDL4-0.27050)-1.13973*(HDL5-0.11410)-0.00207*(EXSMOK-0.23029)+ 0.60138*(CUSMOK-

0.53016)+ 0.49443*(DM-0.08389)

Female:

FRS=0.12962*(AGE-47.5808)-0.0003965*(AGESQ-2363.65)+ 0.41491*(HTN2-0.32308)+ 0.66187*(HTN3-0.14102)+ 1.10282*(HTN4-0.06657)+ 0.20005*(TC2-0.41642)+ 0.44176*(TC3-0.29841)+ 0.52267*(TC4-0.09640)+ 1.03573*(TC5-0.02196)-0.28121*(HDL2-0.18651)-0.18543*(HDL3-0.16015)-0.47018*(HDL4-0.30597)-0.72046*(HDL5-0.31451)+ 0.23099*(EXSMOK-0.03970)+ 0.67653*(CUSMOK-0.05079)+ 0.58729*(DM-0.06026)

The calculated FRS was used as a continuous variable.

FRAILTY STATUS

The dependent variable of the study was frailty status categorized by Fried's criteria (Fried et al., 2001). There are 5 categories in Fried's CHS index: weight loss, weakness, exhaustion, slowness and low activity.

Weight loss: Based on the question "Have you experienced an unintentional weight loss of 4.5kg or more in the last year?". A response of "yes" was scored as 1, and "no" was scored as 0.

Weakness: Based on grip strength, and adjusted for gender and BMI.

Male: 0≤BMI≤22.0 and 0≤Grip strength≤25.0, 22.0<BMI≤24.0 and 0≤Grip strength≤27.0, 24.0<BMI≤26.0 and 0≤Grip strength≤27.8, or 26.0<BMI and 0≤Grip strength≤28.5 were scored as 1, otherwise 0.

Female: 0≤BMI≤23.0 and 0≤Grip strength≤16.8, 23.0<BMI≤25.0 and 0≤Grip strength≤17.7, 25.0<BMI≤27.0 and 0≤Grip strength≤17.8, or 27.0<BMI and 0≤Grip strength≤17.7 were scored as 1, otherwise 0.

Exhaustion: Based on the questions "Everything felt difficult for the last week", and "I could not get myself to do anything for the last week". If participants answered "3 to 4 days in the last week" or "5 or more days in the last week", they scored 1, otherwise 0.

Slowness: Based on 4-meter walking test. Speed was measured in m/s, and adjusted for gender and height.

Male: Height≤165 and 0≤Walking speed≤.93, or 165<Height and 0≤Walking speed≤.98 were scored as 1, otherwise 0.

Female: Height≤152 and 0≤Walking speed≤.85, or 152<Height and 0≤Walking speed≤.93 were scored as 1, otherwise 0.

Low activity: The amount of low intensity, moderate intensity, and high intensity daily activities were measured in minutes through survey questions. Once the minutes were determined, the following equation was used to calculate the amount of activity of participants. ((Low intensity

activity (in minutes)/60*3)+ (Moderate intensity activity (in minutes)/60*4.5)+ (High intensity activity (in minutes)/60*6))*1.05*weight=Activity in kcal. If male activity amount ranged 0≤Activity<495.65 or female activity ranged 0≤Activity<283.50 then they scored 1, otherwise 0.

Presence of 0 component was considered Non-frail, 1-2 components Pre-frail, and 3 or more components Frail.

SOCIAL CONTACT FREQUENCY

There were three types of social contact (e.g., family, friend, or neighbors). Social contact frequency was based on the question "How often do you meet or have a chat with … ?" For each question, participants responded by one of the following: daily, 2-3 times a week, at least once weekly, at least once monthly, less than once monthly, or no contact person. These responses were grouped into 3 categories: Daily (everyday), Weekly (1-3 times a week), Monthly or less (once a month or less). This variable was used as a categorical variable.

Dependent variable

The dependent variables of the study was participants' cognitive scores on 5 domains: Episodic memory, Perceptual speed, Working memory, Frontal lobe assessment, and Global cognition.

Episodic memory: Measured using the word list memory, recall, and recognition tests from the Korean Version of the Consortium to Establish a Registry for Alzheimer's Disease Assessment Packet (CERAD-K) (Lee et al., 2002; Lee et al., 2004). The scores of all the trials were added and was turned into a Z-score.

Perceptual speed: Measured using the trail making test (TMT-A) from CERAD-K. The time spent completing the task was used as a perceptual speed score. Unlike other tests, in which higher score indicates better cognitive function, more time spent completing TMT-A indicated worse cognitive function. In order to maintain consistent direction in results, the time outcome was inverted, and was turned into a Z-score.

Working memory: Measured using the digit span test from Seoul Neuropsychological Screening Battery (SNSB) (Ahn et al., 2010). There were forward and backward trials. The scores from both trials were added and was turned into a Z-score.

Frontal lobe function: Measured based on the Frontal Assessment Battery (FAB) developed by Dubois and colleagues (Dubois et al., 2000). The battery consists of conceptualization, mental flexibility, motor programming, sensitivity to interference, inhibitory control, and environmental autonomy. A Korean version of this battery proposed by Kim et al. (Kim et al., 2010) was used, and the total score of this battery was turned into a Z-score.

Global cognition: Z-scores of the previous cognitive functions were

averaged to create a global cognition score. This variable was used as a continuous variable.

Control variables

Based on previous studies (Bennett et al., 2006; Liu et al., 2018; Han et al., 2019) covariates were collected: gender (male or female), age, education level (<elementary, elementary graduate, middle school graduate, high school graduate, ≥college), monthly household income (<1 million, 1-2 million, >2 million in Korean Won), marriage status (yes or no), number of chronic diseases (0, 1, 2 or ≥3), drinking status (never, <1 monthly, 1-4 monthly, or ≥2 weekly), and Nutritional status (Mini Nutritional Assessment score was used as a continuous variable), depression (yes or no), and IADL (yes or no).

SOCIAL SUPPORT

Although contact frequency is a relatively objective measure of an individual's social network, its representation could seem shallow. To account for this limitation, the ENRICHD Social Support Instrument (ESSI) was included as a control variable (Vaglio et al., 2004). Except for the question regarding marriage, which was already included as a control variable, there were 6 questions in this instrument: "Is there someone you could talk to or rely on in times of need?", "Is there someone to give you advice in difficult situations?", "Is there someone who treats you with concern and affection?", "Is there someone to help you with small favors

such as house chores when necessary?", "Is there someone who helps you whole heartedly in times of need?", "Is there someone who you trust and could call whenever necessary?". For each of the 6 questions, the participants answered by one of the following: 1. No, 2. Scarcely, 3. Sometimes, 4. Often, 5. Always, 9. Do not know. 9 was treated as a null value, and the other responses were summed and used as a continuous variable.

Statistical analysis

The general characteristics of the study participants were described with mean±SD, or n and (%) depending on the type of variable. Then the study characteristics based on each of the independent variables were analyzed by t-test, ANOVA, χ^2, or correlation. Simple linear regression was used to analyze the unadjusted association between each variable included in the study and each cognitive function. In the adjusted model, multiple linear regression analysis was conducted in two separate models. The linear regression was performed using PROC REG function in the SAS software.

Model 1:

$$Y = \beta_o + \beta_1(FRS) + \beta_2(Frailty) + \sum_{i=1}^{k} \beta_i(Covariates)_k$$

The regression values between independent variables for each cognitive function were compared using the equation below:

$$t = \frac{\beta_1 - \beta_2}{\sqrt{S.E._1{}^2 + S.E._2{}^2}}$$

Model 2:

$$Y = \beta_o + \beta_1(FRS) + \beta_2(Frailty) + \beta_j(Interaction) + \sum_{i=1}^{k} \beta_i(Covariates)_k$$

When model 2 was used, three different interaction terms were included in separate analyses. The interaction terms that were statistically significant in the linear regression analysis were analyzed further, using the PROC GLM, and PROC PLM functions in the SAS software, to calculate the differences in slopes.

First, there was the social contact and FRS interaction (Figure 4):

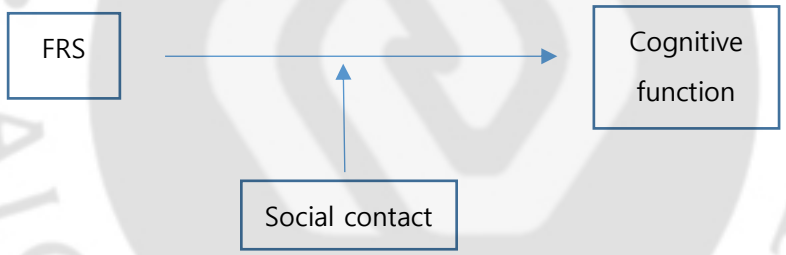

Figure 4. Interaction between FRS and contact frequency

Vascular risks have shown association with cognitive decline in previous studies (Villeneuve et al., 2009; Kaffashian et al., 2011), and our first hypothesis was to find which cognitive functions are influenced by vascular risks the most. Also, according to our third hypothesis, we included an interaction term between FRS and the frequency of contact with others to see if the social contact variable had an interaction effect with FRS in terms

of cognitive function.

Second, there was the social contact and frailty interaction (Figure 5):

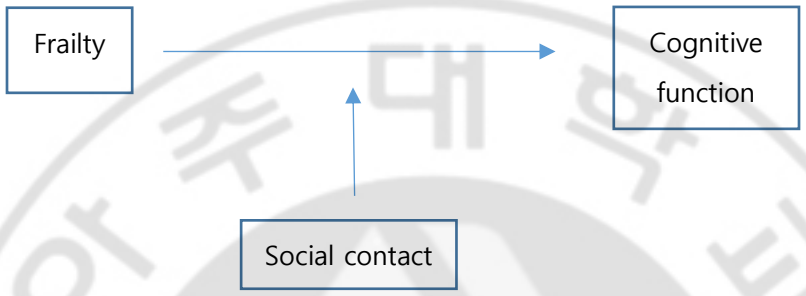

Figure 5. Interaction between frailty and contact frequency

Frailty has shown association with cognitive decline in the past (Chen et al., 2018), and accordingly, our third hypothesis was to find which cognitive functions are most significantly associated with frailty status. Also, in order to analyze the interaction effect of social contact in the relationship between frailty and cognitive function, an interaction term of social contact and frailty status was included in our analysis.

Third, an interaction between frailty status and FRS was included (Figure 6):

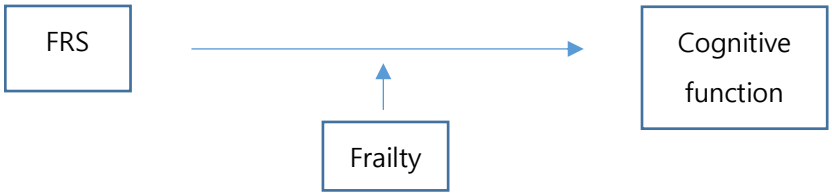

Figure 6. Interaction between FRS and frailty

The interaction between frailty and FRS was added into the analysis, because in the past, studies showing associations between frailty and FRS has proposed vascular risks as possible mechanisms linking frailty and cognitive function (Robertson et al., 2013; Panza et al., 2015a). Accordingly, we hypothesized that the association between FRS and cognitive function would differ depending on the frailty status.

Sensitivity analysis

To account for the differences between people who were excluded from the study and the people who remained in the final analysis, additional sensitivity analysis was conducted. Not accounting for the people who were excluded due to poor cognitive function or presence of dementia, the general characteristics between those who were excluded and those remaining were analyzed. Also, to elucidate the possible differences in results, with or without the excluded participants, a multiple imputation using PROC MI was used.

For all analyses, the criterion for statistical significance was $p < 0.05$, two-tailed. All analyses were conducted using the SAS statistical software

package, version 9.4 (SAS Institute Inc., Cary, NC, USA).

