HEARING IMPAIRMENT, CARDIOVASCULAR DISEASE RISK FACTORS, METHYLMALONIC ACID, AND VITAMIN B_{12} STATUS IN OLDER ADULTS

by

SOHYUN PARK

(Under the Direction of Mary Ann Johnson, Ph.D.)

ABSTRACT

Hearing impairment is a common chronic health condition in older adults and is associated with impaired quality of life. However, there is limited comprehensive research concerning interactions among poor diets and hearing loss. In the first study, the prevalence of hearing impairment and the relationship of Hearing Handicap Inventory for the Elderly with pure-tone average threshold (PTA) were evaluated. Approximately 63% of participants had hearing impairment in the best ear [PTA across 1, 2, and 4 kHz > 25 dB hearing level (HL)]. A moderate correlation was found between Hearing Handicap Inventory for the Elderly and PTA. In the second study, the relationship between hearing loss and cardiovascular disease (CVD) risk factors was examined. Low-density lipoprotein cholesterol, total cholesterol, and triglycerides were not significantly associated with hearing loss. However, PTA was significantly correlated with high-density lipoprotein (HDL) cholesterol in the poorest ear and total cholesterol/HDL cholesterol ratio in both ears. Participants with impaired hearing had significantly lower HDL cholesterol concentration than those with normal hearing (≤ 25 dB HL) in the worst ear. Participants with PTA > 40 dB HL had significantly lower HDL cholesterol level than those with PTA ≤ 40 dB HL in both ears. Thus, HDL cholesterol may be a modifiable risk factor for hearing loss. In the third study, the relationship between age-related hearing loss (ARHL) and poor vitamin B_{12} status in older adults was examined, using multiple measures of vitamin B_{12} status and by repletion with a vitamin B_{12} supplement. A consistent relationship of vitamin B_{12} with auditory function was found in the worst ear. Participants with impaired hearing in the worst ear had a significantly higher prevalence of vitamin B_{12} deficiency, higher mean serum MMA concentration, higher prevalence of elevated MMA (> 271 nmol/L), and a non-significantly higher prevalence of low serum vitamin B_{12} than those with normal hearing (≤ 25 dB HL). Hearing thresholds were not improved in any group after three months of vitamin B_{12} supplementation (0-1000 μg/d). Impaired vitamin B_{12} status may be a modifiable risk factor for ARHL in older adults. Since vitamin B_{12} repletion did not improve hearing function in vitamin B_{12} deficient participants, this suggests that prevention of vitamin B_{12} deficiency may be important. This research adds to the growing body of literature that suggests CVD- and nutrition-related risk factors are associated with hearing loss in older people.

INDEX WORDS: Vitamin B_{12}, Methylmalonic acid, Intervention, Hearing loss, CVD risk factors, Older adults

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DEDICATION

I would like to dedicate this achievement to my parents, Sungman Park and Malpil Lee, for their unconditional love and immeasurable support. My achievement of this higher degree would not have been possible without them. With this opportunity, I would like to let my parents know how much I love them and appreciate their sacrifice. I would also like to dedicate this accomplishment to my husband Antonio, my family, and my friends, for their love, encouragement, and unfailing support of my advanced education. Their love and support have sustained me during this long journey. Thank you all!

감사의 글

오늘이 있기까지 헌신적인 사랑으로 저에게 모든 것을 베풀어 주신 사랑하는 나의 부모님 (아버지 박성만님 과 어머니 이말필님)께 박사과정의 결실인 이 논문을 받칩니다. 부모님의 헌신적인 사랑, 희생, 그리고 뒷받침 없이는 오늘의 결실이 없다고 해도 과언이 아닙니다. 이 기회를 통해, 부모님께 제가 얼마나 부모님을 사랑하고, 존경하고, 그리고 부모님의 희생에 감사 드리는지를 진심으로 전하고 싶습니다. 사랑, 격려, 그리고 응원을 해준 사랑하는 나의 남편 (안토니오), 가족들, 친구들, 그리고 교수님들에게 이 결실을 받칩니다. 박사과정 기간 동안 사랑으로 나를 격려해 주신 모든 분들께 이 결실을 드리면서 기쁨을 함께 하고자 합니다. 정말 감사 드립니다.

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CHAPTER 1

INTRODUCTION

Hearing impairment is the third most common chronic health condition in older adults (Lethbridge-Cejku and Vickerie, 2005). The human ear has a conductive component (the outer and middle ear) and a sensorineural component (the inner ear and auditory nerve). Frequently, a person's pure-tone average, the mean of three or four contiguous frequencies, is used to predict the degree of communication impact imposed by hearing loss (Martin and Clark, 2002; Newman and Sandridge, 2004). Higher hearing threshold indicates poorer hearing sensitivity and greater difficulty hearing and understanding speech. Hearing impairment may result from numerous factors including genetics, noise, acoustic trauma, viral or bacterial infections, sensitivity to certain drugs or medications, and aging (Johnson et al., 2004). In the 2003 National Health Interview Survey, 17.6% of people aged 45 to 64 years, 29.7% of people aged 65 to 74 years, and 46.4% of people aged 75 or older reported difficulty in hearing (Lethbridge-Cejku and Vickerie, 2005). The prevalence of hearing impairment increases with advanced age (Gates and Mills, 2005). Men typically have poorer hearing status than women (Torre et al., 2005).

Hearing impairment adversely affects the lives of older adults. Even mild hearing loss is associated with impaired quality of life, functional disabilities, and adverse effects on physical, cognitive, emotional, behavioral, and social function (Jerger et al., 1995; Dalton et al., 2003; Bazargan et al., 2001; Gates and Mills, 2005). Despite the high prevalence of hearing loss in older adults, there is limited comprehensive and systematic research concerning the possible interactions among poor diet and hearing loss (Johnson et al., 2004). Several lines of evidence suggest that cardiovascular diseases (CVD) and CVD risk factors may be related to hearing loss. Hearing loss was associated with high intake of saturated fats in humans (Rosen et al., 1970) and with high dietary cholesterol in chinchillas (Sikora et al., 1986). Abnormal blood lipids may enhance the adverse effects of noise on hearing loss (Axelsson and Lindgren, 1985). Auditory dysfunction was associated with hyperlipidemia or hypercholesterolemia in some (Rosen and Olin, 1965; Torre et al., 2005), but not all studies (Jones and Davis, 1999, 2000). Other CVD risk factors, self-reported or quantitatively measured, such as stroke, hypertension, heart disease, coronary heart disease, myocardial infarction, smoking, and diabetes mellitus, also have been associated with hearing loss in some (Gates et al., 1993; Torre et al., 2005; Cruickshanks et al., 1998a, 1998b; Frisina et al., 2006; Uchida et al., 2005), but not all studies (Drettner et al., 1975; Jones and Davis, 1999, 2000; Nondahl et al., 2004).

Hearing loss may be related to vascular disease and neural degeneration or disorders (Gate et al., 1993; Seidman et al., 1996), and the vascular and neural systems depend on certain nutrients, such as vitamin B_{12} or folate, for optimal structure and function (Johnson et al., 2004). Vitamin B_{12} deficiency is common in older adults (Wolters et al., 2004; Baik and Russell, 1999). The prevalence of vitamin B_{12} deficiency (5% to 23% in people aged 60 years or older) increases with advanced age, mainly because atrophic gastritis decreases the production of the acid and digestive enzymes needed to cleave protein-bound vitamin B_{12} from the natural chemical form of vitamin B_{12} (Baik and Russell, 1999; IOM, 1998; Wolters et al., 2004; Johnson et al., 2003). Risk factors for vitamin B_{12} deficiency include low animal protein intake, no crystalline vitamin B_{12} from supplements or fortified foods, malabsorption associated with atrophic gastritis or *Helicobacter pylori* infection, pancreatic or intestinal pathology, and gastric acid-reducing medications (Baik and Russell, 1999; IOM, 1998, Johnson et al., 2003; Wolters et al., 2004).

Several studies suggest that vitamin B_{12} deficiency may be related to hearing loss. Poor vitamin B_{12} status was associated with auditory dysfunction in some (Houston et al., 1999; Gok et al., 2004; Shemesh et al., 1993), but not all studies (Berner et al., 2000; Fine et al., 1990; Fine and Hallett, 1980). Tinnitus (ringing in the ears) (Shemesh et al., 1993) and auditory hallucinations (Hector and Burton, 1988) have been recorded as symptoms of vitamin B_{12} deficiency. However, none of these studies have assessed the relationship of hearing with measures of vitamin B_{12} status such as methylmalonic acid (MMA) other than serum vitamin B_{12} and homocysteine (Hcy). MMA and Hcy are sensitive indicators of vitamin B_{12} status (Wolters et al., 2004; Baik and Russell, 1999).

Therefore, the purposes of this dissertation were to evaluate the prevalence of hearing impairment, to examine a possible relationship of hearing impairment with CVD risk factors among a sample of older adults, and to evaluate a possible relationship of age-related hearing loss with poor vitamin B_{12} status in older adults, using multiple measures of vitamin B_{12} status and by repletion with a vitamin B_{12} supplement.

Chapter 2 in this dissertation is a review of the literature. The literature review explores the human auditory system, assessment of auditory function, prevalence and biological basis of hearing loss in older adults, the association of hearing loss with CVD, CVD risk factors, and vitamin B_{12} status as well as functions and diagnosis of vitamin B_{12}.

Chapter 3 describes the methods used and the results obtained concerning the prevalence of hearing impairment and the relationship between Hearing Handicap Inventory for the Elderly and pure-tone average thresholds.

Chapter 4 describes the methods used and the results obtained concerning the relationships between hearing impairment and CVD risk factors.

Chapter 5 describes the methods and the results obtained concerning a possible relationship between age-related hearing loss and poor vitamin B_{12} status in older adults, using multiple measures of vitamin B_{12} status and by repletion with a vitamin B_{12} supplement.

Chapter 6 presents a summary of the major findings of this dissertation.

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CHAPTER 2

LITERATURE REVIEW

Background and Significance

The growth rate of the elderly population (over 65 years) has increased rapidly during the last few decades and will continue to increase for the next 50 years in the United States (U.S. Census, 2004). The number of people over 65 years was 36 million in 2003 and is expected to increase to nearly 55 million in 2020 and to 87 million in 2050 (U.S. Census, 2004; Federal Interagency Forum, 2004). About 88% of older adults were aged 65 to 84 years and 12% were aged 85 years and older in 2000 (U.S. Census, 2004). More than 96% of older adults live in the community rather than in long-term care facilities (Federal Interagency Forum, 2004). Human life expectancy also has increased dramatically during the last few decades. Those who are 65 years old today can expect to live more than 18 additional years, and 85-year-olds can expect to live more than six additional years (Federal Interagency Forum, 2004). With increased human longevity, healthy aging and well-being are important issues. As Americans live longer lives, more people will experience hearing loss, and hearing loss adversely affects the lives of older adults. Although hearing loss is common in older adults, healthy diet and lifestyle may delay the onset of hearing loss and diminish the severity of hearing impairment.

Many studies have tried to find the possible association between auditory dysfunction and certain nutrients, life styles, or certain diseases. Research indicates that cardiovascular diseases (CVD) and CVD risk factors may contribute to hearing loss. Hearing loss was associated with high intake of saturated fats or cholesterol (Rosen et al., 1970; Sikora et al., 1986). Abnormal blood lipids may enhance the adverse effects of noise on hearing loss, and auditory dysfunction was associated with hyperlipidemia or hypercholesterolemia (Axelsson and Lindgren, 1985; Rosen and Olin, 1965; Torre et al., 2005). Other CVD and CVD risk factors, such as stroke, hypertension, heart disease, coronary heart disease, myocardial infarction, smoking status, and diabetes mellitus, also have been associated with hearing loss (Gates et al., 1993; Torre et al., 2005; Cruickshanks et al., 1998a, 1998b; Frisina et al., 2006; Uchida et al., 2005).

Research also has demonstrated that vitamin B_{12} deficiency may be linked to hearing loss. Poor vitamin B_{12} status was associated with auditory dysfunction in some studies (Houston et al., 1999; Quaranta et al., 2004; Gok et al., 2004; Shemesh et al., 1993), but not all studies (Berner et al., 2000; Durga et al., 2006). Tinnitus (ringing in the ears) (Shemesh et al., 1993) and auditory hallucinations (Hector and Burton, 1988) have been recorded as symptoms of vitamin B_{12} deficiency.

Purpose

The purpose of this literature review is to discuss the general knowledge of the human auditory system, the potential risk factors for hearing loss, and the possible role of CVD, CVD risk factors, and vitamin B_{12} in auditory function. First, the anatomy and function of the human auditory system, assessments of auditory function, exogenous factors affecting auditory dysfunction, and effects of the aging process on the auditory system will be reviewed. Second, the prevalence of hearing loss and the possible risk factors for hearing loss, such as cardiovascular disease events, cigarette smoking, diabetes, hyperlipidemia, and hypertension, will be reviewed. Third, the prevalence of vitamin B_{12} deficiency and functions of vitamin B_{12} will be reviewed. Fourth, the possible association between auditory dysfunction and poor vitamin B_{12} status will be reviewed.

The Human Auditory System

Anatomy and Function

The human auditory system is divided into four components: outer ear, middle ear, inner ear, and auditory nerve and central auditory pathways (Figure 2.1).

Outer Ear

The outer ear, consisting of the auricle (or pinna), external auditory canal, and tympanic membrane, is the canal by which sounds are initially introduced to the hearing mechanism (Martin and Clark, 2002). The auricle assists in gathering the sound, and the external auditory canal efficiently transfers the acoustic energy. The tympanic membrane, which is located at the end of the auditory canal, vibrates by the acoustic energy. The outer third of the external auditory canal contains hair follicles and cerumen, which help to prevent foreign objects from passing into the inner two-thirds of the external auditory canal. Deformities of the outer ear do not affect the sensorineural mechanism, but do affect the conductive mechanism.

Middle Ear

The middle ear is an air-filled cavity consisting of bones, windows, ligaments, and muscles (Martin and Clark, 2002). The mastoid is a non-solid bone surrounding the ear and honeycombed with air cells. These cells form the pneumatic mastoid of the temporal bone. Three miniature bones (malleus, incus, and stapes) are called the ossicles. The manubrium (handle) of the malleus is connected to the tympanic membrane, and the head part of the malleus is connected to the incus. The incus is connected to the stapes, which is the smallest bone in the human body. Vibrations of the tympanic membrane are transmitted to this ossicular chain and then to the oval window. The ossicles contribute to the transformation of acoustic energy to mechanical energy.

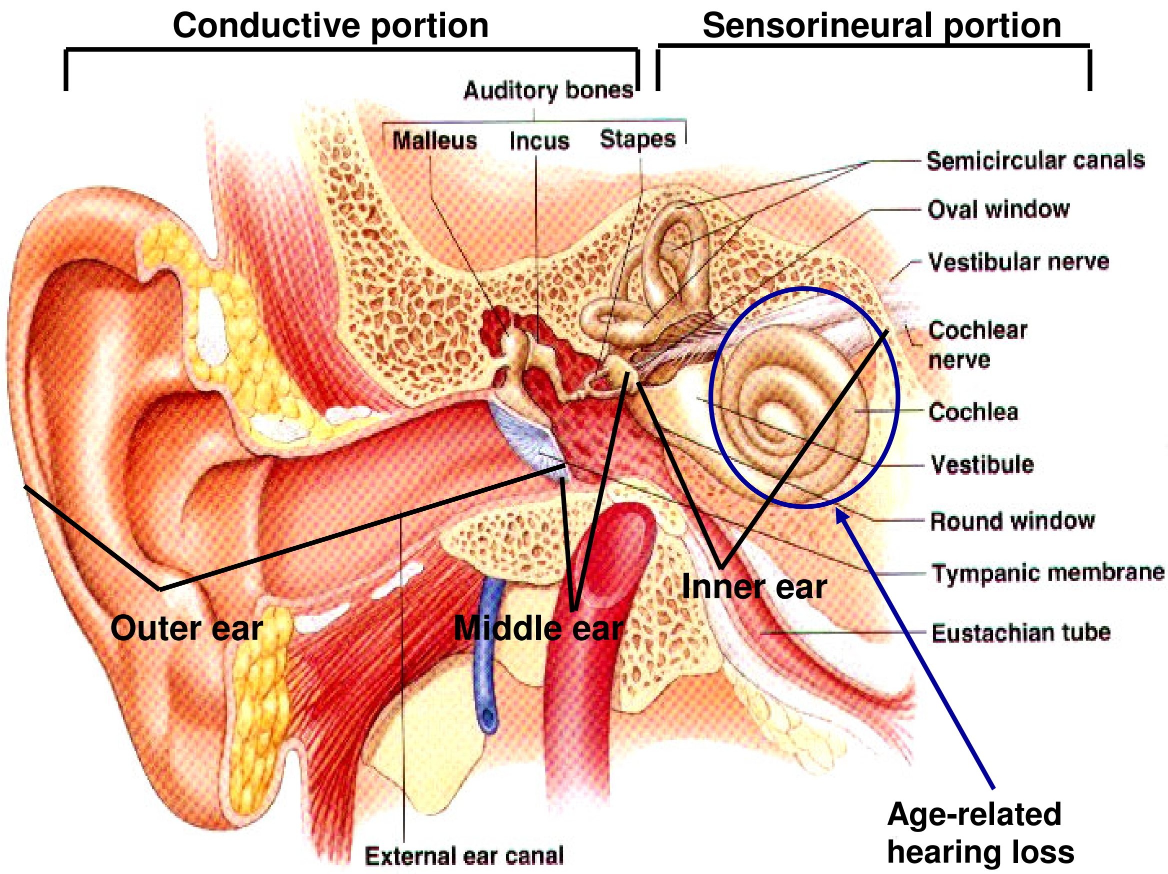

FIGURE 2.1 Human auditory system
(Adapted from http://www.sirinet.net/~jgjohnso/earparts. jpg.)

There are two windows (oval and round) in the middle ear. The foot-plate of the stapes fits into the oval window. The sound pressure collected by tympanic membrane is concentrated on this oval window, consequently increasing the sound pressure. The promontory is positioned between the oval window and round window.

There are two muscles (stapedius and tensor tympani) in the middle ear, and these muscles may protect the inner ear by stiffening the ossicular chain and thereby decreasing sound pressure reaching the inner ear. The stapedius muscle is innervated by a branch of the facial nerve. Upon contraction of the muscle, it is pulled posteriorly and stiffens the ossicle chain and tympanic membrane. The tensor tympani muscle is innervated by the trigeminal (Vth) cranial nerve, and the contraction of tensor tympani muscle moves the malleus, making the tympanic membrane tense. Abnormalities in the middle ear affect the conductive mechanism, but do not affect the sensorineural mechanism.

Inner Ear

The cochlea is located in the inner ear (Gate and Mills, 2005; Martin and Clark, 2002). The snail shell-like, fluid-filled cochlea (35 mm in length) consists of the scala vestibuli, scala media (cochlear duct), scala tympani, Reissner's membrane (located between the scala vestibuli and scala media), basilar membrane (located between the scala media and scala tympani), and helicotrema (apex of the cochlea, which localizes low frequency). Energy transformation occurs in the inner ear from mechanical energy into electrochemical energy for transmission to the brain.

The spiral ligament supports the scala media and stria vascularis. The stria vascularis, located on the lateral wall of the cochlea, produces the endolymph and provides nutrients and oxygen to the cochlea. The organ of Corti, which is the end organ of hearing system and contains sensory cells, is located on the basilar membrane in the scala media. The organ of Corti contains outer hair cells, inner hair cells, the tunnel of Corti, and the tectorial membrane. Stereocilia (hairs) on the top of outer hair cells are embedded in the tectorial membrane. The direction of stereocilia has an important role. The bending of stereocilia one direction activates the hair cells and bending in the opposite direction inhibits the hair cells.

Sound vibrations transmitted from the middle ear to the inner ear cause a disturbance of the fluids within the cochlea, which results in the deflection of the basilar membrane in a wavelike motion. This wavelike motion, referred to as the traveling wave, always moves from the base (detecting high frequency with shorter wavelengths) of the cochlea to the apex (detecting low frequencies with longer wavelengths). When the basilar membrane moves up and down, the hair cells are twisted in an intricate way. The exact mechanism of the organ of Corti is very complicated and is not fully understood. Twisted hair cells cause the cilia of hair cells to bend, which releases a chemical. This in-and-out cycle of the stereocilia of the outer hair cells stimulates auditory neurons, ultimately causing action potential.

Fluids

The cochlea has two different types of fluids (perilymph and endolymph). The scala vestibuli and scala tympani contain perilymph that is high in sodium and low in potassium. The scala media contains endolymph that is high in potassium and low in sodium. Due to high potassium content in endolymph, a strong positive potential (averaging 80 millivolts) is observed in endolymph when compared to perilymph in the scala tympani. Perilymph in the scala vestibuli exhibits positive and small potential (3 milivolts) compared to perilymph in the scala tympani. The remaining part of the cochlea shows negative direct current potential, and all of those potentials change.

Hair Cells and Auditory Neuron

There are approximately three to five rows of 12,000 to 15,000 outer hair cells and one row of 3,000 inner hair cells on the basilar membrane (Martin and Clark, 2002). In the outer hair cells, the neuron contacts about 10 hair cells. Inner hair cells consist of approximately 25 nerve fibers, and each nerve fiber contacts one hair cell. The cochlea contains 30,000 afferent (sensory) neurons and 1,800 efferent neurons. The cell bodies for these neurons are located in the modiolus (central core of the cochlea) (Gate and Mills, 2005; Martin and Clark, 2002). The afferent neurons transmit electrical impulses from the cochlea to the central auditory nerve system, and the efferent axons project from the medial and lateral superior olivary complex in the brainstem to make contact with the hair cells.

Auditory Nerve and Central Auditory Pathways

The auditory nerves have two different types of fibers (type I and type II). Approximately 90% to 95% are type I fibers, which are big, myelinated, and bipolar neurons that stimulate inner hair cells. About 5% to 10% of fibers are type II fibers, which are small, unmyelinated neurons that supply efferent synapses with the outer hair cells (Gate and Mills, 2005). The nerve fibers course through the modiolus and through the internal auditory canal, which carries the cochlear branch of the auditory nerve (VIIIth cranial) (Martin and Clark, 2002). The auditory nerve fibers synapse at the level of the cochlear nucleus in the caudal portion of the brainstem. From the cochlear nucleus nerve fibers ascend in the central auditory nervous system synapsing with several nuclei along the way, including the superior olivary complex, lateral lemniscus, inferior colliculus, and medial geniculate body. From the medial geniculate body, auditory radiations project to the primary and secondary auditory cortex.

Assessment of Auditory Function

The human auditory system has a conductive component (the outer ear and the middle ear) and a sensorineural component (the inner ear and the auditory nerve). During air-conduction measurements, sound travels through the outer ear, middle ear, inner ear, and neural pathways (Martin and Clark, 2002). During bone-conduction measurements, sound energy bypasses the outer ear and the middle ear, with minor exceptions, and reaches the inner ear directly. During a hearing assessment, pure tones of several different frequencies are presented to the listener. Audiometric results plotted on a graph with intensity represented on the Y axis and frequency shown on the X axis. The unit of measurement of sound intensity is the decibel (dB). Hearing threshold is defined as the lowest sound level that an individual can detect 50% of the time when it is presented and is expressed in dB hearing level (HL). Zero dB HL represents the average normal hearing of young adults. The ear exhibits different amounts of sensitivity to various frequencies. Most sensitive frequencies are in the range of 1000 hertz (Hz) to 4000 Hz in humans. Different amounts of pressure are required for 0 dB HL at various frequencies. Hearing thresholds can be determined by pure-tone audiometers, which generate a number of pure tones at various frequencies (from 125 to 8000 Hz).

Air-conduction audiometry is used to specify the degree of hearing loss at different frequencies (from 250 to 8000 Hz). However, it cannot specify whether the hearing loss is produced by a defect in the conductive mechanism or the sensorineural mechanism, or both (Martin and Clark, 2002). Bone-conduction audiometry is used to determine the sensorineural activity level. The measurement can be done by placing a bone vibrator on the mastoid (bone behind the ears) or forehead. Various ranges of frequencies can be tested with bone-conduction audiometry. Depending on the difference between the air-conduction and bone-conduction thresholds (called air-bone gap), the types of hearing loss can be defined (e.g. conductive hearing loss, sensorineural hearing loss, or mixed hearing loss). If the air-bone gap is greater than 10 dB, it indicates a possible pathology in the middle ear. Conductive hearing loss demonstrates an impaired air-conduction threshold and a normal bone-conduction threshold due to damage, disease, or dysfunction of the outer or middle ear. Sensorineural hearing loss is one in which the hearing impairment results from structural damage or alteration to the inner ear (sensory) or auditory nerve dysfunction (neural). Sensorineural hearing loss displays impaired thresholds in both air-conduction and bone-conduction due to damage, disease, or dysfunction of the inner ear. Mixed hearing loss is a combination of conductive and sensorineural hearing loss due to dysfunction of the outer or middle ear and inner ear (Martin and Clark, 2002).

Frequently, a person's pure-tone average (PTA), the mean of three or four contiguous frequencies, is used to predict the degree of communication impact imposed by hearing loss. There are different categories to define hearing loss by the severity of hearing loss. When PTA is 25 dB or less, it is considered normal hearing. PTA from 26 to 40 dB is considered mild hearing loss, and hearing aids are probably considered. PTA from 41 to 55 dB is considered moderate hearing loss, and hearing aids are definitely considered. When PTA is between 56 and 70 dB, it is a moderately severe hearing loss. PTA from 71 to 90 dB is considered severe hearing loss. Lastly, when PTA is greater than 90 dB, it is considered profound hearing loss (Martin and Clark, 2002; Newman and Sandridge, 2004). Higher hearing threshold indicates poorer hearing sensitivity and greater difficulty hearing and understanding speech.

The auditory brainstem response (ABR) measures responses from the synchronized activity of the auditory nerve and neural structures within the brainstem using an electrophysiological technique consisting of a series of waveforms. The ABR is used to monitor the auditory system and to evaluate the neurological intactness of the brainstem (Martin and Clark, 2002; Boettcher, 2002). Each wave has different generating sites. Wave I and II are generated from the VIIIth cranial nerve. For the later waves that comprise the ABR, there is not a 1:1 correspondence between the generating site and the wave component. Clear responses are observed from waves I, III, and V. The ABR provides information on wave latency, interwave latency, and wave amplitudes. Hearing thresholds can be estimated by determining the lowest intensity for which wave V can be identified. The ABR is not affected by sleeping condition, and only one ear is tested at a time. The ABR is used to evaluate the neurological intactness of the brainstem and to estimate hearing sensitivity. Prolonged interwave intervals, wave V interaural latency difference, abnormal amplitude ratios, and prolonged or disappearance of the waves that comprise the ABR is an abnormal finding.

Acoustic immittance measurements are used to identify abnormality in middle ear function, but do not provide information on the hearing levels (Martin and Clark, 2002). Three tests in acoustic immittance measurements are used in determining the presence or absence of normal middle ear function. These measurements include static acoustic immitance, tympanometric width, and middle ear pressure. Static acoustic compliance provides information on the compliance of the tympanic membrane as a function of the air pressure in the outer ear canal. Normal compliance values are between 0.3 and 1.6 cm^3. A compliance value below the normal range is indicative of a stiffened middle ear system. The compliance value above the normal range is indicative of a hypercompliant middle ear system. Tympanometric width provides information about the shape of the tympanogram. The peak in the tympanogram defines middle ear pressure values. In the normal ear, peak compliance generally occurs between + 50 and - 150 decaPascals (the unit of measurement) (Martin and Clark, 2002).

The acoustic reflex is another component of the acoustic immittance battery. This reflex measures the contraction of the middle ear muscles in response to intense sounds. In individuals with normal hearing, the middle ear reflex will occur at the 85 dB sensation level. The reflex will be absent in individuals with conductive hearing loss or cochlear hearing loss.

The Biological Basis of Hearing Loss in Older Adults

Age-related hearing loss, known as presbycusis, is a loss of hearing caused by the aging process and is usually a sensorineural hearing disorder (Gates and Mills, 2005; NIDCD, 2006a). Presbycusis is related to deterioration of cochlear hair cells and spiral ganglion cells (Schuknecht and Gacek, 1993) and is one of most common chronic impairments in older adults (Cruickshanks et al., 1998a, 1998b; Gates and Mills, 2005). The progressive loss of hearing sensitivity with advanced age is due largely to disorders of the peripheral auditory system, specifically abnormalities within the cochlea (Jerger et al., 1995; Mosciki et al., 1985). The cochlea is the auditory portion of the inner ear that rests within a bony spiral canal that contains fluid-filled membranous channels (Martin and Clark, 2002). Although the nature of the impairment associated with presbycusis is well-documented and some areas in the auditory system that are affected have been identified, the causes of hearing loss remain unknown. It is likely that accumulation of chronic noise exposure and other environmental agents (e.g., toxic substances or drugs) in daily life contribute to hearing loss in some older adults (Brant et al., 1996; Gates et al., 1990). Furthermore, there is a genetic link to the degree to which someone loses hearing with advanced age (Gates et al., 1990; Moscicki et al., 1985).

Older adults with presbycusis have difficulty understanding speech (worse with presence of background noise) and high-pitch sounds (e.g., ringing of a telephone or high-pitched women's voices) (Johnson et al., 2004; Gate and Mills, 2005; Martin and Clark, 2002).

Individuals with presbycusis may experience a variety of difficulties such as people's speech seems mumbled, slurred, unclear and low in volume; high-pitched sounds such as "s" and "th" are difficult to hear and distinguish; conversations are difficult to understand, particularly with background noise; higher pitched women's voices are more difficult to hear than men's voices; and some sounds seem annoying or overly loud (Johnson et al., 2004; NIDCD, 2006a). The characteristic of presbycusis is elevated hearing thresholds at high frequencies at the beginning and then progressing to low frequencies with the passage of time (Parham, 1997; Gates and Mills, 2005). Some older adults also experience tinnitus, which is a ringing, roaring and/or hissing sound in one or both ears. Hearing problems can make it very difficult for an older adult to understand and follow health advice from their physician and other health professionals (Johnson et al., 2004; NIDCD, 2006b).

Presbycusis can be classified into four categories (Martin and Clark, 2002). First, sensory presbycusis is caused by a loss of sensory cells of hearing such as outer hair cells and supporting cells in the cochlea. Individuals with sensory presbycusis experience greater hearing loss at higher frequencies. Second, neural presbycusis is caused by a loss of neurons in the cochlea, resulting in poor speech recognition. Third, strial presbycusis is caused by atrophy of the stria vascularis in the cochlea, which does not affect speech recognition. Fourth, cochlear conductive presbycusis is caused by impaired mobility of the cochlear divisions, resulting in sensorineural hearing loss.

The Prevalence of Hearing Loss

Approximately 31 million Americans have hearing impairment (Kochkin, 2005). The prevalence of hearing loss increases greatly with advanced age and is greater in men than in women (Torre et al., 2005; Moscicki et al., 1985; Cruickshanks et al., 1998b). In the 2003 National Health Interview Survey, 6.9 % of people aged 18 to 44 years, 17.6% of people aged 45 to 64 years, 29.7% of people aged 65 to 74 years, and 46.4% of people aged 75 or older had self-reported difficulty in hearing (Lethbridge-Cejku and Vickerie, 2005). In the Framingham Heart Study Cohort, 83.0% had age-related hearing loss in 2,293 participants aged 57 to 89 years (Moscicki et al., 1985). This may be due to a strict definition of hearing loss (defined as hearing thresholds > 20 dB HL in any one of frequencies from 0.5 to 4 kHz) in the study. In the Health, Aging, and Body Composition study, 59.9% had hearing loss (defined as PTA across 0.5, 1, and 2 kHz > 25 dB HL in the worse ear; N = 2,052; aged 73 to 84 years, Helzner et al., 2005).

The high prevalence of hearing loss is a worldwide problem among adults. In Israel, the prevalence of hearing loss was 4.5% in adults younger than 35 years and 10.5% over 35 years old in 13,308 men (aged 20 to 68 years) (Sharabi et al., 2002). In an Italian study, 27.2% of older adults (N = 1,332; aged 65 to 96 years) had self-reported hearing loss (Cacciatore et al., 1999). In an Australian study, 86% had hearing loss (defined as PTA across 0.5, 1, 2, and 4 kHz > 25 dB HL in the best ear) in 93 community-dwelling older adults (aged 65 to 99 years) with poor health status (Jee et al., 2005). Of those with hearing loss, 35.5% had mild hearing loss (PTA 26 to 40 dB HL), 33.3% had moderate hearing loss (PTA 41 to 60 dB HL), and 17.2% had severe hearing loss (PTA > 60 dB HL).

Hearing Loss and Quality of Life in Older Adults

Hearing loss adversely affects the lives of older adults and has enormous costs related to poor quality of life (Johnson et al., 2004). Even mild hearing loss is associated with impaired quality of life and functional disabilities, and adverse effects on physical, cognitive, emotional, behavioral, and social function (Jerger et al., 1995; Dalton et al., 2003; Bazargan et al., 2001; Gates and Mills, 2005) as well as mental and emotional problems such as fear, anger, depression, frustration, embarrassment, anxiety, withdrawal, emotional ability, aloofness, paucity of speech, and confusion or dementia (Mader, 1984; Cacciatore et al., 1999).

Hearing loss and activity limitation was examined in participants (N = 8,767) aged 70 years or older from the 1994 National Health Interview Second Supplement on Aging (Campbell et al., 1999). Older adults with impaired hearing were more likely to report activity limitations than those with normal hearing, such as difficulties in walking (30.7% vs. 21.3%, respectively), getting outside (17.3% vs. 12.0%), getting into and out of bed or a chair (15.1% vs. 9.8%), managing medication (7.7% vs. 4.8%), and preparing meals (11.6% vs. 7.6%). Thus, hearing impairment in older adults can lead to frustrating, embarrassing, and even dangerous situations (Johnson et al., 2004; NIDCD, 2006a, 2006b). For example, older adults with impaired hearing cannot hear others trying to alert them when dangers are nearby, such as sirens, horns, and other types of alarms.

Risk Factors for Hearing Loss

Hearing loss or deafness has been associated with a variety of factors including genetics, noise or trauma, sensitivity to certain drugs or medications, viral or bacterial infections, lifestyles (diets, alcohol drinking, physical activities, and smoking), health status, environment, and aging process (Gates and Mills, 2005; Johnson et al., 2004). Despite the prevalence of high hearing loss among older adults, there has been no comprehensive and systematic research effort directed toward understanding the possible interactions among poor diet, genetic disorders, and age-related hearing loss. Thus, there is a profound gap in our knowledge concerning the role of these factors in hearing loss in older adults (Johnson et al., 2004).

Research on the relationships of age-related hearing loss with nutritional status may lead to identification of risk factors for age-related hearing loss and possibly to prevention and treatment strategies aimed at reducing the prevalence and progression of this devastating disorder. Age-related hearing loss has been related to vascular disease and neural degeneration or disorder (Gate et al., 1993; Seidman et al., 1996). The vascular and neural systems depend on certain nutrients, such as vitamin B_{12} and folate, for optimal structures and functions (Johnson et al., 2004). The working model for exploring the associations of nutrition and age-related hearing loss is illustrated in Figure 2.2 (Johnson et al., 2004).

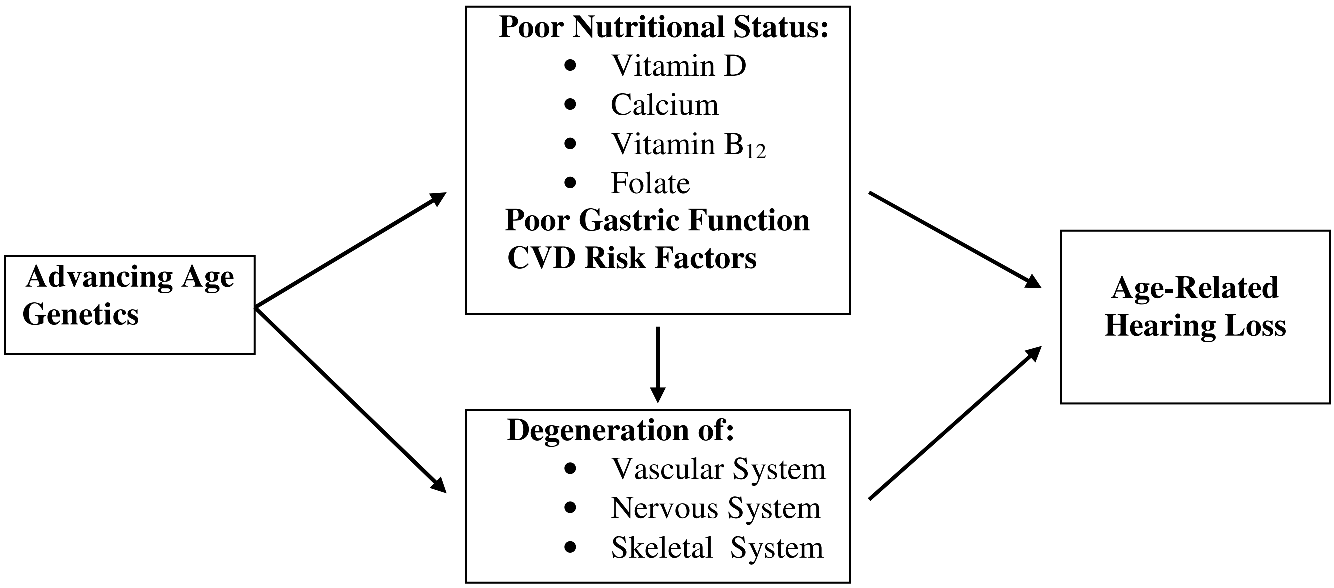

FIGURE 2.2 Working model for hypothesized relationships of nutrition with age-related hearing loss (Adapted from Johnson et al., 2004 with permission)

Cardiovascular Disease and Hearing Loss

Vascular disorders in the cochlea and arteriosclerosis may contribute to sudden deafness, presbycusis, and inherited deafness (Kimura, 1986; Makishima, 1978). Several lines of evidence suggest that hearing impairment may be associated with cardiovascular disease (CVD) (e.g., coronary heart disease, heart attack, and intermittent claudication) and/or CVD risk factors (e.g., diabetes, hypertension, hyperlipidemia, and smoking habit) (Brant et al., 1996; Gates et al., 1993; Cruickshanks et al., 1998b; Pillsbury, 1986; Gates and Mills, 2005; Rosen and Olin, 1965; Torre et al., 2005; Durga et al., 2006).

In the Epidemiology of Hearing Loss Study, self-reported histories of CVD, pure-tone air- and bone-conduction audiometry, and distortion product otoacoustic emissions were obtained in 1,501 participants aged 43 to 84 years in the United States (Torre et al., 2005). Cochlear function was measured based on distortion product otoacoustic emissions, and cochlear impairment was defined as < +9 dB distortion product otoacoustic emissions/noise ratio at 2, 3, and 4 kHz. Self-reported history of myocardial infarction was correlated with cochlear dysfunction in women, but not in men, after controlling for lifestyle factors (e.g. smoking, diabetes, noise exposure, activity, alcohol, and age). However, other CVD variables (e.g. self-reported stroke, brain hemorrhage, and angina) were not correlated with cochlear dysfunction. In the Framingham cohort study, hearing loss at low frequencies in the worse ear (0.25, 0.5, and 1 kHz) was significantly correlated with documented coronary heart disease (CHD) while hearing impairment at low frequencies in the better ear was significantly correlated with stroke (676 men; Gates et al., 1993). In women (n = 996), hearing loss at low frequencies in the better ear was correlated with CVD, CHD, and intermittent claudication, whereas hearing loss at low frequencies in the worse ear was correlated with CVD and stroke.

In a cross-sectional study in the Netherlands, self-reported family history of premature vascular disease (onset < 60 years in first degree family) was significantly associated with PTA-low frequencies (0.5, 1, and 2 kHz), and self-reported vascular diseases were significantly related with PTA-high frequencies (4, 6, and 8 kHz) in 728 older adults (aged 50 to 70 years) (Durga et al., 2006).

In contrast, in a cross-sectional analysis of the Health, Aging, and Body Composition study, myocardial infarction or congestive heart failure were not associated with hearing loss (defined as PTA across 0.5, 1, and 2 kHz > 25 dB HL in the worse ear; N = 2,052; aged 73 to 84 years) (Helzner et al., 2005). Cerebrovascular disease significantly increased risk of hearing loss by 56%. Drettner et al. (1975) found no significant relationship between CVD risk factors and sensorineural hearing loss (SNHL) in 1,000 men with a mean age of 50 years. Kent et al. (1986) found no significant correlation between noise-induced hearing loss (NIHL) and CVD in 2,250 air force aircrew population (aged 19 to 57 years). In this study, cardiovascular function was measured by systolic and diastolic blood pressure and clinical diagnoses of CVD.

It is not clearly understood whether there is a direct relationship between hearing loss and CVD, or if the association is mediated indirectly (Gates et al., 1993). CVD may decrease blood supply to the cochlea and cause cochlea degeneration and cochlear dysfunction (Torre et al., 2005). Severe spiral ganglion atrophy was observed in patients with arterial and arteriolar sclerosis (N = 40; > 50 years) (Makishima, 1978). Also, a positive correlation was found between the degree of lumen narrowing of the internal auditory artery and the degree of spiral ganglion atrophy in the patients. This study suggested that spiral ganglion atrophy caused by chronic reduction of blood supply due to arteriolar sclerosis might be the primary cause of the hair cell lesion. Additional research is needed to identify the mechanisms and metabolic defects responsible for the auditory dysfunction associated with CVD.

Cigarette Smoking Status and Hearing Loss

Many studies have examined the possible relationship between auditory dysfunction and cigarette smoking (Barone et al., 1987; Cunningham et al., 1983; Nakanishi et al., 2000; Sharabi et al., 2002; Siegelaub et al., 1974; Nomura et al., 2005a, 2005b; Burr et al., 2005; Ferrite and Santana, 2005; Itoh et al., 2001; Cruickshanks et al., 1998b).

Several large population-based studies have shown the possible association between hearing loss and smoking status. In a cross-sectional study [Epidemiology of Hearing Loss Study (EHLS)], self-reported history of cigarette smoking and PTA (0.5, 1, 2, and 4 kHz) were obtained in 3,753 adults (aged 48 to 92 years) (Cruickshanks et al., 1998b). The prevalence of hearing loss (defined as PTA > 25 dB HL in the worse ear) was significantly higher in current smokers than in nonsmokers. After controlling for other factors (age, history of CVD, alcohol consumption, occupational noise exposure, and education), smokers were more likely to have hearing loss than the nonsmokers [odd ratio, 1.69; 95% confidence interval (CI), 1.31-2.17]. Furthermore, a significant association was found between hearing loss and pack-years of smoking; heavy smokers (≥ 40 pack-years) were more likely to have hearing loss than non-heavy smokers (0 pack-years; odd ratio, 1.3; 95% CI, 1.04-1.63). Nondahl et al. (2004) examined a possible relationship between serum cotinine and hearing loss in a nested cross-sectional and case-control study in the EHLS (197 participants with hearing loss and age matched 394 controls; aged 53 to 75 years). Cotinine is a metabolite of nicotine and a biomarker of measuring short-term tobacco exposure (Bramer and Kallungal, 2003). No significant association of hearing loss with serum cotinine or self-reported smoking status was found in this study.

In a cross-sectional analysis of the Health, Aging, and Body Composition study, current smokers had a significantly higher risk (by 68%) of hearing loss (defined as PTA across 0.5, 1, and 2 kHz > 25 dB HL in the worse ear) than non-smokers in older adults (N = 2,052; aged 73 to 84 years) (Helzner et al., 2005). Additionally, past smoking status was not associated with hearing loss.

In a Japanese Longitudinal Study of Aging, air-conduction pure-tone thresholds at octave intervals from 0.5 to 8 kHz and self-reported smoking status were obtained in adults (N = 1,478; aged 40 to 79 years) (Uchida et al., 2005). Smokers had significantly higher hearing thresholds at 4 kHz (but not other test frequencies) than non-smokers in men (but not in women) in the better ear and the worse ear.

Itoh et al. (2000) conducted an epidemiological study in Japan, and information on air-conduction thresholds and self-reported smoking habits was collected in older adults (n = 496; aged 60 to 80 years) with bilateral hearing loss (hearing threshold > 40 dB HL at 4 kHz) and in the age-matched controls (n = 2,807) without bilateral hearing loss (hearing threshold ≤ 40 dB HL at 4 kHz for both ears). Current smokers had a significantly higher risk for developing hearing loss than non-smokers after controlling for age and gender (odd ratio, 2.29; 95% CI, 1.68-3.12). However, pure-tone thresholds and otoscopic evaluation were not performed in this study. In contrast, in the Baltimore Longitudinal Study of Aging, cigarette smoking was not significantly associated with hearing loss (defined as PTA across 0.5, 1, 2, and 3 kHz ≥ 30 dB HL in either ear) in 531 men and 310 women (Brant et al., 1996).

In the Danish Work Environment Cohort Study, information on the self-reported hearing loss and smoking status was obtained in adults (N = 7,221; aged 18 to 59 years) (Burr et al., 2005). Significantly higher risk for hearing loss was found in smokers than non-smokers among women, but not among men. In a five-year follow-up study, participants did not have hearing loss or head injury at baseline (n = 4,766). Five-year incidence of hearing loss was significantly higher in smokers than non-smokers among men, but not among women. However, data for hearing loss was obtained by a self-reported questionnaire, so the prevalence of hearing loss may be underestimated.

In a retrospective cross-sectional study conducted in Israel, pure-tone hearing thresholds were measured from 0.25 to 8 kHz in men (N = 13,308; aged 20 to 68 years) (Sharabi et al., 2002). Smoking increased the risk for developing hearing loss by 45% compared to nonsmokers. Current smokers had significantly higher risk for developing conductive hearing loss (odd ratio, 1.85; 95% CI, 1.31-2.27) and SNHL (odd ratio, 2.16; 95% CI, 1.06-3.26) than non-smokers. In contrast, Pyykkö et al. (1988) found no significant relationship between SNHL and smoking status in 199 professional forest workers at 4 kHz. In a cross-sectional study conducted in the Netherlands, hearing thresholds were not independently associated with smoking status in 728 older adults (aged 50 to 70 years) (Durga et al., 2006).

A possible association among cigarette smoking, occupational exposure to noise, and hearing loss were examined in several studies. Nakanishi et al. (2000) found that the higher number of cigarettes smoked per day the greater the risk for developing hearing loss at high frequency (≥ 40 dB HL at 4 kHz at least one ear) but not at low frequency (≥ 30 dB HL at 1 kHz at least one ear) in 1,554 male office workers (aged 30 to 59 years) with low noise exposure during five years of follow-up in Japan. In another Japanese study, pure-tone threshold at 4 kHz were measured in 397 metal factory workers [mean age (± SD): 42 ± 11 years] with occupational noise exposure (Nomura et al., 2005a). Participants with hearing loss (≥ 40 dB HL at 4 kHz) were more likely to be past smokers. Hearing loss was associated with smoking and occupational noise exposure. Ferrite and Santana (2005) conducted a cross-sectional study in Brazil, and pure-tone thresholds were obtained in men (N = 535; aged 20 to 55 years) working at a large metal plant. The combination of noise exposure and smoking had a significantly positive association with hearing loss (defined as hearing threshold > 25 dB HL at one of 3, 4, 6, and 8 kHz), but smoking alone did not have a significant effect on hearing loss, which suggests a synergistic effect of smoking and noise exposure on auditory dysfunction. Wild et al. (2005) evaluated a possible association between NIHL and long-term occupational noise exposure (≥ 10 years working at the brick manufacturing plant) in 88 men (mean age, 46.7 years) in a prospective observational cohort study. Smokers had significantly higher hearing thresholds at 3 and 4 kHz than non-smokers, which indicates poorer hearing status among the smokers compared to non-smokers. This study suggested that long-term smoking status may exacerbate NIHL. Limitations of this study were that no control group was included in this study, and the sample size was relatively small. Palmer et al. (2004) found that cigarette smoking was a risk factor for self-reported hearing impairment without occupational noise exposure in participants (N = 12,907; aged 16 to 64 years) in the United Kingdom. This risk for hearing loss further increased with the number of years exposed to noise. In contrast, Starck et al. (1999) found no significant difference on hearing thresholds between smokers and non-smokers (199 forest workers and 171 shipyard workers; aged 21 to 60 years) with occupational noise exposure.

In a meta-analysis, 15 observational studies (10 cross-sectional, 4 cohort, and 1 case-control) were included to examine whether smoking caused hearing loss (Nomura et al., 2005b). This study found that smoking increased the risk for developing hearing loss. It is not clear whether or not smoking directly causes hearing loss, but smoking cessation may be a useful tactic for retaining auditory function.

The mechanisms by which smoking may cause hearing loss are not entirely known. Smoking negatively affects the cochlear artery by elevating carbon monoxide and nicotine levels in the blood. High carbon monoxide and nicotine levels may contract blood vessels or cause vasospasm and thrombotic occlusions (Zelman and Kan, 1973). Smoking may cause hearing loss at high frequencies by impairing the vascular system in the cochlear artery (Nakanishi et al., 2000). Another possible mechanism is that smoking may increase blood viscosity and damage sensory cells (Nakanishi et al., 2000). Male smokers had higher hematocrit, plasma fibrinogen concentration, and plasma viscosity than non-smokers (Rampling, 1999). Multi-center longitudinal studies with all age populations and a control group well-matched for all known confounding variables are needed to identify the mechanisms and metabolic defects responsible for the association of auditory dysfunction with smoking status.

Diabetes Mellitus and Hearing Loss

Several studies have examined the association between hearing loss and diabetes mellitus, but the findings are inconsistent (Frisina et al., 2006; Ishii et al., 1992; Assimakopoulos et al., 2001; Niedzielska and Katska, 1998). In a cross-sectional analysis of the Health, Aging, and Body Composition study, diabetes mellitus was significantly associated with a 42% higher risk of hearing loss (defined as PTA across 0.5, 1, and 2 kHz > 25 dB HL in the worse ear; N = 2,052; aged 73 to 84 years) (Helzner et al., 2005).

In a population-based longitudinal study conducted in Beaver Dam, WI (the EHLS and the Beaver Dam Eye Study), PTA (0.5, 1, 2, and 4 kHz) was calculated in older adults with type II diabetes (aged 43 to 84 years, n = 344) and in participants without diabetes (n = 3,029) (Dalton et al., 1998). Participants with type II diabetes had significantly higher hearing thresholds (33.3 vs. 26.9 dB HL, respectively) than those without type II diabetes. A significantly greater prevalence of hearing loss (defined as PTA > 25 dB HL) was found in diabetic participants compared to non-diabetic individuals (59% vs. 44%, respectively), but after controlling for age, this significance disappeared. Subset analyses were conducted after excluding individuals with hearing loss inconsistent with age-related hearing loss. A significant relationship between type II diabetes and age-related hearing loss was found in this subset analyses (odd ratio, 1.41; 95% CI, 1.05-1.88). Additionally, there was a significant association between hearing loss (odd ratio, 2.28; 95% CI, 1.04-5.00) and the presence of complications of diabetes (e.g. nephropathy). However, hemoglobin A1c was not associated with hearing loss. This population-based longitudinal study suggested that there is a weak association between hearing loss and type II diabetes.

In contrast, in the Framingham cohort study, Gates et al. (1993) found no relationship between hearing thresholds and the presence or absence of diabetes mellitus or glucose intolerance in men and women (N = 1,662). In a cross-sectional study in the Netherlands, hearing thresholds were not independently associated with self-reported diabetes mellitus in older adults (N = 728; aged 50 to 70 years) (Durga et al., 2006).

Four different PTAs were measured in 60 older adults with type II diabetes (n = 30; aged 59 to 92 years) and in those without type II diabetes (n = 30; aged 59 to 88 years); PTA-1 (0.5, 1, and 2 kHz), PTA-2 (1, 2, and 4 kHz), PTA-3 (4, 8, and 9 kHz), and PTA-4 (10, 11, 12, and 14 kHz) (Frisina et al., 2006). Participants with type II diabetes had significantly higher hearing thresholds in all four PTAs in both ears than those without type II diabetes, which indicates that diabetic individuals have poorer hearing status than non-diabetic participants. This hearing difference between diabetic and non-diabetic groups was greater at low frequencies than at high frequencies.

In a Mexican study, the association between type II diabetes and auditory function was examined using pure-tone audiometry and auditory brainstem response (ABR) in 188 older adults [mean age ± (SD): 50 ± 6 years; 94 diabetic participants and 94 healthy controls] (Díaz de León-Morales et al., 2005). Participants with type II diabetes had significantly higher PTA at high frequencies (2, 4, and 8 kHz) and higher hearing threshold at 8 kHz than the control group. However, the PTAs at low frequencies (0.125, 0.25, and 0.5 kHz) and at middle frequencies (0.5, 1, and 2 kHz) were not different between the groups. The ABR results showed that diabetic participants had significantly prolonged latency of wave V and interwave I-V and III-V latencies compared to the control group. This study indicated that participants with type II diabetes had impaired hearing status and impaired ABR.

The possible association between diabetes and NIHL has been evaluated in various studies. In a retrospective study, Ishii et al. (1992) examined men with occupational noise exposure of approximately 30 years (N = 229; aged 55 to 68 years). In this study, NIHL was defined as hearing level ≥ 65 dB HL at 3, 4, or 6 kHz in at least one ear with ± 20 dB thresholds in the contralateral ear. A significantly higher prevalence of type II diabetes was observed in men with severe NIHL than in those with non-severe NIHL (16.4% vs. 4.8%, respectively).

Nomura et al. (2005a) found that metal factory workers (n = 55; aged 21 to 66 years) with NIHL (defined as hearing level > 40 dB HL at 4 kHz) had significantly higher hemoglobin A1c than those with normal hearing (n = 342) in Japan. Vaughan et al. (2006) conducted a five-year prospective study examining a veteran population (N = 694; aged 25 to 83 years) at the National Center for Rehabilitative Auditory Research at the Veterans Affairs Medical Center in Portland. Diabetic patients aged 60 or younger had higher prevalence of hearing loss at high frequencies (> 8 kHz) than the age-matched control group, but this pattern was not observed in patients older than 60 years. However, one limitation in this study was not including a control population (only the veteran population was used).

In a retrospective study, the effect of diabetes on SNHL was examined in 66,036 participants (12,575 diabetic patients and 53,461 age-matched non-diabetic patients) (Kakarlapudi et al., 2003). The database at the Veterans Affairs Maryland Health Care System was used, and this database has a large population of patients receiving care for a single problem. A significantly higher prevalence of SNHL was observed in the diabetic group than in the non-diabetic group (13.1% vs. 10.3%, respectively). However, information on age was not provided in this study. In contrast, self-reported diabetes mellitus was not associated with SNHL in men aged 50 to 60 years (197 patients with SNHL; 237 controls from National Study of Hearing data) (Jones and Davis, 1999).

A possible association between idiopathic sudden hearing loss (ISHL) and type II diabetes was evaluated in a Japanese study (Fukui et al., 2004). ISHL is defined as deafness of sudden onset (≤ three days) with unknown origin. Among 148 patients with ISHL, 16.2 % had type II diabetes, and these diabetic patients had more severe hearing loss than non-diabetic patients. One of the limitations of this study was not including a healthy control group such as people without ISHL.

In a case-report study, a 44-year-old man had a sudden sensorineural hearing loss (SSNHL) at all test frequencies from 0.5 to 8 kHz (Assimakopoulos et al., 2001). Biochemical tests showed elevated hemoglobin A1c (8.5%), hyperglycemia, and glycosuria. The diagnosis was made as type II diabetes. Following insulin treatment for four days, rapid hearing improvement was observed, and after the fourth day of insulin treatment, hearing levels were stabilized. Even though this is only one case study, this study suggested that sudden hearing loss may be a symptom of diabetes mellitus.

Few studies have examined the relationship between hearing loss and type I diabetes. Children and adolescents (n = 63; < 18 years) with type I diabetes had hearing loss (> 25 dB HL in any test frequency) at middle and high frequencies (2 to 8 kHz), while the matched non-diabetic group (n = 63) did not have hearing loss (Elamin et al., 2005). In another study, 37 children aged 6 to 18 years with type I diabetes had ABR disturbances, such as elongation of the latency of wave I, III, and V without hearing loss, suggesting a conduction disturbance (Niedzielska and Katska, 1998). In contrast, no significant difference in auditory function was found in children with type I diabetes (n = 51, aged 8 to 21 years) compared to non-diabetic children (n = 13). This may be due to the small sample size (Sieger et al., 1983).

The mechanisms by which diabetes mellitus may cause auditory dysfunction are not fully known. Diabetic patients had 10-20 times thicker capillary walls of the stria vascularis in the cochlea than those without diabetes (Jorgensen, 1961). The changes in the vascular system caused by diabetic complications (angiopathy) may impair inner ear and facial nerve function (Jorgensen, 1961). Elevated glucose concentrations may cause auditory dysfunction. Diabetes may increase outer hair cell loss in the mid-portion of the cochlear (Triana et al., 1991). Non-insulin-dependent diabetic rats had significant outer hair cell loss in the cochlea compared to non-diabetic rats, which suggests possible inner ear damage, particularly outer hair cell loss, may be caused by hyperglycemia (Rust et al., 1992). High glucose levels may damage the cochlear nerves by changing the osmolality, blood viscosity, and aggregation of platelets. These may cause microthromboses related to the cochlear nerve (Assimakopoulos et al., 2001). Patients with type II diabetes had higher whole blood viscosity, plasma viscosity, and fibrinogen level than healthy controls, but no difference was found in hematocrit between groups (Rampling, 1999).

Several reviewers concluded that there may be an association between diabetes and hearing loss, but it is not clear whether or not diabetes mellitus directly causes hearing loss (Fowler and Jones, 1999; Maia and de Campose, 2005). Multi-center longitudinal studies with all age populations with a control group well-matched for all known confounding variables are needed to identify the mechanisms and metabolic defects responsible for the association of diabetes mellitus with auditory dysfunction.

Hyperlipidemia and Hearing Loss

Several studies suggested hyperlipidemia or hypercholesterolemia as risk factors for hearing loss. In a Japanese study (607 men and 317 women; aged 40 to 59 years), mean hearing levels in the better ear were measured from 0.125 to 8 kHz in participants with no history of noise exposure or disease associated with hearing loss (Suzuki et al., 2000). Low serum high-density lipoprotein (HDL) cholesterol concentration was significantly related to hearing loss at 2 and 4 kHz in men. However, total serum cholesterol and total triglyceride concentrations were not significantly associated with hearing loss. In another Japanese study, air-conduction thresholds and concentrations of total cholesterol and triglycerides were measured in older adults (n = 496; aged 60 to 80 years) with bilateral hearing loss (hearing threshold > 40 dB HL at 4 kHz) and age-matched controls (n = 2,807) without bilateral hearing loss (hearing threshold ≤ 40 dB HL at 4 kHz for both ears) (Itoh et al., 2001). Conversely, high fasting total cholesterol concentration significantly lowered the risk for hearing loss. Durga et al. (2006) conducted a cross-sectional study in the Netherlands and found that hearing thresholds were not independently associated with hypercholesterolemia (defined as total cholesterol > 6.5 mmol/L, HDL cholesterol < 0.9 mmol/L, or the use of lipid-lowering medication) in older adults (N = 728; aged 50 to 70 years).

Hyperlipidemia, noise exposure, and auditory dysfunction were examined in animal and human studies. Chinchillas (aged 0.5 to 2 years) were fed either a normal diet or a 1% cholesterol diet for six months (Sikora et al., 1986). In addition to the diet, chinchillas were either exposed to no noise or noise (with intensity levels of either 105 or 114 dB). Without noise exposure, chinchillas fed the 1% cholesterol diet had significantly worse hearing status than those fed the control diet at high frequencies (8, 12, and 16 kHz). Pillsbury (1986) found that with noise exposure, spontaneously hypertensive rats fed an atherogenic diet (high in cholesterols and triglycerides) had worse auditory acuity than hypertensive rats fed a normal diet. Tami et al. (1985) examined the effects of noise exposure and hypercholesterolemia on auditory function measured by ABR in three groups of eight-week-old male rabbits (N = 11; regular diet/noise; 2% cholesterol diet/noise; or regular diet/no noise). Hypercholesterolemia alone had no effect on auditory dysfunction. In a human study, the synergistic effect of noise and hypercholesterolemia on hearing loss was shown in 78 men aged 50 years with serum cholesterol level > 7 mmol/L and 75 men aged 50 years with serum cholesterol level < 7 mmol/L (Axelsson and Lindgren, 1985). Men with high serum cholesterol concentrations and elevated noise exposure had a greater risk (relative risk, 2.6; CI, not provided) for NIHL than participants with low serum cholesterol concentrations and elevated noise exposure (relative risk, 1.8; CI, not provided). Information on noise exposure was obtained by a self-reported questionnaire. In the condition of low noise exposure, high cholesterol concentrations alone did not increase the risk of NIHL. In a Japanese study, concentrations of total cholesterol, HDL cholesterol, and triglycerides and pure-tone threshold at 4 kHz were measured in 397 metal factory workers [mean age (± SD): 42 ± 11 years] with occupational noise exposure (between 85 dB and 95 dB) (Nomura et al., 2005a). These blood lipids (total cholesterol, HDL cholesterol, and triglycerides) were not significantly associated with hearing loss (defined as hearing threshold ≥ 40 dB HL at 4 kHz) in this population.

The effects of a high cholesterol diet on hearing loss were examined in participants aged 40 to 59 years (N = 278) in Finland (Rosen et al., 1970). Participants who consumed a diet with high saturated fatty acids for five years had poorer hearing status than those who consumed a diet with more unsaturated fatty acids and less saturated fatty acids for five years, regardless of age, at all test frequencies (0.5, 1, 2, and 4 kHz). In the same study, when participants switched from a diet with high saturated fatty acids to a diet with low saturated fatty acids for three and a half years, their hearing status was improved. When participants changed from a diet with low saturated fatty acids to a diet with high saturated fatty acids, their hearing status worsened (Rosen et al., 1970). In contrast, Jones and Davis (1999) found no significant associations of fasting low-density lipoprotein (LDL) cholesterol, HDL cholesterol, total cholesterol, and triglycerides with SNHL in 197 men (aged 50 to 60 years) with risk factors for ischemic heart disease.

The mechanisms by which hyperlipidemia may cause hearing impairment are not fully understood. Hyperlipidemia may impair auditory function by causing vascular disease, atherosclerosis, reducing blood and oxygen supply, and agglutination of erythrocytes and platelets in the inner ear (Morizono and Paparella, 1978). Low HDL cholesterol concentration may increase the risk of atherosclerosis-related microcirculatory disorders of the cochlear vascular system and may increase susceptibility to noise in the cochlea (Suzuki et al., 2000).

Additional studies with large populations and well-matched control groups for all known confounding variables are needed to identify the mechanisms and metabolic defects responsible for the association of hyperlipidemia with hearing impairment.

Hypertension and Hearing Loss

The possible connection between hearing loss and hypertension has been examined, but the findings are conflicting. Few population-based studies have examined whether or not hypertension has a negative effect on hearing. In the Baltimore Longitudinal Study of Aging, blood pressure and pure-tone thresholds (0.5, 1, 2, and 3 kHz) were measured in 531 men and 310 women (Brant et al., 1996). All participants had PTA (0.5, 1, 2, and 3 kHz) less than 20 dB HL for either ear at baseline, normal otologic history, and no history of noise exposure. The maximum follow-up was 22.8 years in men and 13 years in women in the longitudinal hearing data. Approximately 8.7% of 531 men and 2.3% of 310 women developed hearing loss (defined as PTA across 0.5, 1, 2, and 3 kHz ≥ 30 dB HL in either ear) during the follow-up period. Systolic blood pressure was significantly associated with hearing loss (relative risk, 1.32 for a 20 mmHg rise in systolic blood pressure after controlling for age). Furthermore, high systolic blood pressure had a statistically significant effect on the onset of hearing loss at all ages. In the EHLS, however, hypertension was not significantly correlated with cochlear dysfunction (defined as $< +9$ dB distortion product otoacoustic emissions/noise ratio at 2, 3, and 4 kHz) in a population based study (N = 1,501; aged 43 to 84 years) (Torre et al., 2005).

Hypertension and auditory dysfunction were examined in other human and animal studies. A positive correlation between hypertension (defined as both a systolic blood pressure >160 mmHg and a diastolic blood pressure > 90 mmHg) and hearing loss was found in patients with arteriolar sclerosis as a cause of age-related hearing loss (N = 40; > 50 years) (Makishima, 1978).

In a Japanese study, air-conduction thresholds and blood pressures were measured in older adults (n = 496; aged 60 to 80 years) with bilateral hearing loss (hearing threshold > 40 dB HL at 4 kHz) and age-matched controls (n = 2,807) without bilateral hearing loss (hearing threshold ≤ 40 dB at 4 kHz for both ears) (Itoh et al., 2001). Systolic blood pressure and diastolic blood pressure were not significantly associated with hearing loss in this study. Pyykkö et al. (1988) found that SNHL was not significantly correlated with diastolic blood pressure or systolic blood pressure in 199 forest workers. In a cross-sectional study in the Netherlands, Durga et al. (2006) found that hearing thresholds were not independently associated with hypertension (defined as systolic blood pressure ≥ 160 mmHg, diastolic blood pressure ≥ 95 mmHg or the use of antihypertensive medication) in older adults (N = 728; aged 50 to 70 years).

Hypertension, noise exposure, and auditory dysfunction were examined in several studies. Tomei et al. (2005) studied whether or not chronic noise exposure could be a risk factor for hypertension and the possible association between hearing impairment and hypertension in 301 pilots [mean age (± SD): 40 ± 8 years]. Blood pressures and hearing thresholds were measured. A significant correlation between degree of hearing loss and flight hours was found. Pilots with audiometric deficits had higher prevalence of basal hypertension than pilots without audiometric deficits. Ishii et al. (1992) conducted a retrospective study in men (N = 229; aged 55 to 68 years) with occupational noise exposure (approximately 30 years). The authors found that the prevalence of hypertension (defined as taking high blood pressure medication or diastolic blood pressure ≥ 90 mmHg) was not significantly different between severe NIHL and non-severe NIHL groups. Similar findings were observed in another study (Nomura et al., 2005a). Blood pressures and pure-tone threshold at 4 kHz were measured in 397 metal factory workers [mean age (± SD): 42 ± 11 years] with occupational noise exposure in Japan. Systolic blood pressure and diastolic blood pressure were not associated with hearing loss (defined as hearing threshold ≥ 40 dB HL at 4 kHz).

In an animal study, a possible relationship between hearing loss and hypertension was examined in non-hypertensive (n = 32, Wistar Kyoto strain) and spontaneous hypertensive rats (n = 32, SHR strain), which were fed with either an atherogenic diet (high in cholesterols and triglycerides) or a normal diet (Pillsbury, 1986). Rats were assigned to a noise-exposed or a quiet group. Blood pressures were measured at 5, 8 and 13 months of age. Auditory functions were measured by the ABR. With noise exposure, spontaneous hypertensive rats had more significant hearing loss than non-hypertensive rats. Without noise exposure, hypertension and an atherogenic diet did not have significant effect on auditory dysfunction. This study found that atherogenic diet and hypertension had synergistic effect on hearing loss with the condition of noise exposure.

Hypotension has been linked to developing SNHL. Participants (n = 20; aged ≤ 50 years) with hypotension (defined as diastolic blood pressure ≤ 60 mmHg and/or systolic blood pressure ≤ 105 mmHg) had SNHL in low frequencies compared to 100 participants with normal blood pressure (Pirodda et al., 1999).

The mechanisms of hearing loss caused by hypertension or hypotension are still unclear. One of possible mechanisms is consequent vasoconstriction induced by hypertension. Vasoconstriction of the inner ear blood vessels has negative effects on the blood and oxygen supply to the inner ear. Lack of oxygen and blood supply to the inner ear may cause auditory insensitivity (Pillsbury, 1986; Hillerdal et al., 1987; Tachibana et al., 1984). Another possible mechanism is ionic changes of cellular potentials. Rarey et al. (1996) found that ionic alternations of cellular potentials may cause hearing loss in the spontaneously hypertensive rat.

Patients with hypertension had higher whole blood and plasma viscosities than those without hypertension, and elevated fibrinogen level was found patients with hypertension (Rampling, 1999). Additional research is needed to identify the mechanisms and metabolic defects responsible for the association of hypertension with auditory dysfunction.

Functions of Vitamin B_{12}

Poor vitamin B_{12} status has been associated with neurological problems (IOM, 1998; Baik and Russell, 1999; Miller et al., 2005; Wolters et al., 2004), hematological disorders (IOM, 1998; Baik and Russell, 1999; Miller et al., 2005), and other health-related conditions including poor cognition, dementia, and Alzheimer's disease (Lewis et al., 2005; Del Parigi et al., 2006), depression (Penninx et al., 2000), hearing loss (Houston et al., 1999; Gok et al., 2004; Shemesh et al., 1993), cancer (Ames and Wakimoto, 2002), and poor bone health (Morris et al., 2005; Dhonukshe-Rutten et al., 2005a, 2005b; Herrmann et al., 2005).

Martin et al. (1992) reported that the cognitive dysfunction associated with vitamin B_{12} deficiency was reversible within one year of onset, but not after one year of onset. Vitamin B_{12} deficiency is associated with high homocysteine (Hcy), which may be a causal factor in vascular disease and dementia (IOM, 1998; Baik and Russell, 1999; Wolters et al., 2004). High serum or plasma total homocysteine (tHcy) is also associated with dementia and other cognitive disorders (Del Parigi et al., 2006; Seshadri et al., 2002). In the Framingham Study, elevated serum tHcy (> 14 μmol/L) doubled the risk of dementia during a 16-year follow-up period (Seshadri et al., 2002). The attributable population risk for development of dementia was 16% for tHcy and 21% for the APOE-4 allele. Currently, evidence is limited that supplements of vitamin B_{12} or other B-vitamins directly benefit dementia or cognition, except for established vitamin deficiencies that are corrected in the early stages (Martin et al., 1992; Del Parigi et al., 2006).

In the National Health and Nutrition Examination Survey (NHANES) III (737 men and 813 women, aged 55 years and older), participants with osteoporosis had significantly lower serum vitamin B_{12}, higher serum methylmalonic acid (MMA), and elevated serum Hcy than those with normal bone mineral density measured by dual-energy X-ray absorptiometry. However, there was no association between red blood cell (RBC) folate or serum folate and osteoporosis status (Morris et al., 2005).

Vitamin B_{12} is required for two mammalian enzymes (IOM, 1998; Baik and Russell, 1999; Wolters et al., 2004). First, vitamin B_{12} (methylcobalamin) is a cofactor for methionine synthase that facilitates the methyl transfer from methyltetrahydrofolate to Hcy to form methionine and tetrahydrofolate. Vitamin B_{12} deficiency is associated with decreased activity of methionine synthase, which leads to increases in Hcy that can be measured in blood (IOM, 1998; Baik and Russell, 1999; Wolters et al., 2004). Elevated serum Hcy is associated with low intake or status of folate, vitamin B_6 and B_{12}, as well as other genetic, physiological, and behavioral factors (Jacques et al., 2001; Selhub, 1999; Wolters et al., 2004). Second, vitamin B_{12} (adenosylcobalamin) is a cofactor for L-methylmalonyl-CoA mutase that catalyzes the conversion of L-methylmalonyl-CoA to succinyl-CoA. Vitamin B_{12} deficiency also is associated with decreases in the activity of L-methylmalonyl-CoA mutase, which leads to increases in MMA that can be measured in serum (IOM, 1998; Baik and Russell, 1999; Wolters et al., 2004).

Biomarkers for Vitamin B_{12} Status

The most widely used markers of vitamin B_{12} status are serum or plasma vitamin B_{12} followed by MMA. Elevated blood concentrations of MMA and Hcy are relatively specific markers for vitamin B_{12} deficiency. However, a confounding factor in using these metabolites to assess vitamin B_{12} status is that both are increased when renal function is poor. Hcy is influenced by other dietary factors including folate and vitamin B_6. MMA can reflect bacterial metabolism of the intestinal microflora (IOM, 1998; Baik and Russell, 1999; Wolters et al., 2004; Sachdev, 2005). Because poor renal function elevates MMA, it has been suggested that other metabolites, such as 2-methylcitrate, be used along with MMA (Allen et al., 1993). When 2-methylcitric acid concentration is greater than MMA concentration, it indicates renal dysfunction as opposed to vitamin B_{12} deficiency (Stabler et al., 1999).

There are three types (I, II, and III) of vitamin B_{12} binding proteins in plasma, called transcobalamins (TC) (Baik and Russell, 1999). TC II binds to small fraction (7% to 20%) of plasma vitamin B_{12} and forms a complex, called holotranscoablamin II (holoTC II) (Baik and Russell, 1999). HoloTC II is released into portal circulation and later transported into cells (Baik and Russell, 1999; Herrmann et al., 2003). HoloTC II is a reasonable marker for assessing vitamin B_{12} status without renal dysfunction (Baik and Russell, 1999; Carmel, 2000; IOM, 1998; Wolters et al., 2004). Higher holoTC II indicates better vitamin B_{12} status (Herrmann et al., 2003). Megaloblastic anemia is not a reliable sign of vitamin B_{12} deficiency (Lindenbaum et al., 1988; Stabler, 2001), because megaloblastic anemia does not always appear in people with vitamin B_{12} deficiency (Camel, 2000).

Defining Vitamin B_{12} Status

Generally, serum vitamin B_{12} < 150 or < 160 pmol/L indicates frank vitamin B_{12} deficiency (Baik and Russell, 1999; Wolters et al., 2004), but there is no widely accepted biochemical cutoff for marginal or pre-clinical vitamin B_{12} deficiency or for vitamin B_{12} adequacy (Allen et al., 1993; Carmel, 2000; Baik and Russell, 1999). Use of both serum vitamin B_{12} and MMA may improve the differential diagnosis of vitamin B_{12} deficiency. Information from several sources suggests that marginal status might be defined as a serum vitamin B_{12} above 160 pmol/L and below 222 to 258 pmol/L (300 to 350 pg/ml) along with serum MMA concentrations > 270 or > 370 nmol/L (+ 2 and + 3 standard deviations (SDs) above the values in young controls) (Moelby et al., 1990; Lindenbaum et al., 1994; Pennypacker et al., 1992; Rasmussen et al., 1996; Stabler et al., 1990, 1997). The age-adjusted geometric mean concentration of plasma MMA was 137 nmol/L in NHANES 1999-2000 (Pfeiffer et al., 2005). There are concerns that raising the lower limit of normal serum vitamin B_{12} will falsely classify many vitamin B_{12} adequate people as deficient (Carmel, 2000), and others question the use of increased MMA as the only marker for diagnosis of vitamin B_{12} deficiency (Hvas et al., 2001). Pennypacker et al. (1992) reported that in older adults at geriatric outpatient clinics with serum vitamin B_{12} < 222 pmol/L and with no previous history of vitamin B_{12} deficiency, the prevalence of elevated serum MMA (> 3 SDs) was similar among those with serum vitamin B_{12} of 75 to 148 pmol/L and 148 to 222 pmol/L. In the Framingham elderly population, serum MMA and tHcy concentrations were similarly elevated among those with serum vitamin B_{12} concentrations of 74 to 147 pmol/L and 148 to 258 pmol/L (Lindenbaum et al., 1994).

In contrast, others reported that the prevalence of elevated serum MMA (>270, > 370, or > 376 nmol/L) is quite different among those with serum vitamin B_{12} in the very low (< 150 pmol/L) versus the moderately low ranges (150 to 250 pmol/L). In older Americans in NHANES III (N = 1,145; ≥ 65 y, multi-ethnic), their serum MMA was > 370 nmol/L (90^{th} percentile in young adults) in 65.2% of those with serum vitamin B_{12} ≤ 148 pmol/L and 14.8% of those with serum vitamin B_{12} > 148 pmol/L (Morris et al., 2002). Similarly, Carmel et al. (1999) found that the prevalence of elevated serum MMA (> 370 or > 376 nmol/L) was 55.1%, 12.4%, and 10.8% in those with serum vitamin B_{12} in the ranges of < 140 pmol/L, 140 to 258 pmol/L, and > 258 pmol/L, respectively in older adults (N = 591; > 60 years, multi-ethnic). Due to high cutoff points for elevated serum MMA concentration (> 370 nmol/L rather than > 270 nmol/L), the prevalence of elevated serum MMA was not strongly related to serum vitamin B_{12} concentration.

Although there is no clear consensus definition of the biochemical cutoffs for poor vitamin B_{12} status, serum vitamin B_{12} < 258 pmol/L and serum MMA > 271 nmol/L seems reasonable and has been linked with health problem such as poor cognition (Lewis et al., 2005; Johnson et al., 2003), anemia (Johnson et al., 2003), and depression (Penninx et al., 2000).

Additional research is needed to identify the concentrations of serum vitamin B_{12} and MMA that are linked with specific biochemical, clinical and physiological measures of obvious vitamin B_{12} deficiency as well as marginal or pre-clinical deficiency.

The Prevalence of Vitamin B_{12} Deficiency

Depending on the biochemical criterion that is used, 5% to more than 23% of older adults are deficient in vitamin B_{12} (Baik and Russell, 1999; Stabler, 2001; Johnson et al., 2003; IOM, 1998; Wolters et al., 2004). Risk factors for deficiency include low animal protein intake, no crystalline vitamin B_{12} from supplements or fortified foods, malabsorption associated with atrophic gastritis or *Helicobacter pylori* infection, pancreatic or intestinal pathology, and gastric acid-reducing medications (Baik and Russell, 1999; IOM, 1998, Garcia et al., 2002; Johnson et al., 2003; Rajan et al., 2002a, 2002b; Stabler, 2001; Wolters et al., 2004). The prevalence of vitamin B_{12} deficiency increases with advanced age, mainly because atrophic gastritis decreases the production of the acid and digestive enzymes needed to cleave protein-bound vitamin B_{12} from the natural chemical form of vitamin B_{12} found in meat, poultry, fish and dairy foods (Baik and Russell, 1999; IOM, 1998; Wolters et al., 2004). Loss of intrinsic factor (causing pernicious anemia), gastrectomy, and ileal disease/resection are less common causes of vitamin B_{12} deficiency. People over 50 years old should consume the Recommended Dietary Allowances for vitamin B_{12} in the crystalline form (i.e., fortified foods or dietary supplements), which does not require gastric acid or enzymes for initial digestion (USDHHS and USDA, 2005; IOM, 1998). Approximately 10% to 30% of older adults have malabsorption of protein-bound vitamin B_{12} and about 1% to 2% lack intrinsic factor (the causal factor in pernicious anemia), which is required for active uptake of vitamin B_{12} in the small intestine (Baik and Russell, 1999; Stabler, 2001).

Vitamin B_{12} and Hearing Loss

Poor vitamin B_{12} status was associated with auditory dysfunction in some (Houston et al., 1999; Quaranta et al., 2004; Gok et al., 2004; Shemesh et al., 1993), but not all studies (Berner et al., 2000; Fine et al., 1990; Fine and Hallett, 1980; Durga et al., 2006) (Table 2.1). Tinnitus (ringing in the ears) (Shemesh et al., 1993) and auditory hallucinations (Hector and Burton, 1988) have been recorded as symptoms of vitamin B_{12} deficiency.

None of these studies, however, has assessed the relationship of hearing with measures of vitamin B_{12} status such as MMA other than serum vitamin B_{12} and Hcy. MMA and Hcy are sensitive indicators of vitamin B_{12} status (Wolters et al., 2004; Baik and Russell, 1999; Savage et al., 1994).

TABLE 2.1 Summary of Research Linking Hearing Impairment, Vitamin B_{12}, and Folate

	Age (years)	N	Type of hearing loss	Serum vitamin B_{12} (pmol/L)	Serum folate (nmol/L)	RBC folate (nmol/L)	Homocysteine (µmol/L)	Findings
Houston et al., 1999 [a]	65 ± 4 [b] (60-71) [c]	55	ARHL [d]	308 ± 152 [NA]	25.8 ± 18.7	522 ± 234	NA [e]	ARHL was associated with poor vitamin B_{12} and folate status.
Berner et al., 2000 [f]	Median: 78 (67-88)	91	ARHL	Median: 237 (79-1160)	NA	Whole blood, median: 295 (90-737)	Median: 11.1 (7.0-33.7)	ARHL was not associated with vitamin B_{12} and folate status.
Durga et al., 2006 [g]	60 ± 6 (50-70)	728	ARHL	Median: 330 (252-382)	12 ± 4	691 ± 260	14.4 ± 2.4	Conversely, hearing loss was associated with low concentration of Hcy and high concentrations of folate, vitamin B_{12} and B_6.
Gok et al., 2004 [h]	36 ± 4	60	NIHL [i]	261.7 ± 98.6	11.7 ± 3.9	NA	12.8 ± 3.8	NIHL was associated with elevated Hcy and poor folate and vitamin B_{12} status.
Shemesh et al., 1993 [j]	39.4 ± 10.5	113	NIHL	NA	NA	NA	NA	NIHL was prevalent participants with vitamin B_{12} deficiency.
Cadoni et al., 2004 [k]	43 (16-70)	67	SSNHL [l]	NA	13.1	NA	9.2	SSNHL was associated with elevated Hcy and low folate concentrations.
Capaccio et al., 2005a [m]	53.6 ±11.3	201	SSHL [n]	NA	21.5	NA	12.7	SSHL was associated with elevated Hcy and low folate concentrations.
Capaccio et al., 2005b [o]	48.5 ±14.9	180	SSHL	NA	21.8	NA	12.4	SSHL was associated with elevated Hcy and low folate concentrations.

[a] Houston DK, Johnson MA, Nozza RJ, et al. Age-related hearing loss, vitamin B-12 and folate in elderly women. Am J Clin Nutr 1999;69:564-71.

[b] Mean ± SD.

[c] Ranges in parentheses.

[d] ARHL, age-related hearing loss.

[e] NA, not available.

[f] Berner B, Ødem L, Parving A. Age-related hearing impairment and B vitamin status. Acta Otolaryngol 2000;120:633-7.

[g] Durga J, Anteunis LJC, Schouten EG, Bots ML, Kok FJ, Verhoef P. Association of folate with hearing in dependent on the 5,10-methylenetetrahydrofolate reductase 677C → T mutation. Neurobiol Aging 2006;27:482-9.

[h] Gok U, Halifeoglu I, Canatan C, Yildiz M, Gursu MF, Gur B. Comparative analysis of serum homocysteine, folic acid levels in patients with noise-induced hearing. Auris Nasus Larynx 2004;31:19-22.

[i] NIHL, noise-induced hearing loss.

[j] Shemesh Z, Attias J, Ornan M, Shapira N, Shahar A. Vitamin B12 deficiency in patients with chronic tinnitus and noise-induced hearing loss. Am J Otolaryngol 1993;2:94-9.

[k] Cadoni G, Agostino S, Scipione S, Galli J. Low serum folate levels: A risk factor for sudden sensorineural hearing loss? Acta Otolaryngol 2004;124:608-11.

[l] SSNHL, sudden sensorineural hearing loss.

[m] Capaccio P, Ottaviani F, Cuccarini V, et al. Methylenetetrahydrofolate reductase gene mutations as risk factors for sudden hearing loss. Am J Otolaryngol 2005a;26(6):383-7.

[n] SNHL, sensorieneural hearing loss.

[o] Capaccio P, Ottaviani F, Cuccarini V, et al. Sudden hearing loss and MTHFR 677C>T/1298A>C gene polymorphisms. Genet Med 2005b;7(3): 206-8.

The influence of vitamin B_{12} status on auditory function has been examined in several studies and the findings are mixed (Houston et al., 1999; Shemesh et al., 1993; Gok et al., 2004; Berner et al., 2000). The associations of age-related hearing loss with vitamin B_{12} and folate in 55 women aged 60 to 71 years were examined (Houston et al., 1999). For the hearing assessment, PTA in the better ear across 4 frequencies (0.5, 1, 2, and 4 kHz) was used. Women with hearing loss (PTA $\geq$ 20 dB HL) had significantly lower mean serum vitamin B_{12} concentration (236 vs. 380 pmol/L, respectively) and significantly lower mean RBC folate concentration (425 vs. 619 nmol/L) than women with normal hearing. In a subgroup of women who did not take a multivitamin containing vitamin B_{12} and folate, women with impaired hearing had a significantly lower mean serum vitamin B_{12} concentration (156 vs. 302 pmol/L, respectively), a significantly lower mean RBC folate concentration (288 vs. 502 nmol/L), and a significantly lower mean serum folate concentration (10.5 vs. 19.6 nmol/L) than women with normal hearing. Significant inverse correlations for PTA with serum vitamin B_{12} concentration ($r = -0.58$) and with RBC folate concentration ($r = -0.37$) were found.

Berner et al. (2000) found no relationship of age-related hearing loss with vitamin B_{12} or folate in 35 men and 56 women (aged 67 to 88 years). PTA (from 0.5 to 4 kHz in the right ear) was not significantly correlated with serum vitamin B_{12}, whole blood folic acid, or plasma Hcy. A limitation of Berner et al.'s study was that there was no normal-hearing group, and all participants were hearing-impaired (PTA > 25 dB HL).

In a cross-sectional study in the Netherlands, the association between hearing thresholds and fasting plasma Hcy, serum folate, RBC folate, serum vitamin B_{12}, and plasma vitamin B_6 were examined in 728 older adults (aged 50 to 70 years) (Durga et al., 2006). Major exclusion criteria for this study were Hcy < 13 µmol/L, vitamin B_{12} < 200 pmol/L, self-reported kidney or thyroid disease, and taking dietary supplements containing B vitamins. PTA-low frequencies (0.5, 1, and 2 kHz) and PTA-high frequencies (4, 6, and 8 kHz) were not associated with concentrations of Hcy, folate, vitamin B_{12}, and plasma vitamin B_6. Contrary to their hypothesis, high concentrations of serum folate and vitamin B_{12} were significantly associated with higher PTA, which indicates poorer hearing status. The lack of association of vitamin B_{12} and folate status with auditory function may be due to their exclusion criteria regarding vitamin B_{12} and Hcy, namely that people with abnormal concentrations were excluded.

In Israel, vitamin B_{12} status in army personnel [N = 113; mean age (± SD): 39.4 ± 10.5 years] with a history of military noise exposure was examined [chronic tinnitus/noise-induced hearing loss (NIHL, n = 57), NIHL alone (n = 29), and normal hearing (n = 27)] (Shemesh et al., 1993). The prevalence of vitamin B_{12} deficiency (serum vitamin B_{12} < 184 pmol/L) was significantly higher in those with tinnitus/NIHL compared with the other groups. Twelve tinnitus participants with vitamin B_{12} deficiency received vitamin B_{12} therapy (1 mg/week, parenteral) until their serum vitamin B_{12} concentrations were above 258 pmol/L in a blood sample taken one month after the last injection. Subjective improvement in tinnitus was observed in all 12 patients following vitamin B_{12} replacement therapy. The tinnitus patients with vitamin B_{12} deficiency had poorer hearing status than tinnitus patients with normal vitamin B_{12} status.

In a Turkish study of NIHL, fasting blood samples (serum concentrations of vitamin B_{12}, folate, and Hcy) and hearing levels were measured in 28 men with NIHL [mean age (± SD): 37 ± 5 years] and 32 men without NIHL [mean age (± SD): 36 ± 4 years] (Gok et al., 2004). Men with NIHL had significantly higher mean serum Hcy concentration, lower mean serum folate concentration, and lower mean serum vitamin B_{12} concentration than the control group.

The associations of folate, Hcy, and polymorphisms in the methylenetetrahydrofolate reductase (MTHFR) with hearing loss have been examined in other studies. Low serum folate and high Hcy concentrations were found in 43 patients (23 women and 20 men; aged 17 to 70 years) with sudden sensorineural hearing loss (SSHL) compared with the control group (n = 24; aged 16 to 62) in Italy (Cadoni et al., 2004). SSHL is a sensorineural hearing loss occurring within ≤ 3 days and hearing thresholds of ≥ 30 dB HL at least three contiguous audiometric frequencies. However, serum vitamin B_{12} concentrations were not reported in this study. In another Italian study, patients with SSHL [n = 67; mean age (± SD): 53.6 ± 11.3 years] had significantly higher serum Hcy and lower serum folate concentrations than the controls (n = 134). SSHL was significantly associated with MTHFR (at nucleotides 677 and 1298) gene mutations in adults (Capaccio et al., 2005a, 2005b). Low dietary intakes of folate and/or vitamin B_{12} elevate Hcy concentrations in the blood (Wolters et al., 2004). MTHFR is a folate-related enzyme catalyzing the reduction of 5, 10-methylene-tetrahydrofolic acid to 5-methyl-tetrahydrofolic acid, followed by methyl transfer from methyltetrahydrofolate to Hcy to form methionine and tetrahydrofolate facilitated by methionine synthase. Reduced activity of MTHFR disrupts folate metabolism and leads to elevation of Hcy concentrations. Vitamin B_{12} is an essential cofactor for methionine synthase, so vitamin B_{12} deficiency decreases the activity of methionine synthase, which leads to increases in Hcy concentrations (IOM, 1998; Baik and Russell, 1999; Shane, 2000).

Hearing thresholds in the right ear were measured before and after treatment in the control group (placebo) and the vitamin B_{12} treatment group (seven doses of 1 mg/d and one dose of 5 mg/d; intramuscularly) in adults [N = 20; aged 20 to 30 years; hearing threshold within 15 dB HL at all test frequencies (0.25 to 8 kHz) at baseline] (Quaranta et al., 2004). Mean (±

SD) vitamin B_{12} concentrations were 278.5 ± 44.9 pmol/L in the control group and 287.8 ± 50.6 pmol/L in the vitamin B_{12} treatment group before the treatment, suggesting that their vitamin B_{12} status was above the level considered deficient (< 258 pmol/L) and was between the 25th and 50th percentile based on NHANES III (Wright et al., 1998). There was no effect of vitamin B_{12} supplements on hearing thresholds. Temporary threshold shift was measured at 1, 2, 3, and 4 kHz after noise exposure. Vitamin B_{12} treatment had a protective effect on auditory function against noise exposure at 3 and 4 kHz only, suggesting that enhanced vitamin B_{12} status may offer some protection against noise exposure.

Some investigators have directly or indirectly assessed the effects of vitamin B_{12} deficiency on the auditory nerves or brainstem (an electrophysiologic response that is generated by the acoustic nerve and auditory structures within the brainstem; Martin and Clark, 2002; Boettcher, 2002). Auditory dysfunction and severe vitamin B_{12} deficiency in rhesus monkeys was examined over a five-year period (Agamanolis et al., 1976). Although peripheral hearing levels were not monitored, the auditory nerve and other nerves had active lesions associated with vitamin B_{12} deficiency. The relationship between brainstem auditory evoked responses (BAERs) and vitamin B_{12} deficiency was examined (N = 7; aged 35 to 72 years) (Krumholz et al., 1981). The diagnosis of vitamin B_{12} deficiency was based on the degree of clinical neurological involvement (such as sensory loss, motor loss, cortical dysfunction, and optic neuropathy), but serum vitamin B_{12} concentrations were not reported. Two of seven participants with vitamin B_{12} deficiency had delayed BAERs without hearing loss. In contrast, in a human study, nine out of 10 men with vitamin B_{12} deficiency (defined as serum vitamin B_{12} < 162 pmol/L; aged 43 to 78 years) had normal BAERs, indicating a normal brainstem auditory pathway (Fine et al., 1990). In three case reports, men with vitamin B_{12} deficiency (serum vitamin B_{12} concentration < 125 pmol/L) had normal BAERs (Fine and Hallett, 1980). The small sample sizes of these human studies and lack of vitamin B_{12} adequate control groups make it difficult to derive meaningful conclusions about the effect of vitamin B_{12} deficiency on BAERs.

The mechanisms by which poor vitamin B_{12} status may cause hearing loss are not entirely known. As previously noted, some studies suggest vitamin B_{12} deficiency may compromise auditory nerve or brainstem (Agamanolis et al., 1976; Krumholz et al., 1981). However, age-related hearing loss is mostly due to disorders of the peripheral auditory system and, more specifically, abnormalities within the cochlea (Jerger et al., 1995; Mosciki et al., 1985). Nerve cells have small stores of vitamin B_{12} and may be particularly sensitive to low vitamin B_{12} status (Herbert, 1994). Poor vitamin B_{12} status may increase susceptibility to the harmful effects of noise in the cochlea, damage myelin, and cause auditory neuropathy (Shemesh et al., 1993). Elevated blood concentrations of MMA and Hcy are relatively specific markers for vitamin B_{12} deficiency, but Hcy may also be elevated in poor folate and/or vitamin B_6 status (Wolters et al., 2004; Sachdev, 2005). MMA is believed to be a neurotoxin (Kölker et al., 2000; Wajner and Coelho, 1997), and Hcy may be a vasculotoxin (Sachdev, 2005) and a neurotoxin (Bleich et al., 2004). Therefore, poor vitamin B_{12} and/or folate status might impair the vascular and nervous components of the auditory system through direct and indirect effects. Animal studies, as well as prospective and/or intervention studies in humans, with all age populations and a control group well-matched for all known confounding variables, are needed to demonstrate a causal role for vitamin B_{12} and to identify the mechanisms and metabolic defects responsible for the association of auditory dysfunction with poor vitamin B_{12} and folate status. Furthermore, research is needed to examine the possible effect of vitamin B_{12} supplement on the auditory system.

Purpose, Specific Aims, Hypotheses, and General Approach

The purpose of this dissertation was to examine the prevalence of hearing impairment among older adults, to evaluate the relationship of hearing impairment with CVD risk factors, and to evaluate the relationship of age-related hearing loss with poor vitamin B_{12} status, using multiple measures of vitamin B_{12} status and by repletion with a vitamin B_{12} supplement.

To the accomplish these goals, the research project was designed to assess the relationship of hearing impairment with CVD risk factors, vitamin B_{12} deficiency, MMA and tHcy elevations, and changes in auditory function through vitamin B_{12} supplementation. The aims of chapter three is to evaluate the prevalence of hearing impairment and to examine a possible relationship of Hearing Handicap Inventory for the Elderly and PTA in older adults. The aim of chapter four is to evaluate a possible relationship of hearing impairment with CVD risk factors in older adults. The aim of chapter five is to evaluate a possible association of age-related hearing loss with poor vitamin B_{12} status in older adults, using multiple measures of vitamin B_{12} status and following repletion with a vitamin B_{12} supplement.

It was hypothesed that: 1) the prevalence of hearing impairment would be higher than general population; 2) hearing status would be negatively associated with CVD risk factors in older adults; and 3) age-related hearing loss would be associated with several indices of poor vitamin B_{12} status including low serum vitamin B_{12}, high MMA, and high Hcy, and that vitamin B_{12} repletion would improve hearing loss in vitamin B_{12}-deficient individuals.

The next three chapters will examine the prevalence of hearing impairment, the role of CVD risk factors, and vitamin B_{12} status with regard to hearing impairment in older adults aged 58 to 97 years.

Future studies are needed to determine if changes in auditory structures secondary to poor intakes of nutrients result in functional changes in the auditory system secondary to alterations in nutritional status.

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CHAPTER 3

PREVALENCE OF HEARING IMPAIRMENT IN OLDER ADULTS IN THE OLDER AMERICANS ACT NUTRITION PROGRAMS[1]

[1] Park S, Johnson MA, Shea-Miller K, and De Chicchis AR. To be submitted to the Journal of Aging and Health.

Abstract

Objective: The prevalence of hearing impairment and a possible relationship of Hearing Handicap Inventory for the Elderly (HHIE) with pure-tone average threshold (PTA) were evaluated in older adults receiving nutrition and health services from the Older Americans Act Nutrition Programs.

Methods: Air-conduction thresholds were obtained at octave intervals from 0.25 to 8 kHz using a diagnostic audiometer, and PTA was calculated at frequencies 1, 2, and 4 kHz in older adults (N = 147; mean age (± SD): 76 ± 8 years; 82% female; 70% Caucasian; 30% African-American). The HHIE was used to measure the perceived effect of hearing handicap.

Results: A high prevalence of hearing impairment (PTA > 25 dB hearing level) was observed in this population (63.3% in the best ear and 74.1% in the worst ear), and this prevalence increased with advanced age. Men had higher prevalence of hearing impairment than women. A moderate correlation was found between HHIE and PTA.

Discussion: More attention needs to be paid to the hearing impairment in older adults who receive community-based nutrition and health services. HHIE may be a reasonable self-assessment tool to identify older adults who should undergo an audiometric assessment of auditory function as part of their routine health assessments.

Keywords: hearing impairment, older adults, prevalence, Older Americans Act Nutrition Program

Introduction

Approximately 31 million Americans have hearing impairment (Kochkin, 2005). The prevalence of hearing loss increases greatly with advanced age and is typically greater in men than in women (Torre et al., 2005; Moscicki et al., 1985; Cruickshanks et al., 1998). In the 2003 National Health Interview Survey, 6.9 % of people aged 18 to 44 years, 17.6% of people aged 45 to 64 years, 29.7% of people aged 65 to 74 years, and 46.4% of people aged 75 or older had self-reported difficulty in hearing (Lethbridge-Cejku and Vickerie, 2005).

Hearing loss adversely affects the lives of older adults. Even mild hearing loss is associated with impaired quality of life, functional disabilities, and adverse effects on physical, cognitive, emotional, behavioral, and social function (Jerger et al., 1995; Dalton et al., 2003; Bazargan et al., 2001; Gates and Mills, 2005).

Hearing sensitivity can be readily assessed in community and clinical settings by presenting a series of pure tones to an individual's ears across a range of test frequencies and determining the lowest stimulus level (threshold) that a tone can be detected. Frequently, a person's pure-tone average (PTA), the mean of three or four contiguous frequencies, is used to predict the degree of communication impact imposed by hearing loss. For example, a PTA between 26 and 40 dB hearing level (HL) is considered mild hearing impairment (Martin and Clark, 2002; Newman and Sandridge, 2004) and would suggest difficulty hearing faint speech. Higher hearing threshold indicates poorer hearing sensitivity and greater difficulty hearing and understanding speech. The Hearing Handicap Inventory for the Elderly (HHIE) is a self-assessment tool that intends to identify self-perceived hearing impairment in non-institutionalized older adults and consists of emotional and social components (Weinstein and Ventry, 1983).

The Older Americans Act Nutrition Program (OAANP) is the largest federally funded community-based elderly nutrition program and is designed to address dietary insufficiency and social isolation among older adults (O'Shaughnessy, 2004; Ponza et al., 1996; AoA, 2006). The OAANP provides grants to state agencies on aging to support a variety of health and wellness services, and congregate and home-delivered meals for people 60 years and older. One goal of the OAANP is to provide health promotion and disease management services (O'Shaughnessy, 2004; Ponza et al., 1996; AoA, 2006). Hearing loss may limit a person's ability to understand verbal information. For example, senior centers often provide health and nutritional information orally, such as through monthly nutrition and health education programs to help older adults improve their eating habits, disease management, and health status. Therefore, older individuals with impaired hearing may experience difficulty in understanding such programs at their senior center. Also, little is known about the prevalence of hearing impairment in this population. The specific aims of this study were to evaluate the prevalence of hearing impairment and to examine a possible relationship of HHIE and PTA in older adults.