III. Results

Baseline characteristics

The baseline distribution and average values of all variables included in the final analysis are shown in Table 1. There were more females (52.3%) compared to males (47.7%) and the average age was 76.0 (SD: 3.9) years old. In terms of education, 18.3% were in the <Elementary group, 27.3% in the Elementary group, 16.1% in the Middle School group, 20.4% in the High School group, and 17.9% in the ≥College group. 67.5% of the participants reported being married and there were 20.5% with 3≤ chronic diseases, 35.5% with 2, 30.8% with 1, and 13.2% with 0. 18.0% reported drinking 2≤weekly, 19.3% 1~4 monthly, 34.0% 1≥monthly, and 28.7% never. The average MNA score was 12.9 (SD: 1.5) and the average ESSI score 23.5 (SD: 7.2). Only 8.0% of the participants reported yes to depression, and 36.7% of the participants had difficulties with at least one IADL. 32.0% of the participants had a monthly income of >2 million won, 25.4% 1~2 million won, and 42.6% <1 million won. The average FRS of our population was 1.8 (SD: 0.8), and 7.8% were frail, 46.9% pre-frail, and 45.3% robust. In terms of contact frequency, the proportion was the highest in the Frequently group when the target of contact was either friend (39.4%) or neighbor (41.3%). However, the proportion was the highest in the Rarely group (38.8%) when the target of contact was family. Finally, as for the scores of each cognitive function: Episodic memory (Mean: 0.1, SD: 0.9), Working memory (Mean: 0.1, SD: 1.0),

Perceptual speed (Mean: 0.0, SD: 0.9), Frontal lobe (Mean: 0.1, SD: 0.9), and global cognition (Mean: 0.1, SD: 0.7) were shown.

Table 1. General distribution of all variables

Variable	Category		Variable	Category	
Gender	Female	1327 (52.3)	IADL	Yes	931 (36.7)
	Male	1211 (47.7)		No	1607 (63.3)
Age		76.0 (3.9)	Income	<1 million	1021 (42.6)
Education	<Elementary	463 (18.3)		1~2 million	607 (25.4)
	Elementary	693 (27.3)		>2 million	767 (32.0)
	Middle School	409 (16.1)	FRS		1.8 (0.8)
	High School	518 (20.4)	Frailty	Frail	197 (7.8)
	≥College	454 (17.9)		Pre-frail	1191 (46.9)
Marriage status	No	825 (32.5)		Robust	1150 (45.3)
	Yes	1710 (67.5)	Friendcontact	Rarely	566 (22.3)
Chronic diseases	3≤	519 (20.5)		Moderately	971 (38.3)
	2	901 (35.5)		Frequently	1001 (39.4)
	1	783 (30.8)	Famcontact	Rarely	986 (38.8)
	0	335 (13.2)		Moderately	756 (29.8)
Drinking	2≤ weekly	455 (18.0)		Frequently	796 (31.4)
	1~4 monthly	489 (19.3)	Neighborcontact	Rarely	747 (29.4)
	1≥ monthly	861 (34.0)		Moderately	744 (29.3)
	Never	726 (28.7)		Frequently	1047 (41.3)
Nutritional Status		12.9 (1.5)	Episodic Memory		0.1 (0.9)
Social support		23.5 (7.2)	Working Memory		0.1 (1.0)
Depression	Yes	204 (8.0)	Perceptual Speed		0.0 (0.9)
	No	2334 (92.0)	Frontal Lobe		0.1 (0.9)
			Global Cognition		0.1 (0.7)

* Characteristics of the categorical variables described as N (%),and characteristics of continuous variables described as Mean (SD)

FRS

Higher FRS was apparent in worse frailty status: Frail (Mean: 2.1, SD: 0.8), Pre-frail (Mean: 1.9, SD: 0.8), and Robust (Mean: 1.7, SD: 0.8) (p-value: <.001). FRS was also higher for females (Mean: 2.4, SD: 0.5) compared to males (Mean: 1.2, SD: 1.2) (p-value: <.001). In terms of education, FRS was the highest in the <Elementary group (Mean: 2.2, SD: 0.8), and declined with higher educational attainments (p-value: <.001). FRS was also higher for people who were not married (Mean: 2.3, SD: 2.3, p-value: <.001), reported depression (Mean: 2.1, SD: 0.8, p-value: <.001), but was lower in those with problems in at least one IADL (Mean: 1.6, SD: 0.8, p-value: <.001). FRS was also the highest in those with most chronic diseases (Mean: 2.0, SD: 0.8, p-value: <.001), had the lowest income (Mean: 2.0, SD: 0.8, p-value: <.001), but was the lowest in those that drank most frequently (Mean: 1.3, SD: 0.7, p-value: <.001). FRS was positively correlated with age (r: 0.192, p-value: <.001), but negatively correlated with all cognitive scores. Nutritional status and ESSI were also positively correlated with FRS, but were not statistically significant (Table 2).

FRAILTY

Baseline characteristics of the participants based on Frailty status are displayed in Table 3. In terms of Frailty, female participants tended to be more Frail (8.0%) and Pre-frail (50.0%) compared to male (7.5%; 43.5%) (p-value: .002). Also, people who were in the Frail group tended to be older (Mean: 78.6, SD: 3.7) compared with those in the Pre-frail group (Mean: 76.3, SD: 4.0) and Robust group (Mean: 75.1, SD: 3.6) (p-value: <.001). In terms of education, the proportion of Frailty was the highest in the lowest educational attainment group, and tended to decrease as the educational attainment improved (16.2%, 8.6%, 5.4%, 4.8%, and 3.3%) (p-value: <.001). Proportion of the people in the Frail group was higher for the unmarried participants (9.8%) compared to the married participants (6.8%) (p-value: <.001). Also, as the number of chronic diseases increased, the proportion of Frail participants increased (p-value: <.001). However, people who drank the most frequently (7.9%) had a lower proportion of Frail participants compared to those who were in the Never group (8.4%) and 1 ≥ monthly group (8.7%) (p-value: .004). People in the Frail group had the lowest nutritional status (Mean: 12.0, SD: 2.1) compared to those in the Pre-frail group (Mean: 12.8, SD: 1.6) and the Robust group (Mean: 13.2, SD: 1.2) (p-value: <.001). Subjective social support was the lowest in the Frail group (Mean: 22.8, SD: 7.7) compared to the Pre-frail group (Mean:23.5, SD: 7.1), and the Robust group (Mean: 23.6, SD: 7.1), but the differences were not statistically significant (p-value: .365). Higher proportion of people who reported a presence of depression (31.4%) and IADL (11.0%) were in the Frail group

compared to those who did not report a presence of depression (5.7%) or IADL (5.9%) (p-value's: <.001). There was a higher proportion of people in the Frail group (12.3) for the <1 million Won/month group compared to the <2 million Won/month group (5.3%) (p-value: <.001). Lastly, people in the Frail group had the highest FRS (Mean: 2.1, SD: 0.8) (p-value: <.001), worst Episodic memory score (Mean: -0.597, SD: 0.990) (p-value: <.001), Working memory score (Mean: -0.5, SD: 1.0) (p-value: <.001), Perceptual speed score (Mean: -0.6, SD: 1.2), (p-value: <.001), and Frontal lobe function score (Mean: -0.6, SD: 1.0) (p-value: <.001) compared with the Pre-frail and the Robust group.

Table 2. General characteristics in terms of FRS

Variable	Category	FRS	*p*-value
Frailty	Frail	2.1 (0.8)	<.001
	Pre-frail	1.9 (0.8)	
	Robust	1.7 (0.8)	
Gender	Female	2.4 (0.5)	<.001
	Male	1.2 (1.2)	
Age		0.192	<.001
Education	<Elementary	2.2 (0.8)	<.001
	Elementary	2.0 (0.8)	
	Middle School	1.8 (0.8)	
	High School	1.7 (0.7)	
	≥College	1.5 (0.7)	
Marriage status	No	2.3 (2.3)	<.001
	Yes	1.6 (1.6)	
Chronic diseases	3≤	2.0 (0.8)	<.001
	2	1.9 (0.8)	
	1	1.7 (0.8)	
	0	1.6 (0.7)	
Drinking	2≤ weekly	1.3 (0.7)	<.001
	1~4 monthly	1.7 (0.8)	
	1≥ monthly	1.8 (0.8)	
	Never	2.2 (0.7)	
Nutritional Status		0.034	.084
Social support		0.005	.816
Depression	Yes	2.1 (0.8)	<.001
	No	1.8 (0.8)	
IADL	Yes	1.6 (0.8)	<.001
	No	2.0 (0.8)	
Income	<1 million	2.0 (0.8)	<.001
	1~2 million	1.8 (0.8)	
	>2 million	1.6 (0.7)	
Episodic memory		-0.041	0.039
Working memory		-0.244	<.001
Perceptual speed		-0.283	<.001
Frontal lobe function		-0.225	<.001
Global cognition		-0.268	<.001

* Characteristics of the categorical variables described as N (%), χ^2 and characteristics of continuous variables described as Mean (SD), *F(t)-statistics.*

Table 3. General characteristics in terms of Frailty status

Variable	Category	Frailty			Total	*p*-value
		Robust	Pre-frail	Frail		
Gender	Female	557 (42.0)	664 (50.0)	106 (8.0)	1327 (100.0)	.002
	Male	593 (49.0)	527 (43.5)	91 (7.5)	1211 (100.0)	
Age		75.1 (3.6)	76.3 (4.0)	78.6 (3.7)		<.001
Education	<Elementary	128 (27.6)	260 (56.2)	75 (16.2)	463 (100.0)	<.001
	Elementary	279 (40.3)	354 (51.1)	60 (8.6)	693 (100.0)	
	Middle School	204 (49.9)	183 (44.7)	22 (5.4)	409 (100.0)	
	High School	268 (51.7)	225 (43.5)	25 (4.8)	518 (100.0)	
	≥College	270 (59.5)	169 (37.2)	15 (3.3)	454 (100.0)	
Marriage status	No	320 (38.8)	424 (52.4)	81 (9.8)	825 (100.0)	<.001
	Yes	828 (48.4)	766 (44.8)	116 (6.8)	1710 (100.0)	
Chronic diseases	3≤	179 (34.5)	280 (53.9)	60 (11.6)	519 (100.0)	<.001
	2	371 (41.2)	452 (50.2)	78 (8.6)	901 (100.0)	
	1	399 (50.9)	334 (42.7)	50 (6.4)	783 (100.0)	
	0	201 (60.0)	125 (37.3)	9 (2.7)	335 (100.0)	
Drinking	2≤ weekly	230 (50.6)	189 (41.5)	36 (7.9)	455 (100.0)	.004
	1~4 monthly	243 (49.7)	221 (45.2)	25 (5.1)	489 (100.0)	
	1≥ monthly	475 (43.6)	411 (47.7)	75 (8.7)	861 (100.0)	
	Never	299 (41.2)	366 (50.4)	61 (8.4)	726 (100.0)	
Nutritional Status		13.2 (1.2)	12.8 (1.6)	12.0 (2.1)		<.001
Social support		23.6 (7.1)	23.5 (7.1)	22.8 (7.7)		.365
Depression	Yes	30 (14.7)	110 (53.9)	64 (31.4)	204 (100.0)	<.001
	No	1120 (48.0)	1081 (46.3)	133 (5.7)	2334 (100.0)	
IADL	Yes	393 (42.2)	436 (46.8)	102 (11.0)	931 (100.0)	<.001
	No	757 (47.1)	755 (47.0)	95 (5.9)	1607 (100.0)	
Income	<1 million	375 (36.7)	521 (51.0)	125 (12.3)	1021 (100.0)	<.001
	1~2 million	273 (45.0)	302 (49.7)	32 (5.3)	607 (100.0)	
	>2 million	441 (57.5)	300 (39.1)	26 (3.4)	767 (100.0)	
FRS		1.7 (0.8)	1.9 (0.8)	2.1 (0.8)		<.001
Episodic memory		0.3 (0.8)	-0.2 (0.9)	-0.5 (1.0)		<.001
Working memory		0.3 (0.9)	-0.0 (1.0)	-0.4 (0.9)		<.001
Perceptual speed		0.3 (0.7)	-0.1 (1.0)	-0.6 (1.2)		<.001
Frontal lobe		0.3 (0.8)	-0.0 (0.9)	-0.6 (1.0)		<.001
Global cognition		0.3 (0.6)	-0.1 (0.7)	-0.5 (0.7)		<.001

* Characteristics of the categorical variables described as N (%), χ^2 and characteristics of continuous variables described as Mean (SD), *F-statistics*

SOCIAL CONTACT

Contact with Friends

Baseline characteristics based on contact with friends are shown in Table 4. In contrast to the original hypothesis, people in the Frequently contact group had the worst FRS (Mean: 1.9, SD: 0.8) compared to those in the Moderately group (Mean: 1.8, SD: 0.8), and the Rarely group (Mean: 1.8, SD: 0.8) (p-value: <.001). Notably, people who were in the Frail group had the highest proportion of participants in the Rarely contact group (38.1%) compared to Pre-frail (24.9%) and Robust group (16.9%) (p-value: <.001). Similar trends were noticeable in terms of the cognitive scores. In terms of cognitive scores, the Rarely group showed worst scores on each cognitive function and they were statistically significant.

Contact with Family

The baseline characteristics depending on contact frequency with family did not differ as statistically significantly as in the case with friends (Table 5). The cognitive scores in terms of Perceptual speed (Mean: 0.0, SD: 1.0, p-value: .027), Frontal lobe (Mean: 0.0, SD: 0.9, p-value: .005), and Global cognition (Mean: 0.0, SD: 0.7, p-value: .040) were the lowest in the group of people contacting their family rarely.

Contact with neighbors

Lastly, contact frequency with neighbors was almost as statistically significant with the variables of the study as contacting friends, but the trend was the opposite (Table 6). Participants in the Frequently group had the worst FRS (Mean: 2.0, SD: 0.8, *p*-value: <.001), highest proportion of those who are Frail (51.8%), and all cognitive scores were the lowest (*p*-value's: <.001).

Table 4. Baseline characteristics based on contact frequency with friends

Variable	Category	Friendcontact			Total	*p*-value
		Frequently	Moderately	Rarely		
Gender	Female	591 (44.5)	490 (36.9)	246 (18.6)	1327 (100.0)	<.001
	Male	410 (33.9)	481 (39.7)	320 (26.4)	1211 (100.0)	
Age		76.2 (3.9)	75.8 (3.9)	76.0 (3.9)		.074
Education	<Elementary	201 (43.4)	135 (29.2)	127 (27.4)	463 (100.0)	<.001
	Elementary	305 (44.0)	232 (33.5)	156 (22.5)	693 (100.0)	
	Middle School	179 (43.8)	143 (34.9)	87 (21.3)	409 (100.0)	
	High School	183 (35.3)	223 (43.1)	112 (21.6)	518 (100.0)	
	≥College	133 (29.3)	237 (52.2)	84 (18.5)	454 (100.0)	
Marriage status	No	385 (46.7)	302 (36.6)	138 (16.7)	825 (100.0)	<.001
	Yes	614 (35.9)	668 (39.1)	428 (25.0)	1710 (100.0)	
Chronic diseases	3≤	200 (38.5)	197 (38.0)	122 (23.5)	519 (100.0)	.004
	2	350 (38.8)	315 (35.0)	236 (26.2)	901 (100.0)	
	1	312 (39.9)	325 (41.5)	146 (18.6)	783 (100.0)	
	0	139 (41.5)	134 (40.0)	62 (18.5)	335 (100.0)	
Drinking	2≤ weekly	175 (38.5)	171 (37.6)	109 (23.9)	455 (100.0)	.893
	1~4 monthly	192 (39.3)	186 (38.0)	111 (22.7)	489 (100.0)	
	1≥ monthly	337 (39.1)	327 (38.0)	197 (22.9)	861 (100.0)	
	Never	295 (40.6)	282 (38.9)	149 (20.5)	726 (100.0)	
Nutritional Status		12.9 (1.5)	13.0 (1.4)	12.7 (1.6)		.011
Social support		24.6 (6.4)	22.9 (7.1)	22.5 (8.1)		<.001
Depression	Yes	69 (33.8)	75 (36.8)	60 (29.4)	204 (100.0)	.031
	No	932 (39.9)	896 (38.4)	506 (21.7)	2334 (100.0)	
IADL	Yes	324 (34.8)	333 (35.8)	274 (29.4)	931 (100.0)	<.001
	No	677 (42.1)	638 (39.7)	292 (18.2)	1607 (100.0)	
Income	<1 million	446 (43.7)	340 (33.3)	235 (23.0)	1021 (100.0)	<.001
	1~2 million	211 (34.8)	243 (40.0)	153 (25.2)	607 (100.0)	
	>2 million	273 (35.6)	341 (44.5)	153 (19.9)	767 (100.0)	
FRS		1.9 (0.8)	1.8 (0.8)	1.8 (0.8)		<.001
Frailty	Frail	69 (35.0)	53 (26.9)	75 (38.1)	197 (100.0)	<.001
	Pre-frail	442 (37.1)	452 (38.0)	297 (24.9)	1191 (100.0)	
	Robust	490 (42.6)	466 (40.5)	194 (16.9)	1150 (100.0)	
Episodic memory		0.1 (0.9)	0.2 (0.9)	0.0 (1.0)		.002
Working memory		0.1 (0.9)	0.2 (0.9)	-0.1 (1.0)		<.001
Perceptual speed		0.0 (0.9)	0.2 (0.8)	-0.1 (1.1)		<.001
Frontal lobe		0.1 (0.9)	0.2 (0.9)	-0.1 (1.0)		<.001
Global cognition		0.0 (0.7)	0.2 (0.6)	-0.1 (0.8)		<.001

* Characteristics of the categorical variables described as N (%), χ^2 and characteristics of continuous variables described as Mean (SD), *F-statistics*

Table 5. Baseline characteristics based on contact frequency with family members

Variable	Category	Famcontact			Total	*p*-value
		Frequently	Moderately	Rarely		
Gender	Female	443 (33.4)	382 (38.8)	502 (37.8)	1327 (100.0)	.071
	Male	353 (29.1)	374 (30.9)	484 (40.0)	1211 (100.0)	
Age		75.9 (3.9)	76.0 (4.0)	76.0 (3.8)		.756
Education	<Elementary	150 (32.4)	123 (26.6)	190 (41.0)	463 (100.0)	.354
	Elementary	229 (33.0)	200 (28.9)	264 (38.1)	693 (100.0)	
	Middle School	133 (32.5)	126 (30.8)	150 (36.7)	409 (100.0)	
	High School	141 (27.2)	164 (31.7)	213 (41.1)	518 (100.0)	
	≥College	143 (31.5)	142 (31.3)	169 (37.2)	454 (100.0)	
Marriage status	No	294 (35.6)	222 (26.9)	309 (37.5)	825 (100.0)	.003
	Yes	500 (29.3)	534 (31.2)	676 (39.5)	1710 (100.0)	
Chronic diseases	3≤	165 (31.8)	147 (28.3)	207 (39.9)	519 (100.0)	.767
	2	280 (31.1)	261 (29.0)	360 (39.9)	901 (100.0)	
	1	243 (31.0)	239 (30.5)	301 (38.5)	783 (100.0)	
	0	108 (32.2)	109 (32.6)	118 (35.2)	335 (100.0)	
Drinking	2≤ weekly	130 (28.6)	130 (28.6)	195 (42.8)	455 (100.0)	.120
	1~4 monthly	153 (31.3)	166 (33.9)	170 (34.8)	489 (100.0)	
	1≥ monthly	269 (31.2)	253 (29.4)	339 (39.4)	861 (100.0)	
	Never	242 (33.3)	202 (27.8)	282 (38.9)	726 (100.0)	
Nutritional Status		12.9 (1.5)	13.0 (1.4)	12.8 (1.5)		.026
Social support		24.4 (6.7)	24.1 (6.8)	22.4 (7.6)		<.001
Depression	Yes	57 (27.9)	52 (25.5)	95 (46.6)	204 (100.0)	.061
	No	739 (31.7)	704 (30.1)	891 (38.2)	2334 (100.0)	
IADL	Yes	330 (35.4)	256 (27.5)	345 (37.1)	931 (100.0)	.003
	No	466 (29.0)	500 (31.1)	641 (39.9)	1607 (100.0)	
Income	<1 million	313 (30.7)	268 (26.2)	440 (43.1)	1021 (100.0)	.002
	1~2 million	182 (30.0)	198 (32.6)	227 (37.4)	607 (100.0)	
	>2 million	218 (28.4)	264 (34.4)	285 (37.2)	767 (100.0)	
FRS		1.9 (0.8)	1.8 (0.8)	1.8 (0.8)		.066
Frailty	Frail	60 (30.5)	51 (25.9)	86 (43.6)	197 (100.0)	.092
	Pre-frail	375 (31.5)	335 (28.1)	481 (40.4)	1191 (100.0)	
	Robust	361 (31.4)	370 (32.2)	419 (36.4)	1150 (100.0)	
Episodic memory		0.1 (1.0)	0.1 (0.9)	0.1 (0.9)		.767
Working memory		0.1 (1.0)	0.1 (0.9)	0.1 (1.0)		.570
Perceptual speed		0.0 (1.0)	0.1 (0.8)	0.0 (1.0)		.027
Frontal lobe		0.1 (0.9)	0.2 (0.9)	0.0 (0.9)		.005
Global cognition		0.1 (0.7)	0.1 (0.7)	0.0 (0.7)		.040

* Characteristics of the categorical variables described as N (%), χ^2 and characteristics of continuous variables described as Mean (SD), *F-statistics*

Table 6. Baseline characteristics based on contact frequency with neighbors

Variable	Category	Neicontact			Total	*p*-value
		Frequently	Moderately	Rarely		
Gender	Female	614 (46.3)	384 (28.9)	329 (24.8)	1327 (100.0)	<.001
	Male	433 (35.8)	360 (29.7)	418 (34.5)	1211 (100.0)	
Age		76.1 (4.0)	75.5 (3.9)	76.3 (3.8)		<.001
Education	<Elementary	263 (56.8)	101 (21.8)	99 (21.4)	463 (100.0)	<.001
	Elementary	339 (48.9)	190 (27.4)	164 (23.7)	693 (100.0)	
	Middle School	171 (41.8)	115 (28.1)	123 (30.1)	409 (100.0)	
	High School	166 (32.1)	184 (35.5)	168 (32.4)	518 (100.0)	
	≥College	108 (23.8)	154 (33.9)	192 (42.3)	454 (100.0)	
Marriage status	No	387 (46.9)	219 (26.6)	219 (26.5)	825 (100.0)	<.001
	Yes	658 (38.5)	524 (30.6)	528 (30.9)	1710 (100.0)	
Chronic diseases	3≤	217 (41.8)	126 (24.3)	176 (33.9)	519 (100.0)	.013
	2	388 (43.1)	258 (28.6)	255 (28.3)	901 (100.0)	
	1	299 (38.2)	261 (33.3)	223 (28.5)	783 (100.0)	
	0	143 (42.7)	99 (29.5)	93 (27.8)	335 (100.0)	
Drinking	2≤ weekly	177 (38.9)	137 (30.1)	141 (31.0)	455 (100.0)	.662
	1~4 monthly	202 (41.3)	140 (28.6)	147 (30.1)	489 (100.0)	
	1≥ monthly	348 (40.4)	251 (29.2)	262 (30.4)	861 (100.0)	
	Never	318 (43.8)	211 (29.1)	197 (27.1)	726 (100.0)	
Nutritional Status		12.9 (1.5)	12.9 (1.5)	12.9 (1.5)		.897
Social support		25.4 (6.2)	23.1 (7.2)	21.2 (7.7)		<.001
Depression	Yes	81 (39.7)	51 (25.0)	72 (35.3)	204 (100.0)	.127
	No	966 (41.4)	693 (29.7)	675 (28.9)	2334 (100.0)	
IADL	Yes	380 (40.8)	268 (28.8)	283 (30.4)	931 (100.0)	.714
	No	667 (41.5)	476 (29.6)	464 (28.9)	1607 (100.0)	
Income	<1 million	514 (50.3)	253 (24.8)	254 (24.9)	1021 (100.0)	<.001
	1~2 million	232 (38.2)	186 (30.6)	189 (31.2)	607 (100.0)	
	>2 million	240 (31.3)	256 (33.4)	271 (35.3)	767 (100.0)	
FRS		2.0 (0.8)	1.8 (0.8)	1.7 (0.8)		<.001
Frailty	Frail	102 (51.8)	41 (20.8)	54 (27.4)	197 (100.0)	.008
	Pre-frail	500 (42.0)	348 (29.2)	343 (28.8)	1191 (100.0)	
	Robust	445 (38.7)	355 (30.9)	350 (30.4)	1150 (100.0)	
Episodic memory		-0.0 (0.9)	0.2 (0.9)	0.1 (0.9)		<.001
Working memory		-0.1 (0.9)	0.2 (1.0)	0.2 (1.0)		<.001
Perceptual speed		-0.2 (1.0)	0.2 (0.8)	0.2 (0.8)		<.001
Frontal lobe		-0.1 (0.9)	0.2 (0.9)	0.2 (0.9)		<.001
Global cognition		-0.1 (0.2)	0.2 (0.7)	0.2 (0.6)		<.001

* Characteristics of the categorical variables described as N (%), χ^2 and characteristics of continuous variables described as Mean (SD), *F-statistics*

Global cognition

UNADJUSTED ANALYSIS

In the unadjusted linear regression, as Global cognition as the outcome variable, all variables were significantly associated with Global cognition (Table 7), except for the 1≥ monthly group (p-value: .344) in terms of the drinking variable, Social support (p-value: .477), and in terms of contact frequency with family: Rarely group (p-value: .692) and Moderately group (p-value: .052).