Methods

STUDY POPULATION

The questionnaires and all procedures were approved by the Institutional Review Boards on Human Subjects of the Georgia Department of Human Resources, the University of Georgia, and the Athens Community Council on Aging. Participants were recruited from the OAANP at six senior centers in northeast Georgia, USA. Written informed consent was obtained from each participant. Prior to the auditory assessment, two nurse practitioners conducted otoscopic exams of the outer ear and ear canal to detect excessive cerumen, foreign bodies, or other obvious disorders of the ear canal or tympanic membrane that would prevent a safe and reliable evaluation and to identify obvious disorders that might require a medical referral. Following this exam, 18 individuals were excluded and/or declined further participation in the study. Of the originally enrolled 150 participants, one participant dropped out due to a medical condition and two did not complete the hearing assessment. Participants with abnormal middle ear function were included. Thus, 147 participants (aged 58 to 97 years; 27 men; 120 women; 70% Caucasian; 30% African-American), who were physically and mentally able to participate in the study, had hearing data from the best ear available for statistical analysis. Hearing levels could not be measured in the left ear of four participants at certain frequencies due to the severity of the hearing impairment, so the right ear was used as the best ear, and the worst ear data were missing in those four participants. As a result, worst ear data was available from 143 participants for statistical analysis.

DATA COLLECTION

Assessments were performed in the six senior centers (January through April of 2001). Questionnaires were administered by interviewers trained to collect information on demographics, general health, and auditory function. These interviewers read questions to the participants and recorded their responses. A revised version of the University of Georgia Speech and Hearing Clinic history form was completed to assess family history of hearing loss and noise exposure.

One licensed audiologist with no knowledge about the health or hearing status of the participants conducted the auditory assessments using portable equipment (Grason-Stadler GSI 38, Madison, WI). The assessment was conducted in a quiet area of each senior center because these older adults were not able to travel to the University of Georgia Speech and Hearing Clinic. Air-conduction thresholds were obtained at octave intervals from 0.25 to 8 kHz by using a diagnostic audiometer meeting specifications in accordance with the American National Standards Institute S3.6 (1996) and by following standard audiometric clinical procedures (Yantis, 1994; American Speech-Language-Hearing Association, 1978). For middle ear function, four tympanometric measures were performed using a Grason-Stadler model GSI-38 tympanometer, including static acoustic admittance, tympanometric width, ear canal volume, and tympanometric peak pressure (Wiley et al., 1996).

The HHIE was used to identify social and emotional problems due to hearing impairment (Weinstein et al., 1986; Weinstein and Ventry, 1983). The HHIE contained 25 questions (13 social and 12 emotional) and scored 0, 2, or 4 depending on the answers with a minimum score of 0 and a maximum score of 100 points. Higher scores indicate greater evidence of hearing handicap (Weinstein et al., 1986; Weinstein and Ventry, 1983).

DATA ANALYSIS

For each participant, the ears were classified as the best ear and the worst ear. The best ear was defined as the ear with the lowest hearing levels at 0.5, 1, 2, 4, and 8 kHz. If these were equal, the right ear was labeled the best ear. The statistical analyses were performed independently for the best ear and the worst ear in order not to neglect participants with at least one affected ear. Hearing function was assessed as a modified PTA (1, 2, and 4 kHz) in the best ear and the worst ear. Hearing levels at 0.5 kHz were not included in the PTA, as testing was conducted in a quiet room rather than in a sound-treated audiometric suite. Noise levels were monitored in each facility using a sound level meter, and environmental background noise prohibited reliable measurements at this frequency. Hearing test data were sufficient to permit categorization of participants into normal and impaired hearing based on two cutoffs for poor hearing status of > 25 or > 40 dB HL (Martin and Clark, 2002; Newman and Sandridge, 2004).

Hearing status was dichotomized (normal or impaired hearing). The normality of data was checked by skewness and kurtosis. Spearman's correlation coefficients were used to examine associations between PTA as a continuous variable and HHIE controlling for age, gender, race, family history of hearing loss, and noise exposure. A series of logistic regression analyses were conducted with hearing status as a dependent variable and HHIE, age, gender, race, family history of hearing loss, and noise exposure as independent variables. Some of the differences in categorical variables were tested by use of the chi-square statistic. Data are presented as mean ± standard deviation (SD) or as a percent. Data were analyzed with the Statistical Analysis System (Version 9.1, SAS Institute Inc, Cary, NC). A P value of ≤ 0.05 was considered statistically significant.

Results

A total of 147 participants were included in this study. The prevalence of hearing impairment based on two cutoffs is shown in Table 3.1. Approximately 63% in the best ear and 74% in the worst ear of this population had hearing impairment (PTA > 25 dB HL). The prevalence of hearing impairment was significantly increased with advanced age. Approximately 41% of participants aged ≤ 69 years, 50% of participants aged 70-79 years, and 90% of participants aged ≥ 80 years had hearing impairment (PTA > 25 dB HL in the best ear). This prevalence was further increased in the worst ear (56% of participants aged ≤ 69 years, 66% of participants aged 70-79 years, and 94% of participants aged ≥ 80 years). Men had significantly higher prevalence of hearing impairment than women (85% vs. 58% in the best ear, respectively, P = 0.02 and 92% vs. 71% in the worst ear, P = 0.04) after controlling for age, race, family history of hearing loss, and noise exposure. Mean air-conduction thresholds for frequencies from 0.5 to 8 kHz and PTA (1, 2, and 4 kHz) are shown in Table 3.2 by age, gender, and race. PTA in both ears was significantly correlated with HHIE total, emotional, and social scores (Table 3.3). The prevalence of subjective hearing impairment (HHIE > 16 points; Weinstein and Ventry, 1983) increased as the severity of hearing impairment became worse (Table 3.4). There was a sharp increase in the percentage of participants with HHIE > 16 when PTA was greater than 40 dB HL. More information on the relationship of HHIE with PTA is shown in Appendix A (Tables A.1–A.3).

Discussion

This is a first study to our knowledge that assesses the prevalence of hearing impairment and examines an association between HHIE and PTA in the OAANP. The major findings are that the prevalence of hearing impairment appears to be higher in this OAANP sample (> 25 dB HL: 63.3% in the best ear and 74.1% in the worst ear) compared to other adult populations such as the Epidemiology of Hearing Loss Study (N = 3,753; aged 48 to 92 years; 46% in the worst ear PTA > 25 dB HL across 0.5, 1, 2, and 4 kHz) (Cruickshanks et al., 1998). In the Health, Aging, and Body Composition study, 59.9% had hearing loss (defined as PTA across 0.5, 1, and 2 kHz > 25 dB HL in the worse ear; N = 2,052; aged 73 to 84 years) (Helzner et al., 2005). In an Italian study, 27.2% of older adults (N = 1,332; aged 65 to 96 years) had self-reported hearing loss (Cacciatore et al., 1999). This higher prevalence hearing impairment in the present study was perhaps due to the generally poor health and nutritional status of this population, which is why many of these older people seek services at senior centers (O'Shaughnessy, 2004; Ponza et al., 1996). However, it is difficult to compare the prevalence hearing impairment among studies due to different characteristics (e.g., age, gender, and race) of the study populations, variations in cutoffs for defining hearing impairment, and/or the use of self-reported information or audiometric measures of auditory function.

There was a moderate correlation between HHIE and PTA (rho = 0.45 to 0.53). These correlations of PTA with emotional and social scales indicate that hearing impairment may have both emotional and social impacts. Based on a considerable increase in the handicap category at PTA > 40 dB HL, 40 dB HL may be a reasonable cutoff to use as a basic for referral for audiometric assessment of auditory function. The present study was a partial replication of the Weinstein and Ventry (1983) study that examined the association of PTA (0.5, 1, and 2 kHz) with HHIE in 100 non-institutionalized older adults [mean age (± SD): 75.7 ± 7.2 years with a range from 65 to 92 years]. Similar to the present study, PTA was significantly correlated with HHIE (total, emotional, and social scores). This result may indicate that HHIE is a reasonable self-assessment tool to identify hearing impairment in older adults and the need for referral for further evaluation.

Hearing loss adversely affects the lives of older adults and has enormous costs related to poor quality of life (Johnson et al., 2004). Hearing loss and activity limitation was examined in participants (N = 8,767) aged 70 years or older from the 1994 National Health Interview Second Supplement on Aging (Campbell et al., 1999). Older adults with impaired hearing were more likely to report activity limitations than those with normal hearing, such as difficulties in walking (30.7% vs. 21.3%, respectively), getting outside (17.3% vs. 12.0%), getting into and out of bed or a chair (15.1% vs. 9.8%), managing medication (7.7% vs. 4.8%), and preparing meals (11.6% vs. 7.6%). Thus, hearing impairment in older adults can lead to frustrating, embarrassing, and even dangerous situations (Johnson et al., 2004; NIDCD, 2006a, 2006b). For example, older adults with impaired hearing cannot hear others trying to alert them when dangers are nearby, such as sirens, horns, and other types of alarms.

There are a variety of strategies to assist older adults with hearing impairment including hearing aids (Johnson et al., 2004). Hearing aids are probably considered in older adults with a mild hearing loss (PTA from 26 to 40 dB HL) and definitely considered in older adults with PTA > 40 dB HL (Martin and Clark, 2002). Audiologic services (such as hearing aids) should be available to community-residing adults (Lee et al., 2005) and perhaps could be added to the other health promotion programs and services provided in the OAANP at senior centers (Ponza et al., 1996; National Resource Center on Nutrition, Physical Activity, and Aging, 2002).

There are a few limitations in the present study, such as a convenient sample with wide age ranges and relatively small sample size. Nonetheless, hearing impairment was very prevalent in these participants of the OAANP in northeast Georgia. A moderate correlation between HHIE and PTA may indicate that HHIE is a reasonable self-assessment tool to identify hearing impairment in older adults. More attention may be needed in senior centers to address this high prevalence of hearing loss by providing hearing screenings and referrals, as well as making sure that speakers are amplified appropriately and are aware of the extent of hearing impairment in this population. Also, given the high prevalence of both hearing impairment and nutrition problem, this population may also be useful for examining associations of hearing impairment with cardiovascular disease and nutrition risk factors, as will be discussed in subsequent chapters (4 and 5).

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TABLE 3.1 Prevalence of Hearing Impairment by Age, Gender, and Race based on Pure-tone Average Threshold (1, 2, and 4 kHz)

	Hearing Impairment											
	Pure-tone average threshold > 25 dB hearing level [a]						**Pure-tone average threshold > 40 dB hearing level** [b]					
	Best ear			**Worst ear**			**Best ear**			**Worst ear**		
	N [c]	**n** [d]		**N**	**n**		**N**	**n**		**N**	**n**	
Age (years)												
≤ 69 (%)	34	14	41.2	34	19	55.9	34	6	17.7	34	8	23.5
70-79 (%)	56	28	50.0	55	36	65.5	56	10	17.9	55	15	27.3
≥ 80 (%)	57	51	89.5	54	51	94.4	57	30	52.6	54	38	70.4
P [e]			<0.0001			<0.0001			<0.0001			<0.0001
Gender												
Female (%)	120	70	58.3	119	84	70.6	120	29	24.2	119	44	37.0
Male (%)	27	23	85.2	24	22	91.7	27	17	63.0	24	17	70.8
P [f]			0.003			0.01			<0.0001			0.0005
P [g]			0.02			0.04			0.003			0.003
Race												
Caucasian (%)	103	69	67.0	99	78	78.8	103	39	37.9	99	47	47.5
African-American (%)	44	24	54.6	44	28	63.6	44	7	15.9	44	14	31.8
P [h]			0.19			0.06			0.007			0.05
P [i]			0.26			0.13			0.03			0.18

[a] Hearing impairment was defined as pure-tone average threshold > 25 dB hearing level.

[b] Hearing impairment was defined as pure-tone average threshold > 40 dB hearing level.

[c] Number of total participants.

[d] Number of participants with the condition.

[e] Chi-square analyses.

[f] Logistic regression model controlling for age and race.

[g] Logistic regression model controlling for age, race, family history of hearing loss, and noise exposure.

[h] Logistic regression model controlling for age and gender.

[i] Logistic regression model controlling for age, gender, family history of hearing loss, and noise exposure.

TABLE 3.2 Mean Air-conduction Pure-tone Threshold (dB hearing level), Standard Deviation (SD) for the Best ear and the Worst ear by Age, Gender, Race, and Frequency

	500 Hz		1000 Hz		2000 Hz	
Gender, race, and age	**n**	**Mean ± SD**	**n**	**Mean ± SD**	**n**	**Mean ± SD**
			Best ear			
White female						
58-69 years	14	21.1 ± 12.1	14	23.6 ± 13.1	14	25.0 ± 11.6
70-79 years	36	24.3 ± 9.1	36	23.5 ± 9.6	36	29.4 ± 12.5
80-91 years	31	32.6 ± 10.7	31	36.8 ± 13.5	31	43.4 ± 14.7
All	81	26.9 ± 11.1	81	28.6 ± 13.4	81	34.0 ± 15.1
Black female						
65-68 years	10	21.5 ± 7.1	10	20.0 ± 4.7	10	18.0 ± 8.2
70-78 years	13	21.5 ± 3.8	13	22.7 ± 7.0	13	27.3 ± 11.0
80-97 years	16	31.9 ± 7.5	16	32.5 ± 9.0	16	35.9 ± 11.4
All	39	25.8 ± 8.1	39	26.0 ± 9.1	39	28.5 ± 12.6
White male						
63-69 years	8	25.6 ± 13.2	8	27.5 ± 15.6	8	36.3 ± 21.0
70-79 years	6	30.0 ± 10.5	6	34.2 ± 12.4	6	65.8 ± 15.3
80-92 years	8	33.1 ± 14.6	8	33.8 ± 16.0	8	48.1 ± 19.4
All	22	29.5 ± 12.9	22	31.6 ± 14.6	22	48.6 ± 21.7
Black male						
66-68 years	2	25.0 ± 7.1	2	25.0 ± 14.1	2	27.5 ± 17.7
73 years	1	10.0	1	15.0	1	25.0
84-86 years	2	25.0 ± 7.1	2	32.5 ± 3.5	2	40.0 ± 7.1
All	5	22.0 ± 8.4	5	26.0 ± 10.2	5	32.0 ± 12.0
All Participants	147	26.8 ± 10.6	147	28.3 ± 12.5	147	34.7 ± 16.7
			Worst ear			
White female						
58-69 years	14	26.1 ± 16.1	14	27.9 ± 17.3	14	29.3 ± 14.3
70-79 years	36	29.6 ± 9.3	36	28.5 ± 9.8	36	34.9 ± 13.0
80-91 years	31	38.5 ± 12.7	31	42.3 ± 15.4	31	49.8 ± 15.8
All	81	32.4 ± 12.8	81	33.6 ± 15.0	81	39.6 ± 16.4
Black female						
65-68 years	10	25.0 ± 6.2	10	23.0 ± 4.8	10	24.0 ± 7.4
70-78 years	13	26.2 ± 5.1	13	28.1 ± 7.8	13	31.9 ± 10.3
80-97 years	16	35.9 ± 9.5	16	35.9 ± 9.3	16	42.5 ± 11.7
All	39	29.9 ± 8.9	39	30.0 ± 9.4	39	34.2 ± 12.6
White male						
63-69 years	8	30.6 ± 13.2	8	33.1 ± 16.7	8	48.1 ± 23.0
70-79 years	6	40.0 ± 12.6	6	45.0 ± 20.0	6	66.7 ± 14.0
80-92 years	7	38.6 ± 15.7	7	40.7 ± 17.2	7	56.2 ± 18.0
All	21	36.0 ± 13.9	21	39.0 ± 17.7	21	56.2 ± 19.7
Black male						
66-68 years	2	30.0 ± 7.1	2	30.0 ± 14.1	2	32.5 ± 17.7
73 years	1	15.0	1	20.0	1	35.0
84-86 years	2	30.0 ± 0.0	2	40.0 ± 7.1	2	47.5 ± 17.7
All	5	27.0 ± 7.6	5	32.0 ± 11.5	5	39.0 ± 14.7
All Participants	146	32.1 ± 12.0	146	33.4 ± 14.2	146	40.5 ± 17.2

TABLE 3.2 Continued

	4000 Hz		8000 Hz		PTA (1, 2, and 4 kHz)	
Gender, race, and age	**n**	**Mean ± SD**	**n**	**Mean ± SD**	**n**	**Mean ± SD**
			Best ear			
White female						
58-69 years	14	28.6 ± 14.2	12	36.7 ± 10.5	14	26.1 ± 11.1
70-79 years	36	29.4 ± 15.2	28	40.4 ± 16.0	36	28.2 ± 10.0
80-91 years	31	49.4 ± 13.1	12	53.8 ± 6.1	31	43.7 ± 12.3
All	81	36.9 ± 17.2	52	42.6 ± 14.4	81	33.8 ± 13.5
Black female						
65-68 years	10	15.5 ± 8.0	10	14.5 ± 9.8	10	18.8 ± 5.5
70-78 years	13	23.8 ± 9.8	12	31.3 ±20.2	13	24.6 ± 8.3
80-97 years	16	35.0 ± 12.8	15	41.3 ± 14.7	16	35.4 ± 9.0
All	39	26.3 ± 13.2	37	30.8 ± 18.8	39	27.6 ± 10.5
White male						
63-69 years	8	46.3 ± 18.9	4	47.5 ± 11.9	8	37.1 ± 17.2
70-79 years	6	67.5 ± 5.2	2	57.5 ± 3.5	6	55.8 ± 8.3
80-92 years	8	61.3 ± 13.0	3	53.3 ± 7.6	8	49.0 ± 13.5
All	22	57.5 ± 16.2	9	51.7 ± 9.4	22	46.5 ± 15.4
Black male						
66-68 years	2	40.0 ± 21.2	1	30.0	2	31.7 ± 18.9
73 years	1	40.0	1	45.0	1	28.3
84-86 years	2	52.5 ± 3.5	1	60.0	2	41.7 ± 4.7
All	5	45.0 ± 12.7	3	45.0 ± 15.0	5	35.0 ± 11.5
All Participants	147	37.4 ± 18.6	101	39.2 ± 17.1	147	34.1 ± 14.2
			Worst ear			
White female						
58-69 years	14	35.4 ± 13.2	12	45.0 ± 8.0	14	30.5 ± 12.8
70-79 years	36	36.1 ± 15.1	25	44.0 ± 17.3	36	32.4 ± 11.2
80-91 years	30	56.0 ± 12.2	9	60.0 ± 2.5	30	48.8 ± 13.8
All	80	43.4 ± 16.7	46	47.4 ± 14.7	80	38.2 ± 14.8
Black female						
65-68 years	10	20.5 ± 7.6	10	20.5 ± 9.8	10	21.5 ± 6.2
70-78 years	13	28.1 ± 11.8	11	35.0 ± 19.5	13	29.4 ± 8.5
80-97 years	16	42.5 ± 12.2	12	45.4 ± 15.0	16	39.4 ± 9.1
All	39	32.1 ± 14.3	33	34.4 ± 18.1	39	31.5 ± 10.9
White male						
63-69 years	8	52.5 ± 19.3	2	52.5 ± 10.6	8	44.2 ± 17.4
70-79 years	5	70.0 ± 7.1	1	65.0	5	63.0 ± 11.7
80-92 years	6	70.0 ± 13.0	2	60.0 ± 0.0	6	51.9 ± 12.8
All	19	62.6 ± 16.8	5	58.0 ± 7.6	19	51.6 ± 16.0
Black male						
66-68 years	2	45.0 ± 14.1	1	35.0	2	35.0 ± 14.1
73 years	1	45.0	1	50.0	1	31.7
84-86 years	2	67.5 ± 10.6	-	-	2	51.7 ± 11.8
All	5	54.0 ± 15.2	2	42.5 ± 10.6	5	41.0 ± 13.5
All Participants	143	43.3 ± 18.5	86	42.9 ± 17.2	143	38.2 ± 15.1

- Not applicable.

TABLE 3.3 Association between Hearing Handicap Inventory for the Elderly (HHIE) and Pure-tone Average Threshold in the Best ear and the Worst Ear [a]

Best ear (N = 146)				
	Total HHIE score	Emotional	Social	PTA[b] in the best ear
Total HHIE score	1.00	0.93 *	0.96 *	0.53 *
Emotional		1.00	0.85 *	0.52 *
Social			1.00	0.48 *
PTA in the best ear				1.00
Worst ear (N = 142)				
	Total HHIE score	Emotional	Social	PTA in the worst ear
Total HHIE score	1.00	0.94 *	0.96 *	0.51 *
Emotional		1.00	0.86 *	0.53 *
Social			1.00	0.45 *
PTA in the worst ear				1.00

[a] Partial Spearman correlation coefficient adjusted for age, gender, race, family history of hearing loss, and noise exposure.

[b] PTA, pure-tone average threshold across 1, 2, and 4 kHz.

* $P < 0.0001$.

TABLE 3.4 Number of Participants Self-perceived as being with or without Handicap according to Pure-tone Average Categories

		Hearing Handicap Inventory for the Elderly [a]	
Pure-tone average	**N [b]**	**0 – 16 points**	**> 16 points**
Best ear			
0-25 dB (normal)	54	51 (94.4%)	3 (5.6%)
26-40 dB (mild)	47	41 (87.2%)	6 (12.8%)
41-55 dB (moderate)	34	19 (55.9%)	15 (44.1%)
>55 dB (moderately severe)	12	3 (25.0%)	9 (75.0%)
Total	147	114	33
Worst ear			
0-25 dB (normal)	37	36 (97.3%)	1 (2.7%)
26-40 dB (mild)	45	40 (88.9%)	5 (11.1%)
41-55 dB (moderate)	42	28 (66.7%)	14 (33.3%)
>55 dB (moderately severe)	19	8 (42.1%)	11 (57.9%)
Total	143	112	31

[a] Hearing Handicap Inventory for the Elderly has total 25 questions (score ranged from 0 to 100). Higher number indicates worse hearing impairment.

[b] Number of total participants.

CHAPTER 4

HEARING IMPAIRMENT AND CARDIOVASCULAR DISEASE RISK FACTORS IN OLDER ADULTS[1]

[1] Park S, Johnson MA, Shea-Miller K, and De Chicchis AR. Submitted to Acta Oto-Laryngologica.

ABSTRACT

Conclusion-- Pure-tone average threshold (PTA) in the poorest ear was significantly correlated with high-density lipoprotein (HDL) cholesterol, whereas PTA in both ears was significantly correlated with the total cholesterol/HDL cholesterol ratio. Thus, HDL cholesterol may be a modifiable risk factor for hearing loss.

Objectives-- Hearing impairment is the third most common chronic health condition in older adults and is associated with impaired quality of life. The purpose of this cross-sectional study was to evaluate the relationship of hearing impairment with cardiovascular disease risk factors in older adults.

Method-- PTA was calculated at frequencies 1, 2, and 4 kHz in older adults (N = 146; mean age (± SD): 76 ± 8 years; 82% female; 71% Caucasian; 29% African-American). PTA is the mean of three or four contiguous frequencies and is used to predict the degree of communication impact imposed by hearing loss.

Results-- Based on logistic regression models controlled for age, gender, race, family history of hearing loss, and noise exposure, participants with impaired hearing [> 25 dB hearing level (HL)] had significantly lower HDL cholesterol concentrations than those with normal hearing (≤ 25 dB HL; 1.40 vs. 1.59 mmol/L, respectively, $P = 0.04$) in the worst ear. Participants with impaired hearing (> 40 dB HL) had lower HDL cholesterol than those with PTA ≤ 40 dB HL in the best (1.26 vs. 1.52 mmol/L, respectively, $P = 0.008$) and the worst ear (1.33 vs. 1.53 mmol/L, respectively, $P = 0.02$). LDL cholesterol, total cholesterol, and triglycerides were not significantly associated with hearing loss.

Keywords: hearing impairment, CVD risk factors, older adults, blood lipids

INTRODUCTION

Approximately 31 million Americans have hearing impairment (Kochkin, 2005). The human ear has a conductive component (the outer and middle ear) and a sensorineural component (the inner ear and auditory nerve). In air conduction testing sound travels through the outer ear, middle ear, inner ear, and neural pathways (Martin and Clark, 2002). In bone conduction testing sound energy bypasses the outer ear and middle ear, with minor exceptions and reaches the inner ear directly. Pure-tone average threshold (PTA) is determined by averaging the hearing thresholds at either three or four adjacent octave frequencies and is used to predict the degree of communication impact imposed by hearing loss. For example, a PTA between 26 and 40 dB hearing level (HL) is considered mild hearing impairment (Martin and Clark, 2002) and would suggest difficulty hearing faint speech. Higher hearing thresholds indicate poorer hearing sensitivity and greater difficulty hearing and understanding speech. Hearing impairment may result from numerous factors including genetics, noise, acoustic trauma, viral or bacterial infections, sensitivity to certain drugs or medications, and aging (Johnson et al., 2004). In older adults (65 years and older), hearing impairment is the third most common chronic health condition, exceeded only by arthritis and hypertension (Lethbridge-Cejku and Vickerie, 2005). In the 2003 National Health Interview Survey, 6.9 % of people aged 18 to 44 years, 17.6% of people aged 45 to 64 years, 29.7% of people aged 65 to 74 years, and 46.4% of people aged 75 or older reported difficulty in hearing (Lethbridge-Cejku and Vickerie, 2005). The prevalence of hearing impairment increases with advanced age (Gates and Mills, 2005; Jee et al., 2005). Men typically have poorer hearing status than women (Torre et al., 2005; Moscicki et al., 1985). Hearing impairment adversely affects the lives of older adults. Even mild hearing loss is associated with impaired quality of life, functional disabilities, and adverse effects on physical, cognitive, emotional, behavioral, and social function (Jerger et al., 1995; Dalton et al., 2003; Bazargan et al., 2001; Gates and Mills, 2005).

Several lines of evidence suggest that cardiovascular disease (CVD) risk factors may be related to hearing loss. Hearing loss was associated with high intake of saturated fats in humans (Rosen et al., 1970) and with high dietary cholesterol in chinchillas (Sikora et al., 1986). Abnormal blood lipids may enhance the adverse effects of noise on hearing loss (Axelsson and Lindgren, 1985). Auditory dysfunction was associated with hyperlipidemia or hypercholesterolemia in some (Rosen and Olin, 1965; Torre et al., 2005), but not all studies (Jones and Davis, 1999, 2000; Durga et al., 2006). Other CVD risk factors, self-reported or quantitatively measured, such as stroke, hypertension, heart disease, coronary heart disease, myocardial infarction, smoking, and diabetes mellitus, also have been associated with hearing loss in some (Gates et al., 1993; Torre et al., 2005; Cruickshanks et al., 1998a; Frisina et al., 2006; Uchida et al., 2005), but not all studies (Drettner et al., 1975; Kent et al., 1986; Jones and Davis, 1999, 2000; Nondahl et al., 2004; Pyykkö et al., 1988).

Therefore, the purpose of the present study was to evaluate a possible relationship between hearing impairment and CVD risk factors in older adults. It was hypothesized that hearing status would be negatively associated with CVD risk factors.

MATERIALS AND METHODS

Subjects

The questionnaires and all procedures were approved by the Institutional Review Boards on Human Subjects of the Georgia Department of Human Resources, the University of Georgia, and the Athens Community Council on Aging. Participants were recruited from Older Americans Act Nutrition Program at six senior centers in northeast Georgia, USA. Written informed consent was obtained from each participant. Prior to the auditory assessment, two nurse practitioners conducted otoscopic exams of the outer ear and ear canal to detect excessive cerumen, foreign bodies, or other obvious disorders of the ear canal or tympanic membrane that would prevent a safe and reliable evaluation and to identify obvious disorders that might require a medical referral. Following this exam, 18 individuals were excluded and/or declined further participation in the study. Of the originally enrolled 150 participants, one participant dropped out due to a medical condition, two did not complete the hearing assessment, and one had incomplete blood lipid analysis. Participants with abnormal middle ear function were included. Thus, 146 participants (aged 58 to 97 years; 27 men; 119 women; 70.6% Caucasian; 29.4% African-American), who were physically and mentally able to participate in the study, had hearing data from the best ear available for statistical analysis. Hearing levels could not be measured in the left ear of four participants at certain frequencies due to the severity of the hearing impairment, so the right ear was used as the best ear, and the worst ear data were missing in those four participants. As a result, worst ear data was available from 142 participants for statistical analysis.

Methods

Assessments were performed in the six senior centers (January through April of 2001). Non-fasting blood specimens were collected due to the advanced age and possible frailty of the participants by a licensed phlebotomist. Blood samples for serum concentrations of HDL cholesterol, LDL cholesterol, total cholesterol, and triglycerides were collected by standard methods and were analyzed in a local clinical laboratory (SmithKline-Beecham Clinical Laboratories, Atlanta, GA) within one month prior to auditory assessment. Questionnaires were administered by interviewers trained to collect information on demographics, general health, and auditory function. These interviewers read questions to the participants and recorded their responses. A revised version of the University of Georgia Speech and Hearing Clinic history form was completed to assess family history of hearing loss and noise exposure. A self-reported history of health problems and current medications was obtained including variables related to diabetes mellitus, stroke, heart disease, congestive heart failure, hypertension, and use of tobacco products. Systolic blood pressure and diastolic blood pressure were measured (Critikon DINAMAP™ Vital Signs Monitor 1846 SX, Tampa, FL).

One licensed audiologist with no knowledge about the health or hearing status of the participants conducted the auditory assessments using portable equipment (Grason-Stadler GSI 38, Madison, WI). The assessment was conducted in a quiet area of each senior center because these older adults were not able to travel to the University of Georgia Speech and Hearing Clinic. Air-conduction thresholds were obtained at octave intervals from 0.25 to 8 kHz using a diagnostic audiometer meeting specifications in accordance with the American National Standards Institute S3.6 (1996) and following standard audiometric clinical procedures (Yantis, 1994; American Speech-Language-Hearing Association, 1978). For middle ear function, four tympanometric measures were performed using a Grason-Stadler model GSI-38 tympanometer, including static acoustic admittance, tympanometric width, ear canal volume, and tympanometric peak pressure (Wiley et al., 1996).

Statistical analysis

For each participant, the ears were classified as the best ear and the worst ear, depending on PTA at 1, 2, and 4 kHz. With the exception of one participant, the ears did not differ by more than 15 dB. The statistical analyses were performed independently for the best ear and the worst ear in order not to neglect participants with at least one affected ear. Hearing function was assessed as a modified PTA (1, 2, and 4 kHz) in the best ear and the worst ear. The participants' hearing level at 0.5 kHz was not included in the PTA, as testing was conducted in a quiet room rather than in a sound-treated audiometric suite. Noise levels were monitored in each facility using a sound level meter, and environmental background noise prohibited reliable measurements at this frequency. Hearing test data were sufficient to permit categorization of participants into normal and impaired hearing based on two cutoffs for poor hearing status (> 25 and > 40 dB HL). Hearing status was dichotomized (normal or impaired hearing). Normal distributions of data were checked by skewness and kurtosis. Data were log transformed to approximate normal distributions where necessary. Spearman's correlation coefficients were used to examine association between PTA as a continuous variable and blood lipids and further association with partial correlation controlling for age, gender, race, family history of hearing loss, and noise exposure. A series of logistic regression analyses were conducted with hearing status as a dependent variable and blood lipids, age, gender, race, family history of hearing loss, and noise exposure as independent variables. Data are presented as mean ± standard deviation (SD) or percent. Data were analyzed with the Statistical Analysis System (Version 9.1, SAS Institute Inc, Cary, NC). A *P* value of ≤ 0.05 was considered statistically significant.

RESULTS

A total of 146 participants were included in these analyses and their demographic information and blood lipids are shown in Table 4.1. Based on a definition of hearing loss as PTA > 25 dB HL in the best ear, 63.7% of this population had a hearing impairment. PTA in the worst ear was significantly correlated with HDL cholesterol level and total cholesterol/HDL cholesterol ratio, while PTA in the best ear was significantly correlated with the total cholesterol/HDL cholesterol ratio (Table 4.2). There were no significant correlations of PTA with other blood lipid parameters. The relationship of blood lipid parameters and other factors with PTA using two cutoff limits for poor hearing (> 25 and > 40 dB HL) in the best and the worst ear are shown in Tables 4.3 and 4.4. Based on a series of logistic regression models controlling for age, gender, race, family history of hearing loss, and noise exposure, participants with impaired hearing (PTA > 25 dB HL) in their worst ear had significantly lower mean HDL cholesterol concentrations than individuals with normal hearing (PTA ≤ 25 dB HL) in their worst ear. Participants with hearing impairment (PTA > 40 dB HL) had significantly lower mean HDL cholesterol concentrations than those with PTA ≤ 40 dB HL in the best ear and the worst ear. However, there were no significant differences in concentrations of LDL cholesterol, total cholesterol, and triglycerides between normal hearing and impaired hearing groups. In analyses conducted after excluding participants who were taking a cholesterol lowering medication, the association of low HDL cholesterol with hearing impairment was similar to the results seen for the total sample (Appendix B Tables from B.16 to B.19). Hearing impairment was not significantly associated with self-reported CVD risk factors (e.g. hypertension, diabetes mellitus, use of tobacco products, stroke, heart disease, and congestive heart failure), systolic blood pressure, diastolic blood pressure, or hypertension (defined as systolic blood pressure ≥ 140 mmHg; American Heart Association, 2006a) (Appendix B Tables from B.1 to B.15). Therefore, participants with the poorest hearing (PTA > 40 dB HL) had lower HDL cholesterol concentrations no matter which ear was used to classify them.

DISCUSSION

Low HDL cholesterol concentration was consistently and significantly related to hearing impairment among older adults of the Older Americans Act Nutrition Program in northeast Georgia. This observation adds to the growing body of evidence that CVD risk factors may be related to hearing impairment in older adults. Also, this association of low HDL cholesterol concentration with hearing impairment occurred in a population with a relatively higher prevalence of hearing impairment than other populations, such as the Epidemiology of Hearing Loss Study (Cruickshanks et al., 1998b). However, hearing impairment was not associated with heart disease, stroke, congestive heart failure, hypertension, diabetes mellitus, or use of tobacco products, perhaps because most of these measures (except blood pressure) were self-reported rather than objectively documented by physician report or medical records. Similarly, the relationship of hearing loss with CVD and non-lipid CVD risk factors in other studies is mixed (Gates et al., 1993; Torre et al., 2005; Jones and Davis., 1999).

These findings of blood lipids and hearing loss are consistent with other studies, such as the Framingham cohort study (676 men and 996 women; Gates et al., 1993). In the Framingham study, blood lipids (serum total cholesterol, triglycerides, and HDL) and two PTAs, PTA at low frequencies (0.25, 0.5, and 1 kHz) and PTA at high frequencies (4, 6, and 8 kHz), in the best ear and the worst ear were measured. There was a significant negative relationship between age-adjusted HDL concentration and PTA at low frequency in women in the worst ear. However, similar to the present study, concentrations of total serum cholesterol and triglycerides were not associated with age-related hearing loss. In a Japanese study (607 men and 317 women; aged 40 to 59 years), mean hearing levels in the better ear were measured from 0.125 to 8 kHz in participants with no history of noise exposure or disease associated with hearing loss (Suzuki et al., 2000). Low serum HDL cholesterol concentration was significantly related to hearing loss at 2 and 4 kHz in men. However, similar to the present study, concentrations of total serum cholesterol and triglycerides were not significantly associated with hearing loss. In contrast, a study found no significant associations between hearing loss at any tested frequency (0.25 to 8 kHz) and blood lipids (fasting LDL cholesterol, HDL cholesterol, total cholesterol, and triglycerides) in 197 men (aged 50 to 60 years) with risk factors for ischemic heart disease (Jones and Davis., 1999).

Hyperlipidemia, noise exposure, and auditory dysfunction were examined in animal and human studies. Chinchillas (aged 0.5 to 2 years) were fed either a normal diet or a 1% cholesterol diet for six months (Sikora et al., 1986). In addition to the diet, chinchillas were either exposed to no noise or noise (with intensity levels of either 105 or 114 dB). Without noise exposure, chinchillas fed the 1% cholesterol diet had significantly worse hearing status than those fed with the control diet at high frequencies (8, 12, and 16 kHz). The effects of noise exposure and hypercholesterolemia on auditory function measured by auditory brainstem response (ABR) in three groups of eight weeks old male rabbits (N = 11; regular diet/noise; 2% cholesterol diet/noise; or regular diet/no noise) were also examined (Tami et al., 1985). Hypercholesterolemia alone had no effect on auditory dysfunction in this animal model. In a human study, a synergistic effect of noise and hypercholesterolemia on hearing loss was shown in 78 men aged 50 years with serum cholesterol level > 7 mmol/L and 75 men aged 50 years with serum cholesterol level < 7 mmol/L (Axelsson and Lindgren, 1985). Men with high serum cholesterol levels and elevated noise exposure had greater risk (relative risk of 2.6; CI, not provided) for noise-induced hearing loss (NIHL) than participants with low serum cholesterol concentrations and elevated noise exposure (relative risk of 1.8; CI, not provided). Similar to the present study, noise exposure was assessed by self-reported questionnaire. In the condition of low noise exposure, high cholesterol levels alone did not increase the risk of hearing loss (Axelsson and Lindgren, 1985). In contrast, no interaction between HDL cholesterol levels and noise exposure was found in the present study, perhaps because of the advanced age of the participants and/or high proportion of women participants who generally have less noise exposure than men (Now Hear This, 2004; NIHCS, 1990).

The effects of a high cholesterol diet on hearing loss were examined in participants aged 40 to 59 years (N = 278) in Finland (Rosen et al., 1970). Participants who consumed a diet with high saturated fatty acids for five years had poorer hearing status than those who consumed a diet with more unsaturated fatty acids and less saturated fatty acids for five years, regardless of age, at all test frequencies (0.5, 1, 2, and 4 kHz). In the same study, when participants switched from a diet with high saturated fatty acids to a diet with low saturated fatty acids for three and half years, their hearing status improved. When participants changed from a diet with low saturated fatty acids to a diet with high saturated fatty acids, their hearing status worsened (Rosen et al., 1970).

CVD and related risk factors have been examined in several large studies and the findings are mixed (N = 1,501 to 1,672; Torre et al., 2005; Gates et al., 1993). In the Epidemiology of Hearing Loss Study, self-reported history of CVD, pure-tone air- and bone-conduction audiometry, and distortion product otoacoustic emissions were obtained from 1,501 participants aged 43 to 84 years in the United States (Torre et al., 2005). Cochlear function was measured based on distortion product otoacoustic emissions, and cochlear impairment was defined as < +9 dB distortion product otoacoustic emissions/noise ratio at 2, 3, and 4 kHz. Self-reported history of myocardial infarction was correlated with cochlear dysfunction in women but not in men after controlling for lifestyle factors (e.g. smoking, diabetes, noise exposure, activity, alcohol, and age). However, other CVD variables (e.g. self-reported stroke, brain hemorrhage, angina, and hypertension defined by blood pressure measurement) were not correlated with cochlear dysfunction. In the Framingham cohort study, hearing impairment at low frequencies in the worse ear was significantly correlated with documented coronary heart disease (CHD) while hearing impairment at low frequencies in the better ear was significantly correlated with stroke (676 men; Gates et al., 1993). In women (n = 996), hearing loss at low frequencies in the better ear was correlated with CVD, CHD, and intermittent claudication, whereas hearing loss at low frequencies in the worse ear was correlated with CVD and stroke. Hypertension was significantly associated with PTA in men (at high frequency in the worse ear) and in women (at low frequency in the better ear). However, no significant association of diabetes mellitus, and smoking status with hearing impairment was found. In a cross-sectional study in the Netherlands, hearing thresholds were not independently associated with hypercholesterolemia (defined as total cholesterol > 6.5 mmol/L, HDL cholesterol < 0.9 mmol/L, or the use of lipid-lowering medication), self-reported diabetes mellitus, hypertension (defined as systolic blood pressure ≥ 160 mmHg, diastolic blood pressure ≥ 95 mmHg or the use of antihypertensive medication), and smoking status in 728 older adults (aged 50 to 70 years) (Durga et al., 2006). However, self-reported family history of premature vascular disease (onset < 60 years in first degree family) was significantly associated with PTA-low frequencies (0.5, 1, and 2 kHz), and self-reported vascular diseases were significantly related with PTA-high frequencies (4, 6, and 8 kHz) in this study. In contrast, Drettner et al. (1975) found no significant relationship between CVD risk factors and hearing loss except smoking habits in 1,000 men aged 50 years. Without noise exposure, hearing levels in the right ear were significantly poorer in heavy smokers than in non-smokers (Drettner et al., 1975).

The mechanisms by which hyperlipidemia, other CVD risk factors, and CVD may cause hearing impairment are not entirely known. Hyperlipidemia may impair auditory function by causing vascular disease, atherosclerosis, reducing blood and oxygen supply, and agglutination of erythrocytes and platelets in the inner ear (Morizono and Paparella, 1978). Low HDL cholesterol concentration may increase the risk of atherosclerosis-related microcirculatory disorders of the cochlear vascular system and may increase susceptibility to noise in the cochlea (Suzuki et al., 2000). CVD may decrease blood supply to the cochlea and cause cochlear degeneration and cochlear dysfunction (Torre et al., 2005).

There are some limitations in the present study. Blood lipids were assessed under non-fasting condition. However, non-fasting HDL cholesterol and total cholesterol are similar according to American Heart Association (2006b) and other (Craig et al., 2000). This study was a cross sectional study, so causal relationships between CVD risk factors and hearing impairment cannot be determined.

In summary, hearing impairment was prevalent in these participants of the Older Americans Act Nutrition Program in northeast Georgia. HDL cholesterol level was significantly associated with hearing impairment, but the lack of association with other CVD risk factors may be related to the small sample size and/or the self-reported nature of this information. The observation that HDL cholesterol level was significantly associated with hearing impairment suggests that low HDL cholesterol level may be a modifiable risk factor for hearing impairment. Additional research is needed to identify the mechanisms and metabolic defects responsible for the auditory dysfunction associated with CVD and CVD-related risk factors.

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TABLE 4.1 Characteristics of participants

	N [a]	n [b]	Mean ± SD or %
Age (years)	146	146	76 ± 8 (58-97) [c]
Gender	146		
Female (%)		119	81.5
Male (%)		27	18.5
Race	146		
Caucasian (%)		103	70.6
African-American (%)		43	29.4
Body weight (kg)	146	146	78.4 ± 18.0 (40.8-137.9)
Body mass index (kg/m^2)	146	146	29.2 ± 6.1 (15.2-48.3)
PTA [d] in the best ear (dB HL) [e]	146	146	34 ± 14 (8-73)
PTA in the worst ear (dB HL)	142	142	38 ± 15 (10-83)
PTA > 25 dB HL in the best ear (%)	146	93	63.7
PTA > 25 dB HL in the worst ear (%)	142	106	74.7
PTA > 40 dB HL in the best ear (%)	146	46	31.5
PTA > 40 dB HL in the worst ear (%)	142	61	43.0
Education (years)	143	143	9 ± 4 (0-18)
Family history of hearing loss (%)	146	36	24.7
Number of years exposed to noise (years)	145	145	16 ± 18 (0-83)
HDL cholesterol (mmol/L)	146	146	1.44 ± 0.42 (0.70-2.86)
LDL cholesterol (mmol/L)	141	141	3.07 ± 0.89 (1.43-6.71)
Total cholesterol (mmol/L)	146	146	5.42 ± 1.10 (3.33-10.01)
Total cholesterol/ HDL cholesterol ratio	146	146	4.0 ± 1.3 (2.0-9.0)
Triglycerides (mmol/L)	146	146	1.99 ± 1.16 (0.58-8.78)

[a] Number of total participants.

[b] Number of participants with the condition.

[c] Range in parentheses.

[d] PTA, pure-tone average threshold of 1, 2, and 4 kHz.

[e] dB HL, hearing level in decibel.

TABLE 4.2 Correlation between blood lipids and pure-tone average threshold (PTA; 1, 2, and 4 kHz) in the best ear and the worst ear

	PTA in the best ear (N = 140)	**PTA in the worst ear (N = 136)**
HDL cholesterol	r = -0.14 [a]	r = -0.18 [a]
	P = 0.10 [a]	*P* = 0.04 [a]
	r = -0.14 [b]	r = -0.18 [b]
	P = 0.10 [b]	*P* = 0.04 [b]
LDL cholesterol	r = 0.05 [a]	r = 0.006 [a]
	P = 0.56 [a]	*P* = 0.95 [a]
	r = 0.04 [b]	r = -0.01 [b]
	P = 0.67 [b]	*P* = 0.87 [b]
Total cholesterol	r = 0.003 [a]	r = -0.04 [a]
	P = 0.97 [a]	*P* = 0.65 [a]
	r = -0.01 [b]	r = -0.06 [b]
	P = 0.91 [b]	*P* = 0.50 [b]
Total cholesterol/HDL cholesterol ratio	r = 0.19 [a]	r = 0.18 [a]
	P = 0.03 [a]	*P* = 0.04 [a]
	r = 0.18 [b]	r = 0.17 [b]
	P = 0.04 [b]	*P* = 0.05 [b]
Triglycerides	r = 0.07 [a]	r = 0.09 [a]
	P = 0.41 [a]	*P* = 0.33 [a]
	r = 0.07 [b]	r = 0.09 [b]
	P = 0.40 [b]	*P* = 0.33 [b]

[a] Partial Spearman correlation coefficient controlled for age, gender, race, family history of hearing loss, and noise exposure.

[b] Partial Spearman correlation coefficient controlled for age, gender, race, family history of hearing loss, noise exposure, and taking cholesterol lowering medication.

TABLE 4.3 Demographics, cardiovascular disease risk factors, and auditory function in the best ear and the worst ear (≤ 25 vs. > 25 dB hearing level)

		Hearing						
		Normal (PTA[a] ≤ 25 dB HL[b])		Impaired (PTA > 25 dB HL)				
	N [c]	n [d]	Mean ± SD or %	n [d]	Mean ± SD or %	P value[e]	P value[f]	P value[g]
Best ear								
n	146	53	36.3	93	63.7			
Hearing level (dB)	146	53	19 ± 4	93	43 ± 11			
Age (years)	146	53	72 ± 6	93	79 ± 7	<0.0001	<0.0001	<0.0001
Gender (% of female)	146	49	92.5	70	75.3	0.003	0.02	0.01
Race (% of Caucasian)	146	34	64.2	69	74.2	0.23	0.33	0.19
Body weight (kg)	146	53	82.9 ± 19.7	93	75.8 ± 16.5	0.31	0.28	0.28
Body mass index (kg/m^2)	146	53	30.3 ± 6.8	93	28.5 ± 5.5	0.99	0.98	1.0
Education (years)	143	53	9 ± 3	90	9 ± 4	0.86	0.65	0.24
Family history of hearing loss (%)	146	10	18.9	26	28.0	0.50	0.61	0.47
Number of years exposed to noise (years)	145	52	11 ± 14	93	18 ± 20	0.10	0.11	0.23
HDL cholesterol (mmol/L)	146	53	1.52 ± 0.48	93	1.39 ± 0.37	0.37	0.18	0.29
LDL cholesterol (mmol/L)	141	52	2.97 ± 1.02	89	3.12 ± 0.81	0.99	0.96	0.92
Total cholesterol (mmol/L)	146	53	5.38 ± 1.19	93	5.44 ± 1.05	0.86	0.99	0.96
Total cholesterol/ HDL cholesterol ratio	146	53	3.8 ± 1.5	93	4.1 ± 1.2	0.65	0.53	0.65
Triglycerides (mmol/L)	146	53	1.99 ± 1.25	93	1.99 ± 1.12	0.97	0.98	0.94
Worst ear								
n	142	36	25.3	106	74.7			
Hearing level (dB)	142	36	21 ± 4	106	44 ± 13			
Age (years)	142	36	71 ± 6	106	78 ± 8	<0.0001	<0.0001	<0.0001
Gender (% of female)	142	34	94.4	84	79.3	0.02	0.04	0.05
Race (% of Caucasian)	142	21	58.3	78	73.6	0.09	0.20	0.07
Body weight (kg)	142	36	83.4 ± 20.1	106	76.8 ± 17.1	0.57	0.51	0.55
Body mass index (kg/m^2)	142	36	30.5 ± 7.0	106	28.9 ± 5.7	0.77	0.80	0.65
Education (years)	139	36	9 ± 3	103	9 ± 4	0.54	0.46	0.32
Family history of hearing loss (%)	142	5	13.9	29	27.4	0.23	0.29	0.17
Number of years exposed to noise (years)	141	35	10 ± 13	106	17 ± 19	0.15	0.18	0.12
HDL cholesterol (mmol/L)	142	36	1.59 ± 0.47	106	1.40 ± 0.39	0.08	0.04	0.04
LDL cholesterol (mmol/L)	137	36	3.12 ± 1.08	101	3.06 ± 0.81	0.17	0.15	0.12
Total cholesterol (mmol/L)	142	36	5.54 ± 1.25	106	5.40 ± 1.04	0.28	0.15	0.16
Total cholesterol/ HDL cholesterol ratio	142	36	3.7 ± 1.3	106	4.1 ± 1.3	0.43	0.41	0.47
Triglycerides (mmol/L)	142	36	1.78 ± 0.74	106	2.08 ± 1.28	0.46	0.56	0.49

[a] PTA, pure-tone average threshold of 1, 2, and 4 kHz.

[b] dB HL, hearing level in decibel.

[c] Number of total participants.

[d] Number of participants with the condition.

[e] Logistic regression model controlled for age, gender, and race.

[f] Logistic regression model controlled for age, gender, race, family history of hearing loss, and noise exposure.

[g] Logistic regression model controlled for age, gender, race, family history of hearing loss, noise exposure, and taking cholesterol lowering medication.