Table 7. Unadjusted linear regression in terms of Global cognition

		Global cognition	
Variables	Categories	B (S.E.)	*p*-value
Gender	Female	-0.248 (0.027)	<.001
	Male		
Age		-0.053 (0.003)	<.001
Education	<Elementary	-1.195 (0.037)	<.001
	Elementary	-0.645 (0.034)	<.001
	Middle School	-0.403 (0.038)	<.001
	High School	-0.166 (0.036)	<.001
	≥College		
Marriage status	No	-0.376 (0.283)	<.001
	Yes		
Chronic diseases	3≤	-0.167 (0.048)	<.001
	2	-0.180 (0.044)	<.001
	1	-0.100 (0.045)	.026
	0		
Drinking	2≤ weekly	0.164 (0.041)	<.001
	1~4 monthly	0.151 (0.040)	<.001
	1≥ monthly	0.033 (0.035)	.344
	Never		
Nutritional Status		0.071 (0.009)	<.001
Social support		-0.001 (0.002)	.477
Depression	Yes	-0.530 (0.049)	<.001
	No		

Table 7. *cont.*

Variables	Categories	Global cognition B (S.E.)	*p*-value
IADL	Yes	-0.090 (0.028)	.002
	No		
Income	<1 million	-0.525 (0.030)	<.001
	1~2 million	-0.200 (0.034)	<.001
	>2 million		
FRS		-0.226 (0.017)	<.001
Frailty	Frail	-0.822 (0.050)	<.001
	Pre-frail	-0.360 (0.027)	<.001
	Robust		
Friend	Rarely	-0.134 (0.036)	<.001
	Moderately	0.151 (0.031)	<.001
	Frequently		
Family	Rarely	-0.013 (0.033)	.692
	Moderately	0.068 (0.035)	.052
	Frequently		
Neighbor	Rarely	0.262 (0.032)	<.001
	Moderately	0.266 (0.033)	<.001
	Frequently		

ADJUSTED ANALYSIS

The adjusted analysis with the main variables of interest is shown in Table 8. Low Global cognition was associated with high FRS (B: -0.053, S.E.: 0.021, *p*-value: <.001). Also Global cognition score was worse for Frail (B: -0.302, S.E.: 0.044, *p*-value: .012) and Pre-frail (B: -0.156, S.E.: 0.022, *p*-value: <.001) with Robust as reference. In terms of contact frequency, Rarely contact group (B: -0.131, S.E.: 0.028, *p*-value: <.001) in terms of contacting friends was negatively associated with Global cognition with Frequently as reference. Lastly, both Rarely (B: 0.082, S.E.: 0.027, *p*-value: .003) and Moderately (B: 0.068, S.E.: 0.027, *p*-value: .014) were positively associated

with Global cognition, implying a better cognition score for those contacting their neighbors less frequently, with Frequently as reference in terms of contact frequency with neighbors.

Table 8. Adjusted linear regression in terms of Global cognition

Variables	Categories	Global cognition	
		B (S.E.)	*p*-value
FRS		-0.053 (0.021)	.012
Frailty	Frail	-0.302 (0.044)	.012
	Pre-frail	-0.156 (0.022)	<.001
	Robust		
Friendcontact	Rarely	-0.131 (0.028)	<.001
	Moderately	-0.014 (0.026)	.584
	Frequently		
Famcontact	Rarely	-0.019 (0.025)	.449
	Moderately	0.006 (0.026)	.807
	Frequently		
Neighborcontact	Rarely	0.082 (0.027)	.003
	Moderately	0.068 (0.027)	.014
	Frequently		
Adjusted R^2		0.450	
F-value$_{(df)}$ (*p*-value)		75.20$_{(28)}$ (<.001)	

* Adjusted for gender, age, education, marriage status, number of chronic diseases, drinking status, nutritional status, depression, IADL, Monthly income, and social support

REGRESSION EQUATION FOR GLOBAL COGNITION

$$\widehat{GC} = 2.999 + (0.028)Female - (0.032)Age - (0.923)Below\ elementary$$
$$- (0.503)Elementary\ school - (0.338)Middle\ school$$
$$- (0.108)High\ school - (0.110)Single + (0.031)High\ diseases$$
$$- (0.015)Middle\ diseases - (0.108)Low\ diseases$$
$$+ (0.014)Frequent\ drinking - (0.002)Moderate\ drinking$$
$$+ (0.006)Rarely\ drinking - (0.053)FRS - (0.302)Frail$$
$$- (0.156)Prefrail + (0.020)Nutrional\ status - (0.138)Depression$$
$$- (0.107)IADL - (0.064)Low\ income - (0.010)Middle\ income$$
$$- (0.003)Social\ support - (0.131)Rare\ contact\ with\ friends$$
$$- (0.014)Moderate\ contact\ with\ friends$$
$$- (0.019)Rare\ contact\ with\ family$$
$$- (0.006)Moderate\ contact\ with\ family$$
$$+ (0.082)Rare\ contact\ with\ neighbors$$
$$+ (0.068)Moderate\ contact\ with\ neighbors$$

INTERACTION EFFECTS

Table 9 displays each interaction effect proposed in our hypotheses. In this analysis, the interaction between Frailty and contact frequency with family members (B: 0.046, S.E.: 0.020, p-value: .021) and the interaction between FRS and contact frequency with friends (B: -0.053, S.E.: 0.017, p-value: .002) were significantly associated with Global cognition. These two interaction terms were further analyzed using PROC GLM procedure, and

only the interaction between FRS and contact frequency with friends (B: 3.706, M.S.: 2.407, *p*-value: .003) remained statistically significant (Table 10). Figure 8 illustrates the regression lines based on the frequency of contact with friends. The differences in slopes are shown in Table 11.

Table 9. Adjusted linear regression including the interaction terms

Variables	Categories	Model 1		Model 2		Model 3		Model 4	
		B (S.E.)	*p*-value	B (S.E.)	*p*-value	B (S.E.)	*p*-value	B (S.E.)	*p*-value
FRS		-0.054 (0.021)	.011	-0.053 (0.021)	.012	-0.054 (0.021)	.011	0.042 (0.037)	.258
Frailty	Frail	-0.179 (0.092)	.053	-0.501 (0.095)	<.001	-0.212 (0.085)	.012	-0.301 (0.044)	<.001
	Pre-frail	-0.104 (0.044)	.017	-0.258 (0.047)	<.001	-0.114 (0.044)	.009	-0.162 (0.022)	<.001
	Robust								
Friendcontact	Rarely	-0.078 (0.041)	.058	-0.126 (0.029)	<.001	-0.126 (0.029)	<.001	0.071 (0.068)	.298
	Moderately	0.010 (0.029)	.725	-0.009 (0.026)	.718	-0.010 (0.026)	.700	0.092 (0.041)	.026
	Frequently								
Famcontact	Rarely	-0.012 (0.025)	.629	-0.071 (0.036)	.048	-0.012 (0.025)	.637	-0.014 (0.025)	.563
	Moderately	0.005 (0.026)	.839	-0.023 (0.029)	.422	0.006 (0.026)	.002	0.005 (0.026)	.861
	Frequently								
Neighborcontact	Rarely	0.085 (0.027)	.002	0.085 (0.027)	.002	0.118 (0.037)	.002	0.084 (0.027)	.002
	Moderately	0.068 (0.028)	.014	0.067 (0.028)	.015	0.085 (0.030)	.005	0.070 (0.028)	.012
	Frequently								
Friend_interaction		-0.034 (0.021)	.112						
Fam_interaction				0.046 (0.020)	.021				
Nei_interaction						-0.026 (0.020)	.184		
FRS_friend								-0.053 (0.017)	.002
FRS_Fam									
FRS_Nei									
Frailty_FRS									
Adjusted R^2		0.455		0.455		0.455		0.456	
F-value$_{(df)}$ (*p*-value)		75.34$_{(29)}$ (<.001)		75.52$_{(29)}$ (<.001)		75.30$_{(29)}$ (<.001)		75.82$_{(29)}$ (<.001)	

* Adjusted for gender, age, education, marriage status, number of chronic diseases, drinking status, nutritional status, depression, IADL, Monthly income, and social support

Table 9. *cont.*

Variables	Categories	Model 5		Model 6		Model 7	
		B (S.E.)	*p*-value	B (S.E.)	*p*-value	B (S.E.)	*p*-value
FRS		-0.079 (0.038)	.038	-0.081 (0.036)	.025	-0.041 (0.025)	.102
Frailty	Frail	-0.308 (0.044)	<.001	-0.307 (0.044)	<.001	-0.230 (0.092)	.012
	Pre-frail	-0.164 (0.022)	<.001	-0.164 (0.022)	<.001	-0.128 (0.043)	.003
	Robust						
Friendcontact	Rarely	-0.125 (0.029)	<.001	-0.126 (0.029)	<.001	-0.125 (0.029)	<.001
	Moderately	-0.010 (0.026)	.710	-0.010 (0.026)	.686	-0.009 (0.026)	.721
	Frequently						
Famcontact	Rarely	-0.056 (0.063)	.369	-0.011 (0.025)	.655	-0.012 (0.025)	.641
	Moderately	-0.017 (0.040)	.658	0.005 (0.026)	.843	0.005 (0.026)	.848
	Frequently						
Neighborcontact	Rarely	0.085 (0.027)	.002	0.033 (0.063)	.599	0.084 (0.027)	.002
	Moderately	0.069 (0.028)	.012	0.042 (0.041)	.308	0.068 (0.028)	.014
	Frequently						
Friend_interaction							
Fam_interaction							
Nei_interaction							
FRS_friend							
FRS_Fam		0.012 (0.015)	.439				
FRS_Nei				0.014 (0.016)	.371		
Frailty_FRS						-0.020 (0.021)	.338
Adjusted R^2		0.454		0.454		0.454	
F-value$_{(df)}$ (*p*-value)		$75.22_{(29)}$ (<.001)		$75.23_{(29)}$ (<.001)		$75.24_{(29)}$ (<.001)	

* Adjusted for gender, age, education, marriage status, number of chronic diseases, drinking status, nutritional status, depression, IADL, Monthly income, and social support

Table 10. Analysis of the interaction effect using GLM

		Global Cognition	
Variables	Categories	B (M.S.)	*p*-value
FRS*friendcontact		3.706 (2.407)	.003
		B (S.E.)	*p*-value
FRS*friendcontact	Rarely	-0.131 (0.027)	<.001
	Moderately	-0.036 (0.031)	.246
	Frequently		
R^2		0.444	
F-value$_{(df)}$ (*p*-value)		67.19$_{(28)}$ (<.001)	

* Adjusted for gender, age, education, marriage status, number of chronic diseases, drinking status, nutritional status, depression, IADL, Monthly income, and social support