TABLE 4.4 Demographics, cardiovascular disease risk factors, and auditory function in the best ear and the worst ear (≤ 40 vs. > 40 dB hearing level)

		Hearing						
		PTA[a] ≤ 40 dB HL[b]		PTA > 40 dB HL				
	N[c]	n[d]	Mean ± SD or %	n[d]	Mean ± SD or %	P value[e]	P value[f]	P value[g]
Best ear								
n	146	100	68.5	46	31.5			
Hearing level (dB)	146	100	26 ± 8	46	51 ± 8			
Age (years)	146	100	75 ± 7	46	80 ± 7	<0.0001	<0.0001	<0.0001
Gender (% of female)	146	90	90.0	29	63.0	0.0001	0.003	0.002
Race (% of Caucasian)	146	64	64.0	39	84.8	0.008	0.03	0.03
Body weight (kg)	146	100	79.5 ± 18.4	46	75.9 ± 17.2	0.49	0.44	0.28
Body mass index (kg/m^2)	146	100	29.9 ± 6.4	46	27.7 ± 5.0	0.65	0.58	0.49
Education (years)	143	98	9 ± 4	45	9 ± 3	0.15	0.25	0.72
Family history of hearing loss (%)	146	18	18.0	18	39.1	0.07	0.07	0.07
Number of years exposed to noise (years)	145	99	12 ± 16	46	23 ± 21	0.08	0.08	0.09
HDL cholesterol (mmol/L)	146	100	1.52 ± 0.44	46	1.26 ± 0.29	0.02	0.008	0.01
LDL cholesterol (mmol/L)	141	97	3.08 ± 0.93	44	3.03 ± 0.81	0.38	0.31	0.30
Total cholesterol (mmol/L)	146	100	5.51 ± 1.17	46	5.22 ± 0.91	0.15	0.07	0.07
Total cholesterol/ HDL cholesterol ratio	146	100	3.9 ± 1.4	46	4.3 ± 1.2	0.56	0.50	0.51
Triglycerides (mmol/L)	146	100	1.95 ± 1.20	46	2.09 ± 1.08	0.58	0.61	0.60
Worst ear								
n	142	81	57.0	61	43.0			
Hearing level (dB)	142	81	28 ± 7	61	53 ± 10			
Age (years)	142	81	74 ± 7	61	79 ± 8	<0.0001	<0.0001	<0.0001
Gender (% of female)	142	74	91.4	44	72.1	0.0005	0.003	0.004
Race (% of Caucasian)	142	52	64.2	47	77.1	0.07	0.23	0.19
Body weight (kg)	142	81	80.5 ± 18.7	61	75.7 ± 17.0	0.50	0.47	0.30
Body mass index (kg/m^2)	142	81	30.2 ± 6.6	61	28.1 ± 5.2	0.58	0.53	0.49
Education (years)	139	80	9 ± 4	59	9 ± 3	0.14	0.17	0.19
Family history of hearing loss (%)	142	12	14.8	22	36.1	0.01	0.01	0.009
Number of years exposed to noise (years)	142	80	12 ± 16	61	19 ± 19	0.19	0.23	0.21
HDL cholesterol (mmol/L)	142	81	1.53 ± 0.45	61	1.33 ± 0.34	0.04	0.02	0.02
LDL cholesterol (mmol/L)	137	80	3.05 ± 0.97	57	3.10 ± 0.76	0.56	0.35	0.24
Total cholesterol (mmol/L)	142	81	5.43 ± 1.14	61	5.44 ± 1.05	0.86	0.45	0.38
Total cholesterol/ HDL cholesterol ratio	142	81	3.8 ± 1.3	61	4.3 ± 1.3	0.17	0.20	0.23
Triglycerides (mmol/L)	142	81	1.89 ± 1.15	61	2.17 ± 1.20	0.12	0.13	0.14

[a] PTA, pure-tone average threshold of 1, 2, and 4 kHz.

[b] dB HL, hearing level in decibel.

[c] Number of total participants.

[d] Number of participants with the condition.

[e] Logistic regression model controlled for age, gender, and race.

[f] Logistic regression model controlled for age, gender, race, family history of hearing loss, and noise exposure.

[g] Logistic regression model controlled for age, gender, race, family history of hearing loss, noise exposure, and taking cholesterol lowering medication.

CHAPTER 5

AGE-RELATED HEARING LOSS, METHYLMALONIC ACID, AND VITAMIN B_{12} STATUS IN OLDER ADULTS[1]

[1] Park S, Johnson MA, Shea-Miller K, De Chicchis AR, Allen RH, and Stabler SP. Submitted to The American Journal of Clinical Nutrition.

ABSTRACT

Background: Hearing loss is the third most common chronic condition in older adults and has been associated with poor vitamin B_{12} status.

Objectives: A possible relationship between age-related hearing loss and poor vitamin B_{12} status was evaluated in older adults.

Design: Pure-tone average threshold (PTA; 1, 2, and 4 kHz) > 25 dB hearing level was defined as hearing loss in older adults at six senior centers in northeast Georgia (N = 93; mean age (± SD): 75 ± 7 years; 82.8% female; 64.5% Caucasian). Participants with methylmalonic acid (MMA) > 271 nmol/L at baseline received 1000 µg/d, and those with MMA ≤ 271 nmol/L were randomly assigned to receive 0, 25, or 100 µg/d of vitamin B_{12}. A series of logistic regression analyses were performed with hearing status as a dependent variable and biochemical and demographic characteristics as independent variables.

Results: A consistent relationship of vitamin B_{12} and auditory function was found in the worst ear. Compared to those with normal hearing, those with impaired hearing in the worst ear had a significantly higher prevalence of vitamin B_{12} deficiency (22.8% vs. 0.0%), higher serum MMA concentrations (329 vs. 193 nmol/L), higher prevalence of elevated MMA (> 271 nmol/L, 40.4% vs. 12.1%), and a non-significantly higher prevalence of low vitamin B_{12} concentrations (< 258 pmol/L, 36.8% vs. 15.2%). Hearing thresholds were not improved in any group after three months of vitamin B_{12} supplementation.

Conclusion: Impaired vitamin B_{12} status may be a modifiable risk factor for age-related hearing loss in older adults.

KEYWORDS Vitamin B_{12}, methylmalonic acid, hearing loss, aging, older adults, intervention

INTRODUCTION

Age-related hearing loss, also known as presbycusis, is one of the most common chronic conditions in older adults (Cruickshanks et al., 1998; Gates and Mills, 2005). Presbycusis is a loss of hearing caused by the aging process and is usually a sensorineural hearing disorder (Gates and Mills, 2005; NIDCD, 2006a). In the 2003 National Health Interview Survey, 6.9% of people aged 18 to 44 years, 17.6% of people aged 45 to 64 years, 29.7% of people aged 65 to 74 years, and 46.4% of people aged 75 or older had self-reported difficulty in hearing (Lethbridge-Cejku and Vickerie, 2005). Hearing loss adversely affects the lives of older adults. Even mild hearing loss is associated with impaired quality of life, functional disabilities, and adverse effects on physical, cognitive, emotional, behavioral, and social function (Jerger et al., 1995; Dalton et al., 2003; Bazargan et al., 2001; Gates and Mills, 2005).

Nutrition may play a role in the pathogenesis of auditory dysfunction, and poor micronutrient status may be associated with age-related hearing loss (Johnson et al., 2004). Vitamin B_{12} deficiency is common in older adults (Wolters et al., 2004; Baik and Russell, 1999). The prevalence of vitamin B_{12} deficiency increases with advanced age (5% to 23% in people aged 60 years or older), mainly because atrophic gastritis decreases the production of the acid and digestive enzymes needed to cleave protein-bound vitamin B_{12} from the natural chemical form of vitamin B_{12} in foods (Baik and Russell, 1999; IOM, 1998; Wolters et al., 2004; Johnson et al., 2003). Poor vitamin B_{12} status was associated with auditory dysfunction in some (Houston et al., 1999; Quaranta et al., 2004; Gok et al., 2004; Shemesh et al., 1993), but not all studies (Berner et al., 2000; Fine et al., 1990; Fine and Hallett, 1980). Tinnitus (ringing in the ears) (Shemesh et al., 1993) and auditory hallucinations (Hector and Burton, 1988) have been recorded as symptoms of vitamin B_{12} deficiency. None of these studies, however, has assessed the relationship of hearing with measures of vitamin B_{12} status such as methylmalonic acid (MMA) other than serum vitamin B_{12} and homocysteine (Hcy). MMA and Hcy are sensitive indicators of vitamin B_{12} status (Wolters et al., 2004; Baik and Russell, 1999; Savage et al., 1994).

A sensorineural hearing loss is one in which the hearing impairment results from structural damage or alteration to the inner ear (sensory) or auditory nerve dysfunction (neural). Hearing sensitivity can be readily assessed in community and clinical settings by presenting a series of pure tones to an individual's ears across a range of test frequencies and determining the lowest stimulus level (threshold) that a tone can be detected. Frequently, a person's pure-tone average (PTA), the mean of three or four contiguous frequencies, is used to predict the degree of communication impact imposed by hearing loss. For example, a PTA between 26 and 40 dB hearing level (HL) is considered mild hearing impairment (Martin and Clark, 2002; Newman and Sandridge, 2004) and would suggest difficulty hearing faint speech. Higher hearing threshold indicates poorer hearing sensitivity and greater difficulty hearing and understanding speech.

The purpose of this study was to evaluate a possible relationship between age-related hearing loss and poor vitamin B_{12} status in older adults, using multiple measures of vitamin B_{12} status and following repletion with a vitamin B_{12} supplement. It was hypothesized that age-related hearing loss would be associated with several indices of poor vitamin B_{12} status including low serum vitamin B_{12}, high MMA, and high Hcy, and that vitamin B_{12} repletion would improve hearing loss in vitamin B_{12}-deficient individuals.

SUBJECTS AND METHODS

Subjects

The questionnaires and all procedures were approved by the Institutional Review Boards on Human Subjects of the Georgia Department of Human Resources, the University of Georgia, the University of Colorado, and the Athens Community Council on Aging. Participants were recruited from Older Americans Act Nutrition Program at six senior centers in northeast Georgia, USA. Written informed consent was obtained from each participant. Prior to the auditory assessment, two nurse practitioners conducted otoscopic exams of the outer ear and ear canal to detect excessive cerumen, foreign bodies, or other obvious disorders of the ear canal or tympanic membrane that would prevent a safe and reliable evaluation and to identify obvious disorders that might require a medical referral. Following this exam, 18 individuals were excluded and/or declined further participation in the study. This was a population-based study, so participants taking nutritional supplements, including dietary multi-vitamin and mineral supplements containing vitamin B_{12}, were included in the study. Of the originally enrolled 150 participants, one participant dropped out due to a medical condition and four were excluded because of high serum vitamin B_{12} concentrations (> 95^{th} percentile for their age, gender, and race in the National Health and Nutrition Examination Survey III; Wright et al., 1998), which indicates possible liver dysfunction (Ermens et al., 2003). Two participants did not complete the hearing assessment. Eleven were excluded because they had asymmetrical hearing loss possibly due to etiologies other than age-related hearing loss. Asymmetrical hearing loss was defined as a difference in hearing thresholds between the right and left ear greater than 15 dB HL at any consecutive test frequency from 0.5 to 4 kHz at baseline. Participants with evidence of conductive hearing loss (n = 32) were also excluded. Conductive hearing loss was defined based on tympanometric measurement (> 90^{th} percentile for their age, gender, and ear in the Epidemiology of Hearing Loss Study; Wiley et al., 1996). Seven participants had more than one problem mentioned above. Thus, 93 participants (aged 58 to 92 years; 16 men; 77 women; 64.5% Caucasian; 35.5% African-American), who were physically and mentally able to participate in the study, had hearing data from the best ear available for statistical analysis. Hearing levels could not be measured in the left ear of three participants at certain frequencies due to the severity of the hearing impairment, so the right ear was used as the best ear, and the worst ear data were missing in those three participants. As a result, worst ear data was available from 90 participants for statistical analysis.

Methods

Baseline assessments were performed in the six senior centers (January through April of 2001). After approximately three months of vitamin B_{12} supplementation (described below), post-treatment assessments were completed (May through August of 2001). Non-fasting blood specimens were collected due to the advanced age and possible frailty of the participants. Blood samples for serum folate and vitamin B_{12} were collected by standard methods and were frozen at -70 °C in cryogenic vials with minimal air space (Nalgene Brand Products, Rochester, NY) until analyzed. Serum vitamin B_{12} and folate were analyzed with a radioassay (Quantaphase II Vitamin B_{12}/Folate Radioassay; Bio-Rad, Richmond, CA) (Gunter et al., 1996). Serum MMA, total homocysteine (tHcy), 2-methylcitric acid, and cystathionine were measured by capillary gas chromatography-mass spectrometry (Stabler et al., 1986). Serum pepsinogen I was analyzed by a kit (SORIN/Bio-medica kit P2560; INCSTAR Corporation, Stillwater, MN). Anemia was defined as hemoglobin < 12 g/dL for women and < 13 g/dL for men. Vitamin B_{12} deficiency was defined as serum vitamin B_{12} < 258 pmol/L, serum MMA > 271 nmol/L, and MMA > 2-

methylcitric acid (Stabler et al., 1999; Rajan et al., 2002; Johnson et al., 2003). When 2-methylcitric acid concentration is greater than MMA concentration, it indicates renal dysfunction as opposed to vitamin B_{12} deficiency (Stabler et al., 1999). The previously determined normal ranges were 73 to 271 nmol/L for MMA (Allen et al., 1993), 5.4 to 13.9 µmol/L for tHcy (Stabler et al., 1999), and 60 to 228 nmol/L for 2-methylcitric acid (Stabler et al., 1999). Serum creatinine ≥ 127 µmol/L is indicative of renal failure (Culleton et al., 1999), and MMA and tHcy concentrations have been shown to be elevated in the absence of vitamin B_{12} deficiency in the setting of chronic renal failure (Allen, 1993; Snow, 1999).

One licensed audiologist with no knowledge about the health or hearing status of the participants conducted the auditory assessments using portable equipment (Grason-Stadler GSI 38, Madison, WI). The assessment was conducted in a quiet area of each senior center because these older adults were not able to travel to the University of Georgia Speech and Hearing Clinic. Air-conduction thresholds were obtained at octave intervals from 0.25 to 8 kHz by using a diagnostic audiometer meeting specifications in accordance with the American National Standards Institute S3.6 (1996) and by following standard audiometric clinical procedures (Yantis, 1994; American Speech-Language-Hearing Association, 1978). For middle ear function, four tympanometric measures were performed using a Grason-Stadler model GSI-38 tympanometer, including static acoustic admittance, tympanometric width, ear canal volume, and tympanometric peak pressure (Wiley et al., 1996).

Questionnaires were administered by interviewers trained to collect information on demographics, dietary intake, general health, and auditory function. These interviewers read questions to the participants and recorded their responses. A revised version of the University of Georgia Speech and Hearing Clinic history form was completed to assess family history of hearing loss and noise exposure. A self-reported history of health problems and current medications was obtained. Post-treatment assessments involved the same methods for blood draws, questionnaires, and auditory assessments as baseline.

Supplementation

Prior to assignment to the vitamin B_{12} supplement groups, vitamin B_{12} deficiency for the purposes of this study was defined as serum MMA > 271 nmol/L at baseline. After completing all the assessments at baseline, a randomized, double-blinded, placebo-controlled design was used for the participants with normal MMA concentration (≤ 271 nmol/L). Participants were assigned to receive tablets that contained either 0 µg/d (n = 23), 25 µg/d (n = 20), or 100 µg/d (n = 21) of vitamin B_{12}; these tablets were identical in appearance to each other and to the 1000 µg/d tablet (Sunstar Pharmaceutical, Elgin, IL). Participants with elevated MMA concentration (> 271 nmol/L; n = 29) received 1000 µg/d and were informed of their high MMA concentration and possible vitamin B_{12} deficiency state by the phlebotomist and this information was sent to their physician. However, none of the participants with elevated MMA concentration received medical treatment in the period of study participation. The audiologist and other staff members were blinded to the vitamin B_{12} status of the participants. All participants were instructed to take one tablet daily. Percent compliance was calculated using pill counts. Of the original 93 participants, nine dropped out from the study following baseline assessments at post-treatment for various reasons (deceased, hospitalized, transferred to nursing home, unable to be reached due to extended vacation or change of address, or unwillingness to continue the study). Three did not complete either auditory or blood assessments. One person in the treatment group (1000 µg/d) did not respond metabolically to the vitamin B_{12} supplement (final serum MMA > 271 nmol/L and serum vitamin B_{12} < 258 pmol/L after three months of intervention), and was thus excluded from statistical analyses; possible reasons for non-response include poor compliance, poor gastric function, and/or poor renal clearance of MMA. Therefore, 80 participants were included in statistical analyses in the best ear at post-treatment. Hearing levels could not be measured in the left ear of four participants at certain frequencies due to the severity of hearing impairment at post-treatment. Additionally, one person was found to be a statistical outlier [defined as a greater than 2 standard deviation (SD) difference in hearing level score between baseline and post-treatment] and was excluded from statistical analyses in the worst ear. As a result, 75 participants were included in statistical analyses in the worst ear at post-treatment.

Statistical analysis

For each participant, the ears were classified as the best ear and the worst ear, respectively, depending on PTA at 1, 2, and 4 kHz. The statistical analyses were performed independently for the best ear and the worst ear in order not to neglect participants with at least one affected ear. Hearing function was assessed as a modified PTA (1, 2, and 4 kHz) in the best ear and the worst ear. Hearing levels at 0.5 kHz were not included in the PTA, as testing was conducted in a quiet room rather than in a sound-treated audiometric suite. Noise levels were monitored in each facility using a sound level meter, and environmental background noise prohibited reliable measurements at this frequency. Hearing test data were sufficient to permit categorization of participants into normal and impaired hearing based on a cutoff for poor hearing status of > 25 dB HL (Martin and Clark, 2002; Newman and Sandridge, 2004). Hearing status was dichotomized (normal or impaired hearing). The normality of data was checked by skewness and kurtosis. Data were log transformed to approximate normal distributions where necessary. Data are presented as mean ± SD or as a percent. Spearman's correlation coefficients were used to examine associations between PTA as a continuous variable and serum vitamin B_{12}, MMA, and tHcy (univariate and partial correlations controlling for age, gender, race, creatinine, family history of hearing loss, and noise exposure). A series of logistic regression analyses were conducted with hearing status as a dependent variable and biochemical variables, age, gender, race, family history of hearing loss, and noise exposure as independent variables. Some of the differences in categorical variables were tested by use of the chi-square statistic. For the baseline and post-treatment comparisons within groups, paired *t* tests were used to compare between the baseline and post-treatment variables within the treatment groups. Difference scores were calculated for PTA (1, 2, and 4 kHz) to examine changes in this variable from baseline to post-treatment. Data were analyzed with the Statistical Analysis System (Version 9.1, SAS Institute Inc, Cary, NC). A P value of ≤ 0.05 was considered statistically significant.

RESULTS

A total of 93 participants were included in these analyses and their demographic and biochemical information are shown in Table 5.1. In the entire cohort, no participant had folate deficiency (serum folate < 6.8 nmol/L; Wright et al., 1998). In the worst ear, PTA was significantly correlated with serum MMA concentration (Table 5.2). There were no correlations of PTA with serum vitamin B_{12} and tHcy. The relationships of vitamin B_{12} and other metabolites with PTA (normal hearing ≤ 25 vs. impaired hearing > 25 dB HL) in the best and the worst ear are shown in Tables 5.3 and 5.4. In the best ear (Table 5.3), participants with impaired hearing had significantly higher mean serum MMA concentrations and non-significantly higher prevalence of low pepsinogen I concentrations (≤ 20 ng/mL; Sepulveda, 2004) than individuals with normal hearing. In the worst ear (Table 5.4), participants with impaired hearing had significantly higher mean serum MMA concentrations, higher prevalence of elevated MMA concentrations (> 271 nmol/L), higher prevalence of vitamin B_{12} deficiency (as defined by vitamin B_{12} < 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid), higher prevalence of low serum vitamin B_{12} (< 185 and < 258 pmol/L), and non-significantly lower mean vitamin B_{12} concentrations than individuals with normal hearing. These associations were strengthened or attenuated depending on the other factors included in the models, such as age, gender, race, creatinine, family history of hearing loss, and noise exposure. There was no association of mean tHcy concentrations, the prevalence of taking dietary supplements, and intakes of synthetic vitamin B_{12} or folate with PTA in either ear. Mean serum concentrations of vitamin B_{12} and MMA and the prevalence of vitamin B_{12} deficiency based on three different cutoffs for poor hearing (> 20, > 25, and > 40 dB HL) in the best and the worst ear are shown in Figures 5.1, 5.2, and 5.3, and similar patterns were observed regardless of cutoff levels for poor hearing. More information is shown in Appendix C (Tables from C.1 to C.16). The mean PTA before and after vitamin B_{12} supplement is shown in Figure 5.4. Paired *t* tests showed no significant changes in mean PTA between baseline and post-treatment within groups (placebo, 25, 100, and 1000 µg/d) after three months of supplementation with vitamin B_{12}.

The association between age-related hearing loss and vitamin B_{12} status were examined separately in each ethnicity (Appendix C Tables from C.17 to C.23). In full models (controlling for age, gender, creatinine, family history of hearing loss, and noise exposure) in the worst ear in Caucasians (Table 5.5), those with impaired hearing (PTA > 25 dB HL) had higher mean serum MMA concentration (382 ± 355 vs. 213 ± 74, respectively, $P = 0.008$), higher prevalence of elevated MMA concentration (> 271 nmol/L; 51.3% vs. 16.7%, $P = 0.03$), lower mean serum vitamin B_{12} (282.8 ± 123.0 vs. 354.7 ± 72.9, $P = 0.02$), and higher prevalence of low serum vitamin B_{12} concentration (< 285 pmol/L; 43.6% vs. 16.7%, $P = 0.04$), and there was a trend for mean serum tHcy to be higher (11.3 ± 4.3 vs. 9.6 ± 3.9, $P = 0.06$). Furthermore, in chi-square analyses, Caucasians with impaired hearing had significantly higher prevalence of vitamin B_{12} deficiency (vitamin B_{12} < 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid; 30.8% vs. 0.0%, respectively, $P = 0.01$), and higher prevalence of low serum vitamin B_{12} (< 185 pmol/L; 20.5% vs. 0.0%, $P = 0.05$) than those with normal hearing (PTA ≤ 25 dB HL). These relationships were not seen in African-Americans (Appendix C Tables from C.20 to C.23).

DISCUSSION

The main finding of this study is that impaired hearing in older adults was associated with several indices of poor vitamin B_{12} status including low serum vitamin B_{12} and high MMA concentrations. Most of these associations remained when controlled for other factors that might impair hearing or vitamin B_{12} status such as age, gender, race, family history of hearing loss, noise exposure, and serum creatinine. Associations of impaired hearing with vitamin B_{12} deficiency were not as apparent in the best ear, perhaps because of the overall mild degree of hearing loss in this study and/or the relatively small sample size that limited the power to detect these associations. These findings complement emerging evidence that vitamin B_{12} status, as well as folate status, may be related to hearing loss (Houston et al., 1999; Gok et al., 2004; Shemesh et al., 1993; Cadoni et al., 2004). Other studies have focused on the relationship of hearing loss with blood concentrations of vitamin B_{12} and related metabolites, the influence of vitamin B_{12} deficiency on nerve damage and conduction velocities in the auditory brainstem response, interactions of B-vitamin metabolism with noise exposure, and polymorphisms in genes related to B-vitamin metabolism (Agamanolis et al., 1976; Shemesh et al., 1993; Cadoni et al., 2004). Our research team previously reported that low serum vitamin B_{12} was associated with hearing loss in older Caucasian women (Houston et al., 1999). The present findings extend these findings to another sample of older people that includes men, women, Caucasians and

African-Americans, with an overall higher degree of hearing impairment. We did not confirm our previous finding that poor folate status was related to hearing loss in older women (Houston et al., 1999), perhaps because in the present study folate status was better than in our previous study (e.g., serum folate: 43.2 vs. 25.8 nmol/L, respectively). Thus, poor vitamin B_{12} status may have overshadowed any contributions of folate status to hearing impairment in the present study.

In analyses conducted separately for Caucasians (n = 57 to 60) and African-Americans (n = 33), the associations of vitamin B_{12} status and related metabolites with hearing loss in Caucasians, but not African-Americans, were similar to the results seen for the total sample. The reasons for the difference between Caucasians and African-Americans are not clear, but may be related to the small sample size of African-Americans or to real differences in the metabolism of vitamin B_{12} and related metabolites between Caucasians and African-Americans (Stabler et al., 1999; Wright et al., 1998).

To our knowledge, this is the first study to report an association of elevated serum MMA with hearing loss. MMA accumulates as a result of vitamin B_{12} deficiency. L-methylmalonyl-CoA mutase catalyzes the conversion of L-methylmalonyl-CoA to succinyl-CoA and requires vitamin B_{12} as a cofactor. Therefore, vitamin B_{12} deficiency is associated with a decrease in the activity of L-methylmalonyl-CoA mutase, which leads to increases in MMA concentration (IOM, 1998; Baik and Russell, 1999; Wolters et al., 2004). Serum MMA concentration may be a particularly sensitive index of hearing problems related to poor vitamin B_{12} status as it was the only marker of poor vitamin B_{12} status that was associated with poor hearing in both the best and worst ear.

The influence of vitamin B_{12} status on auditory function has been examined in several studies and the findings are mixed (Houston et al., 1999; Shemesh et al., 1993; Gok et al., 2004;

Berner et al., 2000). Berner et al. (2000) found no relationship of vitamin B_{12} or folate with age-related hearing loss in 35 men and 56 women (aged 67 to 88 years). PTA (from 0.5 to 4 kHz in the right ear) was not significantly correlated with serum vitamin B_{12}, whole blood folic acid, or plasma Hcy. A limitation of Berner et al.'s study was that there was no normal hearing group, and all participants were hearing impaired (PTA > 25 dB HL).

In a cross-sectional study in the Netherlands, the association between hearing thresholds and fasting plasma Hcy, serum folate, RBC folate, serum vitamin B_{12}, and plasma vitamin B_6 were examined in 728 older adults (aged 50 to 70 years) (Durga et al., 2006). Major exclusion criteria for this study were Hcy < 13 µmol/L, vitamin B_{12} < 200 pmol/L, self-reported kidney or thyroid disease, and taking dietary supplements containing B vitamins. PTA-low frequencies (0.5, 1, and 2 kHz) and PTA-high frequencies (4, 6, and 8 kHz) were not associated with concentrations of Hcy, folate, vitamin B_{12}, and plasma vitamin B_6. Contrary to their hypothesis, high concentrations of serum folate and vitamin B_{12} were significantly associated with higher PTA, which indicates poorer hearing status. The lack of association of vitamin B_{12} and folate status with poor auditory function may be due to their exclusion criteria regarding vitamin B_{12} and Hcy.

In Israel, vitamin B_{12} status in army personnel [N = 113; mean age (± SD): 39.4 ± 10.5 years] with a history of military noise exposure was examined [chronic tinnitus/noise-induced hearing loss (NIHL, n = 57), NIHL alone (n = 29), and normal hearing (n = 27)] (Shemesh et al., 1993). The prevalence of vitamin B_{12} deficiency (serum vitamin B_{12} < 184 pmol/L) was significantly higher in those with tinnitus/NIHL compared with the other groups. Twelve tinnitus participants with vitamin B_{12} deficiency received vitamin B_{12} therapy (1 mg/week, parenteral) until their serum vitamin B_{12} concentrations were above 258 pmol/L in a blood sample taken one month after the last injection. Subjective improvement in tinnitus was observed in all 12 patients following vitamin B_{12} replacement therapy. Prior to supplementation, the tinnitus patients with vitamin B_{12} deficiency had poorer hearing status than tinnitus patients with normal vitamin B_{12}. In contrast, there was no association between tinnitus and vitamin B_{12} status in the present study, perhaps because our population was older (older male and female adults) with less noise exposure compared with the previous study (army personnel).

In a Turkish study of NIHL, fasting blood samples (serum concentrations of vitamin B_{12}, folate, and Hcy) and hearing levels were measured in 28 men with NIHL [mean age (± SD): 37 ± 5 years] and 32 men without NIHL [mean age (± SD): 36 ± 4 years] (Gok et al., 2004). Men with NIHL had significantly higher mean serum Hcy concentration, lower mean serum folate concentration, and lower mean serum vitamin B_{12} concentration than the control group. In contrast, Hcy and folate were not associated with auditory function in the present study, perhaps because of the advanced age and better status of folate and Hcy than in the study by Gok et al. (2004) (e.g., serum folate: 43.2 vs. 11.7 nmol/L; serum Hcy: 10.5 vs. 12.8 µmol/L, respectively). In addition, no interaction of noise exposure with MMA or vitamin B_{12} was found in the present study, perhaps because of the advanced age of the participants and/or high number of women participants. Women are less likely to have NIHL (Now Hear This, 2004; National Institute of Health Consens Statement, 1990) and have less hearing impairment overall than men (Lethbridge-Cejku and Vickerie, 2005; NAAS, 1999).

The associations of folate, Hcy, and polymorphisms in the methylenetetrahydrofolate reductase (MTHFR) with hearing loss have been examined in other studies. Low serum folate and high Hcy concentrations were found in 43 patients (23 women and 20 men; aged 17 to 70 years) with sudden sensorineural hearing loss (SSHL) compared with the control group (n = 24;

aged 16 to 62 years) in Italy. SSHL is a sensorineural hearing loss occurring within ≤ 3 days and characterized by hearing thresholds of ≥ 30 dB HL in at least 3 contiguous audiometric frequencies (Cadoni et al., 2004). However, serum vitamin B_{12} concentrations were not reported in this study. In another Italian study, patients with SSHL [n = 67; mean age (± SD): 53.6 ± 11.3 years] had significantly higher serum Hcy and lower serum folate concentrations than the controls (n = 134). SSHL was significantly associated with MTHFR gene mutations (at nucleotides 677 and 1298) in adults (Capaccio et al., 2005a, 2005b). Low dietary intakes of folate and/or vitamin B_{12} elevate Hcy concentrations in the blood (Wolters et al., 2004). MTHFR is a folate-related enzyme catalyzing the reduction of 5, 10-methylene-tetrahydrofolic acid to 5-methyl-tetrahydrofolic acid, followed by methyl transfer from methyltetrahydrofolate to Hcy to form methionine and tetrahydrofolate facilitated by methionine synthase. Reduced activity of MTHFR disrupts folate metabolism and leads to elevation of Hcy concentrations. Vitamin B_{12} is an essential cofactor for methionine synthase, so vitamin B_{12} deficiency decreases activity of methionine synthase, which leads to increases in Hcy concentrations (IOM, 1998; Baik and Russell, 1999; Shane, 2000).

Hearing thresholds in the right ear were measured before and after treatment with either placebo or vitamin B_{12} (seven doses of 1 mg/d and one dose of 5 mg/d; intramuscularly) in adults [N = 20; aged 20 to 30 years; hearing thresholds within 15 dB HL at all test frequencies (0.25-8 kHz) at baseline] (Quaranta et al., 2004). Mean (± SD) vitamin B_{12} concentrations were 278.5 ± 44.9 pmol/L in the control group and 287.8 ± 50.6 pmol/L in the vitamin B_{12} treatment group before the treatment, suggesting that their vitamin B_{12} status was above the level considered deficient (< 258 pmol/L) and was between the 25th and 50th percentile based on National Health and Nutrition Examination Survey III (Wright et al., 1998). Similar to the present study, there was no effect of vitamin B_{12} supplements on hearing thresholds. Temporary threshold shift was measured at 1, 2, 3, and 4 kHz after noise exposure (Quaranta et al., 2004). Vitamin B_{12} treatment had a protective effect on auditory function against noise exposure at 3 and 4 kHz only, suggesting that enhanced vitamin B_{12} status may offer some protection against noise exposure.

Some investigators have directly or indirectly assessed the effects of vitamin B_{12} deficiency on the auditory nerves or brainstem response (an electrophysiologic response that is generated by the acoustic nerve and auditory structures within the brainstem; Martin and Clark, 2002; Boettcher, 2002). Auditory dysfunction and severe vitamin B_{12} deficiency in rhesus monkeys was examined over a five year period (Agamanolis et al., 1976). Although peripheral hearing levels were not monitored, the auditory nerve and other nerves had active lesions associated with vitamin B_{12} deficiency. The relationship between brainstem auditory evoked responses (BAERs) and vitamin B_{12} deficiency was examined (N = 7; aged 35 to 72 years) (Krumholz et al., 1981). The diagnosis of vitamin B_{12} deficiency was based on the degree of clinical neurological involvement (such as sensory loss, motor loss, cortical dysfunction, and optic neuropathy), but serum vitamin B_{12} concentrations were not reported. Two of seven participants with vitamin B_{12} deficiency had delayed BAERs without hearing loss. In contrast, in a human study, nine out of 10 men with vitamin B_{12} deficiency (defined as serum vitamin B_{12} < 162 pmol/L; aged 43 to 78 years) had normal BAERs, indicating a normal brainstem auditory pathway (Fine et al., 1990). In three case reports, men with vitamin B_{12} deficiency (serum vitamin B_{12} concentration < 125 pmol/L) had normal BAERs (Fine and Hallett, 1980). The small sample sizes of these human studies and lack of vitamin B_{12} adequate control groups make it difficult to derive meaningful conclusions about the effect of vitamin B_{12} deficiency on BAERs.

The mechanisms by which poor vitamin B_{12} status may cause hearing loss are not entirely known. As previously noted, some studies suggest vitamin B_{12} deficiency may compromise the auditory nerve or brainstem (Agamanolis et al., 1976; Krumholz et al., 1981). However, age-related hearing loss is mostly due to disorders of the peripheral auditory system and, more specifically, abnormalities within the cochlea (Jerger et al., 1995; Mosciki et al., 1985). Nerve cells have small stores of vitamin B_{12} and may be particularly sensitive to low vitamin B_{12} status (Herbert, 1994). Poor vitamin B_{12} status may increase susceptibility to the harmful effects of noise in the cochlea, damage myelin, and cause auditory neuropathy (Shemesh et al., 1993). Elevated concentrations of MMA and Hcy are relatively specific markers for vitamin B_{12} deficiency, but Hcy may also be elevated in poor folate and/or vitamin B_6 status (Wolters et al., 2004; Sachdev, 2005). MMA is believed to be a neurotoxin (Kölker et al., 2000; Wajner and Coelho, 1997), and Hcy maybe a vasculotoxin (Sachdev, 2005) and a neurotoxin (Bleich et al., 2004). Therefore, poor vitamin B_{12} and/or folate status might impair the vascular and nervous components of the auditory system through direct and indirect effects.

There are some limitations in the present study. Blood samples were assessed under non-fasting condition. However, fasting status had no effect on serum MMA (Rasmussen, 1989), vitamin B_{12}, and serum folate (Wright et al., 1998). Compared with fasting concentrations, non-fasting plasma Hcy concentration increased after a high protein diet (21.2% of energy) but not after a low protein diet (9.3% of energy) (Verhoef et al., 2005). Although vitamin B_{12} supplementation may not improve hearing thresholds, it is also possible that the three months of vitamin B_{12} supplementation might have been too short to observe significant improvements in auditory function in older adults.

In summary, this study suggests that several indices of vitamin B_{12} status, particularly serum MMA, are associated with auditory dysfunction in older people. Because vitamin B_{12} repletion did not improve hearing function in vitamin B_{12} deficient participants, this suggests that prevention of vitamin B_{12} deficiency is important. Additional research is needed to identify the mechanisms and metabolic defects responsible for the association of vitamin B_{12} with auditory dysfunction, as well as the auditory benefits associated with treating vitamin B_{12} deficiency and elevated MMA and tHcy concentrations with vitamin B_{12} supplementation.

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TABLE 5.1 Characteristics of participants at baseline

	N [a]	n [b]	Mean ± SD or %
Age (years)	93	93	75 ± 7 (58-92) [c]
Gender	93		
Female (%)		77	82.8
Male (%)		16	17.2
Race	93		
Caucasian (%)		60	64.5
African-American (%)		33	35.5
Hearing level in the best ear (dB)	93	93	31 ± 14 (8-73)
Hearing level in the worst ear (dB)	90	90	34 ± 14 (10-77)
Education (years)	91	91	9 ± 4 (0-16)
Family history of hearing loss (%)	93	19	20.4
Number of years exposed to noise (years)	92	92	15 ± 17 (0-62)
Number of medications	93	93	6 ± 3 (0-15)
Anemic (%) [d]	92	21	22.8
Serum vitamin B_{12} (pmol/L)	93	93	339.9 ± 135.8 (76.5-746.3)
< 185 pmol/L (%)	93	10	10.8
< 258 pmol/L (%)	93	26	28.0
< 258 pmol/L, methylmalonic acid > 271 nmol/L, and methylmalonic acid > 2-methylcitric acid (%)	93	13	14.0
Serum methylmalonic acid (nmol/L)	93	93	280 ± 251 (104-1972)
> 271 nmol/L (%)	93	29	31.3
Serum total homocysteine (µmol/L)	93	93	10.5 ± 3.8 (5.1-27.0)
Serum folate (nmol/L)	93	93	43.2 ± 26.2 (10.0-163.3)
Serum pepsinogen I (ng/mL)	92	92	100.9 ± 76.3 (8.6-549.9)
≤ 20 ng/mL (%)	92	9	9.8
Serum creatinine (µmol/L)	92	92	94.0 ± 40.1 (61.9-406.6)
≥ 127 µmol/L (%)	92	10	10.9
Serum albumin (g/L)	92	92	4.1 ± 0.3 (3.4-4.9)
Hemoglobin (g/dL)	92	92	13.1 ± 1.3 (9.4-16.8)
Mean cell volume (fl)	92	92	89 ± 5 (68-100)
Multivitamin use (%)	93	30	32.3
Synthetic vitamin B_{12} intake (µg/d)	93	93	11.6 ± 62.5 (0.0-600.6)
≥ 2.4 µg/d (%)	93	33	35.5
Synthetic folate intake (µg/d)	93	93	178.6 ± 215.6 (0.0-1000.0)
≥ 400 µg/d (%)	93	25	26.9

[a] Number of total participants.

[b] Number of participants with the condition.

[c] Range in parentheses.

[d] Anemic defined as hemoglobin ≤ 12 g/dL for females, ≤ 13 g/dL for males.

TABLE 5.2 Correlations of vitamin B_{12}, methylmalonic acid, and total homocysteine with pure-tone average threshold (1, 2, and 4 kHz) in the best ear and the worst ear at baseline [a]

	Pure-tone average threshold in the best ear (N = 91) [b]	**Pure-tone average threshold in the worst ear (N = 88)** [b]
Vitamin B_{12}	r = -0.06	R = -0.13
	P = 0.58	*P* = 0.26
Methylmalonic acid	r = 0.19	R = 0.27
	P = 0.07	*P* = 0.02
Total homocysteine	r = -0.02	R = -0.02
	P = 0.84	*P* = 0.83

[a] Partial Spearman correlation coefficient, controlled for age, gender, race, creatinine, family history of hearing loss, and noise exposure.

[b] Number of total participants.

TABLE 5.3 Demographics, nutrition and auditory function in the best ear at baseline

Best ear		Hearing						
		Normal (PTA [a] ≤ 25 dB HL[b])		**Impaired (PTA >25 dB HL)**				
	N [c]	n [d]	Mean ± SD or %	n [d]	Mean ± SD or %	P value[e]	P value[f]	P value[g]
n	93	43		50				
Hearing level (dB)	93	43	19 ± 4	50	42 ± 11			
Age (years)	93	43	71 ± 6	50	78 ± 7	<0.0001	<0.0001	<0.0001
Gender (% of female)	93	41	95.4	36	72.0	0.004	0.004	0.02
Race (% of Caucasian)	93	24	55.8	36	72.0	0.18	0.19	0.21
Education (years)	91	43	9 ± 3	48	9 ± 4	0.51	0.69	0.68
Family history of hearing loss (%)	93	9	20.9	10	20.0	0.88	0.79	0.70
Number of years exposed to noise (years)	92	42	11 ± 14	50	18 ± 19	0.58	0.55	0.51
Number of medications	93	43	6 ± 3	50	5 ± 3	0.34	0.29	0.25
Anemic (%) [h]	92	10	23.8	11	22.0	0.17	0.31	0.27
Serum vitamin B_{12} (pmol/L)	93	43	372.4 ± 134.0	50	312.0 ± 132.3	0.09	0.17	0.15
< 185 pmol/L (%)	93	1	2.3	9	18.0	0.10	0.14	0.12
< 258 pmol/L (%)	93	9	20.9	17	34.0	0.18	0.30	0.31
< 258 pmol/L, MMA[i] > 271 nmol/L, and MMA > 2-methylcitric acid (%)	93	4	9.3	9	18.0	0.32	0.51	0.54
Serum MMA (nmol/L)	93	43	210 ± 91	50	341 ± 321	0.04	0.05	0.04
> 271 nmol/L (%)	93	9	20.9	20	40.0	0.45	0.56	0.50
Serum total homocysteine (µmol/L)	93	43	9.8 ± 3.3	50	11.0 ± 4.1	0.86	0.66	0.57
Serum folate (nmol/L)	93	43	40.9 ± 23.8	50	45.2 ± 28.2	0.29	0.43	0.43
Serum pepsinogen I (ng/mL)	92	42	103.6 ± 85.0	50	98.7 ± 69.0	0.27	0.27	0.21
≤ 20 ng/mL (%)	92	1	2.4	8	16.0	0.07	0.08	-
Serum creatinine (µmol/L)	92	42	92.0 ± 53.6	50	95.6 ± 24.1	0.73	0.65	0.64
≥ 127 µmol/L (%)	92	3	7.1	7	14.0	0.76	0.76	0.75
Serum albumin (g/L)	92	42	4.1 ± 0.3	50	4.1 ± 0.3	0.69	0.96	0.99
Hemoglobin (g/dL)	92	42	12.9 ± 1.3	50	13.2 ± 1.2	0.20	0.37	0.31
Mean cell volume (fl)	92	42	89 ± 6	50	89 ± 5	0.60	0.43	0.44
Multivitamin use (%)	93	14	32.6	16	32.0	0.33	0.55	0.53
Synthetic B_{12} intake (µg/d)	93	43	17.3 ± 91.2	50	6.6 ± 12.1	0.86	0.92	0.99
≥ 2.4 µg/d (%)	93	15	34.9	18	36.0	0.84	0.77	0.79
Synthetic folate intake (µg/d)	93	43	188.9 ± 227.0	50	169.8 ± 207.2	0.61	0.24	0.27
≥ 400 µg/d (%)	93	12	27.9	13	26.0	0.96	0.56	0.58

[a] PTA, pure-tone average threshold of 1, 2, and 4 kHz.

[b] HL, hearing level.

[c] Number of total participants.

[d] Number of participants with the condition.

[e] Logistic regression model controlled for age and gender.

[f] Logistic regression model controlled for age, gender, race, and creatinine.

[g] Logistic regression model controlled for age, gender, race, creatinine, family history of hearing loss, and noise exposure.

[h] Anemic defined as hemoglobin ≤ 12 g/dL for females, ≤ 13 g/dL for males.

[i] MMA, methylmalonic acid.

- Not applicable. There was possibly a quasi-complete separation of data points.

TABLE 5.4 Demographics, nutrition and auditory function in the worst ear at baseline

Worst ear	N [c]	Normal (PTA[a] ≤ 25 dB HL[b]) n [d]	Normal Mean ± SD or %	Impaired (PTA > 25 dB HL) n [d]	Impaired Mean ± SD or %	P value[e]	P value[f]	P value[g]
n	90	33		57				
Hearing level (dB)	90	33	21 ± 4	57	42 ± 12			
Age (years)	90	33	71 ± 5	57	77 ± 7	0.0003	0.0002	0.0003
Gender (% of female)	90	31	93.9	45	79.0	0.05	0.04	0.14
Race (% of Caucasian)	90	18	54.6	39	68.4	0.25	0.26	0.38
Education (years)	88	33	9 ± 3	55	9 ± 4	0.83	0.96	0.97
Family history of hearing loss (%)	90	6	18.2	12	21.1	0.66	0.59	0.77
Number of years exposed to noise (years)	89	32	10 ± 14	57	17 ± 18	0.26	0.24	0.26
Number of medications	90	33	7 ± 3	57	6 ± 3	0.44	0.43	0.37
Anemic (%) [h]	89	6	18.8	14	24.6	0.85	0.78	0.92
Serum vitamin B_{12} (pmol/L)	90	33	382.6 ± 125.2	57	314.3 ± 138.8	0.08	0.13	0.14
< 185 pmol/L (%)	90	0	0.0	10	17.5	0.01 [i]	-	-
< 258 pmol/L (%)	90	5	15.2	21	36.8	0.04	0.07	0.09
< 258 pmol/L, MMA[j] > 271 nmol/L, and MMA > 2-methylcitric acid (%)	90	0	0.0	13	22.8	0.002 [i]	-	-
Serum MMA (nmol/L)	90	33	193 ± 70	57	329 ± 306	0.01	0.009	0.005
> 271 nmol/L (%)	90	4	12.1	23	40.4	0.05	0.05	0.02
Serum total homocysteine (µmol/L)	90	33	9.8 ± 3.6	57	10.8 ± 3.9	0.81	0.49	0.47
Serum folate (nmol/L)	90	33	42.7 ± 24.8	57	42.9 ± 26.9	0.92	0.67	0.80
Serum pepsinogen I (ng/mL)	89	33	106.4 ± 94.5	56	96.9 ± 63.8	0.53	0.60	0.41
≤ 20 ng/mL (%)	89	1	3.0	7	12.5	0.24	0.29	-
Serum creatinine (µmol/L)	89	32	93.9 ± 60.9	57	93.8 ± 23.4	0.69	0.62	0.57
≥ 127 µmol/L (%)	89	3	9.4	7	12.3	0.79	0.79	0.75
Serum albumin (g/L)	89	32	4.1 ± 0.2	57	4.1 ± 0.3	0.63	0.78	0.91
Hemoglobin (g/dL)	89	32	13.1 ± 1.3	57	13.0 ± 1.3	0.99	0.58	0.74
Mean cell volume (fl)	89	32	90 ± 4	57	89 ± 6	0.47	0.35	0.39
Multivitamin use (%)	90	12	36.4	17	29.8	0.87	0.76	0.81
Synthetic B_{12} intake (µg/d)	90	33	21.9 ± 104.1	57	6.1 ± 11.4	0.62	0.66	0.63
≥ 2.4 µg/d (%)	90	11	33.3	21	36.8	0.59	0.97	0.87
Synthetic folate intake (µg/d)	90	33	196.3 ± 241.0	57	168.8 ± 203.0	0.48	0.15	0.20
≥ 400 µg/d (%)	90	10	30.3	14	24.6	0.65	0.30	0.37

[a] PTA, pure-tone average threshold of 1, 2, and 4 kHz.

[b] HL, hearing level.

[c] Number of total participants.

[d] Number of participants with the condition.

[e] Logistic regression model controlled for age and gender.

[f] Logistic regression model controlled for age, gender, race, and creatinine.

[g] Logistic regression model controlled for age, gender, race, creatinine, family history of hearing loss, and noise exposure.

[h] Anemic defined as hemoglobin ≤ 12 g/dL for females, ≤ 13 g/dL for males.

[i] Chi-square analyses.

[j] MMA, methylmalonic acid.

- Not applicable. There was possibly a quasi-complete separation of data points.

TABLE 5.5 Demographics, nutrition and auditory function in the worst ear at baseline in Caucasians

Worst ear	N [c]	Hearing: Normal (PTA[a] ≤ 25 dB HL[b]) n [d]	Mean ± SD or %	Hearing: Impaired (PTA > 25 dB HL) n [d]	Mean ± SD or %	P value[e]	P value[f]	P value[g]
n	57	18		39				
Hearing level (dB)	57	18	21 ± 3	39	43 ± 13			
Age (years)	57	18	71 ± 5	39	77 ± 8	0.009	0.007	0.007
Gender (% of female)	57	17	94.4	30	76.9	0.12	0.09	0.17
Education (years)	55	18	10 ± 3	37	10 ± 3	0.31	0.32	0.23
Family history of hearing loss (%)	57	4	22.2	10	25.6	0.93	0.85	0.71
Number of years exposed to noise (years)	57	18	11 ± 15	39	17 ± 18	0.35	0.37	0.34
Number of medications	57	18	7 ± 3	39	6 ± 4	0.59	0.63	0.60
Anemic (%) [h]	57	2	11.1	7	18.0	0.68	0.38	0.48
Serum vitamin B_{12} (pmol/L)	57	18	354.7 ± 72.9	39	282.8 ± 123.0	0.02	0.03	0.02
< 185 pmol/L (%)	57	0	0.0	8	20.5	0.05[i]	-	-
< 258 pmol/L (%)	57	3	16.7	17	43.6	0.03	0.04	0.04
< 258 pmol/L, MMA[j] > 271 nmol/L, and MMA > 2-methylcitric acid (%)	57	0	0.0	12	30.8	0.01[i]	-	-
Serum MMA (nmol/L)	57	18	213 ± 74	39	382 ± 355	0.03	0.008	0.008
> 271 nmol/L (%)	57	3	16.7	20	51.3	0.06	0.03	0.03
Serum tHcy (µmol/L)	57	18	9.6 ± 3.9	39	11.3 ± 4.3	0.33	0.07	0.06
Serum folate (nmol/L)	57	18	52.9 ± 26.5	39	46.1 ± 30.0	0.32	0.41	0.41
Serum pepsinogen I (ng/mL)	56	18	133.6 ± 116.3	38	98.9 ± 67.1	0.13	0.19	0.19
≤ 20 ng/mL (%)	56	0	0.0	5	13.2	0.16[i]	-	-
Serum creatinine (µmol/L)	57	18	100.2 ± 79.2	39	95.9 ± 23.5	0.68	0.29	0.20
≥ 127 µmol/L (%)	57	2	11.1	5	12.8	0.37	0.74	0.82
Serum albumin (g/L)	57	18	4.2 ± 0.2	39	4.1 ± 0.3	0.84	0.82	0.85
Hemoglobin (g/dL)	57	18	13.5 ± 1.4	39	13.3 ± 1.3	0.67	0.41	0.55
Mean cell volume (fl)	57	18	91 ± 3	39	90 ± 6	0.29	0.29	0.30
Multivitamin use (%)	57	9	50.0	13	33.3	0.78	0.65	0.69
Synthetic B_{12} intake (µg/d)	57	18	5.9 ± 1.6	39	7.4 ± 13.0	0.44	0.48	0.49
≥ 2.4 µg/d (%)	57	9	50.0	17	43.6	0.88	0.76	0.81
Synthetic folate intake (µg/d)	57	18	302.2 ± 266.6	39	202.1 ± 217.3	0.11	0.07	0.10
≥ 400 µg/d (%)	57	9	50.0	12	30.8	0.20	0.15	0.19

[a] PTA, pure-tone average threshold of 1, 2, and 4 kHz.

[b] HL, hearing level.

[c] Number of total participants.

[d] Number of participants with the condition.

[e] Logistic regression model controlled for age and gender.

[f] Logistic regression model controlled for age, gender, and creatinine.

[g] Logistic regression model controlled for age, gender, creatinine, family history of hearing loss, and noise exposure.

[h] Anemic defined as hemoglobin ≤ 12 g/dL for females, ≤ 13 g/dL for males.

[i] Chi-square analyses.

[j] MMA, methylmalonic acid.

- Not applicable. There was possibly a quasi-complete separation of data points.

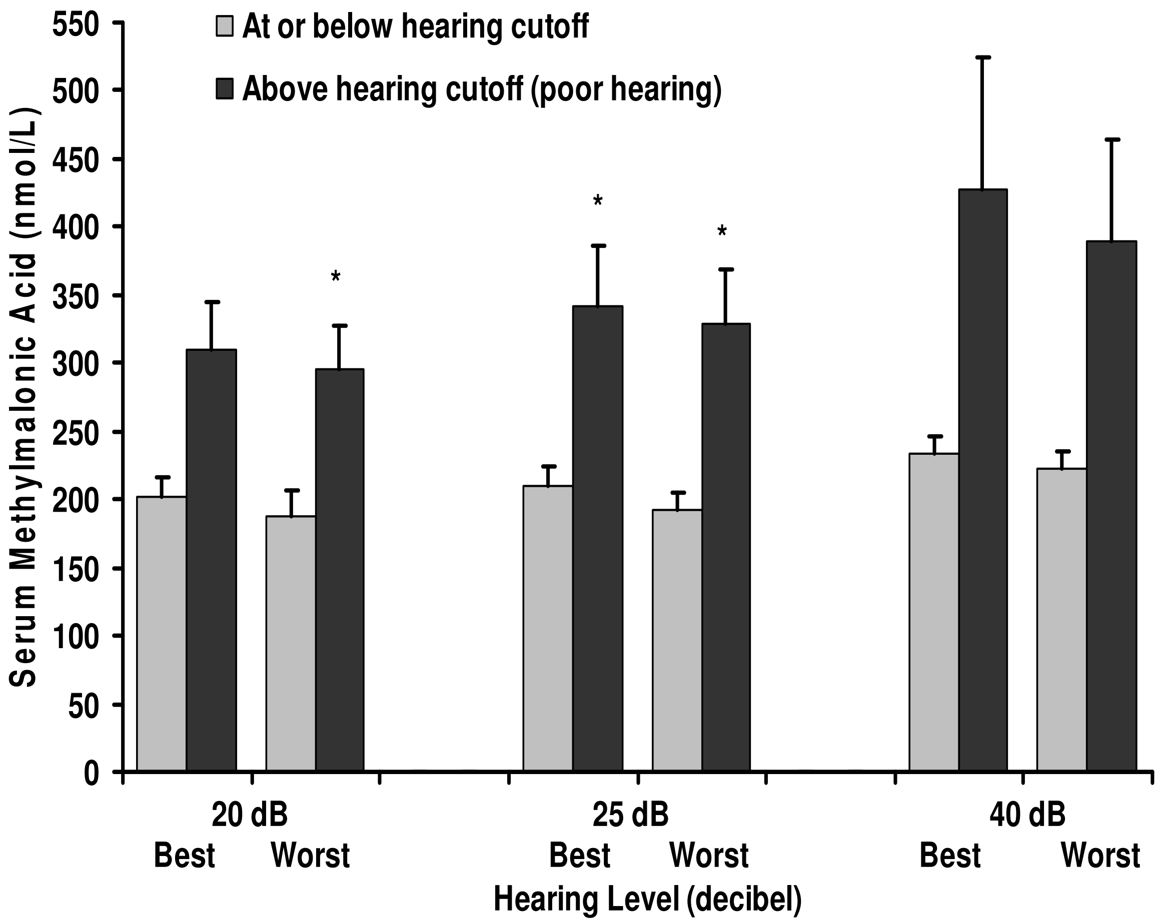

FIGURE 5.1 Serum methylmalonic acid concentration (nmol/L) and poor hearing status in the best ear and the worst ear at baseline analyzed using 3 different cutoffs (> 20, > 25, or > 40 dB hearing level). Values are mean ± SEM. For each pair (e.g., ≤ 20 vs. > 20 dB hearing level in the best ear), logistic regression analyses were conducted to determine the relationship of serum methylmalonic acid with hearing levels; models were controlled for age, gender, race, and serum creatinine. Other models for ≤ 25 vs. > 25 dB hearing level are shown in Tables 5.3 and 5.4. * indicates a significant difference within the pair, $P \leq 0.05$.

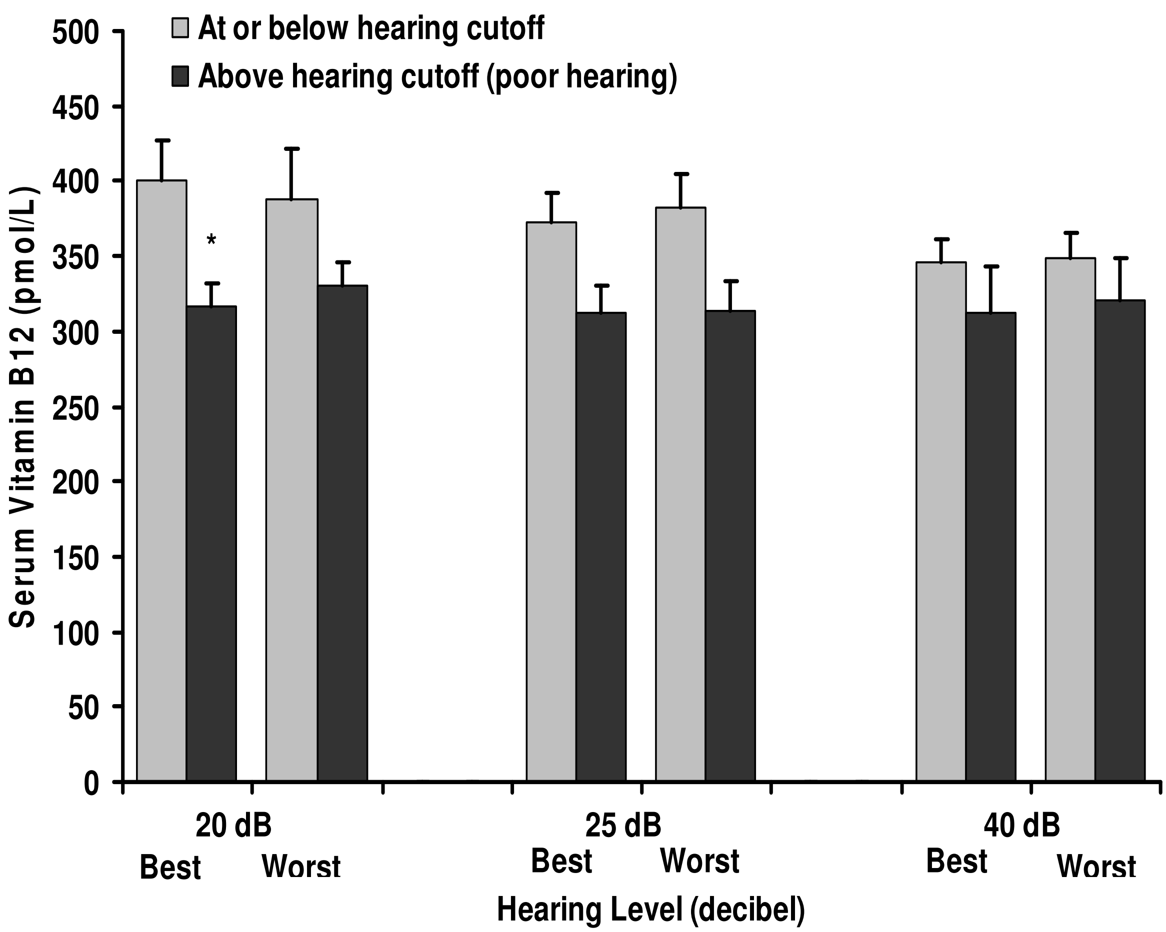

FIGURE 5.2 Serum vitamin B_{12} concentration (pmol/L) and poor hearing status using 3 different cutoffs (> 20, > 25, or > 40 dB hearing level) in the best ear and the worst ear at baseline. Values are mean ± SEM. For each pair (e.g., ≤ 20 vs. > 20 dB hearing level in the best ear), logistic regression analyses were conducted to determine the relationship of serum vitamin B_{12} with hearing levels; models were controlled for age, gender, race, and serum creatinine. Other models for ≤ 25 vs. > 25 dB hearing level are shown in Tables 5.3 and 5.4. * indicates a significant difference within the pair, $P \leq 0.05$.

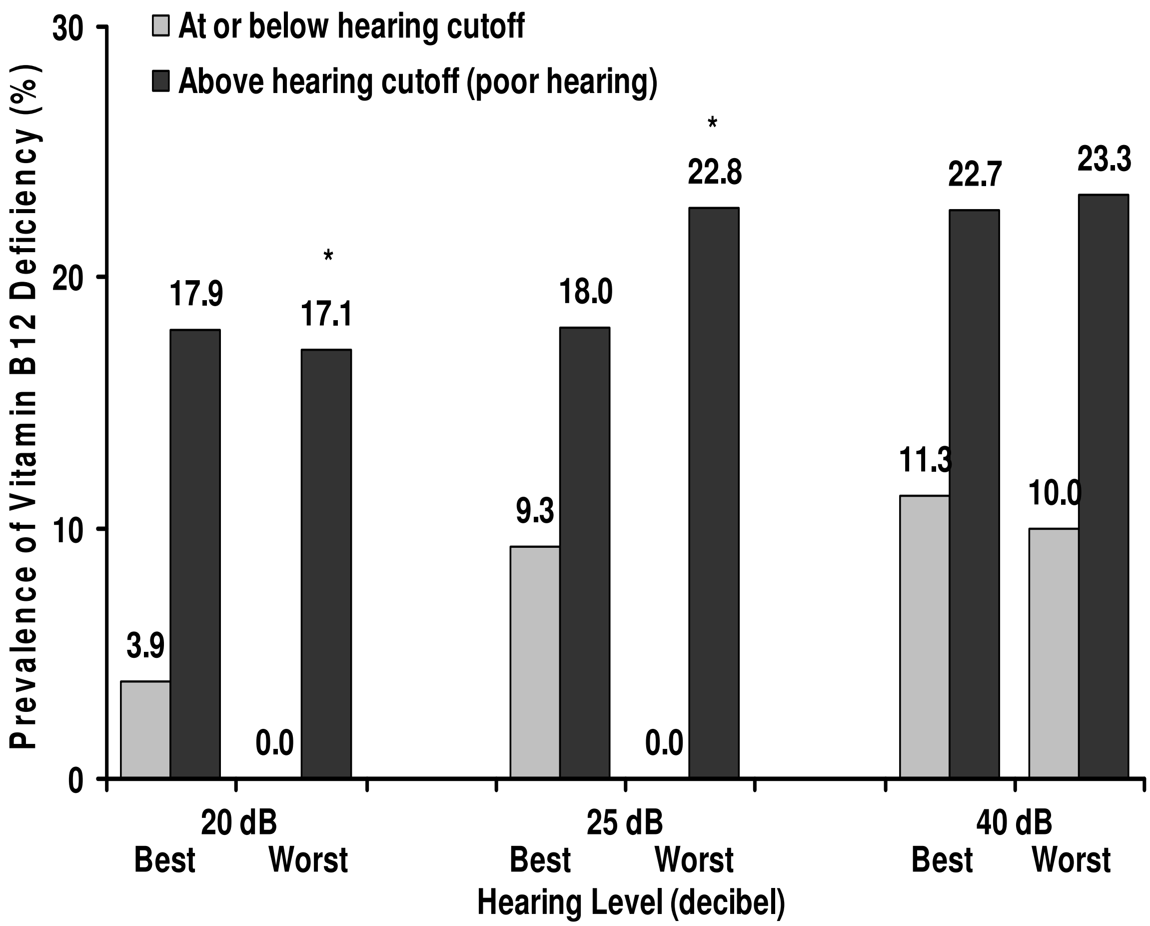

FIGURE 5.3 Prevalence (%) of vitamin B_{12} deficiency (defined as serum vitamin B_{12} < 258 pmol/L, methylmalonic acid > 271 nmol/L, and methylmalonic acid > 2-methylcitric acid) in participants with poor hearing status using 3 different cutoffs (> 20, > 25, and > 40 dB hearing level) at baseline. Values are mean ± SEM. For each pair (e.g., ≤ 20 vs. > 20 dB hearing level in the best ear), logistic regression analyses were conducted to determine the relationship of prevalence of vitamin B_{12} deficiency with hearing levels; models were controlled for age, gender, race, and creatinine. Other models for ≤ 25 vs. > 25 dB hearing level are shown in Tables 5.3 and 5.4. * indicates a significant difference within the pair, $P \leq 0.05$.

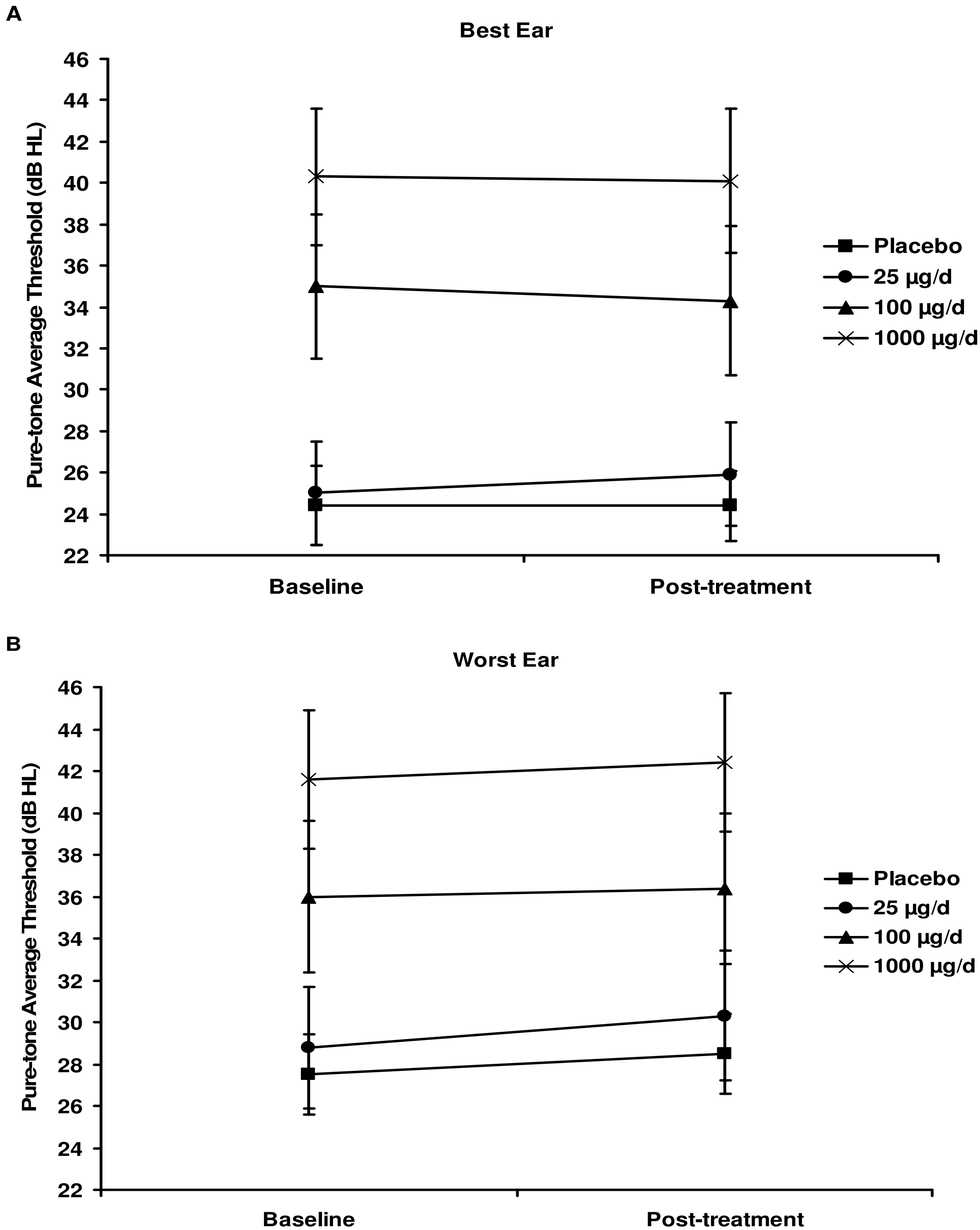

FIGURE 5.4 Pure-tone average threshold (1, 2, and 4 kHz) before vitamin B_{12} supplementation (baseline) and after three months of supplementation (post-treatment) with different levels of vitamin B_{12} (0, 25, 100 and 1000 µg/day) in the best ear (A) and the worst ear (B).

CHAPTER 6

CONCLUSIONS

The purpose of this dissertation was to: 1) examine the prevalence of hearing impairment among a sample of older adults receiving nutrition services from senior centers in northeast Georgia, 2) evaluate a possible relationship of hearing impairment with CVD and CVD risk factors, and 3) further evaluate a possible relationship of age-related hearing loss with poor vitamin B_{12} status, using multiple measures of vitamin B_{12} status and by repletion with a vitamin B_{12} supplement.

Hearing impairment was prevalent among the 147 older adults in this study [pure-tone average threshold (PTA) > 25 dB hearing level; 63% in the best ear and 74% in the worst ear]. Consistent with previous findings, the prevalence of hearing impairment increased with advanced age, and men had poorer hearing status than women. PTA was significantly correlated with self-reported Hearing Handicap Inventory for the Elderly (HHIE) in this population. Participants with impaired hearing scored significantly higher in HHIE than those with normal hearing, which indicates greater evidence of hearing handicap. This result suggests that HHIE may be a reasonable self-assessment tool to identify hearing impairment among older adults.

Low HDL cholesterol concentration was consistently and significantly related to hearing impairment. This observation adds to the growing body of evidence that CVD risk factors may be related to hearing impairment in older adults. Therefore, the observation that HDL cholesterol concentration was significantly associated with hearing impairment suggests that low HDL cholesterol concentration may be a modifiable risk factor for hearing impairment.

However, hearing impairment was not significantly associated with other self-reported CVD risk factors (e.g., hypertension, diabetes mellitus, use of tobacco product, stroke, heart disease, and congestive heart failure), systolic blood pressure, diastolic blood pressure, hypertension, low-density lipoprotein cholesterol, total cholesterol, and triglycerides.

Additional research is needed to identify whether or not CVD and CVD-related risk factors directly cause hearing loss. Multi-center longitudinal studies with all age populations with a control group well matched for all known confounding variables are needed to identify the mechanisms and metabolic defects responsible for the auditory dysfunction associated with CVD and CVD-related risk factors. Histological studies using experimental animals are necessary to decipher the exact mechanisms.

Elevations in MMA concentration (> 271 nmol/L) were prevalent among 93 older adults (31.3%). No participant had folate deficiency (defined as serum folate < 6.8 nmol/L), but 14% of participants had vitamin B_{12} deficiency (defined as serum vitamin B_{12} < 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid). The findings were that impaired hearing in the worst ear was associated with several indices of poor vitamin B_{12} status including low serum vitamin B_{12} and high MMA concentrations. PTA in the worst ear was significantly correlated with serum MMA concentrations, but not with serum concentrations of vitamin B_{12} and tHcy. Most of these associations remained when controlled for other factors that might impair hearing or vitamin B_{12} status such as age, gender, race, family history of hearing loss, noise exposure, and serum creatinine concentrations. The stronger associations of vitamin B_{12} status with hearing in Caucasians compared to African-Americans may suggest a real biological difference in the influence of vitamin B_{12} on hearing loss or may be due to the limited power to detect such an association in the small number of African-Americans in this study (n = 33). These findings complement emerging evidence that vitamin B_{12} status, as well as folate status may be related to hearing loss. To my knowledge, this is the first study to report an association of elevated MMA with hearing loss. Elevated concentrations of MMA and Hcy are relatively specific markers for vitamin B_{12} deficiency, but Hcy may also be elevated in poor folate and/or vitamin B_6 status. The metabolite MMA appeared to be a sensitive indicator of cellular vitamin B_{12} deficiency and a better predictor of hearing impairment than measures of serum vitamin B_{12} or total Hcy. Measurement of serum vitamin B_{12} concentration alone accounted for little of the variance in auditory function among older adults in this study.

This raises the question of whether interventions designed to lower serum MMA and increase vitamin B_{12} concentrations will prevent or reverse auditory dysfunction in older adults. The current study did not support this possibility. Following three months of supplementation with vitamin B_{12}, those persons with high levels of MMA (> 271 nmol/L) at baseline showed no significant change in the PTA between baseline and post-treatment. Thus, prevention of vitamin B_{12} deficiency may be important, because vitamin B_{12} repletion did not improve hearing function in vitamin B_{12}-deficient participants.

Prospective and/or intervention studies in humans, with all age populations with a control group well matched for all known confounding variables are needed to demonstrate a causal role for vitamin B_{12} and to identify the mechanisms and metabolic defects responsible for the association of auditory dysfunction with poor vitamin B_{12} and folate status. Histological studies using experimental animals are required to understand the exact mechanisms. Investigation of gene defects, such as *cblA* (*MMAA*), *cblB* (*MMAB*), *cblC*, *cblD*, *cblE*, *cblF*, *cblG* (*MTR*), and *cblH,* causing vitamin B_{12}-responsive methylmalonic aciduria and/or homocystinuria, and their association with auditory dysfunction are necessary to examine the effects of gene and diet interactions on auditory function. Furthermore, double-blinded randomized clinical trials with long term vitamin B_{12} supplementation are needed to examine the possible effect of vitamin B_{12} supplement on the auditory system.

Together, these studies suggest that hearing impairment is prevalent in these older adults and that future studies are needed to explore the underlying mechanisms, nutrition-related preventive measures, and the therapeutic effects of optimal nutrition among those with hearing impairment. Research strategies involving animal and human models of hearing impairment, nutrient deficiencies and nutrient excesses, and interaction among nutrition, genetic susceptibility via genes that influence hearing impairment and/or nutrient metabolism and the environment (e.g. noise) may be fruitful.

APPENDICES

APPENDIX A

THE PURPOSE OF APPENDIX A IS TO FURTHER EXAMINE A POSSIBLE RELATIONSHIP OF HEARING HANDICAP INVENTORY FOR THE ELDERLY AND PURE-TONE AVERAGE IN OLDER ADULTS RECEIVING NUTRITION AND HEALTH SERVICES FROM THE OLDER AMERICANS ACT NUTRITION PROGRAMS (TABLES A.1 - A.3).

Table A.1 Hearing impairment and Hearing Handicap Inventory for the Elderly based on pure-tone average (PTA; 1, 2, and 4 kHz) [a]

	All Participants		**Normal (PTA ≤ 25 dB hearing level)**		**Impaired (PTA > 25 dB hearing level)**			
	N [b]	**Mean ± SD**	**n [c]**	**Mean ± SD**	**n [c]**	**Mean ± SD**	**P value [d]**	**P value [e]**
Best ear								
Social [f]	147	4.7 ± 8.1	54	1.3 ± 3.3	93	6.6 ± 9.3	0.002	0.002
Emotional [g]	147	5.4 ± 10.4	54	1.5 ± 5.2	93	7.6 ± 12.0	0.002	0.002
Total [h]	147	10.0 ± 17.7	54	2.8 ± 8.1	93	14.2 ± 20.3	0.002	0.002
Worst ear								
Social	143	4.4 ± 7.9	37	1.1 ± 2.9	106	5.6 ± 8.7	0.02	0.02
Emotional	143	5.1 ± 10.0	37	0.8 ± 2.2	106	6.7 ± 11.2	0.01	0.02
Total	143	9.6 ± 17.2	37	1.9 ± 4.8	106	12.3 ± 19	0.009	0.01
	All Participants		**PTA ≤ 40 dB hearing level**		**PTA > 40 dB hearing level**			
	N [b]	**Mean ± SD**	**n [c]**	**Mean ± SD**	**n [c]**	**Mean ± SD**	**P value [d]**	**P value [e]**
Best ear								
Social	147	4.7 ± 8.1	101	2.2 ± 5.9	46	10.1 ± 9.4	0.0003	0.001
Emotional	147	5.4 ± 10.4	101	2.8 ± 8.9	46	11.0 ± 11.4	0.0002	0.0007
Total	147	10.0 ± 17.7	101	5.0 ± 14.4	46	21.1 ± 19.4	0.0002	0.0007
Worst ear								
Social	143	4.4 ± 7.9	82	1.6 ± 4.3	61	8.3 ± 9.8	0.0002	0.0004
Emotional	143	5.1 ± 10.0	82	2.2 ± 7.1	61	9.1 ± 12.0	0.0003	0.0008
Total	143	9.6 ± 17.2	82	3.8 ± 11	61	17.4 ± 20.7	0.0002	0.0004

[a] Hearing Handicap Inventory for the Elderly contains total 25 questions.
[b] Number of total participants.
[c] Number of participants with the condition.
[d] Logistic regression model adjusted for age, gender, and race.
[e] Logistic regression model adjusted for age, gender, race, family history of hearing loss, and noise exposure.
[f] Social/Situational score ranged from 0 to 48. Higher number indicates worst hearing impairment.
[g] Emotional score ranged from 0 to 52. Higher number indicates worse hearing impairment.
[h] Score ranged from 0 to 100. Higher number indicates worse hearing impairment.

Table A.2 Means, standard deviations, and range data for the Hearing Handicap Inventory for the Elderly by hearing level category based on pure-tone average threshold (PTA; 1, 2, and 4 kHz)

Hearing level category	N [b]	PTA in dB hearing level Mean ± SD	Hearing Handicap Inventory for the Elderly [a] Emotional [c] Mean ± SD	Social/Situational [d] Mean ± SD	Total [e] Mean ± SD
Best ear					
Normal (0-25 dB)	54	19.5 ± 3.9 (8-25) [f]	1.5 ± 5.2 (0-28)	1.3 ± 3.3 (0-16)	2.8 ± 8.1 (0-40)
Mild (26-40 dB)	47	34.0 ± 4.1 (27-40)	4.3 ± 11.7 (0-46)	3.2 ± 7.9 (0-34)	7.5 ± 19.1 (0-80)
Moderate (41-55 dB)	34	47.5 ± 4.0 (42-55)	11.2 ± 12.8 (0-48)	8.5 ± 9.0 (0-32)	19.7 ± 21.3 (0-76)
Moderately severe (>55 dB)	12	62.1 ± 4.7 (57-73)	10.3 ± 6.0 (0-24)	14.7 ± 9.5 (4-28)	25.0 ± 12.7 (8-48)
Total	147	34.1 ± 14.2 (8-73)	5.4 ± 10.4 (0-48)	4.7 ± 8.1 (0-38)	10.0 ± 17.7 (0-80)
Worst ear					
Normal (0-25 dB)	37	21.1 ± 3.5 (10-25)	0.8 ± 2.2 (0-10)	1.1 ± 2.9 (0-12)	1.9 ± 4.8 (0-18)
Mild (26-40 dB)	45	32.8 ± 4.3 (27-40)	3.4 ± 9.2 (0-38)	1.9 ± 5.3 (0-30)	5.4 ± 14.0 (0-68)
Moderate (41-55 dB)	42	47.0 ± 4.8 (42-55)	8.4 ± 13.8 (0-48)	7.0 ± 9.8 (0-34)	15.4 ± 23.2 (0-80)
Moderately severe (>55 dB)	19	65.1 ± 7.9 (57-83)	10.6 ± 6.4 (2-24)	11.1 ± 9.3 (0-38)	21.7 ± 13.1 (6-48)
Total	143	38.2 ± 15.1 (10-83)	5.1 ± 10.0 (0-48)	4.4 ± 7.9 (0-38)	9.6 ± 17.2 (0-80)

[a] Hearing Handicap Inventory for the Elderly has total 25 questions.
[b] Number of total participants.
[c] Emotional score ranged from 0 to 52. Higher number indicates worse hearing impairment.
[d] Social/Situational score ranged from 0 to 48. Higher number indicates worse hearing impairment.
[e] Score ranged from 0 to 100. Higher number indicates worse hearing impairment.
[f] Range in parentheses.

Table A.3 Hearing Handicap Inventory for the Elderly scores as a function of handicap category and pure-tone average threshold (1, 2, and 4 kHz)

		Hearing Handicap Inventory for the Elderly [a]		
Pure-tone average	**N [b]**	**0-16 points (No handicap)**	**18-42 points (Mild to moderate handicap)**	**> 42 points (Significant handicap)**
Best ear				
0-25 dB (normal)	54	51 (94.4%)	3 (5.6%)	0 (0.0%)
26-40 dB (mild)	47	41 (87.2%)	2 (4.3%)	4 (8.5%)
41-55 dB (moderate)	34	19 (55.9%)	10 (29.4%)	5 (14.7%)
>55 dB (moderately severe)	12	3 (25.0%)	7 (58.3%)	2 (16.7%)
Total	147	114	22	11
Worst ear				
0-25 dB (normal)	37	36 (97.3%)	1 (2.7%)	0 (0.0%)
26-40 dB (mild)	45	40 (88.9%)	3 (6.7%)	2 (4.4%)
41-55 dB (moderate)	42	28 (66.7%)	8 (19.1%)	6 (14.3%)
>55 dB (moderately severe)	19	8 (42.1%)	9 (47.4%)	2 (10.5%)
Total	143	112	21	10

[a] Hearing Handicap Inventory for the Elderly has total 25 questions (score ranged from 0 to 100). Higher number indicates worse hearing impairment.
[b] Number of total participants.

APPENDIX B

THE PURPOSE OF APPENDIX B IS TO FURTHER EXAMINE A POSSIBLE RELATIONSHIP OF HEARING IMPAIRMENT WITH CARDIOVASCULAR DISEASE RISK FACTORS IN OLDER ADULTS AT DIFFERENT FREQUENCIES (PTA, 0.5, 1, 2, 4, AND 8 kHz) IN THE BEST AND THE WORST EAR. TWO DIFFERENT CUTOFFS FOR POOR HEARING (25 AND 40 dB HL) WERE USED (TABLES B.1 - B.11).

Table B.1 Characteristics of participants

	N [a]	n [b]	Mean ± SD or %
Age (years)	146	146	76 ± 8 (58-97) [c]
Gender	146		
Female (%)		119	81.5
Male (%)		27	18.5
Race	146		
Caucasian (%)		103	70.6
African-American (%)		43	29.4
Hearing level in the best ear (dB)	146	146	34 ± 14 (8-73)
Hearing level in the worst ear (dB)	142	142	38 ± 15 (10-83)
Education (years)	143	143	9 ± 4 (0-18)
Family history of hearing loss (%)	146	36	24.7
Number of years exposed to noise (years)	145	145	16 ± 18 (0-83)
Hypertension (%) [d]	146	82	56.2
Self-reported hypertension and/or taking medication for hypertension (%)	146	89	61.0
Systolic blood pressure (mmHg)	146	146	145 ± 23 (89-236)
Diastolic blood pressure (mmHg)	146	146	70 ± 10 (49-103)
Self-reported diabetes and/or taking medication for diabetes (%)	146	40	27.4
Self-reported stroke (%)	146	17	11.6
Self-reported heart disease (%)	146	24	16.4
Self-reported congestive heart failure (%)	146	13	8.9
Use of tobacco products (%)	146	29	19.9
HDL cholesterol (mg/dL)	146	146	55 ± 16 (27-110)
HDL cholesterol < 40 mg/dL (%)	146	26	18.0
LDL cholesterol (mg/dL)	141	141	118 ± 34 (55-258)
LDL cholesterol ≥ 130 mg/dL (%)	141	48	34.0
Total cholesterol (mg/dL)	146	146	208 ± 42 (128-385)
Total cholesterol ≥ 200 mg/dL (%)	146	78	53.4
Total cholesterol/ HDL cholesterol ratio	146	146	4.0 ± 1.3 (2-9)
Total cholesterol/ HDL cholesterol ratio ≥ 3.5 (%)	146	93	63.7
Triglycerides (mg/dL)	146	146	176 ± 103 (51-777)
Triglycerides ≥ 200 mg/dL (%)	146	45	31.0

[a] Number of total participants.
[b] Number of participants with the condition.
[c] Range in parentheses.
[d] Hypertension was defined as systolic blood pressure ≥ 140 mmHg.

Table B.2 Demographics, cardiovascular disease risk factors, and auditory function based on ***pure-tone average threshold*** (PTA; 1, 2, and 4 kHz) in the best ear and the worst ear ***(≤ 25 vs. > 25 dB HL)***

		Hearing					
		Normal (PTA ≤ 25 dB HL)		**Impaired (PTA >25 dB HL)**			
	N [a]	n [b]	Mean ± SD or %	n [b]	Mean ± SD or %	P value [c]	P value [d]
Best ear							
n	146	53	36.3	93	63.7		
Hearing level (dB)	146	53	19 ± 4	93	43 ± 11		
Age (years)	146	53	72 ± 6	93	79 ± 7	< 0.0001	< 0.0001
Gender (% of female)	146	49	92.5	70	75.3	0.003	0.02
Race (% of Caucasian)	146	34	64.2	69	74.2	0.23	0.33
Education (years)	143	53	9 ± 3	90	9 ± 4	0.86	0.65
Family history of hearing loss (%)	146	10	18.9	26	28.0	0.50	0.61
Number of years exposed to noise (years)	145	52	11 ± 14	93	18 ± 20	0.10	0.11
Hypertension (%) [e]	146	27	50.9	55	59.1	0.39	0.37
Self-reported hypertension and/or taking medication for hypertension (%)	146	33	62.3	56	60.2	0.66	0.72
Systolic blood pressure (mmHg)	146	53	142 ± 19	93	147 ± 25	0.50	0.42
Diastolic blood pressure (mmHg)	146	53	70 ± 9	93	70 ± 11	0.31	0.38
Self-reported diabetes and/or taking medication for diabetes (%)	146	16	30.2	24	25.8	0.94	0.93
Self-reported stroke (%)	146	6	11.3	11	11.8	0.41	0.38
Self-reported heart disease (%)	146	12	22.6	12	12.9	0.12	0.14
Self-reported congestive heart failure (%)	146	7	13.2	6	6.5	0.06	0.09
Use of tobacco products (%)	146	9	17.0	20	21.5	0.69	0.60
HDL cholesterol (mg/dL)	146	53	58 ± 19	93	53 ± 14	0.37	0.18
HDL cholesterol < 40 mg/dL (%)	146	8	15.1	18	19.4	0.95	0.94
LDL cholesterol (mg/dL)	141	52	114 ± 39	89	120 ± 31	0.99	0.96
LDL cholesterol ≥ 130 mg/dL (%)	141	14	26.9	34	38.2	0.46	0.38
Total cholesterol (mg/dL)	146	53	207 ± 46	93	209 ± 40	0.86	0.99
Total cholesterol ≥ 200 mg/dL (%)	146	29	54.7	49	52.7	0.94	0.94
Total cholesterol/ HDL cholesterol ratio	146	53	3.8 ± 1.5	93	4.1 ± 1.2	0.65	0.53
Total cholesterol/ HDL cholesterol ratio ≥ 3.5 (%)	146	29	54.7	64	68.8	0.28	0.27
Triglycerides (mg/dL)	146	53	176 ± 111	93	176 ± 99	0.97	0.98
Triglycerides ≥ 200 mg/dL (%)	146	18	34.0	27	29.0	0.58	0.53
Worst ear							
n	142	36	25.3	106	74.7		
Hearing level (dB)	142	36	21 ± 4	106	44 ± 13		
Age (years)	142	36	71 ± 6	106	78 ± 8	< 0.0001	< 0.0001

Gender (% of female)	142	34	94.4	84	79.3	0.02	0.04
Race (% of Caucasian)	142	21	58.3	78	73.6	0.09	0.20
Education (years)	139	36	9 ± 3	103	9 ± 4	0.54	0.46
Family history of hearing loss (%)	142	5	13.9	29	27.4	0.23	0.29
Number of years exposed to noise (years)	141	35	10 ± 13	106	17 ± 19	0.15	0.18
Hypertension (%) [e]	142	20	55.6	60	56.6	0.77	0.83
Self-reported hypertension and/or taking medication for hypertension (%)	142	23	63.9	63	59.4	0.89	0.93
Systolic blood pressure (mmHg)	142	36	143 ± 18	106	145 ± 24	0.83	0.96
Diastolic blood pressure (mmHg)	142	36	70 ± 10	106	70 ± 11	0.27	0.37
Self-reported diabetes and/or taking medication for diabetes (%)	142	10	27.8	29	27.4	0.52	0.43
Self-reported stroke (%)	142	4	11.1	13	12.3	0.53	0.57
Self-reported heart disease (%)	142	7	19.4	16	15.1	0.58	0.63
Self-reported congestive heart failure (%)	142	3	8.3	10	9.4	0.98	0.95
Use of tobacco products (%)	142	7	19.4	20	18.9	0.77	0.90
HDL cholesterol (mg/dL)	142	36	61 ± 18	106	54 ± 15	0.08	0.04
HDL cholesterol < 40 mg/dL (%)	142	4	11.1	21	19.8	0.46	0.40
LDL cholesterol (mg/dL)	137	36	120 ± 41	101	118 ± 31	0.17	0.15
LDL cholesterol ≥ 130 mg/dL (%)	137	11	30.6	36	35.6	0.84	0.83
Total cholesterol (mg/dL)	142	36	213 ± 48	106	208 ± 40	0.28	0.15
Total cholesterol ≥ 200 mg/dL (%)	142	21	58.3	56	52.8	0.56	0.49
Total cholesterol/ HDL cholesterol ratio	142	36	3.7 ± 1.3	106	4.1 ± 1.3	0.43	0.41
Total cholesterol/ HDL cholesterol ratio ≥ 3.5 (%)	142	19	52.8	71	67.0	0.33	0.37
Triglycerides (mg/dL)	142	36	158 ± 66	106	184 ± 113	0.46	0.56
Triglycerides ≥ 200 mg/dL (%)	142	10	27.8	35	33.0	0.63	0.75

[a] Number of total participants.
[b] Number of participants with the condition.
[c] Logistic regression model adjusted for age, gender, and race.
[d] Logistic regression model adjusted for age, gender, race, family history of hearing loss, and noise exposure.
[e] Hypertension was defined as systolic blood pressure ≥ 140 mmHg.

Table B.3 Demographics, cardiovascular disease risk factors, and auditory function ***at 1 kHz*** in the best ear and the worst ear ***(≤ 25 vs. > 25 dB HL)***

		Hearing					
		Normal (≤ 25 dB HL)		Impaired (>25 dB HL)			
	N [a]	n [b]	Mean ± SD or %	n [b]	Mean ± SD or %	P value [c]	P value [d]
Best ear							
n	146	82	56.2	64	43.8		
Hearing level (dB)	146	82	19 ± 5	64	40 ± 9		
Age (years)	146	82	73 ± 7	64	80 ± 7	< 0.0001	< 0.0001
Gender (% of female)	146	69	84.2	50	78.1	0.17	0.53
Race (% of Caucasian)	146	57	69.5	46	71.9	0.64	0.90
Education (years)	143	81	10 ± 3	62	9 ± 4	0.25	0.30
Family history of hearing loss (%)	146	17	20.7	19	29.7	0.32	0.35
Number of years exposed to noise (years)	145	81	13 ± 16	64	18 ± 20	0.21	0.23
Hypertension (%) [e]	146	47	57.3	35	54.7	0.35	0.38
Self-reported hypertension and/or taking medication for hypertension (%)	146	51	62.2	38	59.4	0.73	0.78
Systolic blood pressure (mmHg)	146	82	143 ± 20	64	147 ± 26	0.81	0.73
Diastolic blood pressure (mmHg)	146	82	70 ± 10	64	69 ± 11	0.73	0.70
Self-reported diabetes and/or taking medication for diabetes (%)	146	22	26.8	18	28.1	0.49	0.56
Self-reported stroke (%)	146	9	11.0	8	12.5	0.26	0.26
Self-reported heart disease (%)	146	14	17.1	10	15.6	0.83	0.83
Self-reported congestive heart failure (%)	146	7	8.5	6	9.4	0.53	0.48
Use of tobacco products (%)	146	18	22.0	11	17.2	0.40	0.50
HDL cholesterol (mg/dL)	146	82	57 ± 18	64	53 ± 14	0.20	0.11
HDL cholesterol < 40 mg/dL (%)	146	13	15.9	13	20.3	0.40	0.33
LDL cholesterol (mg/dL)	141	79	114 ± 36	62	123 ± 32	0.54	0.56
LDL cholesterol ≥ 130 mg/dL (%)	141	22	27.9	26	41.9	0.21	0.22
Total cholesterol (mg/dL)	146	82	207 ± 45	64	210 ± 39	0.81	0.96
Total cholesterol ≥ 200 mg/dL (%)	146	41	50.0	37	57.8	0.33	0.35
Total cholesterol/ HDL cholesterol ratio	146	82	3.9 ± 1.4	64	4.1 ± 1.3	0.31	0.24
Total cholesterol/ HDL cholesterol ratio ≥ 3.5 (%)	146	48	58.5	45	70.3	0.22	0.23
Triglycerides (mg/dL)	146	82	176 ± 105	64	177 ± 100	0.58	0.59
Triglycerides ≥ 200 mg/dL (%)	146	26	31.7	19	29.7	0.67	0.67
Worst ear							
n	145	62	42.8	83	57.2		
Hearing level (dB)	145	62	21 ± 4	83	43 ± 12		
Age (years)	145	62	73 ± 6	83	79 ± 7	< 0.0001	< 0.0001

Gender (% of female)	145	52	83.9	67	80.7	0.35	0.73
Race (% of Caucasian)	145	43	69.4	59	71.1	0.76	0.87
Education (years)	142	62	10 ± 3	80	9 ± 4	0.35	0.37
Family history of hearing loss (%)	145	11	17.7	25	30.1	0.12	0.14
Number of years exposed to noise (years)	144	61	13 ± 15	83	17 ± 20	0.27	0.33
Hypertension (%) [e]	145	32	51.6	50	60.2	0.67	0.59
Self-reported hypertension and/or taking medication for hypertension (%)	145	40	64.5	49	59.0	0.85	0.83
Systolic blood pressure (mmHg)	145	62	141 ± 20	83	148 ± 24	0.36	0.30
Diastolic blood pressure (mmHg)	145	62	69 ± 9	83	70 ± 11	0.19	0.21
Self-reported diabetes and/or taking medication for diabetes (%)	145	14	22.6	26	31.3	0.10	0.10
Self-reported stroke (%)	145	7	11.3	10	12.1	0.44	0.52
Self-reported heart disease (%)	145	10	16.1	14	16.9	0.57	0.60
Self-reported congestive heart failure (%)	145	6	9.7	7	8.4	0.86	0.85
Use of tobacco products (%)	145	15	24.2	13	15.7	0.21	0.29
HDL cholesterol (mg/dL)	145	62	57 ± 19	83	54 ± 14	0.21	0.14
HDL cholesterol < 40 mg/dL (%)	145	10	16.1	16	19.3	0.44	0.42
LDL cholesterol (mg/dL)	140	60	119 ± 37	80	118 ± 32	0.22	0.17
LDL cholesterol ≥ 130 mg/dL (%)	140	18	30.0	30	37.5	0.81	0.93
Total cholesterol (mg/dL)	145	62	212 ± 48	83	206 ± 37	0.20	0.11
Total cholesterol ≥ 200 mg/dL (%)	145	35	56.5	43	51.8	0.43	0.36
Total cholesterol/ HDL cholesterol ratio	145	62	4.0 ± 1.4	83	4.0 ± 1.3	0.96	0.99
Total cholesterol/ HDL cholesterol ratio ≥ 3.5 (%)	145	38	61.3	55	66.3	0.79	0.87
Triglycerides (mg/dL)	145	62	171 ± 85	83	181 ± 115	0.47	0.55
Triglycerides ≥ 200 mg/dL (%)	145	18	29.0	27	32.5	0.21	0.25

[a] Number of total participants.
[b] Number of participants with the condition.
[c] Logistic regression model adjusted for age, gender, and race.
[d] Logistic regression model adjusted for age, gender, race, family history of hearing loss, and noise exposure.
[e] Hypertension was defined as systolic blood pressure ≥ 140 mmHg.

Table B.4 Demographics, cardiovascular disease risk factors, and auditory function ***at 2 kHz*** in the best ear and the worst ear ***(≤ 25 vs. > 25 dB HL)***

		Hearing					
		Normal (≤ 25 dB HL)		Impaired (>25 dB HL)			
	N [a]	n [b]	Mean ± SD or %	n [b]	Mean ± SD or %	P value [c]	P value [d]
Best ear							
n	146	56	38.4	90	61.6		
Hearing level (dB)	146	56	19 ± 5	90	45 ± 13		
Age (years)	146	56	72 ± 6	90	79 ± 7	< 0.0001	< 0.0001
Gender (% of female)	146	48	85.7	71	78.9	0.17	0.34
Race (% of Caucasian)	146	37	66.1	66	73.3	0.33	0.49
Education (years)	143	56	9 ± 4	87	9 ± 3	0.92	0.92
Family history of hearing loss (%)	146	11	19.6	25	27.8	0.48	0.52
Number of years exposed to noise (years)	145	55	13 ± 18	90	17 ± 18	0.50	0.53
Hypertension (%) [e]	146	28	50.0	54	60.0	0.42	0.38
Self-reported hypertension and/or taking medication for hypertension (%)	146	34	60.7	55	61.1	0.49	0.50
Systolic blood pressure (mmHg)	146	56	141 ± 20	90	148 ± 24	0.22	0.18
Diastolic blood pressure (mmHg)	146	56	69 ± 10	90	70 ± 11	0.19	0.23
Self-reported diabetes and/or taking medication for diabetes (%)	146	17	30.4	23	25.6	0.83	0.78
Self-reported stroke (%)	146	6	10.7	11	12.2	0.37	0.41
Self-reported heart disease (%)	146	11	19.6	13	14.4	0.54	0.53
Self-reported congestive heart failure (%)	146	6	10.7	7	7.8	0.68	0.70
Use of tobacco products (%)	146	13	23.2	16	17.8	0.39	0.43
HDL cholesterol (mg/dL)	146	56	59 ± 19	90	53 ± 14	0.04	0.03
HDL cholesterol < 40 mg/dL (%)	146	8	14.3	18	20.0	0.36	0.35
LDL cholesterol (mg/dL)	141	55	118 ± 37	86	118 ± 33	0.40	0.39
LDL cholesterol ≥ 130 mg/dL (%)	141	17	30.9	31	36.1	0.98	0.99
Total cholesterol (mg/dL)	146	56	210 ± 44	90	207 ± 42	0.49	0.39
Total cholesterol ≥ 200 mg/dL (%)	146	32	57.1	46	51.1	0.43	0.38
Total cholesterol/ HDL cholesterol ratio	146	56	3.8 ± 1.4	90	4.1 ± 1.3	0.29	0.28
Total cholesterol/ HDL cholesterol ratio ≥ 3.5 (%)	146	31	55.4	62	68.9	0.19	0.19
Triglycerides (mg/dL)	146	56	171 ± 109	90	180 ± 99	0.37	0.43
Triglycerides ≥ 200 mg/dL (%)	146	17	30.4	28	31.1	0.64	0.69
Worst ear							
n	145	41	28.3	104	71.7		
Hearing level (dB)	145	41	21 ± 4	104	48 ± 14		
Age (years)	145	41	71 ± 6	104	78 ± 7	< 0.0001	< 0.0001

Gender (% of female)	145	37	90.2	82	78.9	0.04	0.06
Race (% of Caucasian)	145	28	68.3	74	71.2	0.86	0.86
Education (years)	142	41	9 ± 3	101	9 ± 4	0.46	0.62
Family history of hearing loss (%)	145	7	17.1	29	27.9	0.29	0.30
Number of years exposed to noise (years)	144	40	14 ± 18	104	16 ± 18	0.99	0.90
Hypertension (%) [e]	145	21	51.2	61	58.7	0.74	0.62
Self-reported hypertension and/or taking medication for hypertension (%)	145	24	58.5	65	62.5	0.36	0.31
Systolic blood pressure (mmHg)	145	41	141 ± 18	104	147 ± 24	0.52	0.41
Diastolic blood pressure (mmHg)	145	41	70 ± 10	104	70 ± 11	0.73	0.84
Self-reported diabetes and/or taking medication for diabetes (%)	145	12	29.3	28	26.9	0.99	0.98
Self-reported stroke (%)	145	4	9.8	13	12.5	0.33	0.42
Self-reported heart disease (%)	145	8	19.5	16	15.4	0.76	0.67
Self-reported congestive heart failure (%)	145	3	7.3	10	9.6	0.58	0.58
Use of tobacco products (%)	145	8	19.5	20	19.2	0.87	0.94
HDL cholesterol (mg/dL)	145	41	61 ± 19	104	53 ± 14	0.02	0.02
HDL cholesterol < 40 mg/dL (%)	145	5	12.2	21	20.2	0.26	0.27
LDL cholesterol (mg/dL)	140	41	117 ± 38	99	119 ± 33	0.44	0.38
LDL cholesterol ≥ 130 mg/dL (%)	140	11	26.8	37	37.4	0.59	0.70
Total cholesterol (mg/dL)	145	41	211 ± 45	104	208 ± 41	0.51	0.37
Total cholesterol ≥ 200 mg/dL (%)	145	23	56.1	55	52.9	0.72	0.58
Total cholesterol/ HDL cholesterol ratio	145	41	3.7 ± 1.3	104	4.1 ± 1.3	0.16	0.19
Total cholesterol/ HDL cholesterol ratio ≥ 3.5 (%)	145	22	53.7	71	68.3	0.20	0.19
Triglycerides (mg/dL)	145	41	163 ± 66	104	183 ± 114	0.33	0.40
Triglycerides ≥ 200 mg/dL (%)	145	12	29.3	33	31.7	0.35	0.41

[a] Number of total participants.
[b] Number of participants with the condition.
[c] Logistic regression model adjusted for age, gender, and race.
[d] Logistic regression model adjusted for age, gender, race, family history of hearing loss, and noise exposure.
[e] Hypertension was defined as systolic blood pressure ≥ 140 mmHg.