Table 11. Differences in slope depending on contact frequency with friends

	Global Cognition	
Variables	B (S.E.)	*p*-value
Frequently vs. Moderately	0.096 (0.036)	.008
Frequently vs. Rarely	0.132 (0.035)	<.001
Moderately vs. Rarely	0.036 (0.031)	.246

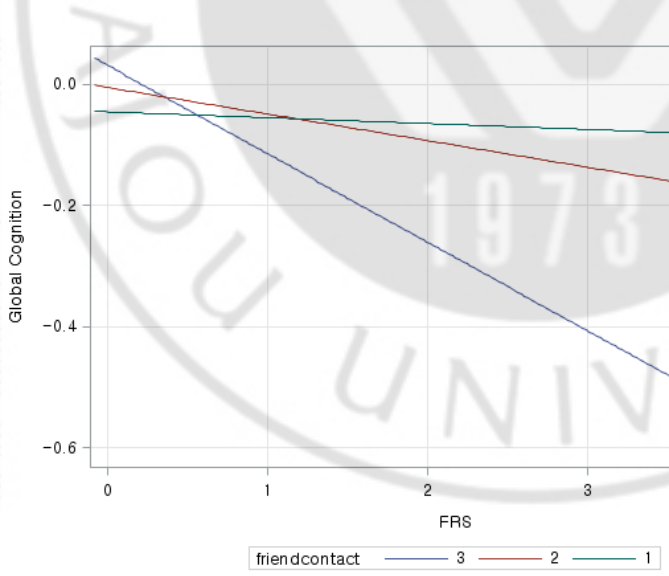

Figure 7. Regression lines depending on contact frequency with friends

Cognitive function

UNADJUSTED LINEAR REGRESSION FOR EACH COGNITIVE FUNCTION

Table 12 shows the unadjusted regression values between all variables and each cognitive function. FRS was significantly associated with all cognitive functions except for episodic memory. Frailty status, both Frail and Pre-frail, were significantly associated with all cognitive functions. The direction of the association implicated that worsening of either FRS or Frailty status was associated with lower cognitive scores. In terms of contact frequency, the associations with cognitive scores were mostly significantly associated when the target of contact was either friends or neighbors. Notably, most of the results in this analysis indicated a reversed effect between friends and neighbors.

Table 12. Unadjusted linear regression as each cognitive function as outcome

		Episodic Memory		Perceptual speed		Working memory		Frontal lobe	
Variables	Categories	B (S.E.)	*p*-value	B (S.E.)	*p*-value	B (S.E.)	*p*-value	B (S.E.)	*p*-value
Gender	Female	0.181 (0.037)	<.001	-0.442 (0.036)	<.001	-0.407 (0.037)	<.001	-0.326 (0.036)	<.001
	Male								
Age		-0.069 (0.005)	<.001	-0.056 (0.005)	<.001	-0.043 (0.005)	<.001	-0.041 (0.005)	<.001
Education	<Elementary	-0.612 (0.059)	<.001	-1.475 (0.052)	<.001	-1.355 (0.056)	<.001	-1.338 (0.053)	<.001
	Elementary	-0.304 (0.054)	<.001	-0.651 (0.047)	<.001	-0.858 (0.051)	<.001	-0.768 (0.048)	<.001
	Middle School	-0.219 (0.061)	<.001	-0.327 (0.054)	<.001	-0.566 (0.058)	<.001	-0.499 (0.054)	<.001
	High School	0.016 (0.058)	.779	-0.116 (0.051)	.022	-0.294 (0.055)	<.001	-0.269 (0.051)	<.001
	≥College								
Marriage status	No	-0.150 (0.039)	<.001	-0.482 (0.039)	<.001	-0.478 (0.040)	<.001	-0.395 (0.038)	<.001
	Yes								
Chronic diseases	3≤	-0.103 (0.065)	.112	-0.168 (0.065)	.010	-0.197 (0.067)	.004	-0.202 (0.064)	.002
	2	-0.125 (0.059)	.034	-0.205 (0.060)	<.001	-0.194 (0.062)	.002	-0.195 (0.058)	<.001
	1	-0.087 (0.060)	.151	-0.081 (0.061)	.184	-0.135 (0.063)	.031	-0.097 (0.059)	.101
	0								
Drinking	2≤ weekly	-0.106 (0.055)	.054	0.234 (0.056)	<.001	0.318 (0.057)	<.001	0.210 (0.053)	.003
	1~4 monthly	0.065 (0.054)	.231	0.200 (0.054)	<.001	0.184 (0.056)	.001	0.156 (0.053)	.003
	1≥ monthly	-0.066 (0.046)	.157	0.073 (0.047)	.120	0.079 (0.048)	.099	0.044 (0.046)	.332
	Never								
Nutritional status		0.070 (0.012)	<.001	0.068 (0.013)	<.001	0.070 (0.013)	<.001	0.076 (0.012)	<.001
Social support		-0.000 (0.003)	.933	-0.006 (0.003)	.023	-0.001 (0.003)	.639	0.002 (0.003)	.441
Depression	Yes	-0.402 (0.067)	<.001	-0.659 (0.067)	<.001	-0.515 (0.070)	<.001	-0.545 (0.066)	<.001
	No								

Table 12. *cont.*

Variables	Categories	Episodic Memory		Perceptual speed		Working memory		Frontal lobe	
		B (S.E.)	*p*-value	B (S.E.)	*p*-value	B (S.E.)	*p*-value	B (S.E.)	*p*-value
IADL	Yes	-0.220 (0.038)	<.001	-0.034 (0.039)	.383	0.015 (0.040)	.704	-0.121 (0.037)	.001
	No								
Income	<1 million	-0.320 (0.042)	<.001	-0.652 (0.041)	<.001	-0.573 (0.042)	<.001	-0.554 (0.040)	<.001
	1~2 million	-0.096 (0.048)	.044	-0.201 (0.047)	<.001	-0.248 (0.049)	<.001	-0.254 (0.046)	<.001
	>2 million								
FRS		-0.036 (0.023)	.124	-0.328 (0.023)	<.001	-0.290 (0.024)	<.001	-0.252 (0.022)	<.001
Frailty	Frail	-0.847 (0.069)	<.001	-0.840 (0.070)	<.001	-0.686 (0.072)	<.001	-0.915 (0.067)	<.001
	Pre-frail	-0.325 (0.037)	<.001	-0.389 (0.037)	<.001	-0.350 (0.039)	<.001	-0.377 (0.036)	<.001
	Robust								
Friend	Rarely	-0.049 (0.049)	.311	-0.142 (0.049)	.004	-0.177 (0.050)	<.001	-0.167 (0.047)	<.001
	Moderately	0.111 (0.042)	.008	0.185 (0.042)	<.001	0.148 (0.043)	<.001	0.161 (0.041)	<.001
	Frequently								
Family	Rarely	-0.007 (0.044)	.874	0.013 (0.045)	.766	-0.025 (0.046)	.586	-0.033 (0.043)	.440
	Moderately	0.025 (0.047)	.600	0.116 (0.048)	.015	0.024 (0.049)	.621	0.107 (0.046)	.021
	Frequently								
Neighbor	Rarely	0.140 (0.044)	.002	0.342 (0.044)	<.001	0.318 (0.046)	<.001	0.248 (0.043)	<.001
	Moderately	0.157 (0.044)	<.001	0.323 (0.044)	<.001	0.303 (0.046)	<.001	0.282 (0.043)	<.001
	Frequently								

ADJUSTED LINEAR REGRESSION FOR EACH COGNITIVE FUNCTION

In the adjusted analysis (Table 13), contrasting to our hypothesis, FRS was not significantly associated with specific cognitive functions. However, Frailty was significantly associated with all cognitive functions. The strengths of association between each cognitive function and Frailty were compared using a t-test, and the results are shown in Figure 9. When the regression coefficients were compared, Episodic memory was more strongly associated with Frailty compared to Perceptual speed (t: 2.616, *p*-value: <.01), and Working memory (t: 3.026, <.002). Also, Frontal lobe was more strongly associated with Frailty compared to Perceptual speed (t: 2.241, *p*-value: <.05), and Working memory (t: 2.682, *p*-value<.01) (Table 14). In terms of contact frequency, Rarely group was significantly associated with Perceptual speed (B: -0.175, S.E.: 0.041, *p*-value: <.001), Working memory (B: -0.228, S.E.: 0.046, *p*-value: <.001), and Frontal lobe (B: -0.139, S.E.: 0.043, *p*-value: .001). Contacting neighbors was significantly associated with Perceptual speed (B: 0.099, S.E.: 0.040, *p*-value: .012), and Working memory (B: 0.127, S.E.: 0.044, *p*-value: .004) for those in the Rarely group with Frequently group as reference, but the direction was the opposite to that of contacting friends (Table 13).

Table 13. Adjusted linear regression as each cognitive function as outcome

Variables	Categories	Episodic memory		Perceptual speed		Working memory		Frontal lobe	
		B (S.E.)	*p*-value	B (S.E.)	*p*-value	B (S.E.)	*p*-value	B (S.E.)	*p*-value
FRS		-0.058 (0.035)	.094	-0.058 (0.031)	.060	-0.045 (0.034)	.187	-0.052 (0.032)	.104
Frailty	Frail	-0.453 (0.072)	<.001	-0.201 (0.064)	.002	-0.147 (0.071)	.038	-0.407 (0.066)	<.001
	Pre-frail	-0.198 (0.036)	<.001	-0.137 (0.035)	<.001	-0.121 (0.036)	<.001	-0.166 (0.033)	<.001
	Robust								
Friendcontact	Rarely	0.018 (0.047)	.695	-0.175 (0.041)	<.001	-0.228 (0.046)	<.001	-0.139 (0.043)	.001
	Moderately	0.031 (0.042)	.462	-0.016 (0.037)	.661	-0.060 (0.041)	.147	-0.011 (0.038)	.780
	Frequently								
Famcontact	Rarely	0.004 (0.041)	.915	-0.001 (0.036)	.974	-0.038 (0.040)	.338	-0.040 (0.037)	.282
	Moderately	-0.004 (0.043)	.920	0.041 (0.038)	.289	-0.044 (0.042)	.296	0.034 (0.039)	.392
	Frequently								
Neighborcontact	Rarely	0.052 (0.045)	.239	0.099 (0.040)	.012	0.127 (0.044)	.004	0.051 (0.041)	.215
	Moderately	0.015 (0.045)	.739	0.070 (0.040)	.079	0.112 (0.044)	.012	0.074 (0.041)	.072
	Frequently								
Adjusted R^2		0.179		0.366		0.266		0.291	
F-value$_{(df)}$ (*p-value*)		$20.80_{(28)}$ (<.001)		$53.35_{(28)}$ (<.001)		$33.76_{(28)}$ (<.001)		$38.10_{(28)}$ (<.001)	

* Adjusted for gender, age, education, marriage status, number of chronic diseases, drinking status, nutritional status, depression, IADL, Monthly income, and social support

REGRESSION EQUATION FOR EPISODIC MEMORY

$$\widehat{\mathrm{EM}} = 3.600 + (0.398)Female - (0.046)Age - (0.527)Below\ elementary$$
$$- (0.304)Elementary\ school - (0.252)Middle\ school$$
$$- (0.013)High\ school - (0.100)Single + (0.058)High\ diseases$$
$$- (0.023)Middle\ diseases - (0.050)Low\ diseases$$
$$+ (0.030)Frequent\ drinking + (0.076)Moderate\ drinking$$
$$+ (0.004)Rarely\ drinking - (0.058)FRS - (0.453)Frail$$
$$- (0.198)Prefrail + (0.025)Nutrional\ status - (0.120)Depression$$
$$- (0.063)IADL - (0.005)Low\ income + (0.026)Middle\ income$$
$$- (0.002)Social\ support + (0.018)Rare\ contact\ with\ friends$$
$$+ (0.031)Moderate\ contact\ with\ friends$$
$$+ (0.004)Rare\ contact\ with\ family$$
$$- (0.004)Moderate\ contact\ with\ family$$
$$+ (0.052)Rare\ contact\ with\ neighbors$$
$$+ (0.015)Moderate\ contact\ with\ neighbors$$