Table B.5 Demographics, cardiovascular disease risk factors, and auditory function ***at 4 kHz*** in the best ear and the worst ear ***(≤ 25 vs. > 25 dB HL)***

		Hearing					
		Normal (≤ 25 dB HL)		Impaired (>25 dB HL)			
	N [a]	n [b]	Mean ± SD or %	n [b]	Mean ± SD or %	P value [c]	P value [d]
Best ear							
n	146	53	36.3	93	63.7		
Hearing level (dB)	146	53	18 ± 6	93	49 ± 13		
Age (years)	146	53	72 ± 7	93	79 ± 7	< 0.0001	< 0.0001
Gender (% of female)	146	50	94.3	69	74.2	0.0009	0.004
Race (% of Caucasian)	146	31	58.5	72	77.4	0.01	0.05
Education (years)	143	52	9 ± 3	91	9 ± 4	0.53	0.48
Family history of hearing loss (%)	146	6	11.3	30	32.3	0.02	0.03
Number of years exposed to noise (years)	145	52	11 ± 14	93	18 ± 20	0.10	0.16
Hypertension (%) [e]	146	27	50.9	55	59.1	0.27	0.22
Self-reported hypertension and/or taking medication for hypertension (%)	146	32	60.4	57	61.3	0.28	0.29
Systolic blood pressure (mmHg)	146	53	142 ± 18	93	147 ± 25	0.28	0.21
Diastolic blood pressure (mmHg)	146	53	70 ± 10	93	70 ± 11	0.16	0.20
Self-reported diabetes and/or taking medication for diabetes (%)	146	17	32.1	23	24.7	0.79	0.97
Self-reported stroke (%)	146	3	5.7	14	15.1	0.01	0.009
Self-reported heart disease (%)	146	11	20.8	13	14.0	0.16	0.17
Self-reported congestive heart failure (%)	146	5	9.4	8	8.6	0.46	0.55
Use of tobacco products (%)	146	13	24.5	16	17.2	0.07	0.13
HDL cholesterol (mg/dL)	146	53	61 ± 19	93	52 ± 13	0.03	0.01
HDL cholesterol < 40 mg/dL (%)	146	7	13.2	19	20.4	0.96	0.86
LDL cholesterol (mg/dL)	141	52	107 ± 29	89	124 ± 35	0.02	0.03
LDL cholesterol ≥ 130 mg/dL (%)	141	10	19.2	38	42.7	0.01	0.009
Total cholesterol (mg/dL)	146	53	199 ± 36	93	214 ± 45	0.05	0.11
Total cholesterol ≥ 200 mg/dL (%)	146	27	50.9	51	54.8	0.39	0.43
Total cholesterol/ HDL cholesterol ratio	146	53	3.5 ± 1.1	93	4.3 ± 1.3	0.008	0.008
Total cholesterol/ HDL cholesterol ratio ≥ 3.5 (%)	146	25	47.2	68	73.1	0.01	0.02
Triglycerides (mg/dL)	146	53	162 ± 109	93	184 ± 99	0.14	0.18
Triglycerides ≥ 200 mg/dL (%)	146	14	26.4	31	33.3	0.39	0.54
Worst ear							
n	142	34	23.9	108	76.1		
Hearing level (dB)	142	34	20 ± 5	108	51 ± 14		
Age (years)	142	34	71 ± 6	108	78 ± 7	< 0.0001	< 0.0001

Gender (% of female)	142	33	97.1	85	78.7	0.01	0.02
Race (% of Caucasian)	142	18	52.9	81	75.0	0.02	0.04
Education (years)	139	33	9 ± 3	106	9 ± 4	0.83	0.77
Family history of hearing loss (%)	142	5	14.7	29	26.9	0.40	0.47
Number of years exposed to noise (years)	141	33	10 ± 13	108	16 ± 19	0.38	0.42
Hypertension (%) [e]	142	20	58.8	60	55.6	0.50	0.56
Self-reported hypertension and/or taking medication for hypertension (%)	142	21	61.8	65	60.2	0.57	0.58
Systolic blood pressure (mmHg)	142	34	143 ± 19	108	145 ± 24	0.99	0.85
Diastolic blood pressure (mmHg)	142	34	71 ± 9	108	70 ± 11	0.85	0.70
Self-reported diabetes and/or taking medication for diabetes (%)	142	11	32.4	28	25.9	0.95	0.89
Self-reported stroke (%)	142	2	5.9	15	13.9	0.09	0.09
Self-reported heart disease (%)	142	6	17.7	17	15.7	0.77	0.80
Self-reported congestive heart failure (%)	142	4	11.8	9	8.3	0.20	0.21
Use of tobacco products (%)	142	6	17.7	21	19.4	0.99	0.95
HDL cholesterol (mg/dL)	142	34	60 ± 17	108	54 ± 16	0.31	0.22
HDL cholesterol < 40 mg/dL (%)	142	3	8.8	22	20.4	0.36	0.32
LDL cholesterol (mg/dL)	137	33	107 ± 32	104	122 ± 34	0.10	0.11
LDL cholesterol ≥ 130 mg/dL (%)	137	6	18.2	41	39.4	0.05	0.06
Total cholesterol (mg/dL)	142	34	197 ± 39	108	213 ± 43	0.08	0.12
Total cholesterol ≥ 200 mg/dL (%)	142	16	47.1	61	56.5	0.19	0.23
Total cholesterol/ HDL cholesterol ratio	142	34	3.4 ± 1.0	108	4.2 ± 1.4	0.03	0.03
Total cholesterol/ HDL cholesterol ratio ≥ 3.5 (%)	142	15	44.1	75	69.4	0.03	0.03
Triglycerides (mg/dL)	142	34	157 ± 123	108	184 ± 97	0.13	0.15
Triglycerides ≥ 200 mg/dL (%)	142	7	20.6	38	35.2	0.17	0.19

[a] Number of total participants.
[b] Number of participants with the condition.
[c] Logistic regression model adjusted for age, gender, and race.
[d] Logistic regression model adjusted for age, gender, race, family history of hearing loss, and noise exposure.
[e] Hypertension was defined as systolic blood pressure ≥ 140 mmHg.

Table B.6 Demographics, cardiovascular disease risk factors, and auditory function ***at 8 kHz*** in the best ear and the worst ear ***(≤ 25 vs. > 25 dB HL)***

		Hearing					
		Normal (≤ 25 dB HL)		**Impaired (>25 dB HL)**			
	N [a]	n [b]	Mean ± SD or %	n	Mean ± SD or %	P value [c]	P value [d]
Best ear							
n	100	24	24.0	76	76.0		
Hearing level (dB)	100	24	14 ± 8	76	47 ± 10		
Age (years)	100	24	72 ± 8	76	76 ± 7	0.02 [f]	-
Gender (% of female)	100	24	100.0	64	84.2	0.06 [g]	-
Race (% of Caucasian)	100	8	33.3	53	69.7	0.002 [g]	-
Education (years)	98	24	9 ± 3	74	9 ± 4	0.80 [f]	-
Family history of hearing loss (%)	100	4	16.7	15	19.7	1.0 [g]	-
Number of years exposed to noise (years)	100	24	10 ± 14	76	14 ± 17	0.33 [f]	-
Hypertension (%) [e]	100	16	66.7	44	57.9	0.48 [g]	-
Self-reported hypertension and/or taking medication for hypertension (%)	100	15	62.5	50	65.8	0.81 [g]	-
Systolic blood pressure (mmHg)	100	24	145 ± 19	76	145 ± 23	0.93 [f]	-
Diastolic blood pressure (mmHg)	100	24	73 ± 10	76	69 ± 11	0.17 [f]	-
Self-reported diabetes and/or taking medication for diabetes (%)	100	7	29.2	24	31.6	1.0 [g]	-
Self-reported stroke (%)	100	3	12.5	11	14.5	1.0 [g]	-
Self-reported heart disease (%)	100	1	4.2	14	18.4	0.11 [g]	-
Self-reported congestive heart failure (%)	100	1	4.2	9	11.8	0.44 [g]	-
Use of tobacco products (%)	100	4	16.7	20	26.3	0.42 [g]	-
HDL cholesterol (mg/dL)	100	24	63 ± 18	76	55 ± 17	0.05 [f]	-
HDL cholesterol < 40 mg/dL (%)	100	2	8.3	16	21.1	0.23 [g]	-
LDL cholesterol (mg/dL)	97	23	112 ± 26	74	119 ± 37	0.43 [f]	-
LDL cholesterol ≥ 130 mg/dL (%)	97	4	17.4	29	39.2	0.08 [g]	-
Total cholesterol (mg/dL)	100	24	207 ± 31	76	210 ± 48	0.73 [f]	-
Total cholesterol ≥ 200 mg/dL (%)	100	16	66.7	40	52.6	0.25 [g]	-
Total cholesterol/ HDL cholesterol ratio	100	24	3.4 ± 0.9	76	4.1 ± 1.5	0.02 [f]	-
Total cholesterol/ HDL cholesterol ratio ≥ 3.5 (%)	100	11	45.8	47	61.8	0.24 [g]	-
Triglycerides (mg/dL)	100	24	174 ± 139	76	173 ± 94	0.85 [h]	-
Triglycerides ≥ 200 mg/dL (%)	100	5	20.8	25	32.9	0.32 [g]	-
Worst ear							
n	85	18	21.2	67	78.8		
Hearing level (dB)	85	18	15 ± 7	67	50 ± 10		
Age (years)	85	18	71 ± 5	67	75 ± 8	0.02 [f]	-

Gender (% of female)	85	18	100.0	60	89.6	0.34 [g]	-
Race (% of Caucasian)	85	5	27.8	46	68.7	0.003 [g]	-
Education (years)	84	18	9 ± 3	66	9 ± 4	0.52 [f]	-
Family history of hearing loss (%)	85	2	11.1	13	19.4	0.51 [g]	-
Number of years exposed to noise (years)	85	18	11 ± 13	67	11 ± 16	0.98 [f]	-
Hypertension (%) [e]	85	14	77.8	36	53.7	0.10 [g]	-
Self-reported hypertension and/or taking medication for hypertension (%)	85	12	66.7	42	62.7	1.0 [g]	-
Systolic blood pressure (mmHg)	85	18	148 ± 15	67	143 ± 21	0.39 [f]	-
Diastolic blood pressure (mmHg)	85	18	74 ± 11	67	69 ± 9	0.06 [f]	-
Self-reported diabetes and/or taking medication for diabetes (%)	85	6	33.3	20	29.9	0.78 [g]	-
Self-reported stroke (%)	85	3	16.7	7	10.5	0.44 [g]	-
Self-reported heart disease (%)	85	1	5.6	12	17.9	0.28 [g]	-
Self-reported congestive heart failure (%)	85	1	5.6	7	10.5	1.0 [g]	-
Use of tobacco products (%)	85	3	16.7	17	25.4	0.54 [g]	-
HDL cholesterol (mg/dL)	85	18	66 ± 18	67	55 ± 17	0.02 [f]	-
HDL cholesterol < 40 mg/dL (%)	85	1	5.6	13	19.4	0.28 [g]	-
LDL cholesterol (mg/dL)	82	18	108 ± 27	64	117 ± 38	0.38 [f]	-
LDL cholesterol ≥ 130 mg/dL (%)	82	3	16.7	21	32.8	0.25 [g]	-
Total cholesterol (mg/dL)	85	18	204 ± 34	67	209 ± 49	0.70 [f]	-
Total cholesterol ≥ 200 mg/dL (%)	85	10	55.6	36	53.7	1.0 [g]	-
Total cholesterol/ HDL cholesterol ratio	85	18	3.2 ± 0.8	67	4.0 ± 1.4	0.002 [f]	-
Total cholesterol/ HDL cholesterol ratio ≥ 3.5 (%)	85	6	33.3	42	62.7	0.03 [g]	-
Triglycerides (mg/dL)	85	18	148 ± 57	67	184 ± 116	0.38 [h]	-
Triglycerides ≥ 200 mg/dL (%)	85	3	16.7	24	35.8	0.16 [g]	-

[a] Number of total participants.
[b] Number of participants with the condition.
[c] Logistic regression model adjusted for age, gender, and race.
[d] Logistic regression model adjusted for age, gender, race, family history of hearing loss, and noise exposure.
[e] Hypertension was defined as systolic blood pressure ≥ 140 mmHg.
[f] Independent-sample *t* test.
[g] Chi-square analyses.
[h] Wilcoxon-Mann-Whitney test.
- Not applicable. There was possibly a quasi-complete separation of data points.

Table B.7 Demographics, cardiovascular disease risk factors, and auditory function based on ***pure-tone average threshold*** (PTA; 1, 2, and 4 kHz) in the best ear and the worst ear ***(≤ 40 vs. > 40 dB HL)***

		Hearing					
		PTA ≤ 40 dB HL		**PTA > 40 dB HL**			
	N [a]	n [b]	Mean ± SD or %	n [b]	Mean ± SD or %	P value [c]	P value [d]
Best ear							
n	146	100	68.5	46	31.5		
Hearing level (dB)	146	100	26 ± 8	46	51 ± 8		
Age (years)	146	100	75 ± 7	46	80 ± 7	< 0.0001	< 0.0001
Gender (% of female)	146	90	90.0	29	63.0	0.0001	0.003
Race (% of Caucasian)	146	64	64.0	39	84.8	0.008	0.03
Education (years)	143	98	9 ± 4	45	9 ± 3	0.15	0.25
Family history of hearing loss (%)	146	18	18.0	18	39.1	0.07	0.07
Number of years exposed to noise (years)	145	99	12 ± 16	46	23 ± 21	0.08	0.08
Hypertension (%) [e]	146	55	55.0	27	58.7	0.35	0.29
Self-reported hypertension and/or taking medication for hypertension (%)	146	61	61.0	28	60.9	0.41	0.42
Systolic blood pressure (mmHg)	146	100	144 ± 22	46	148 ± 25	0.21	0.17
Diastolic blood pressure (mmHg)	146	100	70 ± 10	46	70 ± 11	0.48	0.44
Self-reported diabetes and/or taking medication for diabetes (%)	146	28	28.0	12	26.1	0.73	0.86
Self-reported stroke (%)	146	12	12.0	5	10.9	0.54	0.69
Self-reported heart disease (%)	146	15	15.0	9	19.6	0.55	0.57
Self-reported congestive heart failure (%)	146	9	9.0	4	8.7	0.51	0.61
Use of tobacco products (%)	146	22	22.0	7	15.2	0.12	0.22
HDL cholesterol (mg/dL)	146	100	58 ± 17	46	48 ± 11	0.02	0.008
HDL cholesterol < 40 mg/dL (%)	146	13	13.0	13	28.3	0.29	0.25
LDL cholesterol (mg/dL)	141	97	119 ± 36	44	117 ± 31	0.38	0.31
LDL cholesterol ≥ 130 mg/dL (%)	141	33	34.0	15	34.1	0.95	0.89
Total cholesterol (mg/dL)	146	100	212 ± 45	46	201 ± 35	0.15	0.07
Total cholesterol ≥ 200 mg/dL (%)	146	57	57.0	21	45.7	0.45	0.39
Total cholesterol/ HDL cholesterol ratio	146	100	3.9 ± 1.4	46	4.3 ± 1.2	0.56	0.50
Total cholesterol/ HDL cholesterol ratio ≥ 3.5 (%)	146	56	56.0	37	80.4	0.03	0.04
Triglycerides (mg/dL)	146	100	172 ± 106	46	185 ± 96	0.58	0.61
Triglycerides ≥ 200 mg/dL (%)	146	30	30.0	15	32.6	0.85	0.83
Worst ear							
n	142	81	57.0	61	43.0		
Hearing level (dB)	142	81	28 ± 7	61	53 ± 10		
Age (years)	142	81	74 ± 7	61	79 ± 8	< 0.0001	< 0.0001
Gender (% of female)	142	74	91.4	44	72.1	0.0005	0.003

Race (% of Caucasian)	142	52	64.2	47	77.1	0.07	0.23
Education (years)	139	80	9 ± 4	59	9 ± 3	0.14	0.17
Family history of hearing loss (%)	142	12	14.8	22	36.1	0.01	0.01
Number of years exposed to noise (years)	141	80	12 ± 16	61	19 ± 19	0.19	0.23
Hypertension (%) [e]	142	43	53.1	37	60.7	0.26	0.23
Self-reported hypertension and/or taking medication for hypertension (%)	142	49	60.5	37	60.7	0.33	0.30
Systolic blood pressure (mmHg)	142	81	143 ± 21	61	148 ± 25	0.28	0.28
Diastolic blood pressure (mmHg)	142	81	70 ± 11	61	71 ± 10	0.27	0.30
Self-reported diabetes and/or taking medication for diabetes (%)	142	25	30.9	14	23.0	0.59	0.62
Self-reported stroke (%)	142	10	12.4	7	11.5	0.53	0.78
Self-reported heart disease (%)	142	14	17.3	9	14.8	0.64	0.55
Self-reported congestive heart failure (%)	142	8	9.9	5	8.2	0.34	0.40
Use of tobacco products (%)	142	17	21.0	10	16.4	0.30	0.53
HDL cholesterol (mg/dL)	142	81	59 ± 17	61	51 ± 13	0.04	0.02
HDL cholesterol < 40 mg/dL (%)	142	9	11.1	16	26.2	0.10	0.09
LDL cholesterol (mg/dL)	137	80	117 ± 37	57	119 ± 29	0.56	0.35
LDL cholesterol ≥ 130 mg/dL (%)	137	25	31.3	22	38.6	0.70	0.93
Total cholesterol (mg/dL)	142	81	209 ± 44	61	209 ± 40	0.86	0.45
Total cholesterol ≥ 200 mg/dL (%)	142	45	55.6	32	52.5	0.81	0.61
Total cholesterol/ HDL cholesterol ratio	142	81	3.8 ± 1.3	61	4.3 ± 1.3	0.17	0.20
Total cholesterol/ HDL cholesterol ratio ≥ 3.5 (%)	142	44	54.3	46	75.4	0.05	0.08
Triglycerides (mg/dL)	142	81	167 ± 101	61	192 ± 106	0.12	0.13
Triglycerides ≥ 200 mg/dL (%)	142	23	28.4	22	36.1	0.40	0.44

[a] Number of total participants.
[b] Number of participants with the condition.
[c] Logistic regression model adjusted for age, gender, and race.
[d] Logistic regression model adjusted for age, gender, race, family history of hearing loss, and noise exposure.
[e] Hypertension was defined as systolic blood pressure ≥ 140 mmHg.

Table B.8 Demographics, cardiovascular disease risk factors, and auditory function ***at 1 kHz*** in the best ear and the worst ear ***(≤ 40 vs. > 40 dB HL)***

		Hearing					
		≤ 40 dB HL		> 40 dB HL			
	N [a]	n [b]	Mean ± SD or %	n [b]	Mean ± SD or %	P value [c]	P value [d]
Best ear							
n	146	123	84.0	23	16.0		
Hearing level (dB)	146	123	24 ± 9	23	50 ± 6		
Age (years)	146	123	75 ± 7	23	81 ± 8	0.002	0.003
Gender (% of female)	146	101	82.1	18	78.3	0.65	0.76
Race (% of Caucasian)	146	83	67.5	20	87.0	0.04	0.07
Education (years)	143	120	9 ± 4	23	10 ± 3	0.48	0.45
Family history of hearing loss (%)	146	27	22.0	9	39.1	0.31	0.31
Number of years exposed to noise (years)	145	122	15 ± 18	23	17 ± 17	0.98	1.0
Hypertension (%) [e]	146	70	56.9	12	52.2	0.55	0.59
Self-reported hypertension and/or taking medication for hypertension (%)	146	77	62.6	12	57.2	0.73	0.79
Systolic blood pressure (mmHg)	146	123	144 ± 22	23	149 ± 28	0.51	0.56
Diastolic blood pressure (mmHg)	146	123	70 ± 10	23	68 ± 10	0.88	0.94
Self-reported diabetes and/or taking medication for diabetes (%)	146	32	26.0	8	34.8	0.11	0.09
Self-reported stroke (%)	146	15	12.2	2	8.7	0.97	0.85
Self-reported heart disease (%)	146	21	17.1	3	13.0	0.57	0.56
Self-reported congestive heart failure (%)	146	12	9.8	1	4.4	0.54	0.57
Use of tobacco products (%)	146	28	22.8	1	4.4	0.11	0.12
HDL cholesterol (mg/dL)	146	123	56 ± 17	23	49 ± 11	0.06	0.05
HDL cholesterol < 40 mg/dL (%)	146	21	17.1	5	21.7	0.62	0.68
LDL cholesterol (mg/dL)	141	120	118 ± 35	21	116 ± 31	0.50	0.39
LDL cholesterol ≥ 130 mg/dL (%)	141	42	35.0	6	28.6	0.50	0.39
Total cholesterol (mg/dL)	146	123	210 ± 43	23	198 ± 36	0.13	0.08
Total cholesterol ≥ 200 mg/dL (%)	146	68	55.3	10	43.5	0.29	0.22
Total cholesterol/ HDL cholesterol ratio	146	123	4 ± 1.3	23	4.2 ± 1.3	0.63	0.73
Total cholesterol/ HDL cholesterol ratio ≥ 3.5 (%)	146	76	61.8	17	73.9	0.50	0.53
Triglycerides (mg/dL)	146	123	176 ± 102	23	178 ± 112	0.71	0.67
Triglycerides ≥ 200 mg/dL (%)	146	40	32.5	5	21.7	0.24	0.22
Worst ear							
n	145	109	75.2	36	24.8		
Hearing level (dB)	145	109	27 ± 7	36	54 ± 10		
Age (years)	145	109	75 ± 7	36	80 ± 8	0.0003	0.0005
Gender (% of female)	145	93	85.3	26	72.2	0.06	0.29

Race (% of Caucasian)	145	71	65.1	31	86.1	0.01	0.05
Education (years)	142	107	9 ± 4	35	9 ± 3	0.31	0.47
Family history of hearing loss (%)	145	20	18.4	16	44.4	0.03	0.03
Number of years exposed to noise (years)	144	108	14 ± 17	36	21 ± 20	0.27	0.29
Hypertension (%) [e]	145	63	57.8	19	52.8	0.53	0.63
Self-reported hypertension and/or taking medication for hypertension (%)	145	68	62.4	21	58.3	0.87	0.82
Systolic blood pressure (mmHg)	145	109	145 ± 22	36	146 ± 26	0.91	0.90
Diastolic blood pressure (mmHg)	145	109	70 ± 10	36	69 ± 11	0.86	0.94
Self-reported diabetes and/or taking medication for diabetes (%)	145	30	27.5	10	27.8	0.54	0.54
Self-reported stroke (%)	145	12	11.0	5	13.9	0.23	0.37
Self-reported heart disease (%)	145	17	15.6	7	19.4	0.68	0.72
Self-reported congestive heart failure (%)	145	9	8.3	4	11.1	0.58	0.48
Use of tobacco products (%)	145	23	21.1	5	13.9	0.53	0.81
HDL cholesterol (mg/dL)	145	109	57 ± 16	36	49 ± 14	0.06	0.03
HDL cholesterol < 40 mg/dL (%)	145	16	14.7	10	27.8	0.21	0.18
LDL cholesterol (mg/dL)	140	106	119 ± 35	34	117 ± 31	0.43	0.30
LDL cholesterol ≥ 130 mg/dL (%)	140	36	34.0	12	35.3	0.95	0.85
Total cholesterol (mg/dL)	145	109	210 ± 44	36	204 ± 37	0.32	0.16
Total cholesterol ≥ 200 mg/dL (%)	145	60	55.1	18	50.0	0.76	0.61
Total cholesterol/ HDL cholesterol ratio	145	109	3.9 ± 1.3	36	4.3 ± 1.3	0.36	0.37
Total cholesterol/ HDL cholesterol ratio ≥ 3.5 (%)	145	65	59.6	28	77.8	0.21	0.25
Triglycerides (mg/dL)	145	109	170 ± 101	36	196 ± 109	0.39	0.39
Triglycerides ≥ 200 mg/dL (%)	145	32	29.4	13	36.1	0.64	0.66

[a] Number of total participants.
[b] Number of participants with the condition.
[c] Logistic regression model adjusted for age, gender, and race.
[d] Logistic regression model adjusted for age, gender, race, family history of hearing loss, and noise exposure.
[e] Hypertension was defined as systolic blood pressure ≥ 140 mmHg.

Table B.9 Demographics, cardiovascular disease risk factors, and auditory function ***at 2 kHz*** in the best ear and the worst ear ***(≤ 40 vs. > 40 dB HL)***

		Hearing					
		≤ 40 dB HL		> 40 dB HL			
	N [a]	n [b]	Mean ± SD or %	n [b]	Mean ± SD or %	P value [c]	P value [d]
Best ear							
n	146	105	71.9	41	28.1		
Hearing level (dB)	146	105	26 ± 9	41	57 ± 10		
Age (years)	146	105	75 ± 8	41	80 ± 7	0.0001	0.0002
Gender (% of female)	146	92	87.6	27	65.9	0.002	0.03
Race (% of Caucasian)	146	68	64.8	35	85.4	0.01	0.04
Education (years)	143	104	9 ± 4	39	9 ± 4	0.44	0.62
Family history of hearing loss (%)	146	20	19.1	16	39.0	0.11	0.12
Number of years exposed to noise (years)	145	104	13 ± 16	41	22 ± 21	0.16	0.17
Hypertension (%) [e]	146	61	58.1	21	51.2	0.53	0.59
Self-reported hypertension and/or taking medication for hypertension (%)	146	65	61.9	24	58.5	0.74	0.77
Systolic blood pressure (mmHg)	146	105	145 ± 22	41	145 ± 25	0.95	0.99
Diastolic blood pressure (mmHg)	146	105	70 ± 10	41	69 ± 11	0.93	0.97
Self-reported diabetes and/or taking medication for diabetes (%)	146	28	26.7	12	29.3	0.34	0.41
Self-reported stroke (%)	146	12	11.4	5	12.2	0.37	0.46
Self-reported heart disease (%)	146	16	15.2	8	19.5	0.59	0.62
Self-reported congestive heart failure (%)	146	9	8.6	4	9.8	0.95	0.95
Use of tobacco products (%)	146	24	22.9	5	12.2	0.07	0.13
HDL cholesterol (mg/dL)	146	105	58 ± 17	41	49 ± 12	0.07	0.03
HDL cholesterol < 40 mg/dL (%)	146	14	13.3	12	29.3	0.16	0.13
LDL cholesterol (mg/dL)	141	102	116 ± 36	39	124 ± 30	0.33	0.35
LDL cholesterol ≥ 130 mg/dL (%)	141	32	31.4	16	41.0	0.24	0.26
Total cholesterol (mg/dL)	146	105	208 ± 45	41	208 ± 35	0.86	0.93
Total cholesterol ≥ 200 mg/dL (%)	146	55	52.4	23	56.1	0.29	0.31
Total cholesterol/ HDL cholesterol ratio	146	105	3.8 ± 1.3	41	4.4 ± 1.2	0.19	0.15
Total cholesterol/ HDL cholesterol ratio ≥ 3.5 (%)	146	58	55.2	35	85.4	0.005	0.006
Triglycerides (mg/dL)	146	105	173 ± 105	41	186 ± 99	0.60	0.64
Triglycerides ≥ 200 mg/dL (%)	146	33	31.4	12	29.3	0.44	0.40
Worst ear							
n	145	83	57.2	62	42.8		
Hearing level (dB)	145	83	28 ± 8	62	57 ± 11		
Age (years)	145	83	74 ± 7	62	79 ± 7	< 0.0001	< 0.0001
Gender (% of female)	145	75	90.4	44	71.0	0.001	0.01

Race (% of Caucasian)	145	55	66.3	47	75.8	0.19	0.48
Education (years)	142	82	9 ± 3	60	9 ± 4	0.30	0.39
Family history of hearing loss (%)	145	14	16.9	22	35.5	0.04	0.05
Number of years exposed to noise (years)	144	82	12 ± 15	62	20 ± 20	0.16	0.18
Hypertension (%) [e]	145	44	53.0	38	61.3	0.27	0.23
Self-reported hypertension and/or taking medication for hypertension (%)	145	50	60.2	39	62.9	0.32	0.32
Systolic blood pressure (mmHg)	145	83	143 ± 22	62	148 ± 24	0.28	0.25
Diastolic blood pressure (mmHg)	145	83	70 ± 11	62	70 ± 10	0.65	0.67
Self-reported diabetes and/or taking medication for diabetes (%)	145	22	26.5	18	29.0	0.39	0.39
Self-reported stroke (%)	145	8	9.6	9	14.5	0.08	0.11
Self-reported heart disease (%)	145	14	16.9	10	16.1	0.99	0.96
Self-reported congestive heart failure (%)	145	8	9.6	5	8.1	0.45	0.53
Use of tobacco products (%)	145	19	22.9	9	14.5	0.06	0.12
HDL cholesterol (mg/dL)	145	83	59 ± 17	62	50 ± 12	0.005	0.002
HDL cholesterol < 40 mg/dL (%)	145	10	12.1	16	25.8	0.15	0.13
LDL cholesterol (mg/dL)	140	81	116 ± 37	59	121 ± 29	0.89	0.98
LDL cholesterol ≥ 130 mg/dL (%)	140	24	29.6	24	40.7	0.29	0.34
Total cholesterol (mg/dL)	145	83	210 ± 48	62	207 ± 33	0.65	0.39
Total cholesterol ≥ 200 mg/dL (%)	145	44	53.0	34	54.9	0.56	0.65
Total cholesterol/ HDL cholesterol ratio	145	83	3.8 ± 1.4	62	4.3 ± 1.2	0.07	0.06
Total cholesterol/ HDL cholesterol ratio ≥ 3.5 (%)	145	43	51.8	50	80.7	0.002	0.003
Triglycerides (mg/dL)	145	83	168 ± 105	62	189 ± 99	0.06	0.08
Triglycerides ≥ 200 mg/dL (%)	145	24	28.9	21	33.9	0.46	0.49

[a] Number of total participants.
[b] Number of participants with the condition.
[c] Logistic regression model adjusted for age, gender, and race.
[d] Logistic regression model adjusted for age, gender, race, family history of hearing loss, and noise exposure.
[e] Hypertension was defined as systolic blood pressure ≥ 140 mmHg.

Table B.10 Demographics, cardiovascular disease risk factors, and auditory function ***at 4 kHz*** in the best ear and the worst ear ***(≤ 40 vs. > 40 dB HL)***

		Hearing					
		≤ 40 dB HL		**> 40 dB HL**			
	N [a]	n [b]	Mean ± SD or %	n [b]	Mean ± SD or %	P value [c]	P value [d]
Best ear							
n	146	86	58.9	60	41.1		
Hearing level (dB)	146	86	24 ± 10	60	56 ± 10		
Age (years)	146	86	74 ± 7	60	80 ± 7	< 0.0001	< 0.0001
Gender (% of female)	146	80	93.0	39	65.0	< 0.0001	0.0002
Race (% of Caucasian)	146	50	58.1	53	88.3	< 0.0001	0.0001
Education (years)	143	85	9 ± 4	58	9 ± 3	0.21	0.41
Family history of hearing loss (%)	146	14	16.3	22	36.7	0.12	0.15
Number of years exposed to noise (years)	145	85	11 ± 14	60	22 ± 21	0.01	0.02
Hypertension (%) [e]	146	47	54.7	35	58.3	0.15	0.09
Self-reported hypertension and/or taking medication for hypertension (%)	146	52	60.5	37	61.7	0.13	0.12
Systolic blood pressure (mmHg)	146	86	144 ± 22	60	146 ± 24	0.27	0.14
Diastolic blood pressure (mmHg)	146	86	70 ± 10	60	70 ± 11	0.10	0.07
Self-reported diabetes and/or taking medication for diabetes (%)	146	28	32.6	12	20.0	0.28	0.20
Self-reported stroke (%)	146	12	14.0	5	8.3	0.79	0.70
Self-reported heart disease (%)	146	15	17.4	9	15.0	0.24	0.23
Self-reported congestive heart failure (%)	146	8	9.3	5	8.3	0.20	0.34
Use of tobacco products (%)	146	19	22.1	10	16.7	0.20	0.34
HDL cholesterol (mg/dL)	146	86	59 ± 17	60	51 ± 13	0.40	0.13
HDL cholesterol < 40 mg/dL (%)	146	10	11.6	16	26.7	0.46	0.34
LDL cholesterol (mg/dL)	141	85	116 ± 35	56	122 ± 33	0.71	0.65
LDL cholesterol ≥ 130 mg/dL (%)	141	26	30.6	22	39.3	0.32	0.20
Total cholesterol (mg/dL)	146	86	207 ± 41	60	211 ± 44	0.41	0.56
Total cholesterol ≥ 200 mg/dL (%)	146	47	54.7	31	51.7	0.72	0.62
Total cholesterol/ HDL cholesterol ratio	146	86	3.8 ± 1.3	60	4.3 ± 1.3	0.40	0.26
Total cholesterol/ HDL cholesterol ratio ≥ 3.5 (%)	146	47	54.7	46	76.7	0.14	0.15
Triglycerides (mg/dL)	146	86	166 ± 100	60	191 ± 106	0.67	0.65
Triglycerides ≥ 200 mg/dL (%)	146	24	27.9	21	35.0	0.88	0.83
Worst ear							
n	142	66	46.5	76	53.5		
Hearing level (dB)	142	66	27 ± 9	76	58 ± 11		
Age (years)	142	66	73 ± 7	76	79 ± 7	< 0.0001	< 0.0001
Gender (% of female)	142	63	95.5	55	72.4	< 0.0001	0.0004

Race (% of Caucasian)	142	40	60.6	59	77.6	0.01	0.04
Education (years)	139	65	9 ± 4	74	9 ± 4	0.52	0.74
Family history of hearing loss (%)	142	9	13.6	25	32.9	0.02	0.04
Number of years exposed to noise (years)	141	65	10 ± 13	76	19 ± 20	0.009	0.01
Hypertension (%) [e]	142	35	53.0	45	59.2	0.24	0.21
Self-reported hypertension and/or taking medication for hypertension (%)	142	40	60.6	46	60.5	0.27	0.29
Systolic blood pressure (mmHg)	142	66	144 ± 20	76	146 ± 25	0.58	0.48
Diastolic blood pressure (mmHg)	142	66	70 ± 10	76	70 ± 11	0.26	0.31
Self-reported diabetes and/or taking medication for diabetes (%)	142	22	33.3	17	22.4	0.39	0.44
Self-reported stroke (%)	142	8	12.1	9	11.8	0.41	0.41
Self-reported heart disease (%)	142	13	19.7	10	13.2	0.14	0.14
Self-reported congestive heart failure (%)	142	6	9.1	7	9.2	0.34	0.61
Use of tobacco products (%)	142	14	21.2	13	17.1	0.21	0.41
HDL cholesterol (mg/dL)	142	66	60 ± 19	76	52 ± 13	0.14	0.02
HDL cholesterol < 40 mg/dL (%)	142	9	13.6	16	21.1	0.76	0.98
LDL cholesterol (mg/dL)	137	65	116 ± 36	72	120 ± 32	0.73	0.61
LDL cholesterol ≥ 130 mg/dL (%)	137	19	29.2	28	38.9	0.60	0.58
Total cholesterol (mg/dL)	142	66	208 ± 43	76	210 ± 42	0.94	0.53
Total cholesterol ≥ 200 mg/dL (%)	142	37	56.1	40	52.6	0.76	0.67
Total cholesterol/ HDL cholesterol ratio	142	66	3.7 ± 1.3	76	4.2 ± 1.3	0.50	0.39
Total cholesterol/ HDL cholesterol ratio ≥ 3.5 (%)	142	36	54.6	54	71.1	0.29	0.39
Triglycerides (mg/dL)	142	66	169 ± 106	76	185 ± 102	0.49	0.48
Triglycerides ≥ 200 mg/dL (%)	142	20	30.3	25	32.9	0.89	0.86

[a] Number of total participants.
[b] Number of participants with the condition.
[c] Logistic regression model adjusted for age, gender, and race.
[d] Logistic regression model adjusted for age, gender, race, family history of hearing loss, and noise exposure.
[e] Hypertension was defined as systolic blood pressure ≥ 140 mmHg.

Table B.11 Demographics, cardiovascular disease risk factors, and auditory function ***at 8 kHz*** in the best ear and the worst ear ***(≤ 40 vs. > 40 dB HL)***

		Hearing					
		≤ 40 dB HL		**> 40 dB HL**			
	N [a]	n [b]	Mean ± SD or %	n [b]	Mean ± SD or %	P value [c]	P value [d]
Best ear							
n	100	48	48.0	52	52.0		
Hearing level (dB)	100	48	24 ± 13	52	53 ± 6		
Age (years)	100	48	72 ± 8	52	78 ± 6	< 0.0001	< 0.0001
Gender (% of female)	100	45	93.8	43	82.7	0.04	0.05
Race (% of Caucasian)	100	23	47.9	38	73.1	0.0006	0.001
Education (years)	98	48	9 ± 4	50	9 ± 4	0.06	0.08
Family history of hearing loss (%)	100	6	12.5	13	25.0	0.20	0.20
Number of years exposed to noise (years)	100	48	12 ± 14	52	14 ± 18	0.87	0.99
Hypertension (%) [e]	100	28	58.3	32	61.5	0.57	0.47
Self-reported hypertension and/or taking medication for hypertension (%)	100	29	60.4	36	69.2	0.12	0.11
Systolic blood pressure (mmHg)	100	48	143 ± 20	52	147 ± 24	0.84	0.93
Diastolic blood pressure (mmHg)	100	48	72 ± 10	52	68 ± 11	0.42	0.34
Self-reported diabetes and/or taking medication for diabetes (%)	100	17	35.4	14	26.9	0.91	0.69
Self-reported stroke (%)	100	4	8.3	10	19.2	0.04	0.05
Self-reported heart disease (%)	100	6	12.5	9	17.3	0.42	0.31
Self-reported congestive heart failure (%)	100	4	8.3	6	11.5	0.89	0.98
Use of tobacco products (%)	100	13	27.1	11	21.2	0.20	0.24
HDL cholesterol (mg/dL)	100	48	60 ± 18	52	54 ± 16	0.16	0.14
HDL cholesterol < 40 mg/dL (%)	100	6	12.5	12	23.1	0.66	0.60
LDL cholesterol (mg/dL)	97	47	108 ± 28	50	125 ± 39	0.04	0.05
LDL cholesterol ≥ 130 mg/dL (%)	97	10	21.3	23	46.0	0.02	0.02
Total cholesterol (mg/dL)	100	48	201 ± 36	52	217 ± 51	0.10	0.14
Total cholesterol ≥ 200 mg/dL (%)	100	25	52.1	31	59.6	0.47	0.54
Total cholesterol/ HDL cholesterol ratio	100	48	3.5 ± 1.2	52	4.3 ± 1.5	0.04	0.05
Total cholesterol/ HDL cholesterol ratio ≥ 3.5 (%)	100	22	45.8	36	69.2	0.02	0.03
Triglycerides (mg/dL)	100	48	165 ± 111	52	181 ± 101	0.76	0.83
Triglycerides ≥ 200 mg/dL (%)	100	13	27.1	17	32.7	0.91	0.99
Worst ear							
n	85	36	42.0	49	58.0		
Hearing level (dB)	85	36	26 ± 12	49	55 ± 6		
Age (years)	85	36	71 ± 7	49	76 ± 7	0.0003	0.0003
Gender (% of female)	85	35	97.2	43	87.8	0.06	0.06

Race (% of Caucasian)	85	15	41.7	36	73.5	0.0005	0.0006
Education (years)	85	36	8 ± 3	48	10 ± 3	0.007	0.006
Family history of hearing loss (%)	85	6	16.7	9	18.4	0.74	0.75
Number of years exposed to noise (years)	85	36	11 ± 14	49	11 ± 17	0.65	0.65
Hypertension (%) [e]	85	22	61.1	28	57.1	0.19	0.19
Self-reported hypertension and/or taking medication for hypertension (%)	85	21	58.3	33	67.4	0.18	0.17
Systolic blood pressure (mmHg)	85	36	144 ± 18	49	144 ± 21	0.26	0.24
Diastolic blood pressure (mmHg)	85	36	72 ± 9	49	68 ± 10	0.28	0.28
Self-reported diabetes and/or taking medication for diabetes (%)	85	13	36.1	13	26.5	0.90	0.93
Self-reported stroke (%)	85	4	11.1	6	12.2	0.46	0.46
Self-reported heart disease (%)	85	4	11.1	9	18.4	0.26	0.30
Self-reported congestive heart failure (%)	85	2	5.6	6	12.2	0.37	0.41
Use of tobacco products (%)	85	10	27.8	10	20.4	0.23	0.21
HDL cholesterol (mg/dL)	85	36	64 ± 18	49	53 ± 16	0.01	0.01
HDL cholesterol < 40 mg/dL (%)	85	3	8.3	11	22.5	0.34	0.40
LDL cholesterol (mg/dL)	82	35	109 ± 25	47	120 ± 42	0.14	0.14
LDL cholesterol ≥ 130 mg/dL (%)	82	6	17.1	18	38.3	0.02	0.02
Total cholesterol (mg/dL)	85	36	203 ± 32	49	212 ± 55	0.48	0.42
Total cholesterol ≥ 200 mg/dL (%)	85	20	55.6	26	53.1	0.85	0.87
Total cholesterol/ HDL cholesterol ratio	85	36	3.3 ± 0.9	49	4.3 ± 1.5	0.01	0.01
Total cholesterol/ HDL cholesterol ratio ≥ 3.5 (%)	85	15	41.7	33	67.4	0.03	0.02
Triglycerides (mg/dL)	85	36	162 ± 119	49	188 ± 96	0.65	0.64
Triglycerides ≥ 200 mg/dL (%)	85	9	25.0	18	36.7	0.96	0.96

[a] Number of total participants.
[b] Number of participants with the condition.
[c] Logistic regression model adjusted for age, gender, and race.
[d] Logistic regression model adjusted for age, gender, race, family history of hearing loss, and noise exposure.
[e] Hypertension was defined as systolic blood pressure ≥ 140 mmHg.
[f] Chi-square analyses.
- Not applicable. There was possibly a quasi-complete separation of data points.

A POSSIBLE RELATIONSHIP OF AGE-RELATED HEARING LOSS WITH CARDIOVASCULAR DISEASE RISK FACTORS IN OLDER ADULTS WAS EXAMINED USING TWO DIFFERENT CUTOFFS FOR POOR HEARING (25 AND 40 dB HL). PARTICIPANTS WITH CONDUCTIVE HEARING LOSS AND ASYMMETRICAL HEARING LOSS WERE EXCLUDED IN THIS ANALYSIS (TABLES B.12 – B.15).

Table B.12 Characteristics of participants

	N [a]	**n** [b]	**Mean ± SD or %**
Age (years)	96	96	75 ± 7 (58-92) [c]
Gender	96		
Female (%)		79	82.3
Male (%)		17	17.7
Race	96		
Caucasian (%)		64	66.7
African-American (%)		32	33.3
PTA [d] in the best ear (dB HL) [e]	96	96	31 ± 14 (8-73)
PTA in the worst ear (dB HL)	93	93	34 ± 14 (10-77)
PTA > 25 dB HL in the best ear (%)	96	51	53.1
PTA > 25 dB HL in the worst ear (%)	93	61	65.6
PTA > 40 dB HL in the best ear (%)	96	22	22.9
PTA > 40 dB HL in the worst ear (%)	93	30	32.3
Education (years)	94	94	9 ± 4 (0-16)
Family history of hearing loss (%)	96	18	18.8
Number of years exposed to noise (years)	95	95	14 ± 17 (0-62)
HDL cholesterol (mg/dL)	96	96	55 ± 16 (27-110)
LDL cholesterol (mg/dL)	93	93	116 ± 34 (55-258)
Total cholesterol (mg/dL)	96	96	204 ± 41 (128-369)
Total cholesterol/ HDL cholesterol ratio	96	96	3.9 ± 1.3 (2.2-9.0)
Triglycerides (mg/dL)	96	96	169 ± 103 (51-777)

[a] Number of total participants without conductive hearing loss and asymmetrical hearing loss.
[b] Number of participants with the condition.
[c] Range in parentheses.
[d] PTA, pure-tone average threshold of 1, 2, and 4 kHz.
[e] dB HL, hearing level in decibel.

Table B.13 Correlation between blood cholesterols and pure-tone average (1, 2, and 4 kHz) in the best ear and the worst ear [a]

	PTA [b] in the best ear (N = 92)	PTA in the worst ear (N = 89)
HDL cholesterol	r = -0.16 *P* = 0.13	r = -0.23 *P* = 0.04
LDL cholesterol	r = 0.04 *P* = 0.72	r = -0.04 *P* = 0.75
Total cholesterol	r = -0.01 *P* = 0.90	r = -0.11 *P* = 0.30
Total cholesterol/HDL cholesterol ratio	r = 0.22 *P* = 0.04	r = 0.20 *P* = 0.06
Triglycerides	r = 0.12 *P* = 0.26	r = 0.08 *P* = 0.47

[a] Partial Spearman correlation coefficient controlled for age, gender, race, family history of hearing loss, and noise exposure.
[b] PTA, pure-tone average threshold of 1, 2, and 4 kHz.

Table B.14 Demographics, cardiovascular disease risk factors, and auditory function in the best ear and the worst ear ***(PTA[a] ≤ 25 vs. > 25 dB hearing level)***

		Hearing					
		Normal (PTA ≤ 25 dB HL[b])		**Impaired (PTA > 25 dB HL)**			
	N [c]	n [d]	Mean ± SD or %	n [d]	Mean ± SD or %	P value [e]	P value [f]
Best ear							
n	96	45	46.9	51	53.1		
Hearing level (dB)	96	45	19 ± 4	51	42 ± 11		
Age (years)	96	45	71 ± 6	51	78 ± 7	< 0.0001	< 0.0001
Gender (% of female)	96	42	93.3	37	72.6	0.006	0.03
Race (% of Caucasian)	96	27	60.0	37	72.6	0.33	0.35
Education (years)	94	45	9 ± 3	49	9 ± 4	0.79	0.72
Family history of hearing loss (%)	96	8	17.8	10	19.6	1.00	0.84
Number of years exposed to noise (years)	95	44	11 ± 14	51	18 ± 19	0.32	0.31
HDL cholesterol (mg/dL)	96	45	58 ± 18	51	53 ± 14	0.34	0.14
LDL cholesterol (mg/dL)	93	44	113 ± 39	49	118 ± 30	0.89	0.86
Total cholesterol (mg/dL)	96	45	204 ± 45	51	203 ± 37	0.79	0.71
Total cholesterol/ HDL cholesterol ratio	96	45	4.0 ± 1.0	51	4.0 ± 1.0	0.77	0.60
Triglycerides (mg/dL)	96	45	173 ± 114	51	166 ± 93	0.73	0.77
Worst ear							
n	93	32	34.4	61	65.6		
Hearing level (dB)	93	32	21 ± 4	61	41 ± 12		
Age (years)	93	32	71 ± 5	61	77 ± 7	0.0002	0.0003
Gender (% of female)	93	30	93.8	48	78.7	0.04	0.10
Race (% of Caucasian)	93	18	56.3	43	70.5	0.23	0.32
Education (years)	91	32	9 ± 3	59	9 ± 4	0.97	0.95
Family history of hearing loss (%)	93	5	15.6	12	19.7	0.66	0.81
Number of years exposed to noise (years)	92	31	10 ± 14	61	16 ± 17	0.34	0.37
HDL cholesterol (mg/dL)	93	32	60 ± 17	61	53 ± 16	0.09	0.03
LDL cholesterol (mg/dL)	90	32	120 ± 42	58	113 ± 29	0.14	0.14
Total cholesterol (mg/dL)	93	32	211 ± 48	61	200 ± 36	0.10	0.07
Total cholesterol/ HDL cholesterol ratio	93	32	4.0 ± 1.0		4.0 ± 1.0	0.68	0.55
Triglycerides (mg/dL)	93	32	155 ± 67	61	180 ± 119	0.50	0.52

[a] PTA, pure-tone average threshold of 1, 2, and 4 kHz.
[b] dB HL, hearing level in decibel.
[c] Number of total participants without conductive and asymmetrical hearing loss.
[d] Number of participants with the condition.
[e] Logistic regression model controlled for age, gender, and race.
[f] Logistic regression model controlled for age, gender, race, family history of hearing loss, and noise exposure.

Table B.15 Demographics, cardiovascular disease risk factors, and auditory function in the best ear and the worst ear ***(PTA[a] ≤ 40 vs. > 40 dB hearing level)***

		Hearing					
		PTA ≤ 40 dB HL[b]		**PTA > 40 dB HL**			
	N [c]	n [d]	Mean ± SD or %	n [d]	Mean ± SD or %	P value [e]	P value [f]
Best ear							
n	96	74	77.1	22	22.9		
Hearing level (dB)	96	74	25 ± 8	22	52 ± 9		
Age (years)	96	74	74 ± 7	22	79 ± 7	0.001	0.001
Gender (% of female)	96	67	90.5	12	54.6	0.0004	0.009
Race (% of Caucasian)	96	46	62.2	18	81.8	0.15	0.22
Education (years)	94	73	9 ± 4	21	9 ± 4	0.73	0.90
Family history of hearing loss (%)	96	11	14.9	7	31.8	0.22	0.31
Number of years exposed to noise (years)	95	73	11 ± 14	22	25 ± 22	0.05	0.07
HDL cholesterol (mg/dL)	96	74	57 ± 17	22	49 ± 12	0.24	0.09
LDL cholesterol (mg/dL)	93	72	117 ± 37	21	111 ± 26	0.31	0.33
Total cholesterol (mg/dL)	96	74	207 ± 43	22	191 ± 26	0.13	0.12
Total cholesterol/ HDL cholesterol ratio	96	74	4.0 ± 1.0	22	4.0 ± 1.0	0.73	0.91
Triglycerides (mg/dL)	96	74	170 ± 108	22	167 ± 85	0.86	0.96
Worst ear							
n	93	63	67.7	30	32.3		
Hearing level (dB)	93	63	26 ± 7	30	51 ± 9		
Age (years)	93	63	73 ± 6	30	79 ± 8	0.0002	0.0002
Gender (% of female)	93	59	93.4	19	63.3	0.0002	0.001
Race (% of Caucasian)	93	40	63.5	21	70.0	0.71	0.93
Education (years)	91	62	9 ± 3	29	9 ± 4	0.34	0.36
Family history of hearing loss (%)	93	9	14.3	8	26.7	0.11	0.13
Number of years exposed to noise (years)	92	62	11 ± 14	30	19 ± 20	0.37	0.48
HDL cholesterol (mg/dL)	93	63	59 ± 17	30	49 ± 12	0.02	0.007
LDL cholesterol (mg/dL)	90	62	116 ± 38	28	115 ± 25	0.58	0.51
Total cholesterol (mg/dL)	93	63	207 ± 45	30	199 ± 28	0.35	0.26
Total cholesterol/ HDL cholesterol ratio	93	63	4.0 ± 1.0	30	4.0 ± 1.0	0.19	0.12
Triglycerides (mg/dL)	93	63	165 ± 105	30	185 ± 102	0.12	0.09

[a] PTA, pure-tone average threshold of 1, 2, and 4 kHz.
[b] dB HL, hearing level in decibel.
[c] Number of total participants without conductive and asymmetrical hearing loss.
[d] Number of participants with the condition.
[e] Logistic regression model controlled for age, gender, and race.
[f] Logistic regression model controlled for age, gender, race, family history of hearing loss, and noise exposure.

A POSSIBLE RELATIONSHIP OF HEARING IMPAIRMENT WITH CARDIOVASCULAR DISEASE RISK FACTORS IN OLDER ADULTS WAS EXAMINED USING TWO DIFFERENT CUTOFFS FOR POOR HEARING (25 AND 40 dB HL). PARTICIPANTS WHO WERE TAKING A CHOLESTEROL LOWERING MEDICATION WERE EXCLUDED IN THIS ANALYSIS (TABLES B.16 – B.19).

Table B.16 Characteristics of participants

	N [a]	**n** [b]	**Mean ± SD or %**
Age (years)	115	115	77 ± 8 (58-97) [c]
Gender	115		
Female (%)		93	80.9
Male (%)		22	19.1
Race	115		
Caucasian (%)		75	65.2
African-American (%)		40	34.8
Body weight (kg)	115	115	77.7 ± 18.2 (40.8-137.9)
Body mass index	115	115	29.0 ± 6.2 (15.2-48.3)
PTA [d] in the best ear (dB HL) [e]	115	115	35 ± 14 (8-67)
PTA in the worst ear (dB HL)	112	112	39 ± 15 (10-83)
PTA > 25 dB HL in the best ear (%)	115	77	67.0
PTA > 25 dB HL in the worst ear (%)	112	88	78.6
PTA > 40 dB HL in the best ear (%)	115	37	32.2
PTA > 40 dB HL in the worst ear (%)	112	51	45.5
Education (years)	112	112	9 ± 4 (0-18)
Family history of hearing loss (%)	115	24	20.9
Number of years exposed to noise (years)	114	114	15 ± 18 (0-83)
HDL cholesterol (mmol/L)	115	115	1.44 ± 0.43 (0.70-2.86)
LDL cholesterol (mmol/L)	111	111	3.14 ± 0.83 (1.43-5.59)
Total cholesterol (mmol/L)	115	115	5.45 ± 0.98 (3.33-8.48)
Total cholesterol/ HDL cholesterol ratio	115	115	4.0 ± 1.3 (2.0-8.1)
Triglycerides (mmol/L)	115	115	1.96 ± 1.22 (0.58-8.78)

[a] Number of total participants.
[b] Number of participants with the condition.
[c] Range in parentheses.
[d] PTA, pure-tone average threshold of 1, 2, and 4 kHz.
[e] dB HL, hearing level in decibel.

Table B.17 Correlation between blood cholesterols and pure-tone average (1, 2, and 4 kHz) in the best ear and the worst ear [a]

	PTA [b] in the best ear (N = 110)	**PTA in the worst ear (N = 107)**
HDL cholesterol	r = -0.20	r = -0.23
	P = 0.05	*P* = 0.02
LDL cholesterol	r = 0.07	r = 0.03
	P = 0.48	*P* = 0.80
Total cholesterol	r = 0.001	r = -0.04
	P = 0.92	*P* = 0.70
Total cholesterol/HDL cholesterol ratio	r = 0.23	r = 0.22
	P = 0.02	*P* = 0.03
Triglycerides	r = 0.13	r = 0.15
	P = 0.18	*P* = 0.12

[a] Partial Spearman correlation coefficient controlled for age, gender, race, family history of hearing loss, and noise exposure.
[b] PTA, pure-tone average threshold of 1, 2, and 4 kHz.

Table B.18 Demographics, cardiovascular disease risk factors, and auditory function in the best ear and the worst ear ***(PTA[a] ≤ 25 vs. > 25 dB hearing level)***

		Hearing					
		Normal (PTA ≤ 25 dB HL[b])		Impaired (PTA > 25 dB HL)			
	N [c]	n [d]	Mean ± SD or %	n [d]	Mean ± SD or %	P value [e]	P value [f]
Best ear							
n	115	38	33.0	77	67.0		
Hearing level (dB)	115	38	19 ± 4	77	42 ± 10		
Age (years)	115	38	72 ± 6	77	79 ± 7	< 0.0001	< 0.0001
Gender (% of female)	115	34	89.5	59	76.6	0.10	0.21
Race (% of Caucasian)	115	20	52.6	55	71.4	0.05	0.10
Body weight (kg)	115	38	83.3 ± 20.7	77	75.0 ± 16.2	0.28	0.21
Body mass index	115	38	30.4 ± 7.4	77	28.3 ± 5.5	0.83	0.77
Education (years)	112	38	9 ± 4	74	9 ± 4	0.73	0.91
Family history of hearing loss (%)	115	6	15.8	18	23.4	0.98	0.95
Number of years exposed to noise (years)	114	37	10 ± 14	77	18 ± 19	0.19	0.19
HDL cholesterol (mmol/L)	115	38	1.54 ± 0.50	77	1.39 ± 0.38	0.24	0.11
LDL cholesterol (mmol/L)	111	37	3.01 ± 0.93	74	3.21 ± 0.78	0.96	0.97
Total cholesterol (mmol/L)	115	38	5.38 ± 1.12	77	5.48 ± 0.92	0.59	0.57
Total cholesterol/ HDL cholesterol ratio	115	38	3.8 ± 1.4	77	4.2 ± 1.3	0.64	0.44
Triglycerides (mmol/L)	115	38	1.91 ± 1.40	77	1.98 ± 1.13	0.93	0.99
Worst ear							
n	112	24	21.4	88	78.6		
Hearing level (dB)	112	24	21 ± 4	88	44 ± 13		
Age (years)	112	24	71 ± 6	88	78 ± 7	0.0001	0.0003
Gender (% of female)	112	22	91.7	70	79.6	0.21	0.29
Race (% of Caucasian)	112	10	41.7	62	70.5	0.01	0.03
Body weight (kg)	112	24	83.6 ± 21.2	88	76.0 ± 17.1	0.69	0.61
Body mass index	112	24	30.5 ± 7.7	88	28.6 ± 5.8	0.81	0.82
Education (years)	109	24	9 ± 3	85	9 ± 4	0.83	0.82
Family history of hearing loss (%)	112	3	12.5	20	22.7	0.80	0.77
Number of years exposed to noise (years)	111	23	10 ± 14	88	16 ± 18	0.54	0.52
HDL cholesterol (mmol/L)	112	24	1.62 ± 0.46	88	1.40 ± 0.41	0.08	0.05
LDL cholesterol (mmol/L)	108	24	3.19 ± 0.92	84	3.13 ± 0.80	0.11	0.09
Total cholesterol (mmol/L)	112	24	5.56 ± 1.13	88	5.44 ± 0.93	0.08	0.06
Total cholesterol/ HDL cholesterol ratio	112	24	3.6 ± 1.1	88	4.2 ± 1.4	0.37	0.33
Triglycerides (mmol/L)	112	24	1.59 ± 0.66	88	2.07 ± 1.33	0.44	0.46

[a] PTA, pure-tone average threshold of 1, 2, and 4 kHz.
[b] dB HL, hearing level in decibel.
[c] Number of total participants.
[d] Number of participants with the condition.
[e] Logistic regression model controlled for age, gender, and race.
[f] Logistic regression model controlled for age, gender, race, family history of hearing loss, and noise exposure.

Table B.19 Demographics, cardiovascular disease risk factors, and auditory function in the best ear and the worst ear ***(PTA[a] ≤ 40 vs. > 40 dB hearing level)***

		Hearing					
		PTA ≤ 40 dB HL[b]		**PTA > 40 dB HL**			
	N [c]	n [d]	Mean ± SD or %	n [d]	Mean ± SD or %	P value [e]	P value [f]
Best ear							
n	115	78	67.8	37	32.2		
Hearing level (dB)	115	78	27 ± 9	37	51 ± 7		
Age (years)	115	78	75 ± 8	37	81 ± 6	0.0001	0.0004
Gender (% of female)	115	68	87.2	25	67.6	0.02	0.11
Race (% of Caucasian)	115	44	56.4	31	83.8	0.003	0.02
Body weight (kg)	115	78	79.4 ± 18.9	37	74.1 ± 16.3	0.36	0.22
Body mass index	115	78	29.8 ± 6.6	37	27.2 ± 4.9	0.33	0.25
Education (years)	112	76	9 ± 4	36	9 ± 4	0.19	0.27
Family history of hearing loss (%)	115	12	15.4	12	32.4	0.38	0.31
Number of years exposed to noise (years)	114	77	12 ± 16	37	22 ± 19	0.12	0.10
HDL cholesterol (mmol/L)	115	78	1.53 ± 0.46	37	1.26 ± 0.29	0.02	0.004
LDL cholesterol (mmol/L)	111	76	3.12 ± 0.87	35	3.18 ± 0.75	0.58	0.58
Total cholesterol (mmol/L)	115	78	5.48 ± 1.04	37	5.38 ± 0.86	0.23	0.16
Total cholesterol/ HDL cholesterol ratio	115	78	3.8 ± 1.4	37	4.4 ± 1.1	0.31	0.16
Triglycerides (mmol/L)	115	78	1.87 ± 1.26	37	2.15 ± 1.11	0.31	0.24
Worst ear							
n	112	61	54.5	51	45.5		
Hearing level (dB)	112	61	28 ± 7	51	53 ± 11		
Age (years)	112	61	74 ± 7	51	81 ± 7	< 0.0001	< 0.0001
Gender (% of female)	112	54	88.5	38	74.5	0.04	0.07
Race (% of Caucasian)	112	33	54.1	39	76.5	0.007	0.03
Body weight (kg)	112	61	81.0 ± 19.2	51	73.7 ± 16.3	0.30	0.22
Body mass index	112	61	30.3 ± 6.8	51	27.6 ± 5.2	0.32	0.29
Education (years)	109	60	9 ± 4	49	8 ± 4	0.08	0.08
Family history of hearing loss (%)	112	8	13.1	15	29.4	0.26	0.24
Number of years exposed to noise (years)	111	60	12 ± 17	51	18 ± 19	0.55	0.50
HDL cholesterol (mmol/L)	112	61	1.56 ± 0.47	51	1.32 ± 0.34	0.02	0.009
LDL cholesterol (mmol/L)	108	60	3.09 ± 0.92	48	3.21 ± 0.70	0.53	0.36
Total cholesterol (mmol/L)	112	61	5.45 ± 1.09	51	5.48 ± 0.81	0.28	0.14
Total cholesterol/ HDL cholesterol ratio	112	61	3.7 ± 1.3	51	4.4 ± 1.3	0.15	0.14
Triglycerides (mmol/L)	112	61	1.80 ± 1.25	51	2.17 ± 1.19	0.14	0.13

[a] PTA, pure-tone average threshold of 1, 2, and 4 kHz.
[b] dB HL, hearing level in decibel.
[c] Number of total participants.
[d] Number of participants with the condition.
[e] Logistic regression model controlled for age, gender, and race.
[f] Logistic regression model controlled for age, gender, race, family history of hearing loss, and noise exposure.

APPENDIX C

THE PURPOSE OF APPENDIX C IS TO FURTHER EXAMINE A POSSIBLE RELATIONSHIP OF HEARING IMPAIRMENT WITH MULTIPLE MEASURES OF VITAMIN B_{12} STATUS IN OLDER ADULTS USING TWO DIFFERENT CUTOFFS (25 AND 40 dB HL) IN THE BEST AND THE WORST EAR.

A POSSIBLE RELATIONSHIP OF AGE-RELATED HEARING LOSS WITH MULTIPLE MEASURES OF VITAMIN B_{12} STATUS IN OLDER ADULTS USING THREE DIFFERENT CUTOFFS (20, 25, AND 40 dB HL) IN THE BEST AND THE WORST EAR. PARTICIPANTS WITH CONDUCTIVE HEARING LOSS AND ASYMMETRICAL HEARING LOSS WERE EXCLUDED (TABLES C.1 – C.4).

Table C.1 Characteristics of participants at baseline

	N [a]	**n** [b]	**Mean ± SD or %**
Age (years)	93	93	75 ± 7 (58-92) [c]
Gender	93		
Female (%)		77	82.8
Male (%)		16	17.2
Race	93		
Caucasian (%)		60	64.5
African-American (%)		33	35.5
Hearing level in the best ear (dB)	93	93	31 ± 14 (8-73)
Hearing level in the worst ear (dB)	90	90	34 ± 14 (10-77)
Education (years)	91	91	9 ± 4 (0-16)
Family history of hearing loss (%)	93	19	20.4
Number of years exposed to noise (years)	92	92	15 ± 17 (0-62)
Body mass index (kg/m^2)	93	93	30.2 ± 7.0 (20.0-53.8)
Nutritional Health Score [d]	92	92	5 ± 4 (0-19)
Overall health [e]	93	93	1.6 ± 0.7 (0-3)
Number of medications	93	93	6 ± 3 (0-15)
Impaired cognition (%) [f]	93	27	29.0
Anemic (%) [g]	92	21	22.8
Serum vitamin B_{12} (pmol/L)	93	93	339.9 ± 135.8 (76.5-746.3)
< 148 pmol/L (%)	93	8	8.6
< 185 pmol/L (%)	93	10	10.8
< 221 pmol/L (%)	93	19	20.4
< 258 pmol/L (%)	93	26	28.0
< 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid (%)	93	13	14.0

Serum methylmalonic acid (nmol/L)	93	93	280 ± 251 (104-1972)
> 271 nmol/L (%)	93	29	31.3
> 376 nmol/L (%)	93	12	12.9
Serum total homocysteine (µmol/L)	93	93	10.5 ± 3.8 (5.1-27.0)
> 9.0 µmol/L (%)	93	51	54.8
> 11.0 µmol/L (%)	93	35	37.6
> 13.9 µmol/L (%)	93	11	11.8
Serum folate (nmol/L)	93	93	43.2 ± 26.2 (10.0-163.3)
Cystathionine (nmol/L)	93	93	260 ± 141 (89-968)
2-methylcitric acid (nmol/L)	93	93	184 ± 68 (58-453)
Serum pepsinogen I (ng/mL)	92	92	100.9 ± 76.3 (8.6-549.9)
≤ 20 ng/mL (%)	92	9	9.8
≤ 50 ng/mL (%)	92	22	23.9
Serum creatinine (µmol/L)	92	92	94.0 ± 40.1 (61.9-406.6)
≥ 127 µmol/L (%)	92	10	10.9
Serum albumin (g/L)	92	92	4.1 ± 0.3 (3.4-4.9)
Blood urea nitrogen (mmol/L)	92	92	18 ± 9 (8-79)
Hemoglobin (g/dL)	92	92	13.1 ± 1.3 (9.4-16.8)
Mean cell volume (fl)	92	92	89 ± 5 (68-100)
S-adenosyl-methionine (nmol/L)	92	92	114 ± 67 (42-511)
S-adenosyl-homocysteine (nmol/L)	93	93	34 ± 20 (10-144)
SAM/SAH ratio	92	92	4.0 ± 2.0 (0.9-9.4)
Multivitamin use (%)	93	30	32.3
Synthetic vitamin B_{12} intake (µg/d)	93	93	11.6 ± 62.5 (0.0-600.6)
≥ 2.4 µg/d (%)	93	33	35.5
≥ 6 µg/d (%)	93	30	32.3
≥ 12 µg/d (%)	93	11	11.8
≥ 25 µg/d (%)	93	10	10.8
Synthetic folate intake (µg/d)	93	93	178.6 ± 215.6 (0.0-1000.0)
≥ 400 µg/d (%)	93	25	26.9

[a] Number of total participants.
[b] Number of participants with the condition.
[c] Range in parentheses.
[d] NHS: Nutritional Screening Initiative Questionnaire. Higher number indicates greater nutritional risk.
[e] 0 = poor, 1 = fair, 2 = good, and 3 = excellent. Higher number indicates better health status.
[f] Impaired cognition defined as ≥ 9 on Orientation Memory Concentration test.
[g] Anemic defined as hemoglobin ≤ 12 g/dL for females, ≤ 13 g/dL for males.

Table C.2 Demographics, nutrition and auditory function in the best ear and the worst ear at baseline ***(PTA ≤ 25 vs. > 25 dB hearing level)****

		Hearing						
		Normal (PTA ≤ 25 dB HL)		Impaired (PTA >25 dB HL)				
	N [a]	n [b]	Mean ± SD or %	n [b]	Mean ± SD or %	P value[c]	P value[d]	P value[e]
Best ear								
n	93	43		50				
Hearing level (dB)	93	43	19 ± 4	50	42 ± 11			
Age (years)	93	43	71 ± 6	50	78 ± 7	<0.0001	<0.0001	<0.0001
Gender (% of female)	93	41	95.4	36	72.0	0.004	0.004	0.02
Race (% of Caucasian)	93	24	55.8	36	72.0	0.18	0.19	0.21
Education (years)	91	43	9 ± 3	48	9 ± 4	0.51	0.69	0.68
Family history of hearing loss (%)	93	9	20.9	10	20.0	0.88	0.79	0.70
Number of years exposed to noise (years)	92	42	11 ± 14	50	18 ± 19	0.58	0.55	0.51
Body mass index (kg/m^2)	93	43	31.5 ± 7.7	50	29.0 ± 6.2	0.95	0.69	0.67
Nutritional Health Score [f]	92	43	6 ± 4	49	5 ± 4	0.10	0.13	0.13
Overall health [g]	93	43	1.5 ± 0.7	50	1.6 ± 0.8	0.62	0.77	0.75
Number of medications	93	43	6 ± 3	50	5 ± 3	0.34	0.29	0.25
Impaired cognition (%) [h]	93	9	20.9	18	36.0	0.51	0.35	0.28
Anemic (%) [i]	92	10	23.8	11	22.0	0.17	0.31	0.27
Serum vitamin B_{12} (pmol/L)	93	43	372.4 ± 134.0	50	312.0 ± 132.3	0.09	0.17	0.15
< 148 pmol/L (%)	93	1	2.3	7	14.0	0.25	0.32	0.31
< 185 pmol/L (%)	93	1	2.3	9	18.0	0.10	0.14	0.12
< 221 pmol/L (%)	93	6	14.0	13	26.0	0.16	0.23	0.26
< 258 pmol/L (%)	93	9	20.9	17	34.0	0.18	0.30	0.31
< 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid (%)	93	4	9.3	9	18.0	0.32	0.51	0.54
Serum methylmalonic acid (nmol/L)	93	43	210 ± 91	50	341 ± 321	0.04	0.05	0.04
> 271 nmol/L (%)	93	9	20.9	20	40.0	0.45	0.56	0.50
> 376 nmol/L (%)	93	3	7.0	9	18.0	0.91	0.89	0.85
Serum total homocysteine (µmol/L)	93	43	9.8 ± 3.3	50	11.0 ± 4.1	0.86	0.66	0.57
> 9.0 µmol/L (%)	93	22	51.2	29	58.0	0.70	0.76	0.82
> 11.0 µmol/L (%)	93	13	30.2	22	44.0	0.72	0.54	0.54
> 13.9 µmol/L (%)	93	4	9.3	7	14.0	0.80	0.93	0.85
Serum folate (nmol/L)	93	43	40.9 ± 23.8	50	45.2 ± 28.2	0.29	0.43	0.43
Cystathionine (nmol/L)	93	43	254 ± 156	50	265 ± 128	0.48	0.53	0.59
2-methylcitric acid (nmol/L)	93	43	175 ± 68	50	191 ± 69	0.85	0.75	0.77
Serum pepsinogen I (ng/mL)	92	42	103.6 ± 85.0	50	98.7 ± 69.0	0.27	0.27	0.21
≤ 20 ng/mL (%)	92	1	2.4	8	16.0	0.07	0.08	-
≤ 50 ng/mL (%)	92	9	21.4	13	26.0	0.57	0.46	0.38

Serum creatinine (µmol/L)	92	42	92.0 ± 53.6	50	95.6 ± 24.1	0.73	0.65	0.64
≥ 127 µmol/L (%)	92	3	7.1	7	14.0	0.76	0.76	0.75
Serum albumin (g/L)	92	42	4.1 ± 0.3	50	4.1 ± 0.3	0.69	0.96	0.99
Blood urea nitrogen (mmol/L)	92	42	18 ± 11	50	19 ± 7	0.51	0.22	0.19
Hemoglobin (g/dL)	92	42	12.9 ± 1.3	50	13.2 ± 1.2	0.20	0.37	0.31
Mean cell volume (fl)	92	42	89 ± 6	50	89 ± 5	0.60	0.43	0.44
S-adenosyl-methionine (nmol/L)	92	43	115 ± 76	49	113 ± 57	0.93	0.87	0.89
S-adenosyl-homocysteine (nmol/L)	93	43	33 ± 23	50	34 ± 17	0.78	0.69	0.71
SAM/SAH ratio	92	43	4.0 ± 1.9	49	4.0 ± 2.1	0.87	0.99	0.98
Multivitamin use (%)	93	14	32.6	16	32.0	0.33	0.55	0.53
Synthetic B_{12} intake (µg/d)	93	43	17.3 ± 91.2	50	6.6 ± 12.1	0.86	0.92	0.99
≥ 2.4 µg/d (%)	93	15	34.9	18	36.0	0.84	0.77	0.79
≥ 6 µg/d (%)	93	13	30.2	17	34.0	0.32	0.56	0.52
≥ 12 µg/d (%)	93	4	9.3	7	14.0	0.17	0.23	0.22
≥ 25 µg/d (%)	93	3	7.0	7	14.0	0.12	0.17	0.17
Synthetic folate intake (µg/d)	93	43	188.9 ± 227.0	50	169.8 ± 207.2	0.61	0.24	0.27
≥ 400 µg/d (%)	93	12	27.9	13	26.0	0.96	0.56	0.58
Worst ear								
n	90	33		57				
Hearing level (dB)	90	33	21 ± 4	57	42 ± 12			
Age (years)	90	33	71 ± 5	57	77 ± 7	0.0003	0.0002	0.0003
Gender (% of female)	90	31	93.9	45	79.0	0.05	0.04	0.14
Race (% of Caucasian)	90	18	54.6	39	68.4	0.25	0.26	0.38
Education (years)	88	33	9 ± 3	55	9 ± 4	0.83	0.96	0.97
Family history of hearing loss (%)	90	6	18.2	12	21.1	0.66	0.59	0.77
Number of years exposed to noise (years)	89	32	10 ± 14	57	17 ± 18	0.26	0.24	0.26
Body mass index (kg/m^2)	90	33	31.7 ± 7.7	57	29.6 ± 6.5	0.82	0.78	0.79
Nutritional Health Score [f]	89	33	6 ± 4	56	5 ± 4	0.38	0.48	0.47
Overall health [g]	90	33	1.6 ± 0.7	57	1.6 ± 0.8	0.61	0.42	0.50
Number of medications	90	33	7 ± 3	57	6 ± 3	0.44	0.43	0.37
Impaired cognition (%) [h]	90	6	18.2	20	35.1	0.35	0.27	0.13
Anemic (%) [i]	89	6	18.8	14	24.6	0.85	0.78	0.92
Serum vitamin B_{12} (pmol/L)	90	33	382.6 ± 125.2	57	314.3 ± 138.8	0.08	0.13	0.14
< 148 pmol/L (%)	90	0	0.0	8	14.0	0.02 [j]	-	-
< 185 pmol/L (%)	90	0	0.0	10	17.5	0.01 [j]	-	-
< 221 pmol/L (%)	90	3	9.1	16	28.1	0.05	0.08	0.10
< 258 pmol/L (%)	90	5	15.2	21	36.8	0.04	0.07	0.09
< 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid (%)	90	0	0.0	13	22.8	0.002 [j]	-	-
Serum methylmalonic acid (nmol/L)	90	33	193 ± 70	57	329 ± 306	0.01	0.009	0.005
> 271 nmol/L (%)	90	4	12.1	23	40.4	0.05	0.05	0.02
> 376 nmol/L (%)	90	1	3.0	10	17.5	0.36	0.24	0.22

Serum total homocysteine (µmol/L)	90	33	9.8 ± 3.6	57	10.8 ± 3.9	0.81	0.49	0.47
> 9.0 µmol/L (%)	90	15	45.5	34	59.7	0.50	0.37	0.36
> 11.0 µmol/L (%)	90	11	33.3	23	40.4	0.81	0.99	0.92
> 13.9 µmol/L (%)	90	4	12.1	6	10.5	0.34	0.54	0.71
Serum folate (nmol/L)	90	33	42.7 ± 24.8	57	42.9 ± 26.9	0.92	0.67	0.80
Cystathionine (nmol/L)	90	33	258 ± 167	57	262 ± 128	0.45	0.69	0.79
2-methylcitric acid (nmol/L)	90	33	174 ± 72	57	191 ± 67	0.98	0.90	0.87
Serum pepsinogen I (ng/mL)	89	33	106.4 ± 94.5	56	96.9 ± 63.8	0.53	0.60	0.41
≤ 20 ng/mL (%)	89	1	3.0	7	12.5	0.24	0.29	-
≤ 50 ng/mL (%)	89	9	27.3	12	21.4	0.42	0.49	0.67
Serum creatinine (µmol/L)	89	32	93.9 ± 60.9	57	93.8 ± 23.4	0.69	0.62	0.57
≥ 127 µmol/L (%)	89	3	9.4	7	12.3	0.79	0.79	0.75
Serum albumin (g/L)	89	32	4.1 ± 0.2	57	4.1 ± 0.3	0.63	0.78	0.91
Blood urea nitrogen (mmol/L)	89	32	19 ± 13	57	18 ± 7	0.98	0.54	0.47
Hemoglobin (g/dL)	89	32	13.1 ± 1.3	57	13.0 ± 1.3	0.99	0.58	0.74
Mean cell volume (fl)	89	32	90 ± 4	57	89 ± 6	0.47	0.35	0.39
S-adenosyl-methionine (nmol/L)	89	33	119 ± 86	56	112 ± 54	0.75	0.79	0.81
S-adenosyl-homocysteine (nmol/L)	90	33	33 ± 25	57	34 ± 16	0.59	0.40	0.45
SAM/SAH ratio	89	33	4.1 ± 1.9	56	3.9 ± 2.1	0.72	0.60	0.63
Multivitamin use (%)	90	12	36.4	17	29.8	0.87	0.76	0.81
Synthetic B_{12} intake (µg/d)	90	33	21.9 ± 104.1	57	6.1 ± 11.4	0.62	0.66	0.63
≥ 2.4 µg/d (%)	90	11	33.3	21	36.8	0.59	0.97	0.87
≥ 6 µg/d (%)	90	11	33.3	18	31.6	0.74	0.88	0.97
≥ 12 µg/d (%)	90	4	12.1	7	12.3	0.69	0.79	0.84
≥ 25 µg/d (%)	90	3	9.1	7	12.3	0.48	0.61	0.68
Synthetic folate intake (µg/d)	90	33	196.3 ± 241.0	57	168.8 ± 203.0	0.48	0.15	0.20
≥ 400 µg/d (%)	90	10	30.3	14	24.6	0.65	0.30	0.37

* PTA, pure-tone average threshold of 1, 2, and 4 kHz.
[a] Number of total participants.
[b] Number of participants with the condition.
[c] Logistic regression model adjusted for age and gender.
[d] Logistic regression model adjusted for age, gender, race, and creatinine.
[e] Logistic regression model adjusted for age, gender, race, creatinine, family history of hearing loss, and noise exposure.
[f] NHS: Nutritional Screening Initiative Questionnaire. Higher number indicates greater nutritional risk.
[g] 0 = poor, 1 = fair, 2 = good, and 3 = excellent. Higher number indicates better health status.
[h] Impaired cognition defined as ≥ 9 on Orientation Memory Concentration test.
[i] Anemic defined as hemoglobin ≤ 12 g/dL for females, ≤ 13 g/dL for males.
[j] Chi-square analyses.
- Not applicable. There was possibly a quasi-complete separation of data points.

Table C.3 Demographics, nutrition and auditory function in the best ear and the worst ear at baseline ***(PTA ≤ 40 vs. > 40 dB hearing level)****

		Hearing						
		PTA ≤ 40 dB HL		PTA > 40 dB HL				
	N [a]	n [b]	Mean ± SD or %	n [b]	Mean ± SD or %	P value[c]	P value[d]	P value[e]
Best ear								
n	93	71		22				
Hearing level (dB)	93	71	25 ± 8	22	52 ± 9			
Age (years)	93	71	73 ± 7	22	79 ± 7	0.001	0.002	0.001
Gender (% of female)	93	65	91.6	12	54.6	0.0003	0.0008	0.0009
Race (% of Caucasian)	93	42	59.2	18	81.8	0.10	0.09	0.18
Education (years)	91	70	9 ± 4	21	9 ± 4	0.66	0.75	0.90
Family history of hearing loss (%)	93	12	16.9	7	31.8	0.17	0.28	0.35
Number of years exposed to noise (years)	92	70	12 ± 14	22	25 ± 22	0.09	0.09	0.11
Body mass index (kg/m^2)	93	71	30.7 ± 7.2	22	28.5 ± 6.3	0.74	0.57	0.63
Nutritional Health Score [f]	92	70	5 ± 4	22	5 ± 4	0.92	0.95	0.95
Overall health [g]	93	71	1.6 ± 0.8	22	1.5 ± 0.7	0.47	0.31	0.48
Number of medications	93	71	6 ± 3	22	6 ± 3	0.76	0.80	0.87
Impaired cognition (%) [h]	93	18	25.4	9	40.9	0.45	0.20	0.15
Anemic (%) [i]	92	17	24.3	4	18.2	0.08	0.18	0.15
Serum vitamin B_{12} (pmol/L)	93	71	345.7 ± 133.0	22	321.4 ± 146.0	0.88	0.76	0.60
< 148 pmol/L (%)	93	5	7.0	3	13.6	0.89	0.77	0.76
< 185 pmol/L (%)	93	6	8.5	4	18.2	0.83	0.86	0.92
< 221 pmol/L (%)	93	13	18.3	6	27.3	0.53	0.61	0.77
< 258 pmol/L (%)	93	19	26.8	7	31.8	0.96	0.92	0.82
< 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid (%)	93	8	11.3	5	22.7	0.24	0.37	0.56
Serum methylmalonic acid (nmol/L)	93	71	234 ± 109	22	428 ± 454	0.17	0.23	0.29
> 271 nmol/L (%)	93	17	23.9	12	54.6	0.13	0.18	0.20
> 376 nmol/L (%)	93	7	9.9	5	22.7	0.53	0.31	0.29
Serum total homocysteine (µmol/L)	93	71	10.2 ± 3.6	22	11.2 ± 4.4	0.50	0.66	0.74
> 9.0 µmol/L (%)	93	37	52.1	14	63.6	0.76	0.92	0.76
> 11.0 µmol/L (%)	93	26	36.6	9	40.9	0.29	0.56	0.48
> 13.9 µmol/L (%)	93	8	11.3	3	13.6	0.37	0.47	0.67
Serum folate (nmol/L)	93	71	42.5 ± 23.5	22	45.4 ± 34.1	0.56	0.99	0.69
Cystathionine (nmol/L)	93	71	254 ± 138	22	278 ± 149	0.42	0.33	0.19
2-methylcitric acid (nmol/L)	93	71	182 ± 68	22	189 ± 72	0.37	0.24	0.21
Serum pepsinogen I (ng/mL)	92	70	100.1 ± 75.3	22	103.6 ± 81.2	0.52	0.52	0.29
≤ 20 ng/mL (%)	92	6	8.6	3	13.6	0.57	0.61	0.50
≤ 50 ng/mL (%)	92	17	24.3	5	22.7	0.90	0.99	0.73
Serum creatinine (µmol/L)	92	70	92.6 ± 44.4	22	98.4 ± 21.4	0.71	0.58	0.57

≥ 127 µmol/L (%)	92	7	10.0	3	13.6	0.25	0.22	0.18
Serum albumin (g/L)	92	70	4.1 ± 0.3	22	4.1 ± 0.2	0.74	0.35	0.30
Blood urea nitrogen (mmol/L)	92	70	18 ± 10	22	19 ± 7	0.83	0.60	0.70
Hemoglobin (g/dL)	92	70	13.0 ± 1.3	22	13.4 ± 1.2	0.21	0.42	0.35
Mean cell volume (fl)	92	70	90 ± 5	22	89 ± 6	0.33	0.16	0.21
S-adenosyl-methionine (nmol/L)	92	71	113 ± 67	21	119 ± 67	0.79	0.95	0.92
S-adenosyl-homocysteine (nmol/L)	93	71	34 ± 20	22	33 ± 18	0.23	0.15	0.16
SAM/SAH ratio	92	71	3.9 ± 2.1	21	4.3 ± 1.7	0.16	0.27	0.37
Multivitamin use (%)	93	24	33.8	6	27.3	0.90	0.76	0.79
Synthetic B_{12} intake (µg/d)	93	71	12.7 ± 71.3	22	7.8 ± 13.1	0.76	0.68	0.69
≥ 2.4 µg/d (%)	93	24	33.8	9	40.9	0.80	0.72	0.99
≥ 6 µg/d (%)	93	22	31.0	8	36.4	0.66	0.94	0.73
≥ 12 µg/d (%)	93	7	9.9	4	18.2	0.06	0.10	0.11
≥ 25 µg/d (%)	93	6	8.5	4	18.2	0.05	0.10	0.10
Synthetic folate intake (µg/d)	93	71	174.2 ± 216.8	22	193.0 ± 216.1	0.64	0.81	0.97
≥ 400 µg/d (%)	93	18	25.4	7	31.8	0.51	0.96	0.71
Worst ear								
n	90	60		30				
Hearing level (dB)	90	60	26 ± 7	31	51 ± 9			
Age (years)	90	60	73 ± 6	30	79 ± 8	0.0002	0.0002	0.0002
Gender (% of female)	90	57	95.0	19	63.3	0.0002	0.0003	0.001
Race (% of Caucasian)	90	36	60.0	21	70.0	0.47	0.47	0.70
Education (years)	88	59	9 ± 3	29	9 ± 4	0.61	0.41	0.41
Family history of hearing loss (%)	90	10	16.7	8	26.7	0.16	0.17	0.19
Number of years exposed to noise (years)	89	59	12 ± 14	30	19 ± 19	0.68	0.66	0.75
Body mass index (kg/m^2)	90	60	31.0 ± 7.3	30	29.3 ± 6.3	0.60	0.45	0.52
Nutritional Health Score [f]	89	60	6 ± 4	29	5 ± 4	0.34	0.37	0.42
Overall health [g]	90	60	1.6 ± 0.8	30	1.5 ± 0.7	0.59	0.50	0.57
Number of medications	90	60	6 ± 3	30	6 ± 3	0.75	0.74	0.82
Impaired cognition (%) [h]	90	13	21.7	13	43.3	0.13	0.09	0.05
Anemic (%) [i]	89	13	22.0	7	23.3	0.38	0.52	0.47
Serum vitamin B_{12} (pmol/L)	90	60	348.9 ± 127.5	30	320.1 ± 155.6	0.86	0.99	0.81
< 148 pmol/L (%)	90	2	3.3	6	20.0	0.13	0.14	0.17
< 185 pmol/L (%)	90	3	5.0	7	23.3	0.12	0.14	0.20
< 221 pmol/L (%)	90	10	16.7	9	30.0	0.24	0.28	0.35
< 258 pmol/L (%)	90	15	25.0	11	36.7	0.50	0.59	0.68
< 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid (%)	90	6	10.0	7	23.3	0.13	0.17	0.25
Serum methylmalonic acid (nmol/L)	90	60	223 ± 91	30	390 ± 403	0.12	0.10	0.10
> 271 nmol/L (%)	90	13	21.7	14	46.7	0.10	0.10	0.07
> 376 nmol/L (%)	90	5	8.3	6	20.0	0.78	0.72	0.75
Serum total homocysteine (µmol/L)	90	60	10.0 ± 3.3	30	11.3 ± 4.6	0.81	0.92	0.74

> 9.0 µmol/L (%)	90	30	50.0	19	63.3	0.87	0.97	0.97
> 11.0 µmol/L (%)	90	21	35.0	13	43.3	0.47	0.57	0.47
> 13.9 µmol/L (%)	90	6	10.0	4	13.3	0.59	0.70	0.75
Serum folate (nmol/L)	90	60	41.6 ± 23.8	30	45.2 ± 30.4	0.17	0.22	0.10
Cystathionine (nmol/L)	90	60	251 ± 139	30	279 ± 150	0.42	0.37	0.30
2-methylcitric acid (nmol/L)	90	60	182 ± 68	30	191 ± 72	0.23	0.13	0.11
Serum pepsinogen I (ng/mL)	89	59	104.3 ± 77.1	30	92.9 ± 75.2	0.08	0.07	0.04
≤ 20 ng/mL (%)	89	3	5.1	5	16.7	0.08	0.09	0.07
≤ 50 ng/mL (%)	89	12	20.3	9	30.0	0.23	0.18	0.14
Serum creatinine (µmol/L)	89	59	91.5 ± 47.4	30	98.4 ± 22.5	0.98	0.91	0.90
≥ 127 µmol/L (%)	89	5	8.7	5	16.7	0.68	0.66	0.57
Serum albumin (g/L)	89	59	4.1 ± 0.3	30	4.0 ± 0.3	0.53	0.37	0.32
Blood urea nitrogen (mmol/L)	89	59	18 ± 10	30	19 ± 6	0.79	0.60	0.62
Hemoglobin (g/dL)	89	59	13.1 ± 1.4	30	13.1 ± 1.2	0.56	0.38	0.49
Mean cell volume (fl)	89	59	89 ± 5	30	89 ± 6	0.44	0.35	0.39
S-adenosyl-methionine (nmol/L)	89	60	114 ± 71	29	115 ± 60	0.80	0.76	0.84
S-adenosyl-homocysteine (nmol/L)	90	60	33 ± 21	30	36 ± 19	0.45	0.36	0.30
SAM/SAH ratio	89	60	4.1 ± 2.1	29	3.8 ± 1.7	0.56	0.49	0.33
Multivitamin use (%)	90	20	33.3	9	30.0	0.42	0.55	0.56
Synthetic B_{12} intake (µg/d)	90	60	13.8 ± 77.4	30	8.1 ± 12.6	0.76	0.73	0.93
≥ 2.4 µg/d (%)	90	19	31.7	13	43.3	0.23	0.34	0.24
≥ 6 µg/d (%)	90	17	28.3	12	40.0	0.09	0.12	0.09
≥ 12 µg/d (%)	90	5	8.3	6	20.0	0.02	0.02	0.03
≥ 25 µg/d (%)	90	4	6.7	6	20.0	0.02	0.02	0.02
Synthetic folate intake (µg/d)	90	60	177.3 ± 216.8	30	182.0 ± 220.4	0.79	0.94	0.98
≥ 400 µg/d (%)	90	16	26.7	8	26.7	0.78	0.99	0.95

* PTA, pure-tone average threshold of 1, 2, and 4 kHz.
[a] Number of total participants.
[b] Number of participants with the condition.
[c] Logistic regression model adjusted for age and gender.
[d] Logistic regression model adjusted for age, gender, race, and creatinine.
[e] Logistic regression model adjusted for age, gender, race, creatinine, family history of hearing loss, and noise exposure.
[f] NHS: Nutritional Screening Initiative Questionnaire. Higher number indicates greater nutritional risk.
[g] 0 = poor, 1 = fair, 2 = good, and 3 = excellent. Higher number indicates better health status.
[h] Impaired cognition defined as ≥ 9 on Orientation Memory Concentration test.
[i] Anemic defined as hemoglobin ≤ 12 g/dL for females, ≤ 13 g/dL for males.

Table C.4 Demographics, nutrition and auditory function in the best ear and the worst ear at baseline ***(PTA ≤ 20 vs. > 20 dB hearing level)****

		Hearing						
		Normal (PTA ≤ 20 dB HL)		Impaired (PTA > 20 dB HL)				
	N [a]	n [b]	Mean ± SD or %	n [b]	Mean ± SD or %	P value[c]	P value[d]	P value[e]
Best ear								
n	93	26		67				
Hearing level (dB)	93	26	17 ± 3	67	37 ± 13			
Age (years)	93	26	70 ± 5	67	77 ± 7	0.0002	0.0002	0.0001
Gender (% of female)	93	24	92.3	53	79.1	0.13	0.08	0.09
Race (% of Caucasian)	93	15	57.7	45	67.2	0.60	0.41	0.33
Education (years)	91	26	9 ± 3	65	9 ± 4	0.79	0.94	0.76
Family history of hearing loss (%)	93	5	19.2	14	20.9	0.87	0.87	0.93
Number of years exposed to noise (years)	92	26	13 ± 14	66	16 ± 18	0.91	0.84	086
Body mass index (kg/m^2)	93	26	31.0 ± 6.9	67	29.9 ± 7.0	0.57	0.79	0.81
Nutritional Health Score [f]	92	26	6 ± 4	66	5 ± 3	0.22	0.24	0.23
Overall health [g]	93	26	1.5 ± 0.7	67	1.6 ± 0.8	0.42	0.81	0.89
Number of medications	93	26	6 ± 4	67	6 ± 3	0.67	0.61	0.57
Impaired cognition (%) [h]	93	7	26.9	20	29.9	0.45	0.48	0.33
Anemic (%) [i]	92	6	23.1	15	22.7	0.28	0.58	0.64
Serum vitamin B$_{12}$ (pmol/L)	93	26	400.8 ± 137.4	67	316.3 ± 128.5	0.03	0.05	0.06
< 148 pmol/L (%)	93	0	0.0	8	11.9	0.10 [j]	-	-
< 185 pmol/L (%)	93	0	0.0	10	14.9	0.06 [j]	-	-
< 221 pmol/L (%)	93	3	11.5	16	23.9	0.23	0.29	0.26
< 258 pmol/L (%)	93	4	15.4	22	32.8	0.09	0.14	0.12
< 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid (%)	93	1	3.9	12	17.9	0.16	0.19	0.17
Serum methylmalonic acid (nmol/L)	93	26	202 ± 76	67	310 ± 287	0.30	0.09	0.12
> 271 nmol/L (%)	93	5	19.2	24	35.8	0.77	0.54	0.75
> 376 nmol/L (%)	93	1	3.9	11	16.4	0.67	0.29	0.30
Serum total homocysteine (µmol/L)	93	26	9.8 ± 3.7	67	10.7 ± 3.8	0.76	0.15	0.16
> 9.0 µmol/L (%)	93	13	50.0	38	56.7	0.99	0.53	0.61
> 11.0 µmol/L (%)	93	9	34.6	26	38.8	0.68	0.78	0.73
> 13.9 µmol/L (%)	93	3	11.5	8	11.9	0.54	0.69	0.73
Serum folate (nmol/L)	93	26	41.1 ± 26.2	67	44.0 ± 26.4	0.62	0.49	0.50
Cystathionine (nmol/L)	93	26	257 ± 186	67	260 ± 120	0.79	0.50	0.63
2-methylcitric acid (nmol/L)	93	26	183 ± 82	67	184 ± 63	0.31	0.80	0.67
Serum pepsinogen I (ng/mL)	92	25	116.4 ± 103.4	67	95.2 ± 63.4	0.15	0.41	0.55
≤ 20 ng/mL (%)	92	0	0.0	9	13.4	0.11 [j]	-	-
≤ 50 ng/mL (%)	92	5	20.0	17	25.4	0.67	0.99	0.84

Serum creatinine (µmol/L)	92	26	98.6 ± 66.7	66	92.2 ± 23.1	0.19	0.17	0.19
≥ 127 µmol/L (%)	92	3	11.5	7	10.6	0.51	0.52	0.54
Serum albumin (g/L)	92	26	4.1 ± 0.3	66	4.1 ± 0.3	0.13	0.12	0.10
Blood urea nitrogen (mmol/L)	92	26	19 ± 14	66	18 ± 7	0.93	0.23	0.27
Hemoglobin (g/dL)	92	26	13.0 ± 1.6	66	13.1 ± 1.2	0.32	0.67	0.79
Mean cell volume (fl)	92	26	89 ± 6	66	89 ± 5	0.99	0.85	0.87
S-adenosyl-methionine (nmol/L)	92	26	120 ± 91	66	112 ± 54	0.64	0.79	0.78
S-adenosyl-homocysteine (nmol/L)	93	26	35 ± 28	67	33 ± 16	0.88	0.44	0.42
SAM/SAH ratio	92	26	3.9 ± 1.6	66	4.0 ± 2.1	0.64	0.84	0.84
Multivitamin use (%)	93	10	38.5	20	29.9	0.94	0.70	0.75
Synthetic B_{12} intake (µg/d)	93	26	26.5 ± 117.2	67	5.6 ± 10.9	0.53	0.59	0.59
≥ 2.4 µg/d (%)	93	10	38.5	23	34.3	0.83	0.57	0.59
≥ 6 µg/d (%)	93	9	34.6	21	31.3	0.83	0.92	0.96
≥ 12 µg/d (%)	93	3	11.5	8	11.9	0.60	0.60	0.56
≥ 25 µg/d (%)	93	2	7.7	8	11.9	0.34	0.38	0.34
Synthetic folate intake (µg/d)	93	26	175.3 ± 195.6	67	179.9 ± 224.2	0.97	0.71	0.72
≥ 400 µg/d (%)	93	7	26.9	18	26.9	0.88	0.85	0.85
Worst ear								
n	90	14		76				
Hearing level (dB)	90	14	18 ± 3	76	37 ± 13			
Age (years)	90	14	69 ± 4	76	76 ± 7	<0.0001 [k]	-	-
Gender (% of female)	90	14	100.0	62	81.6	0.11 [j]	-	-
Race (% of Caucasian)	90	9	64.3	48	63.2	0.94 [j]	-	-
Education (years)	88	14	11 ± 3	74	9 ± 4	0.11 [k]	-	-
Family history of hearing loss (%)	90	2	14.3	16	21.1	0.72 [j]	-	-
Number of years exposed to noise (years)	89	14	10 ± 15	75	15 ± 17	0.29 [k]	-	-
Body mass index (kg/m^2)	90	14	31.2 ± 7.7	76	30.3 ± 6.9	0.65 [k]	-	-
Nutritional Health Score [f]	89	14	4 ± 3	75	5 ± 4	0.25 [k]	-	-
Overall health [g]	90	14	1.7 ± 0.6	76	1.6 ± 0.8	0.46 [k]	-	-
Number of medications	90	14	5 ± 3	76	6 ± 3	0.27 [k]	-	-
Impaired cognition (%) [h]	90	2	14.3	24	31.6	0.34 [j]	-	-
Anemic (%) [i]	89	3	21.4	17	22.7	1.0 [j]	-	-
Serum vitamin B_{12} (pmol/L)	90	14	388.3 ± 127.0	76	330.3 ± 138.0	0.15 [k]	-	-
< 148 pmol/L (%)	90	0	0.0	8	10.5	0.35 [j]	-	-
< 185 pmol/L (%)	90	0	0.0	10	13.2	0.35 [j]	-	-
< 221 pmol/L (%)	90	2	14.3	17	22.4	0.73 [j]	-	-
< 258 pmol/L (%)	90	3	21.4	23	30.3	0.75 [j]	-	-
< 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid (%)	90	0	0.0	13	17.1	0.21 [j]	-	-
Serum methylmalonic acid (nmol/L)	90	14	187 ± 73	76	296 ± 272	0.003 [l]	-	-
> 271 nmol/L (%)	90	1	7.1	26	34.2	0.06 [j]	-	-
> 376 nmol/L (%)	90	1	7.1	10	13.2	1.0 [j]	-	-

Serum total homocysteine (µmol/L)	90	14	9.4 ± 4.6	76	10.6 ± 3.6	0.05 [l]	-	-
> 9.0 µmol/L (%)	90	5	35.7	44	57.9	0.13 [j]	-	-
> 11.0 µmol/L (%)	90	4	28.6	30	39.5	0.44 [j]	-	-
> 13.9 µmol/L (%)	90	2	14.3	8	10.5	0.65 [j]	-	-
Serum folate (nmol/L)	90	14	43.7 ± 28.6	76	42.6 ± 25.7	0.99 [l]	-	-
Cystathionine (nmol/L)	90	14	262 ± 231	76	260 ± 122	0.15 [l]	-	-
2-methylcitric acid (nmol/L)	90	14	180 ± 96	76	186 ± 64	0.13 [l]	-	-
Serum pepsinogen I (ng/mL)	89	14	136.3 ± 132.8	75	93.7 ± 59.3	0.40 [l]	-	-
≤ 20 ng/mL (%)	89	0	0.0	8	10.7	0.35 [j]	-	-
≤ 50 ng/mL (%)	89	3	21.4	18	24.0	1.0 [j]	-	-
Serum creatinine (µmol/L)	89	14	102.9 ± 89.3	75	92.2 ± 23.4	0.15 [l]	-	-
≥ 127 µmol/L (%)	89	2	14.3	8	10.7	0.65 [j]	-	-
Serum albumin (g/L)	89	14	4.2 ± 0.3	75	4.1 ± 0.3	0.38 [k]	-	-
Blood urea nitrogen (mmol/L)	89	14	21 ± 18	75	18 ± 6	0.45 [l]	-	-
Hemoglobin (g/dL)	89	14	13.1 ± 1.6	75	13.1 ± 1.3	0.98 [k]	-	-
Mean cell volume (fl)	89	14	89 ± 4	75	89 ± 6	0.95 [l]	-	-
S-adenosyl-methionine (nmol/L)	89	14	119 ± 115	75	113 ± 56	0.22 [l]	-	-
S-adenosyl-homocysteine (nmol/L)	90	14	35 ± 35	76	34 ± 16	0.16 [l]	-	-
SAM/SAH ratio	89	14	4.0 ± 1.3	75	4.0 ± 2.1	0.98 [k]	-	-
Multivitamin use (%)	90	7	50.0	22	29.0	0.13 [j]	-	-
Synthetic B_{12} intake (µg/d)	90	14	45.5 ± 159.8	76	5.7 ± 10.6	0.89 [l]	-	-
≥ 2.4 µg/d (%)	90	6	42.9	26	34.2	0.56 [j]	-	-
≥ 6 µg/d (%)	90	6	42.9	23	30.3	0.37 [j]	-	-
≥ 12 µg/d (%)	90	1	7.1	10	13.2	1.0 [j]	-	-
≥ 25 µg/d (%)	90	1	7.1	9	11.8	1.0 [j]	-	-
Synthetic folate intake (µg/d)	90	14	199.2 ± 216.8	76	175.1 ± 218.0	0.76 [k]	-	-
≥ 400 µg/d (%)	90	5	35.7	19	25.0	0.51 [j]	-	-

* PTA, pure-tone average threshold of 1, 2, and 4 kHz.
[a] Number of total participants.
[b] Number of participants with the condition.
[c] Logistic regression model adjusted for age and gender.
[d] Logistic regression model adjusted for age, gender, race, and creatinine.
[e] Logistic regression model adjusted for age, gender, race, creatinine, family history of hearing loss, and noise exposure.
[f] NHS: Nutritional Screening Initiative Questionnaire. Higher number indicates greater nutritional risk.
[g] 0 = poor, 1 = fair, 2 = good, and 3 = excellent. Higher number indicates better health status.
[h] Impaired cognition defined as ≥ 9 on Orientation Memory Concentration test.
[i] Anemic defined as hemoglobin ≤ 12 g/dL for females, ≤ 13 g/dL for males.
[j] Chi-square analyses.
[k] Independent-sample *t* test.
[l] Wilcoxon-Mann-Whitney test.
- Not applicable. There was possibly a quasi-complete separation of data points.