REGRESSION EQUATION FOR PEPCEPTUAL SPEED

$$\widehat{\mathrm{PS}} = 3.628 - (0.161)Female - (0.036)Age - (1.079)Below\ elementary$$
$$- (0.415)Elementary\ school - (0.201)Middle\ school$$
$$- (0.020)High\ school - (0.076)Single + (0.061)High\ diseases$$
$$- (0.006)Middle\ diseases + (0.007)Low\ diseases$$
$$- (0.062)Frequent\ drinking - (0.032)Moderate\ drinking$$
$$- (0.025)Rarely\ drinking - (0.058)FRS - (0.201)Frail$$
$$- (0.137)Prefrail + (0.007)Nutrional\ status - (0.237)Depression$$
$$- (0.119)IADL - (0.141)Low\ income - (0.014)Middle\ income$$
$$- (0.007)Social\ support - (0.175)Rare\ contact\ with\ friends$$
$$- (0.016)Moderate\ contact\ with\ friends$$
$$- (0.001)Rare\ contact\ with\ family$$
$$+ (0.041)Moderate\ contact\ with\ family$$
$$+ (0.099)Rare\ contact\ with\ neighbors$$
$$+ (0.070)Moderate\ contact\ with\ neighbors$$

REGRESSION EQUATION FOR WORKING MEMORY

$$\widehat{\mathrm{WM}} = 2.684 + (0.066)Female - (0.027)Age - (1.050)Below\ elementary$$
$$- (0.687)Elementary\ school - (0.482)Middle\ school$$
$$- (0.022)High\ school - (0.157)Single + (0.003)High\ diseases$$
$$- (0.022)Middle\ diseases - (0.074)Low\ diseases$$
$$+ (0.076)Frequent\ drinking + (0.025)Moderate\ drinking$$
$$+ (0.004)Rarely\ drinking - (0.045)FRS - (0.147)Frail$$
$$- (0.121)Prefrail + (0.026)Nutrional\ status - (0.103)Depression$$
$$- (0.068)IADL - (0.047)Low\ income - (0.006)Middle\ income$$
$$- (0.002)Social\ support - (0.228)Rare\ contact\ with\ friends$$
$$- (0.060)Moderate\ contact\ with\ friends$$
$$- (0.039)Rare\ contact\ with\ family$$
$$+ (0.044)Moderate\ contact\ with\ family$$
$$+ (0.127)Rare\ contact\ with\ neighbors$$
$$+ (0.112)Moderate\ contact\ with\ neighbors$$

REGRESSION EQUATION FOR FRONTAL LOBE FUNCTION

$$\widehat{\mathrm{FL}} = 2.082 - (0.060)Female - (0.019)Age - (1.038)Below\ elementary$$
$$- (0.603)Elementary\ school - (0.416)Middle\ school$$
$$- (0.203)High\ school - (0.106)Single + (0.010)High\ diseases$$
$$- (0.022)Middle\ diseases - (0.029)Low\ diseases$$
$$+ (0.010)Frequent\ drinking - (0.030)Moderate\ drinking$$
$$- (0.007)Rarely\ drinking - (0.052)FRS - (0.407)Frail$$
$$- (0.166)Prefrail + (0.022)Nutrional\ status - (0.091)Depression$$
$$- (0.178)IADL - (0.064)Low\ income - (0.043)Middle\ income$$
$$+ (0.001)Social\ support - (0.139)Rare\ contact\ with\ friends$$
$$- (0.011)Moderate\ contact\ with\ friends$$
$$- (0.040)Rare\ contact\ with\ family$$
$$+ (0.034)Moderate\ contact\ with\ family$$
$$+ (0.051)Rare\ contact\ with\ neighbors$$
$$+ (0.074)Moderate\ contact\ with\ neighbors$$

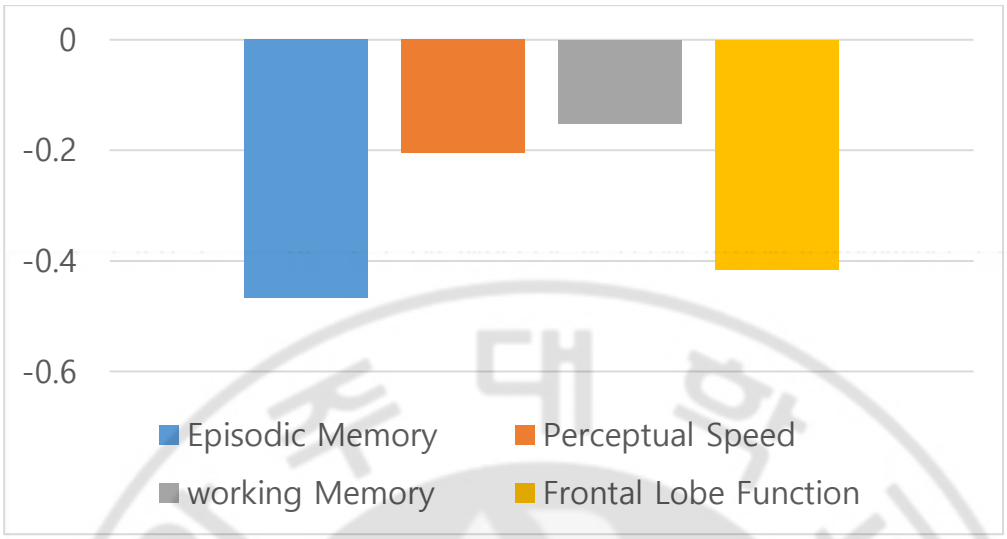

Figure 8. Regression coefficients of the association between Frailty and each cognitive function

Table 14. Comparison of the regression coefficients of the association between Frailty and each cognitive function

Cognitive functions	t-value	*p*-value
Episodic memory>Perceptual speed	2.616	<.01
Episodic memory>Working memory	3.026	<.002
Frontal lobe>Perceptual speed	2.241	<.05
Frontal lobe>Working memory	2.682	<.01

INTERACTION EFFECTS

The interaction effects in regards to each cognitive function are shown in Tables 15, 16, 19 and 20. The interaction between contact frequency with family members and Frailty (B: 0.065, S.E.: 0.029, *p*-

value: .023) as well as the interaction between Frailty and FRS (B: -0.080, S.E.: 0.030, p-value: .007) in regards to Perceptual speed were significant. Also, in regards to Working memory, the interaction between contact frequency with friends and Frailty (B: -0.077, S.E.: 0.034, *p*-value: .022) was significant. However, in the GLM analysis, only the interaction between Frailty and FRS remained statistically significant (B: 5.012, M.S.: 2.506, *p*-value: .014) (Table 17). The regression lines depending on Frailty status are shown in Figure 10, and the differences in slopes between the lines are shown in Table 18.

Table 15. Adjusted analysis with interaction terms in regards to Episodic memory

		Episodic memory							
		Model 1		Model 2		Model 3		Model 4	
Variables	Categories	B (S.E.)	*p*-value	B (S.E.)	*p*-value	B (S.E.)	*p*-value	B (S.E.)	*p*-value
FRS		-0.057 (0.035)	.101	-0.057 (0.035)	.100	-0.058 (0.035)	.097	-0.048 (0.041)	.238
Frailty	Frail	-0.309 (0.150)	.039	-0.585 (0.154)	<.001	-0.364 (0.137)	.008	-0.396 (0.149)	.008
	Pre-frail	-0.131 (0.071)	.065	-0.262 (0.076)	<.001	-0151 (0.071)	.035	-0.171 (0.070)	0.015
	Robust								
Friendcontact	Rarely	0.071 (0.067)	.290	0.018 (0.047)	.694	0.018 (0.047)	.697	0.019 (0.047)	.684
	Moderately	0.053 (0.047)	.255	0.031 (0.042)	.455	0.031 (0.042)	.463	0.031 (0.042)	.456
	Frequently								
Famcontact	Rarely	0.004 (0.041)	.924	-0.035 (0.058)	.540	0.004 (0.041)	.912	0.004 (0.041)	.913
	Moderately	-0.004 (0.043)	.922	-0.024 (0.047)	.619	-004 (0.043)	.929	-0.005 (0.041)	.913
	Frequently								
Neighborcontact	Rarely	0.053 (0.045)	.233	0.052 (0.045)	.239	0.083 (0.060)	.165	0.052 (0.045)	.241
	Moderately	0.015 (0.045)	.742	0.014 (0.045)	.755	0.031 (0.049)	.533	0.015 (0.045)	.742
	Frequently								
Friend_interaction		-0.038 (0.034)	.275						
Fam_interaction				0.031 (0.032)	.335				
Nei_interaction						-0.025 (0.032)	.443		
Frailty_FRS								-0.015 (0.033)	.660
Adjusted R^2		0.179		0.179		0.179		0.179	
F-value$_{(df)}$ (*p-value)*		$20.13_{(29)}$ (<.001)		$20.12_{(29)}$ (<.001)		$20.10_{(29)}$ (<.001)		$20.09_{(29)}$ (<.001)	

* Adjusted for gender, age, education, marriage status, number of chronic diseases, drinking status, nutritional status, depression, IADL, Monthly income, and social support

Table 16. Adjusted analysis with interaction terms in regards to Perceptual speed

		Perceptual speed							
		Model 1		Model 2		Model 3		Model 4	
Variables	Categories	B (S.E.)	*p*-value	B (S.E.)	*p*-value	B (S.E.)	*p*-value	B (S.E.)	*p*-value
FRS		-0.057 (0.031)	.063	-0.056 (0.031)	.069	-0.058 (0.031)	.060	-0.006 (0.037)	.876
Frailty	Frail	-0.115 (0.134)	.388	-0.477 (0.137)	<.001	-0.186 (0.122)	.127	0.111 (0.133)	.403
	Pre-frail	-0.098 (0.063)	0.123	-0.272 (0.068)	<.001	-0.130 (0.064)	.042	0.006 (0.062)	.926
	Robust								
Friendcontact	Rarely	-0.144 (0.060)	.016	-0.175 (0.041)	<.001	-0.175 (0.041)	<.001	-0.171 (0.041)	<.001
	Moderately	-0.003 (0.041)	.939	-0.015 (0.037)	.681	-0.016 (0.037)	.661	-0.014 (0.037)	.704
	Frequently								
Famcontact	Rarely	-0.001 (0.036)	.968	-0.085 (0.052)	.100	-0.001 (0.036)	.975	-0.000 (0.036)	.989
	Moderately	0.041 (0.038)	.288	0.000 (0.042)	.998	0.041 (0.038)	.288	0.039 (0.038)	.302
	Frequently								
Neighborcontact	Rarely	0.100 (0.040)	.012	0.099 (0.040)	.012	0.104 (0.053)	.051	0.098 (0.040)	.014
	Moderately	0.070 (0.040)	.079	0.068 (0.040)	.087	0.073 (0.044)	.098	0.070 (0.040)	.081
	Frequently								
Friend_interaction		-0.022 (0.031)	.466						
Fam_interaction				0.065 (0.029)	.023				
Nei_interaction						-0.004 (0.029)	.887		
Frailty_FRS								-0.080 (0.030)	.007
Adjusted R^2		0.366		0.367		0.366		0.368	
F-value$_{(df)}$ (*p-value)*		51.52$_{(29)}$ (<.001)		51.77$_{(29)}$ (<.001)		51.49$_{(29)}$ (<.001)		51.88$_{(29)}$ (<.001)	

* Adjusted for gender, age, education, marriage status, number of chronic diseases, drinking status, nutritional status, depression, IADL, Monthly income, and social support

Table 17. Analysis of the interaction effect using GLM

Variables	Categories	Perceptual speed	
		B (M.S.)	*p*-value
FRS*frailty		5.012 (2.506)	.014
		B (S.E.)	*p*-value
FRS*Frailty	Frail	-0.163 (0.073)	.026
	Pre-frail	-0.104 (0.042)	.014
	Robust		
R^2		0.377	
F-value$_{(df)}$ (*p*-value)		48.28$_{(30)}$ (<.001)	

* Adjusted for gender, age, education, marriage status, number of chronic diseases, drinking status, nutritional status, depression, IADL, Monthly income, and social support

Table 18. Differences in slope depending on Frailty

Variables	Perceptual speed	
	B (S.E.)	*p*-value
Robust vs. Pre-frail	0.060 (0.073)	.414
Robust vs. Frail	0.163 (0.073)	.026
Pre-frail vs. Frail	0.104 (0.042)	.014

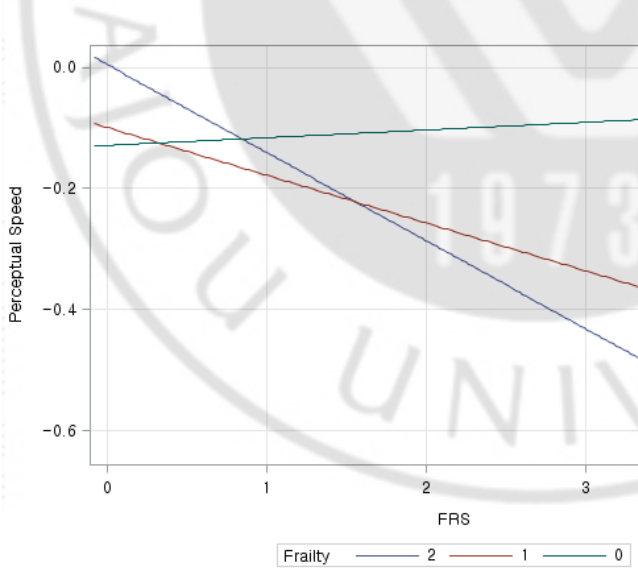

Figure 9. Regression lines depending on Frailty

Table 19. Adjusted analysis with interaction terms in regards to Working memory

		Working memory							
		Model 1		Model 2		Model 3		Model 4	
Variables	Categories	B (S.E.)	*p*-value	B (S.E.)	*p*-value	B (S.E.)	*p*-value	B (S.E.)	*p*-value
FRS		-0.043 (0.034)	.213	-0.043 (0.034)	.205	-0.044 (0.034)	.194	-0.073 (0.040)	.070
Frailty	Frail	0.149 (0.148)	.313	-0.392 (0.152)	.010	-0.042 (0.135)	.753	-0.315 (0.147)	.032
	Pre-frail	0.016 (0.070)	.819	-0.241 (0.075)	.001	-0.066 (0.070)	.347	-0.198 (0.069)	.004
	Robust								
Friendcontact	Rarely	-0.120 (0.066)	.069	-0.228 (0.046)	<.001	-0.228 (0.046)	<.001	-0.230 (0.046)	<.001
	Moderately	-0.014 (0.046)	.754	-0.059 (0.041)	.153	-0.060 (0.041)	.147	-0.061 (0.041)	.139
	Frequently								
Famcontact	Rarely	-0.039 (0.040	.326	-0.113 (0.057)	.049	-0.038 (0.040)	.340	-0.039 (0.040)	.334
	Moderately	-0.044 (0.042)	.297	-0.080 (0.047)	.086	-0.044 (0.042)	.302	-0.044 (0.042)	.303
	Frequently								
Neighborcontact	Rarely	0.128 (0.044)	.003	0.127 (0.044)	.004	0.163 (0.059)	.006	0.128 (0.044)	.004
	Moderately	0.111 (0.04)	.012	0.110 (0.044)	.013	0.130 (0.049)	.008	0.112 (0.044)	.011
	Frequently								
Friend_interaction		-0.077 (0.034)	.022						
Fam_interaction				0.058 (0.032)	.068				
Nei_interaction						-0.029 (0.032)	.363		
Frailty_FRS								0.043 (0.033)	.193
Adjusted R^2		0.267		0.266		0.266		0.266	
F-value$_{(df)}$ (*p-value)*		32.83$_{(29)}$ (<.001)		32.74$_{(29)}$ (<.001)		32.62$_{(29)}$ (<.001)		32.66$_{(29)}$ (<.001)	

* Adjusted for gender, age, education, marriage status, number of chronic diseases, drinking status, nutritional status, depression, IADL, Monthly income, and social support

Table 20. Adjusted analysis with interaction terms in regards to Frontal lobe function

		Frontal Lobe Fuction							
		Model 1		Model 2		Model 3		Model 4	
Variables	Categories	B (S.E.)	*p*-value	B (S.E.)	*p*-value	B (S.E.)	*p*-value	B (S.E.)	*p*-value
FRS		-0.052 (0.032)	.105	-0.051 (0.032)	.108	-0.051 (0.032)	.108	-0.049 (0.038)	.195
Frailty	Frail	-0.401 (0.137)	.004	-0.474 (0.141)	<.001	-0.317 (0.125)	.011	-0.391 (0.137)	.004
	Pre-frail	-0.163 (0.065)	.012	-0.199 (0.070)	.004	-0.119 (0.065)	.068	-0.159 (0.064)	.014
	Robust								
Friendcontact	Rarely	-0.137 (0.061)	.026	-0.139 (0.043)	.001	-0.139 (0.043)	.001	-0.139 (0.043)	.001
	Moderately	-0.010 (0.043)	.819	-0.010 (0.038)	.785	-0.011 (0.038)	.779	-0.011 (0.048)	.783
	Frequently								
Famcontact	Rarely	-0.040 (0.037)	.282	-0.060 (0.053)	.257	-0.040 (0.037)	.284	-0.040 (0.037)	.283
	Moderately	0.034 (0.039)	.392	0.024 (0.043)	.582	0.034 (0.039)	.386	0.034 (0.039)	.393
	Frequently								
Neighborcontact	Rarely	0.051 (0.041)	.215	0.051 (0.041)	.215	0.082 (0.055)	.138	0.051 (0.041)	.215
	Moderately	0.074 (0.041)	.072	0.073 (0.041)	.074	0.090 (0.045)	.047	0.074 (0.041)	.073
	Frequently								
Friend_interaction		-0.002 (0.032)	.959						
Fam_interaction				0.016 (0.029)	.594				
Nei_interaction						-0.025 (0.029)	.400		
Frailty_FRS								-0.004 (0.031)	.889
Adjusted R^2		0.290		0.290		0.290		0.290	
F-value$_{(df)}$ (*p-value)*		36.77$_{(29)}$ (<.001)		36.78$_{(29)}$ (<.001)		36.80$_{(29)}$ (<.001)		36.77$_{(29)}$ (<.001)	

* Adjusted for gender, age, education, marriage status, number of chronic diseases, drinking status, nutritional status, depression, IADL, Monthly income, and social support

IV. Discussion

This is an important study in terms of the impending super-aged society. South Korea has already become an aged society in 2018, and by 2065, the elderly population in Korea is expected to double that of a super-aged society. This study aimed to analyze the association between some of the health related concerns in the elderly population (e.g., vascular risks, frailty and cognitive function). Similar to previous findings (Fougère et al., 2017; Chen et al., 2018), the results of this study showed significant association between FRS and frailty with cognitive function. However, FRS was only significantly associated with global cognition, and the regression coefficient was significantly smaller than that of frailty. Our result differs from those of previous studies, in which vascular risks were associated with impaired executive function (Villeneuve et al., 2009), and vascular dementia, which has a characteristic of damaged frontal lobe function (Alzheimer's, 2015). A possible reason for this difference could be that the participants of this study had relatively lower vascular risks compared to other studies (Forman et al., 2008; Ganguli et al., 2014). Furthermore, an interaction between FRS and social contact was found, in which the cognitive score declined less as FRS increased for people who contacted their friends more frequently. Considering previous studies presenting protective role of social relationship in terms of cognitive decline (Fratiglioni et al., 2000; Fratiglioni et al., 2004), it is possible that contacting one's friends affected the association between cognitive function and FRS, either through the buffering or the main effect model.

In this study, the association between frailty and cognitive function

was the most significant. A number of studies are considering cognitive decline and physical frailty as co-occurring phenomenon with aging (Morley, 2015; Panza et al., 2015a; Panza et al., 2018), so the strong association between frailty and cognitive scores was not surprising. More notable were the strengths of association between each cognitive function and frailty. The strongest association was found between episodic memory function and frailty. A previous study (Buchman et al., 2008) showed an association between Alzheimer's pathology and frailty, and because decline in episodic memory is a key characteristic of Alzheimer's disease (Alzheimer's, 2015), the strong association between frailty and episodic memory in the current study is consistent with existing evidence. The second strongest association was found between the frontal lobe function and frailty. This too was supported in a number of previous studies (Glisky, 2007; Harada et al., 2013; Delrieu et al., 2016). Perceptual speed and working memory scores, although statistically significantly associated with frailty, showed significantly lower regression scores compared with episodic memory and frontal lobe function. Studies considering the relationship between frailty and various cognitive functions are scarce, so the results of this study provide important implications for the future.

The Generalized Linear Model was used for the interaction terms that were significantly associated with the cognitive scores in the linear regression model. The only significant interaction was found between Frailty and FRS in terms of Perceptual speed. Previous studies have proposed the possibility that vascular risk factors could be a part of the mechanism within the relationship between frailty and cognitive function (Fried et al., 2001;

Azzopardi et al., 2018). Accordingly, the interactive effect found in this study indicates the close relationship between frailty, vascular risk and cognitive function. Furthermore, the results propose the possibility that vascular risks not only work as a mechanism between frailty and cognitive function, but also could interact with frailty to worsen cognitive function, in this case perceptual speed. This is an important implication, because it provides information about the specific cognitive function that could be affected by the presence of combined frailty and vascular risk, which then can be used to design future intervention studies.

In line with previous studies indicating the associations between people's social networks and cognitive function (Zunzunegui et al., 2003; Barnes et al., 2004; Kuiper et al., 2016), the findings of our study presented interesting findings in regards to contact frequency and different cognitive functions. Whereas infrequent contact with friends was associated with relatively poorer cognitive function, infrequent contact with neighbors was associated with relatively better cognitive function. A few things could be considered in regards to the differences in results depending on the target of social contact. First, the possibility that the relationship with friends is perceived differently than the one with neighbors. This is important, because despite previous findings indicating beneficial effects of social relationship in terms of an individual's health, there are also findings indicating otherwise. For example, Gale et al. (Gale et al., 2012) found that bad social relationships could in fact negatively affect health. Also, the importance of considering poor social relationships was emphasized by Rook (Rook, 1984), who proposed that negative social relationships impacted health negatively more

than positive social relationships impacted health positively. However, our study was not able to acquire information regarding people's perceptions of their social relationships. Our effort to control for the subjective aspect of social relationships was accounted for by adjusting the overall perceived social support.

Social contact has shown protective effect against cognitive decline in previous studies (Zunzunegui et al., 2003; Barnes et al., 2004; Kuiper et al., 2016). Accordingly, we hypothesized that frequent social contact could buffer against cognitive impairment for people who are frail or have a high vascular risk score. However, the only interaction that was statistically significant was between contact frequency with friends and FRS in terms of Global cognition. Although the social contact variable did not show any other interactive effect, there were main effects in which the social contact variable was significantly associated with cognitive scores. Notably, for Perceptual speed and Working memory, although infrequent contact with friends were associated with lower cognitive scores, infrequent contact with neighbors was associated with higher cognitive scores. Neighborhood cohesion has shown to be beneficial in terms of an individual's health (Cramm and Nieboer, 2012), which contradicts the result of this study. Our study showing harmful effect of contacting one's neighbors in terms of cognitive function may be due to the fact that some relationships bring harmful results to a person (Gale et al., 2012), but the possibility of reverse causality also need to be considered.

The findings of this study bring forth various notions in terms of health related concerns in the elderly population. Worsening of vascular

health, as well as physical and cognitive function with aging has been shown in previous studies (Hultsch et al., 1993; Tabbarah et al., 2002; Heidenreich et al., 2011; North and Sinclair, 2012; Tarazona-Santabalbina et al., 2016). Also, research in this field has tried to figure out the directional relationships between these conditions (Kaffashian et al., 2011; Bouillon et al., 2013; Rogers et al., 2017). The current study provides additional support to the relationship between these conditions, and further suggests new implications for this line of research. All three conditions often co-exist in the elderly population, and share common mechanisms. However, they have also shown to be preventable, so it is important to find ways to best ameliorate these conditions. Notably, the strong association between frailty and cognitive function shown in this study suggests the necessity to research these two concepts more closely. Moreover, frailty was most strongly associated with episodic memory, and studying this relationship more closely could also assist in terms of Alzheimer's research. Alzheimer's disease is the most common form of dementia, and if ameliorating frailty status could contribute in delaying Alzheimer's disease onset, it could significantly reduce Alzheimer's prevalence around the world, as well as mortality due to Alzheimer's (Zissimopoulos et al., 2014).

Vascular risk, measured by FRS, was not as significantly associated with cognitive function in the current study as previous studies (Villeneuve et al., 2009; Kaffashian et al., 2011). However, it was mildly associated with the global cognition, suggesting the need to care for vascular risk for better cognitive reserve. Therefore, reminding people to update their vascular health status regularly, and educating them regarding ways to improve it

could greatly enhance various health concerns in the elderly. Also, considering the interactive effect between FRS and social contact as well as FRS and frailty provides indications for the future. First, the GLM model displayed a steeper decline in global cognition score in relation to increasing FRS for people who contacted their friends rarely compared to those contacting their friends frequently. Although there are limitations in terms of interpreting this result, it suggests a possible necessity to implement an intervention program involving social contact. This notion is also supported by previous studies showing how social contact has shown to buffer against harmful health effects (James et al., 2011; Lee and Kim, 2016). Accordingly, educating people in regards to the benefits of maintaining good social relationships, and developing programs to increase people's social network could prove to be a useful way to achieve healthy aging in the elderly population. In the last interaction between Frailty and FRS, the result of the GLM model displayed a steeper decline in Perceptual speed score for those who were frail and had high FRS. This information could be utilized to help people in various ways, because it not only shows the interaction effect between Frailty and FRS, but also indicates the specific cognitive function that is affected by this interaction.

Finally, although social contact did not show any interaction effects in specific cognitive functions, and did not show the possibility of being a buffer against high FRS or worse frailty status, there were associations between different contact types and multiple cognitive functions. There were no significant differences in terms of the regression coefficients for each of the cognitive functions, but the different direction in the regression value

between the targets of contact was more notable. In a simple interpretation of these results, contacting one's friends more frequently should be recommended for the elderly population, but the results should be interpreted with caution. Even though this study does not provide definitive findings that could be implemented into intervention programs, it does provide useful information for the future. First, the necessity to study the concept of social contact more carefully could be considered. Considering the difference in the type of contact in our study as well as other previous studies (Chon et al., 2018; Kim and Chon, 2018), it is necessary to design studies to better analyze the mechanisms involved. Also, the result of this study provides additional support to the already existing evidence in regards to the benefits of social relationship (Berkman, 1995).

In this study, there are a number of strengths. First, the data used in the study is based on first nation-wide multi-centered frailty research in Korea. Although frailty is a concept that is increasingly being researched around the world, there has not been a study specifically designed to study frailty in Korea. The Korean Frailty and Aging Cohort Study not only initiated a cohort study to study various aspects of frailty, its design is also useful in terms of generalizability of its data. Second, the results of the study provide important implications in regards to health for the elderly population in Korea. Vascular risk, cognitive function, and frailty are all important issues in the elderly population, and the results proposing directional association between these health states provides valuable information for the future, both in terms of research design and government policy implementation. Third, a standardized scores of different cognitive functions were used as the

outcome variables. This allowed the comparison of the strengths of association between each cognitive function in terms of the independent variables. Lastly, the interaction terms included in the analyses implicates the possible synergistic effect between the independent variables. This is useful in regards to considering the outcome, when two different conditions co-occur in an individual.

Despite its various strengths and important results, the limitations of the study need to be taken into careful consideration. First, although this is a nation-wide multi-centered research, the data cannot be generalized to the entire Korean population. This is partly because the participants of the study were people who were able to come to the centers and to communicate, resulting in relatively healthy elderly population. This was especially true in terms of FRS, because it was significantly lower than that of other studies. Also, even though this was based on a cohort study, only the baseline data have been gathered so far, and the analysis was based on a cross-sectional data. This is an important issue in terms of interpreting the results, because it is difficult to clarify the causal direction between the variables of interest. Lastly, there was the problem of the participants who were excluded from the final analysis. Only the participants with no missing values on the main variables of interest were included in the study, and in the end more than 10% of the total population were excluded. This was even more problematic, because the general characteristics of the people who were excluded compared to the people who remained in the study differed (Supplementary Table 1). However, in a separate analysis including the people with the missing values, the result of the linear regression did not differ much from

the original analysis (Supplementary Table 2). In the future, a longitudinal design should be used to better clarify the direction of the association between vascular risk, frailty and cognitive function. Also, the concept of social contact should be measured more systematically to capture a wider sense of a person's social network.

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Korean Abstract

인구 고령화는 전세계 국가에서 눈에 띄며 한국은 인구 고령화가 특히 빠른 국가이다. 주목할 만하게, 각종 문제는 개개인의 나이와 연관해서 세심하게 고려되어야 하는데, 이것은 나이가 증가함에 따라 여러 문제들이 동시에 생겨날 가능성이 높아지기 때문이다. 혈관 위험, 노쇠 및 인지 저하는 노인 인구와 관련하여 연구되고 있는 주요 문제 중 일부이다. 세 가지 건강 상태 모두가 사람의 연령이 증가함에 따라 악화되는 것으로 알려져 있으며, 또한 여러 연구에서 서로 관련이 있음을 발견했다. 이전 연구에서는 세 가지 조건을 예방하고 개선하는 것이 가능함을 보여줌으로써, 이러한 문제를 보다 면밀히 연구해야 하는 중요성을 나타내고 있다. 이러한 문제들과 관련하여 도움이 될 수 있는 한 가지 방법은 지인과 더 자주 접촉하는 것이다. 건강에 대한 사회적 접촉의 이점은 수많은 연구를 통해 보여지기 때문에 이 연구는 그 이점을 더 면밀히 분석하였다. 이 연구의 목적은 혈관 위험, 노쇠 및 인지 기능 간의 연관성을 연구하고 유해한 건강 결과에 대해 완충 작용을 하는 사회적 관계의 가능성을 더 밝히는 것이었다. 이 연구는 한국 노인 노쇠 코호트 Korean Frailty and Aging Cohort Study (KFACS)의 데이터를 사용하여 각 변수 간의 연관성을 분석했다. 우리의 결과는 노쇠와 인지 기능 사이의 강한 연관성을 보여 주었지만, 혈관 위험은 그다지 연관성이 없었다. 또한 빈번하지 않은 사회적 접촉이 인지 기능의 저하와 관련되어 있음에도 불구하고 이는 일부 경우에만 해당되는 것이 나타났다. 마지막으로 우리는 분석에서 상호 작용 변수를 포함시킴으로써 사회적 접촉과 위험변수들의 상호작용 효과를 연구하려고 시도했지만 통계적으로 유의미한 몇 가지 상호 작용만 남았다. 확정적인 결론을 내리기에는 부족하지만, 이 연구는 향후 연구에 가치 있는 통찰력을 제공하고 향후 연구에서 그 결과를 구현하면 한국의 노령 인구의 건강을 크게 향상시킬 수 있을 것이다.

Supplementary Table 1. General characteristics between study participants and dropouts

Variable	Category	Dropout		Total	*p*-value
		Yes	No		
Gender	Female	213 (49.8)	1369 (52.9)	1582 (52.5)	.223
	Male	215 (50.2)	1217 (47.1)	1432 (47.5)	
Age		76.3 (4.0)	76.0 (3.9)		.136
Education	<Elementary	160 (37.5)	482 (18.7)	642 (21.3)	<.001
	Elementary	98 (23.0)	712 (27.5)	810 (26.9)	
	Middle School	53 (12.4)	411 (15.9)	464 (15.4)	
	High School	60 (14.0)	524 (20.3)	584 (19.4)	
	≥College	56 (13.1)	456 (17.6)	512 (17.0)	
Marriage status	No	150 (35.1)	842 (32.6)	992 (32.9)	.318
	Yes	278 (64.9)	1741 (67.4)	20199 (67.1)	
Chronic diseases	3≤	68 (15.9)	528 (20.4)	596 (19.8)	.038
	2	142 (33.2)	919 (35.5)	1061 (35.2)	
	1	155 (36.2)	796 (30.8)	951 (31.5)	
	0	63 (14.7)	343 (13.3)	406 (13.5)	
Drinking	2≤ weekly	82 (19.6)	456 (17.7)	538 (17.9)	.585
	1~4 monthly	81 (19.3)	494 (19.1)	575 (19.2)	
	1≥ monthly	147 (35.1)	881 (34.2)	1028 (34.3)	
	Never	109 (26.0)	748 (19.0)	857 (28.6)	

* Characteristics of the categorical variables described as N (%), χ^2 and characteristics of continuous variables described as Mean (SD), *F-statistics*

Supplementary Table 1. *Cont.*

Variable	Category	Dropout		Total	*p*-value
		Yes	No		
Nutritional Status		12.5 (1.8)	12.9 (1.5)		<.001
Social support		25.2 (6.8)	23.5 (7.2)		<.001
Depression	Yes	57 (13.3)	216 (8.4)	273 (9.1)	<.001
	No	371 (86.7)	2370 (91.6)	2741 (90.9)	
IADL	Yes	188 (43.9)	951 (36.8)	1139 (37.8)	.005
	No	240 (56.1)	1635 (63.2)	1875 (62.2)	
Income	<1 million	207 (53.3)	1044 (42.9)	1251 (44.3)	<.001
	1~2 million	83 (21.4)	617 (25.3)	700 (14.8)	
	>2 million	98 (25.3)	773 (31.8)	871 (30.9)	
FRS		1.8 (0.9)	1.9 (0.8)		.581
Frailty	Frail	22 (15.5)	204 (7.9)	226 (8.3)	<.001
	Pre-frail	83 (58.4)	1224 (47.3)	1307 (47.9)	
	Robust	37 (26.1)	1158 (44.8)	1195 (43.8)	
Episodic Memory		-0.4 (1.2)	0.1 (0.9)		<.001
Working Memory		-0.4 (1.1)	0.1 (1.0)		<.001
Perceptual Speed		-0.1 (1.2)	0.0 (1.0)		.006
Frontal Lobe		-0.5 (1.3)	0.1 (0.9)		<.001
Global Cognition		-0.4 (0.9)	0.1 (0.7)		<.001

* Characteristics of the categorical variables described as N (%), χ^2 and characteristics of continuous variables described as Mean (SD), *F-statistics*

Supplementary Table 2. Adjusted linear regression with Imputed data

Variables	Categories	Episodic memory		Perceptual speed		Working memory		Frontal lobe	
		B (S.E.)	*p*-value	B (S.E.)	*p*-value	B (S.E.)	*p*-value	B (S.E.)	*p*-value
FRS		-0.043 (0.033)	.194	-0.057 (0.031)	.062	-0.010 (0.032)	.755	-0.035 (0.031)	.246
Frailty	Frail	-0.464 (0.071)	<.001	-0.295 (0.073)	<.001	-0.182 (0.065)	.005	-0.419 (0.070)	<.001
	Pre-frail	-0.192 (0.036)	<.001	-0.136 (0.032)	<.001	-0.130 (0.034)	<.001	-0.160 (0.034)	<.001
	Robust								
Friendcontact	Rarely	-0.004 (0.044)	.921	-0.137 (0.041)	<.001	-0.227 (0.042)	<.001	-0.175 (0.041)	<.001
	Moderately	0.035 (0.040)	.378	-0.025 (0.036)	.495	-0.057 (0.038)	.137	-0.029 (0.037)	.423
	Frequently								
Famcontact	Rarely	0.021 (0.039)	.579	-0.001 (0.035)	.973	-0.018 (0.037)	.628	-0.034 (0.036)	.347
	Moderately	-0.002 (0.041)	.953	0.029 (0.038)	.439	-0.046 (0.039)	.244	0.038 (0.038)	.319
	Frequently								
Neighborcontact	Rarely	0.083 (0.043)	.052	0.096 (0.039)	.013	0.134 (0.041)	.001	0.083 (0.039)	.035
	Moderately	0.027 (0.043)	.533	0.063 (0.039)	.105	0.111 (0.041)	.006	0.095 (0.039)	.016
	Frequently								

* Adjusted for gender, age, education, marriage status, number of chronic diseases, drinking status, nutritional status, depression, IADL, Monthly income, and social support