A POSSIBLE RELATIONSHIP OF HEARING IMPAIRMENT WITH MULTIPLE MEASURES OF VITAMIN B_{12} STATUS WAS EXAMINED IN OLDER ADULTS. PARTICIPANTS WITH CONDUCTIVE HEARING LOSS, ASYMMETRICAL HEARING LOSS, AND HIGH VITAMIN B_{12} CONCENTRATIONS WERE INCLUDED (TABLES C.5 - C.8).

Table C.5 Characteristics of participants at baseline

	N [a]	n [b]	Mean ± SD or %
Age (years)	147	147	76 ± 8 (58-97) [c]
Gender	147		
Female (%)		120	81.6
Male (%)		27	18.4
Race	147		
Caucasian (%)		103	70.1
African-American (%)		44	29.9
Hearing level in the best ear (dB)	147	147	34 ± 14 (8-73)
Hearing level in the worst ear (dB)	143	143	38 ± 15 (10-83)
Family history of hearing loss (%)	147	37	25.2
Education (years)	144	144	9 ± 4 (0-18)
Number of years exposed to noise (years)	146	146	15 ± 18 (0-83)
Body mass index (kg/m^2)	147	147	29.3 ± 6.4 (15.2-53.8)
Nutritional Health Score [d]	146	146	5 ± 3
Overall health [e]	147	147	1.7 ± 0.8 (0-3)
Number of medications	147	147	6 ± 4 (0-15)
Impaired cognition (%) [f]	147	39	26.5
Anemic (%) [g]	146	31	21.2
Serum vitamin B_{12} (pmol/L)	147	147	364.1 ± 161.2 (74.3-992.6)
< 148 pmol/L (%)	147	11	7.5
< 185 pmol/L (%)	147	15	10.2
< 221 pmol/L (%)	147	26	17.7
< 258 pmol/L (%)	147	38	25.9
< 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid (%)	147	17	11.6
Serum methylmalonic acid (nmol/L)	147	147	270 ± 213 (85-1972)
> 271 nmol/L (%)	147	43	29.3
> 376 nmol/L (%)	147	18	12.2
Serum total homocysteine (µmol/L)	147	147	10.6 ± 4.2 (5.1-39.5)
> 9.0 µmol/L (%)	147	87	59.2
> 11.0 µmol/L (%)	147	52	35.4
> 13.9 µmol/L (%)	147	19	12.9
Serum folate (nmol/L)	147	147	45.6 ± 26.6 (8.8-163.3)
Cystathionine (nmol/L)	147	147	258 ± 129 (89-968)
2-methylcitric acid (nmol/L)	147	147	187 ± 66 (58-453)
Serum pepsinogen I (ng/mL)	145	145	100.0 ± 70.9 (8.6-549.9)
≤ 20 ng/mL (%)	145	13	9.0

≤ 50 ng/mL (%)	145	33	22.8
Serum creatinine (µmol/L)	146	146	95.5 ± 42.5 (53.0-406.4)
≥ 127 µmol/L (%)	146	17	11.6
Serum albumin (g/L)	146	146	4.1 ± 0.3 (3.4-4.9)
Blood urea nitrogen (mmol/L)	146	146	19 ± 8 (8-79)
Hemoglobin (g/dL)	146	146	13.2 ± 1.3 (9.4-17.3)
Mean cell volume (fl)	146	146	91 ± 5 (68-107)
S-adenosyl-methionine (nmol/L)	146	146	117 ± 60 (42-511)
S-adenosyl-homocysteine (nmol/L)	147	147	34 ± 21 (9-157)
SAM/SAH ratio	146	146	4.0 ± 2.0 (0.9-9.6)
Multivitamin use (%)	147	59	40.1
Synthetic vitamin B_{12} intake (µg/d)	147	147	13.3 ± 54.8 (0.0-600.6)
≥ 2.4 µg/d (%)	147	66	44.9
≥ 6 µg/d (%)	147	63	42.9
≥ 12 µg/d (%)	147	29	19.7
≥ 25 µg/d (%)	147	24	16.3
Synthetic folate intake (µg/d)	147	147	224.7 ± 241.9 (0.0-1200.0)
≥ 400 µg/d (%)	147	55	37.4

[a] Number of total participants.
[b] Number of participants with the condition.
[c] Range in parentheses.
[d] NHS: Nutritional Screening Initiative Questionnaire. Higher number indicates greater nutritional risk.
[e] 0 = poor, 1 = fair, 2 = good, and 3 = excellent. Higher number indicates better health status.
[f] Impaired cognition defined as ≥ 9 on Orientation Memory Concentration test.
[g] Anemic defined as hemoglobin ≤ 12 g/dL for females, ≤ 13 g/dL for males.

Table C.6 Correlations of vitamin B_{12}, methylmalonic acid, and total homocysteine with pure-tone average (1, 2, and 4 kHz) in the best ear and the worst ear at baseline [a]

	Pure-tone average threshold in the best ear (N=145) [b]	**Pure-tone average threshold in the worst ear (N=141)** [b]
Vitamin B_{12}	r = 0.10	r = 0.07
	P = 0.25	*P* = 0.43
Methylmalonic acid	r = -0.03	r = 0.02
	P = 0.75	*P* = 0.78
Total homocysteine	r = -0.08	r = -0.08
	P = 0.37	*P* = 0.36

[a] Partial Spearman correlation coefficient from multivariable linear regression analysis; adjusted for age, gender, race, creatinine, family history of hearing loss, and noise exposure.
[b] Number of total participants.

Table C.7 Demographics, nutrition and auditory function in the best ear and the worst ear at baseline ***(PTA ≤ 25 vs. > 25 dB hearing level)****

		Hearing						
		Normal (PTA ≤ 25 dB HL)		Impaired (PTA >25 dB HL)				
	N [a]	n [b]	Mean ± SD or %	n [b]	Mean ± SD or %	P value[c]	P value[d]	P value[e]
Best ear								
n	147	54		93				
Hearing level (dB)	147	54	19 ± 4	93	43 ± 11			
Age (years)	147	54	72 ± 6	93	79 ± 7	<0.0001	<0.0001	<0.0001
Gender (% of female)	147	50	92.6	70	75.3	0.002	0.002	0.01
Race (% of Caucasian)	147	34	63.0	69	74.2	0.19	0.22	0.32
Education (years)	144	54	9 ± 3	90	9 ± 4	0.65	0.88	0.66
Family history of hearing loss (%)	147	11	20.4	26	28.0	0.44	0.53	0.65
Number of years exposure to noise (years)	146	53	11 ± 14	93	18 ± 20	0.11	0.10	0.11
Body mass index (kg/m^2)	147	54	30.8 ± 7.5	93	28.5 ± 5.5	0.61	0.99	0.95
Nutritional Health Score [f]	146	54	6 ± 4	92	4 ± 3	0.04	0.06	0.05
Overall health [g]	147	54	1.6 ± 0.8	93	1.7 ± 0.8	0.69	0.92	0.73
Number of medications	147	54	6 ± 4	93	6 ± 3	0.98	0.98	0.85
Impaired cognition (%) [h]	147	12	22.2	27	29.0	0.91	0.91	0.66
Anemic (%) [i]	146	12	22.6	19	20.4	0.11	0.19	0.14
Serum vitamin B_{12} (pmol/L)	147	54	383.7 ± 179.2	93	352.7 ± 149.6	0.15	0.22	0.32
< 148 pmol/L (%)	147	3	5.6	8	8.6	0.87	0.96	0.93
< 185 pmol/L (%)	147	3	5.6	12	12.9	0.38	0.50	0.52
< 221 pmol/L (%)	147	8	14.8	18	19.4	0.39	0.52	0.62
< 258 pmol/L (%)	147	12	22.2	26	28.0	0.39	0.58	0.63
< 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid (%)	147	5	9.3	12	12.9	0.57	0.76	0.97
Serum methylmalonic acid (nmol/L)	147	54	219 ± 90	93	299 ± 254	0.34	0.47	0.52
> 271 nmol/L (%)	147	12	22.2	31	33.3	0.95	0.89	0.88
> 376 nmol/L (%)	147	4	7.4	14	15.1	0.90	0.87	0.81
Serum total homocysteine (µmol/L)	147	54	9.7 ± 3.0	93	11.1 ± 4.7	0.78	0.48	0.52
> 9.0 µmol/L (%)	147	29	53.7	58	62.4	0.58	0.70	0.71
> 11.0 µmol/L (%)	147	15	27.8	37	39.8	0.45	0.26	0.30
> 13.9 µmol/L (%)	147	4	7.4	15	16.1	0.80	0.46	0.36
Serum folate (nmol/L)	147	54	43.2 ± 25.4	93	47.0 ± 27.3	0.46	0.65	0.40
Cystathionine (nmol/L)	147	54	248 ± 145	93	264 ± 118	0.53	0.71	0.61
2-methylcitric acid (nmol/L)	147	54	176 ± 62	93	194 ± 68	0.72	0.73	0.73
Serum pepsinogen I (ng/mL)	145	52	102.8 ± 82.1	93	98.4 ± 64.3	0.49	0.54	0.40
≤ 20 ng/mL (%)	145	3	5.8	10	10.8	0.42	0.50	0.38
≤ 50 ng/mL (%)	145	12	23.1	21	22.6	0.87	0.99	0.85

Serum creatinine (µmol/L)	146	53	91.1 ± 49.1	93	98.0 ± 38.4	0.68	0.67	0.64
≥ 127 µmol/L (%)	146	4	7.6	13	14.0	0.89	0.88	0.87
Serum albumin (g/L)	146	53	4.1 ± 0.3	93	4.1 ± 0.3	0.22	0.30	0.30
Blood urea nitrogen (mmol/L)	146	53	18 ± 10	93	19 ± 7	0.44	0.18	0.13
Hemoglobin (g/dL)	146	53	13.1 ± 1.4	93	13.3 ± 1.3	0.35	0.61	0.46
Mean cell volume (fl)	146	53	90 ± 5	93	91 ± 5	0.55	0.77	0.68
S-adenosyl-methionine (nmol/L)	146	54	116 ± 70	92	117 ± 54	0.61	0.57	0.59
S-adenosyl-homocysteine (nmol/L)	147	54	33 ± 21	93	35 ± 21	0.48	0.51	0.46
SAM/SAH ratio	146	54	3.9 ± 1.8	92	4.1 ± 2.1	0.34	0.42	0.39
Multivitamin use (%)	147	19	35.2	40	43.0	0.18	0.36	0.32
Synthetic B_{12} intake (µg/d)	147	54	19.7 ± 87.5	93	9.6 ± 18.0	0.51	0.46	0.52
≥ 2.4 µg/d (%)	147	21	38.9	45	48.4	0.44	0.79	0.63
≥ 6 µg/d (%)	147	19	35.2	44	47.3	0.16	0.34	0.24
≥ 12 µg/d (%)	147	7	13.0	22	23.7	0.18	0.26	0.23
≥ 25 µg/d (%)	147	5	9.3	19	20.4	0.09	0.14	0.13
Synthetic folate intake (µg/d)	147	54	197.4 ± 222.4	93	240.5 ± 252.3	0.55	0.96	0.77
≥ 400 µg/d (%)	147	17	31.5	38	40.9	0.40	0.72	0.57
Worst ear								
n	143	37		106				
Hearing level (dB)	143	37	21 ± 4	106	44 ± 13			
Age (years)	143	37	71 ± 6	106	78 ± 8	<0.0001	<0.0001	<0.0001
Gender (% of female)	143	35	94.6	84	79.3	0.01	0.01	0.03
Race (% of Caucasian)	143	21	56.8	78	73.6	0.06	0.08	0.18
Education (years)	140	37	9 ± 3	103	9 ± 4	0.33	0.53	0.47
Family history of hearing loss (%)	143	6	16.2	29	27.4	0.22	0.24	0.32
Number of years exposure to noise (years)	142	36	10 ± 13	106	17 ± 19	0.14	0.14	0.17
Body mass index (kg/m^2)	143	37	31.1 ± 7.9	106	28.9 ± 5.7	0.61	0.77	0.82
Nutritional Health Score [f]	142	37	5 ± 4	105	5 ± 3	0.61	0.85	0.75
Overall health [g]	143	37	1.6 ± 0.8	106	1.7 ± 0.8	0.71	0.41	0.57
Number of medications	143	37	6 ± 3	106	6 ± 4	0.66	0.63	0.52
Impaired cognition (%) [h]	143	9	24.3	29	27.4	0.56	0.72	0.91
Anemic (%) [i]	142	7	19.4	23	21.7	0.46	0.81	0.72
Serum vitamin B_{12} (pmol/L)	143	37	370.7 ± 130.6	106	361.5 ± 173.4	0.60	0.92	0.88
< 148 pmol/L (%)	143	1	2.7	10	9.4	0.37	0.53	0.56
< 185 pmol/L (%)	143	1	2.7	14	13.2	0.20	0.30	0.34
< 221 pmol/L (%)	143	4	10.8	22	20.8	0.16	0.27	0.32
< 258 pmol/L (%)	143	7	18.9	31	29.3	0.22	0.43	0.49
< 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid (%)	143	1	2.7	16	15.1	0.08	0.13	0.19
Serum methylmalonic acid (nmol/L)	143	37	201 ± 79	106	292 ± 242	0.05	0.09	0.08
> 271 nmol/L (%)	143	5	13.5	35	33.0	0.18	0.19	0.11
> 376 nmol/L (%)	143	2	5.4	15	14.2	0.76	0.70	0.67

Serum total homocysteine (µmol/L)	143	37	9.9 ± 3.4	106	10.8 ± 4.5	0.88	0.71	0.77
> 9.0 µmol/L (%)	143	18	48.7	66	62.3	0.87	0.65	0.64
> 11.0 µmol/L (%)	143	12	32.4	38	35.9	0.70	0.97	0.91
> 13.9 µmol/L (%)	143	4	10.8	13	12.3	0.35	0.64	0.82
Serum folate (nmol/L)	143	37	42.8 ± 24.4	106	46.3 ± 27.4	0.84	0.76	0.91
Cystathionine (nmol/L)	143	37	249 ± 159	106	261 ± 119	0.50	0.86	0.89
2-methylcitric acid (nmol/L)	143	37	175 ± 69	106	192 ± 66	0.85	0.89	0.97
Serum pepsinogen I (ng/mL)	141	36	104.5 ± 90.6	105	97.5 ± 63.1	0.42	0.49	0.31
≤ 20 ng/mL (%)	141	1	2.8	11	10.5	0.23	0.26	-
≤ 50 ng/mL (%)	141	9	25.0	23	21.9	0.62	0.76	0.99
Serum creatinine (µmol/L)	142	36	92.3 ± 57.7	106	96.2 ± 37.0	0.54	0.52	0.49
≥ 127 µmol/L (%)	142	3	8.3	13	12.3	0.74	0.78	0.77
Serum albumin (g/L)	142	36	4.1 ± 0.2	106	4.1 ± 0.3	0.49	0.65	0.74
Blood urea nitrogen (mmol/L)	142	36	18 ± 12	106	19 ± 7	0.73	0.30	0.22
Hemoglobin (g/dL)	142	36	13.1 ± 1.3	106	13.2 ± 1.4	0.73	0.65	0.83
Mean cell volume (fl)	142	36	90 ± 4	106	91 ± 6	0.52	0.84	0.74
S-adenosyl-methionine (nmol/L)	142	37	117 ± 82	105	116 ± 52	0.91	0.92	0.99
S-adenosyl-homocysteine (nmol/L)	143	37	33 ± 24	106	35 ± 20	0.99	0.86	0.98
SAM/SAH ratio	142	37	4.0 ± 1.8	105	4.0 ± 2.1	0.76	0.87	0.75
Multivitamin use (%)	143	13	35.1	44	41.5	0.29	0.69	0.65
Synthetic B_{12} intake (µg/d)	143	37	19.7 ± 98.3	106	11.5 ± 29.0	0.74	0.82	0.72
≥ 2.4 µg/d (%)	143	12	32.4	53	50.0	0.11	0.34	0.27
≥ 6 µg/d (%)	143	12	32.4	50	47.2	0.13	0.40	0.32
≥ 12 µg/d (%)	143	4	10.8	25	23.6	0.15	0.23	0.24
≥ 25 µg/d (%)	143	3	8.1	21	19.8	0.13	0.22	0.26
Synthetic folate intake (µg/d)	143	37	190.6 ± 237.5	106	240.0 ± 245.0	0.55	0.79	0.94
≥ 400 µg/d (%)	143	11	29.7	43	40.6	0.40	0.93	0.78

* PTA, pure-tone average threshold of 1, 2, and 4 kHz.
[a] Number of total participants.
[b] Number of participants with the condition.
[c] Logistic regression model adjusted for age and gender.
[d] Logistic regression model adjusted for age, gender, race, and creatinine.
[e] Logistic regression model adjusted for age, gender, race, creatinine, family history of hearing loss, and noise exposure.
[f] NHS: Nutritional Screening Initiative Questionnaire. Higher number indicates greater nutritional risk.
[g] 0 = poor, 1 = fair, 2 = good, and 3 = excellent. Higher number indicates better health status.
[h] Impaired cognition defined as ≥ 9 on Orientation Memory Concentration test.
[i] Anemic defined as hemoglobin ≤ 12 g/dL for females, ≤ 13 g/dL for males.
- Not applicable. There was possibly a quasi-complete separation of data points.

Table C.8 Demographics, nutrition and auditory function in the best ear and the worst ear at baseline ***(PTA ≤ 40 vs. > 40 dB hearing level)****

		Hearing						
		PTA ≤ 40 dB HL		PTA >40 dB HL				
	N [a]	n [b]	Mean ± SD or %	n[b]	Mean ± SD or %	P value[c]	P value[d]	P value[e]
Best ear								
n	147	101		46				
Hearing level (dB)	147	101	26 ± 8	46	51 ± 8			
Age (years)	147	101	75 ± 7	46	80 ± 7	<0.0001	<0.0001	<0.0001
Gender (% of female)	147	91	90.1	29	63.0	<0.0001	0.0002	0.004
Race (% of Caucasian)	147	64	63.4	39	84.8	0.007	0.008	0.03
Education (years)	144	99	9 ± 4	45	9 ± 3	0.89	0.15	0.24
Family history of hearing loss (%)	147	19	18.8	18	39.1	0.01	0.07	0.07
Number of years exposure to noise (years)	146	100	12 ± 15	46	23 ± 21	0.07	0.07	0.08
Body mass index (kg/m^2)	147	101	30.1 ± 6.8	46	27.7 ± 5.0	0.39	0.65	0.51
Nutritional Health Score [f]	146	100	5 ± 4	46	5 ± 3	0.76	0.91	0.83
Overall health [g]	147	101	1.7 ± 0.8	46	1.7 ± 0.7	0.86	0.89	0.87
Number of medications	147	101	6 ± 4	46	6 ± 3	0.76	0.93	0.86
Impaired cognition (%) [h]	147	24	23.8	15	32.6	0.75	0.22	0.15
Anemic (%) [i]	146	22	22.0	9	19.6	0.17	0.41	0.36
Serum vitamin B_{12} (pmol/L)	147	101	363.5 ± 167.4	46	365.3 ± 148.5	0.88	0.61	0.37
< 148 pmol/L (%)	147	7	6.9	4	8.7	0.93	0.67	0.74
< 185 pmol/L (%)	147	10	9.9	5	10.9	0.67	0.62	0.72
< 221 pmol/L (%)	147	18	17.8	8	17.4	0.97	0.89	0.88
< 258 pmol/L (%)	147	28	27.7	10	21.7	0.30	0.25	0.23
< 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid (%)	147	10	9.9	7	15.2	0.35	0.52	0.74
Serum methylmalonic acid (nmol/L)	147	101	238 ± 103	46	340 ± 341	0.46	0.87	0.80
> 271 nmol/L (%)	147	23	22.8	20	43.5	0.16	0.31	0.34
> 376 nmol/L (%)	147	10	9.9	8	17.4	0.83	0.40	0.39
Serum total homocysteine (µmol/L)	147	101	10.3 ± 3.3	46	11.4 ± 5.7	0.43	0.45	0.49
> 9.0 µmol/L (%)	147	59	58.4	28	60.9	0.17	0.23	0.34
> 11.0 µmol/L (%)	147	35	34.7	17	37.0	0.37	0.56	0.58
> 13.9 µmol/L (%)	147	10	9.9	9	19.6	0.77	0.62	0.64
Serum folate (nmol/L)	147	101	44.4 ± 24.9	46	48.2 ± 30.2	0.37	0.77	0.45
Cystathionine (nmol/L)	147	101	251 ± 126	46	274 ± 134	0.49	0.21	0.09
2-methylcitric acid (nmol/L)	147	101	185 ± 62	46	193 ± 75	0.35	0.11	0.12
Serum pepsinogen I (ng/mL)	145	99	98.4 ± 70.1	46	103.4 ± 73.3	0.98	0.84	0.61
≤ 20 ng/mL (%)	145	8	8.1	5	10.9	0.55	0.52	0.37
≤ 50 ng/mL (%)	145	25	25.3	8	17.4	0.15	0.27	0.37
Serum creatinine (µmol/L)	146	100	91.9 ± 38.8	46	103.2 ± 49.3	0.59	0.70	0.75

≥ 127 µmol/L (%)	146	9	9.0	8	17.4	0.99	0.94	0.96
Serum albumin (g/L)	146	100	4.1 ± 0.3	46	4.1 ± 0.3	0.78	0.35	0.32
Blood urea nitrogen (mmol/L)	146	100	18 ± 9	46	19 ± 7	0.65	0.34	0.31
Hemoglobin (g/dL)	146	100	13.1 ± 1.3	46	13.5 ± 1.4	0.18	0.49	0.46
Mean cell volume (fl)	146	100	90 ± 5	46	91 ± 5	0.97	0.56	0.57
S-adenosyl-methionine (nmol/L)	146	101	116 ± 61	45	118 ± 58	0.63	0.24	0.23
S-adenosyl-homocysteine (nmol/L)	147	101	34 ± 18	46	36 ± 26	0.18	0.10	0.10
SAM/SAH ratio	146	101	4.0 ± 2.1	45	4.1 ± 1.9	0.37	0.64	0.72
Multivitamin use (%)	147	38	37.6	21	45.7	0.24	0.54	0.63
Synthetic B_{12} intake (µg/d)	147	101	15.0 ± 65.7	46	9.6 ± 12.1	0.83	0.64	0.71
≥ 2.4 µg/d (%)	147	41	40.6	25	54.4	0.20	0.60	0.42
≥ 6 µg/d (%)	147	39	38.6	24	52.2	0.15	0.43	0.29
≥ 12 µg/d (%)	147	15	14.9	14	30.4	0.03	0.07	0.07
≥ 25 µg/d (%)	147	13	12.9	11	23.9	0.08	0.20	0.23
Synthetic folate intake (µg/d)	147	101	205.3 ± 236.7	46	267.2 ± 250.2	0.17	0.62	0.53
≥ 400 µg/d (%)	147	33	32.7	22	47.8	0.11	0.35	0.26
Worst ear								
n	143	82		61				
Hearing level (dB)	143	82	28 ± 7	61	53 ± 10			
Age (years)	143	82	74 ± 7	61	79 ± 8	<0.0001	<0.0001	<0.0001
Gender (% of female)	143	75	91.5	44	72.1	0.0003	0.0005	0.003
Race (% of Caucasian)	143	52	63.4	47	77.1	0.05	0.06	0.24
Education (years)	140	81	9 ± 4	59	9 ± 3	0.53	0.13	0.16
Family history of hearing loss (%)	143	13	15.9	22	36.1	0.004	0.01	0.01
Number of years exposure to noise (years)	142	81	12 ± 16	61	19 ± 19	0.21	0.19	0.22
Body mass index (kg/m^2)	143	82	30.5 ± 7.1	61	28.1 ± 5.2	0.34	0.57	0.46
Nutritional Health Score [f]	142	82	5 ± 4	60	4 ± 3	0.22	0.36	0.41
Overall health [g]	143	82	1.6 ± 0.8	61	1.7 ± 0.8	0.71	0.96	0.80
Number of medications	143	82	6 ± 4	61	6 ± 4	0.58	0.63	0.69
Impaired cognition (%) [h]	143	17	20.7	21	34.4	0.32	0.11	0.05
Anemic (%) [i]	142	17	21.0	13	21.3	0.31	0.56	0.51
Serum vitamin B_{12} (pmol/L)	143	82	356.3 ± 164.6	61	374.0 ± 161.7	0.47	0.29	0.14
< 148 pmol/L (%)	143	4	4.9	7	11.5	0.31	0.44	0.36
< 185 pmol/L (%)	143	7	8.5	8	13.1	0.86	0.99	0.90
< 221 pmol/L (%)	143	15	18.3	11	18.0	0.91	0.76	0.68
< 258 pmol/L (%)	143	23	28.1	15	24.6	0.44	0.30	0.24
< 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid (%)	143	8	9.8	9	14.8	0.42	0.60	0.84
Serum methylmalonic acid (nmol/L)	143	82	233 ± 90	61	317 ± 308	0.83	0.71	0.64
> 271 nmol/L (%)	143	18	22.0	22	36.1	0.39	0.47	0.41
> 376 nmol/L (%)	143	7	8.5	10	16.4	0.99	0.77	0.78
Serum total homocysteine (µmol/L)	143	82	10.2 ± 3.2	61	11.3 ± 5.4	0.23	0.28	0.26

> 9.0 µmol/L (%)	143	47	57.3	37	60.7	0.20	0.26	0.33
> 11.0 µmol/L (%)	143	30	36.6	20	32.8	0.12	0.19	0.22
> 13.9 µmol/L (%)	143	8	9.8	9	14.8	0.79	0.94	0.72
Serum folate (nmol/L)	143	82	43.8 ± 25.9	61	47.5 ± 27.7	0.23	0.44	0.14
Cystathionine (nmol/L)	143	82	249 ± 129	61	270 ± 131	0.48	0.42	0.28
2-methylcitric acid (nmol/L)	143	82	185 ± 64	61	192 ± 71	0.16	0.07	0.06
Serum pepsinogen I (ng/mL)	141	80	101.0 ± 73.1	61	97.0 ± 68.3	0.57	0.52	0.33
≤ 20 ng/mL (%)	141	5	6.3	7	11.5	0.29	0.28	0.17
≤ 50 ng/mL (%)	141	18	22.5	14	23.0	0.83	0.96	0.72
Serum creatinine (µmol/L)	142	81	91.8 ± 42.2	61	99.7 ± 44.0	0.54	0.56	0.63
≥ 127 µmol/L (%)	142	7	8.6	9	14.8	0.96	0.97	0.92
Serum albumin (g/L)	142	81	4.2 ± 0.3	61	4.1 ± 0.3	0.60	0.33	0.27
Blood urea nitrogen (mmol/L)	142	81	18 ± 9	61	19 ± 7	0.70	0.64	0.65
Hemoglobin (g/dL)	142	81	13.1 ± 1.4	61	13.3 ± 1.4	0.51	0.92	0.94
Mean cell volume (fl)	142	81	90 ± 5	61	91 ± 5	0.58	0.89	0.82
S-adenosyl-methionine (nmol/L)	142	82	116 ± 66	60	117 ± 54	0.83	0.67	0.79
S-adenosyl-homocysteine (nmol/L)	143	82	33 ± 19	61	36 ± 24	0.87	0.99	0.97
SAM/SAH ratio	142	82	4.1 ± 2.1	60	4.0 ± 1.9	0.98	0.72	0.66
Multivitamin use (%)	143	28	34.2	29	47.5	0.03	0.10	0.10
Synthetic B_{12} intake (µg/d)	143	82	14.9 ± 71.4	61	11.9 ± 20.4	0.94	0.99	0.88
≥ 2.4 µg/d (%)	143	30	36.6	35	57.4	0.23	0.10	0.05
≥ 6 µg/d (%)	143	28	34.2	34	55.7	0.01	0.04	0.02
≥ 12 µg/d (%)	143	10	12.2	19	31.2	0.01	0.02	0.03
≥ 25 µg/d (%)	143	8	9.8	16	26.2	0.01	0.03	0.05
Synthetic folate intake (µg/d)	143	82	188.8 ± 214.3	61	278.8 ± 270.7	0.05	0.18	0.13
≥ 400 µg/d (%)	143	25	30.5	29	47.5	0.06	0.18	0.12

* PTA, pure-tone average threshold of 1, 2, and 4 kHz.
[a] Number of total participants.
[b] Number of participants with the condition.
[c] Logistic regression model adjusted for age and gender.
[d] Logistic regression model adjusted for age, gender, race, and creatinine.
[e] Logistic regression model adjusted for age, gender, race, creatinine, family history of hearing loss, and noise exposure.
[f] NHS: Nutritional Screening Initiative Questionnaire. Higher number indicates greater nutritional risk.
[g] 0 = poor, 1 = fair, 2 = good, and 3 = excellent. Higher number indicates better health status.
[h] Impaired cognition defined as ≥ 9 on Orientation Memory Concentration test.
[i] Anemic defined as hemoglobin ≤ 12 g/dL for females, ≤ 13 g/dL for males.

A POSSIBLE RELATIONSHIP OF HEARING IMPAIRMENT WITH MULTIPLE MEASURES OF VITAMIN B_{12} STATUS WAS EXAMINED IN OLDER ADULTS. PARTICIPANTS WITH CONDUCTIVE HEARING LOSS AND ASYMMETRICAL HEARING LOSS WERE INCLUDED. PARTICIPANTS WITH HIGH VITAMIN B_{12} CONCENTRATIONS (> 95 TH PERCENTILE) WERE EXCLUDED (TABLES C.9 - C.12).

Table C.9 Characteristics of participants at baseline *(Participants with high vitamin B_{12} concentrations were excluded.)*

	N [a]	n [b]	Mean ± SD or %
Age (years)	141	141	76 ± 8 (58-97) [c]
Gender	141		
Female (%)		115	81.6
Male (%)		26	18.4
Race	141		
Caucasian (%)		97	68.8
African-American (%)		44	31.2
Hearing level in the best ear (dB)	141	141	34 ± 14 (8-73)
Hearing level in the worst ear (dB)	137	137	38 ± 15 (10-83)
Education (years)	139	139	9 ± 4 (0-18)
Family history of hearing loss (%)	141	36	25.5
Number of years exposed to noise (years)	140	140	16 ± 18 (0-83)
Body mass index (kg/m^2)	141	141	29.2 ± 6.4 (15.2-53.8)
Nutritional Health Score [d]	140	140	5 ± 3 (0-19)
Overall health [e]	141	141	1.7 ± 0.8
Number of medications	141	141	6 ± 3 (0-15)
Impaired cognition (%) [f]	141	38	27.0
Anemic (%) [g]	140	30	21.4
Serum vitamin B_{12} (pmol/L)	141	141	346.6 ± 138.0 (74.3-746.3)
< 148 pmol/L (%)	141	11	7.8
< 185 pmol/L (%)	141	15	10.6
< 221 pmol/L (%)	141	26	18.4
< 258 pmol/L (%)	141	38	27.0
< 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid (%)	141	17	12.1
Serum methylmalonic acid (nmol/L)	141	141	270 ± 216 (85-1972)
> 271 nmol/L (%)	141	41	29.1
> 376 nmol/L (%)	141	17	12.1
Serum total homocysteine (µmol/L)	141	141	10.7 ± 4.3 (5.1-39.5)
> 9.0 µmol/L (%)	141	83	58.9
> 11.0 µmol/L (%)	141	51	36.2
> 13.9 µmol/L (%)	141	19	13.5
Serum folate (nmol/L)	141	141	44.5 ± 25.7 (8.8-163.3)
Cystathionine (nmol/L)	141	141	256 ± 130 (89-968)
2-methylcitric acid (nmol/L)	141	141	187 ± 68 (58-453)

Serum pepsinogen I (ng/mL)	139	139	98.7 ± 70.8 (8.6-549.9)
≤ 20 ng/mL (%)	139	13	9.4
≤ 50 ng/mL (%)	139	32	23.0
Serum creatinine (µmol/L)	140	140	95.5 ± 43.4 (53.0-406.6)
≥ 127 µmol/L (%)	140	17	12.1
Serum albumin (g/L)	140	140	4.1 ± 0.3 (3.4-4.9)
Blood urea nitrogen (mmol/L)	140	140	18 ± 8 (8-79)
Hemoglobin (g/dL)	140	140	13.2 ± 1.3 (9.4-17.3)
Mean cell volume (fl)	140	140	91 ± 5 (68-107)
S-adenosyl-methionine (nmol/L)	140	140	115 ± 61 (42-511)
S-adenosyl-homocysteine (nmol/L)	141	141	35 ± 21 (9-157)
SAM/SAH ratio	140	140	4.0 ± 1.9 (0.9-9.4)
Multivitamin use (%)	141	56	39.7
Synthetic vitamin B_{12} intake (µg/d)	141	141	10.8 ± 51.1 (0.0-600.6)
≥ 2.4 µg/d (%)	141	61	43.3
≥ 6 µg/d (%)	141	58	41.1
≥ 12 µg/d (%)	141	26	18.4
≥ 25 µg/d (%)	141	21	14.9
Synthetic folate intake (µg/d)	141	141	214.8 ± 230.0 (0.0-1028.6)
≥ 400 µg/d (%)	141	52	36.9

[a] Number of total participants.
[b] Number of participants with the condition.
[c] Range in parentheses.
[d] NHS: Nutritional Screening Initiative Questionnaire. Higher number indicates greater nutritional risk.
[e] 0 = poor, 1 = fair, 2 = good, and 3 = excellent. Higher number indicates better health status.
[f] Impaired cognition defined as ≥ 9 on Orientation Memory Concentration test.
[g] Anemic defined as hemoglobin ≤ 12 g/dL for females, ≤ 13 g/dL for males.

Table C.10 Correlations of vitamin B_{12}, methylmalonic acid, and total homocysteine with pure-tone average (1, 2, and 4 kHz) in the best ear and the worst ear at baseline [a] *(Participants with high vitamin B_{12} concentrations were excluded.)*

	Pure-tone average threshold in the best ear (N=139) [b]	**Pure-tone average threshold in the worst ear (N=135)** [b]
Vitamin B_{12}	r = 0.15 *P* = 0.08	r = 0.12 *P* = 0.18
Methylmalonic acid	r = -0.03 *P* = 0.77	r = 0.03 *P* = 0.74
Total homocysteine	r = -0.10 *P* = 0.25	r = -0.09 *P* = 0.28

[a] Partial Spearman correlation coefficient from multivariable linear regression analysis; adjusted for age, gender, race, creatinine, family history of hearing loss, and noise exposure.
[b] Number of total participants.

Table C.11 Demographics, nutrition and auditory function in the best ear and the worst ear at baseline ***(PTA ≤ 25 vs. > 25 dB hearing level;*** *Participants with high vitamin B_{12} concentrations were excluded.)**

		Hearing						
		Normal (PTA ≤ 25 dB HL)		Impaired (PTA >25 dB HL)				
	N [a]	n [b]	Mean ± SD or %	n [b]	Mean ± SD or %	P value[c]	P value[d]	P value[e]
Best ear								
n	141	51		90				
Hearing level (dB)	141	51	19 ± 4	90	43 ± 11			
Age (years)	141	51	72 ± 6	90	79 ± 7	<0.0001	<0.0001	<0.0001
Gender (% of female)	141	48	94.2	67	74.4	0.002	0.002	0.009
Race (% of Caucasian)	141	31	60.8	66	73.3	0.14	0.16	0.23
Education (years)	139	51	9 ± 3	88	9 ± 4	0.57	0.82	0.67
Family history of hearing loss (%)	141	11	21.6	25	27.8	0.64	0.80	0.91
Number of years exposed to noise (years)	140	50	11 ± 14	90	19 ± 20	0.18	0.17	0.17
Body mass index (kg/m^2)	141	51	30.7 ± 7.7	90	28.4 ± 5.4	0.94	0.89	0.94
Nutritional Health Score [f]	140	51	6 ± 4	89	4 ± 3	0.10	0.16	0.14
Overall health [g]	141	51	1.6 ± 0.8	90	1.7 ± 0.8	0.82	0.92	0.92
Number of medications	141	51	6 ± 4	90	6 ± 3	0.98	0.97	0.81
Impaired cognition (%) [h]	141	12	23.5	26	28.9	0.68	0.87	0.92
Anemic (%) [i]	140	11	22.0	19	21.1	0.13	0.23	0.19
Serum vitamin B_{12} (pmol/L)	141	51	355.8 ± 138.4	90	341.4 ± 138.2	0.59	0.96	0.99
< 148 pmol/L (%)	141	3	5.9	8	8.9	0.93	0.86	0.84
< 185 pmol/L (%)	141	3	5.9	12	13.3	0.43	0.58	0.58
< 221 pmol/L (%)	141	8	15.7	18	20.0	0.46	0.64	0.71
< 258 pmol/L (%)	141	12	23.5	26	28.9	0.49	0.75	0.77
< 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid (%)	141	5	9.8	12	13.3	0.63	0.87	0.92
Serum methylmalonic acid (nmol/L)	141	51	218 ± 92	90	300 ± 258	0.32	0.51	0.53
> 271 nmol/L (%)	141	11	21.6	30	33.3	0.99	0.88	0.91
> 376 nmol/L (%)	141	4	7.8	13	14.4	0.79	0.73	0.67
Serum total homocysteine (µmol/L)	141	51	9.8 ± 3.1	90	11.2 ± 4.8	0.94	0.67	0.67
> 9.0 µmol/L (%)	141	27	52.9	56	62.2	0.58	0.69	0.72
> 11.0 µmol/L (%)	141	14	27.5	37	41.1	0.46	0.27	0.30
> 13.9 µmol/L (%)	141	4	7.8	15	16.7	0.89	0.57	0.48
Serum folate (nmol/L)	141	51	41.5 ± 23.3	90	46.2 ± 26.9	0.39	0.57	0.42
Cystathionine (nmol/L)	141	51	244 ± 146	90	263 ± 120	0.69	0.93	0.84
2-methylcitric acid (nmol/L)	141	51	174 ± 63	90	194 ± 69	0.90	0.92	0.90
Serum pepsinogen I (ng/mL)	139	49	100.3 ± 81.1	90	97.8 ± 64.9	0.56	0.63	0.48
≤ 20 ng/mL (%)	139	3	6.1	10	11.1	0.45	0.55	0.43
≤ 50 ng/mL (%)	139	11	22.5	21	23.3	0.98	0.89	0.75

Serum creatinine (µmol/L)	140	50	90.5 ± 50.5	90	98.3 ± 38.9	0.74	0.73	0.71
≥ 127 µmol/L (%)	140	4	8.0	13	14.4	0.95	0.96	0.99
Serum albumin (g/L)	140	50	4.1 ± 0.3	90	4.1 ± 0.3	0.23	0.33	0.32
Blood urea nitrogen (mmol/L)	140	50	17 ± 11	90	19 ± 7	0.27	0.07	0.06
Hemoglobin (g/dL)	140	50	13.1 ± 1.4	90	13.3 ± 1.3	0.41	0.74	0.58
Mean cell volume (fl)	140	50	90 ± 5	90	91 ± 5	0.39	0.59	0.55
S-adenosyl-methionine (nmol/L)	140	51	114 ± 71	89	116 ± 54	0.83	0.81	0.77
S-adenosyl-homocysteine (nmol/L)	141	51	33 ± 21	90	36 ± 21	0.79	0.85	0.80
SAM/SAH ratio	140	51	3.9 ± 1.8	89	4.0 ± 2.0	0.51	0.59	0.60
Multivitamin use (%)	141	17	33.3	39	43.3	0.12	0.27	0.24
Synthetic B_{12} intake (µg/d)	141	51	15.2 ± 83.8	90	8.3 ± 11.8	0.93	0.99	0.94
≥ 2.4 µg/d (%)	141	18	35.3	43	47.8	0.23	0.49	0.42
≥ 6 µg/d (%)	141	16	31.4	42	46.7	0.06	0.16	0.12
≥ 12 µg/d (%)	141	5	9.8	21	23.3	0.05	0.08	0.08
≥ 25 µg/d (%)	141	3	5.9	18	20.0	0.02	0.03	0.03
Synthetic folate intake (µg/d)	141	51	188.5 ± 222.4	90	229.7 ± 234.2	0.55	0.98	0.89
≥ 400 µg/d (%)	141	15	29.4	37	41.1	0.28	0.58	0.49
Worst ear								
n	137	37		100				
Hearing level (dB)	137	37	21 ± 4	100	45 ± 13			
Age (years)	137	37	71 ± 6	100	78 ± 8	<0.0001	<0.0001	<0.0001
Gender (% of female)	137	35	94.6	79	79.0	0.01	0.01	0.05
Race (% of Caucasian)	137	21	56.8	72	72.0	0.09	0.11	0.25
Education (years)	135	37	9 ± 3	98	9 ± 4	0.31	0.48	0.41
Family history of hearing loss (%)	137	6	16.2	28	28.0	0.21	0.22	0.30
Number of years exposed to noise (years)	136	36	10 ± 13	100	17 ± 19	0.11	0.11	0.13
Body mass index (kg/m^2)	137	37	31.1 ± 7.9	100	28.7 ± 5.6	0.52	0.88	0.99
Nutritional Health Score [f]	136	37	5 ± 4	99	5 ± 3	0.52	0.74	0.62
Overall health [g]	137	37	1.6 ± 0.8	100	1.7 ± 0.8	0.74	0.44	0.63
Number of medications	137	37	6 ± 4	100	6 ± 3	0.51	0.51	0.39
Impaired cognition (%) [h]	137	9	24.3	28	28.0	0.59	0.73	0.84
Anemic (%) [i]	136	7	19.4	22	22.0	0.42	0.75	0.64
Serum vitamin B_{12} (pmol/L)	137	37	370.7 ± 130.6	100	336.7 ± 142.0	0.21	0.47	0.56
< 148 pmol/L (%)	137	1	2.7	10	10.0	0.34	0.49	0.51
< 185 pmol/L (%)	137	1	2.7	14	14.0	0.18	0.27	0.30
< 221 pmol/L (%)	137	4	10.8	22	22.0	0.14	0.23	0.27
< 258 pmol/L (%)	137	7	18.9	31	31.0	0.18	0.36	0.39
< 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid (%)	137	1	2.7	16	16.0	0.07	0.12	0.17
Serum methylmalonic acid (nmol/L)	137	37	201 ± 79	100	294 ± 248	0.06	0.09	0.08
> 271 nmol/L (%)	137	5	13.5	33	33.0	0.19	0.19	0.11
> 376 nmol/L (%)	137	2	5.4	14	14.0	0.72	0.65	0.61

Serum total homocysteine (µmol/L)	137	37	9.9 ± 3.4	100	10.9 ± 4.6	0.94	0.66	0.68
> 9.0 µmol/L (%)	137	18	48.7	62	62.0	0.90	0.67	0.66
> 11.0 µmol/L (%)	137	12	32.4	37	37.0	0.70	0.97	0.93
> 13.9 µmol/L (%)	137	4	10.8	13	13.0	0.40	0.71	0.94
Serum folate (nmol/L)	137	37	42.8 ± 24.4	100	44.8 ± 26.2	0.93	0.63	0.94
Cystathionine (nmol/L)	137	37	249 ± 159	100	259 ± 120	0.45	0.80	0.80
2-methylcitric acid (nmol/L)	137	37	175 ± 69	100	192 ± 68	0.81	0.89	0.95
Serum pepsinogen I (ng/mL)	135	36	104.5 ± 90.6	99	95.6 ± 62.2	0.40	0.49	0.29
≤ 20 ng/mL (%)	135	1	2.8	11	11.1	0.20	0.25	-
≤ 50 ng/mL (%)	135	9	25.0	22	22.2	0.57	0.70	0.93
Serum creatinine (µmol/L)	136	36	92.3 ± 57.7	100	96.3 ± 38.0	0.51	0.50	0.47
≥ 127 µmol/L (%)	136	3	8.3	13	13.0	0.81	0.84	0.86
Serum albumin (g/L)	136	36	4.1 ± 0.2	100	4.1 ± 0.3	0.54	0.69	0.78
Blood urea nitrogen (mmol/L)	136	36	18 ± 12	100	18 ± 7	0.86	0.38	0.31
Hemoglobin (g/dL)	136	36	13.1 ± 1.3	100	13.2 ± 1.4	0.69	0.71	0.92
Mean cell volume (fl)	136	36	90 ± 4	100	91 ± 6	0.54	0.84	0.75
S-adenosyl-methionine (nmol/L)	135	37	117 ± 82	98	114 ± 52	0.76	0.80	0.84
S-adenosyl-homocysteine (nmol/L)	137	37	33 ± 24	100	35 ± 20	0.99	0.85	0.98
SAM/SAH ratio	135	37	4.0 ± 1.8	98	3.9 ± 2.0	0.87	0.96	0.86
Multivitamin use (%)	137	13	35.1	41	41.0	0.35	0.75	0.71
Synthetic B_{12} intake (µg/d)	137	37	19.7 ± 98.3	100	7.8 ± 11.3	0.62	0.69	0.59
≥ 2.4 µg/d (%)	137	12	32.4	48	48.0	0.16	0.43	0.36
≥ 6 µg/d (%)	137	12	32.4	45	45.0	0.20	0.50	0.43
≥ 12 µg/d (%)	137	4	10.8	22	22.0	0.19	0.27	0.30
≥ 25 µg/d (%)	137	3	8.1	18	18.0	0.17	0.26	0.33
Synthetic folate intake (µg/d)	137	37	190.6 ± 237.5	100	226.9 ± 229.4	0.75	0.60	0.77
≥ 400 µg/d (%)	137	11	29.7	40	40.0	0.48	0.99	0.83

* PTA, pure-tone average threshold of 1, 2, and 4 kHz.
[a] Number of total participants.
[b] Number of participants with the condition.
[c] Logistic regression model adjusted for age and gender.
[d] Logistic regression model adjusted for age, gender, race, and creatinine.
[e] Logistic regression model adjusted for age, gender, race, creatinine, family history of hearing loss, and noise exposure.
[f] NHS: Nutritional Screening Initiative Questionnaire. Higher number indicates greater nutritional risk.
[g] 0 = poor, 1 = fair, 2 = good, and 3 = excellent. Higher number indicates better health status.
[h] Impaired cognition defined as ≥ 9 on Orientation Memory Concentration test.
[i] Anemic defined as hemoglobin ≤ 12 g/dL for females, ≤ 13 g/dL for males.
- Not applicable. There was possibly a quasi-complete separation of data points.

Table C.12 Demographics, nutrition and auditory function in the best ear and the worst ear at baseline ***(PTA ≤ 40 vs. > 40 dB hearing level;*** *Participants with high vitamin B_{12} concentrations were excluded.)**

		Hearing						
		PTA ≤ 40 dB HL		PTA >40 dB HL				
	N [a]	n [b]	Mean ± SD or %	n [b]	Mean ± SD or %	P value[c]	P value[d]	P value[e]
Best ear								
n	141	95		46				
Hearing level (dB)	141	95	26 ± 8	46	51 ± 8			
Age (years)	141	95	74 ± 7	46	80 ± 7	<0.0001	<0.0001	<0.0001
Gender (% of female)	141	86	90.5	29	63.0	<0.0001	0.0003	0.004
Race (% of Caucasian)	141	58	61.1	39	84.8	0.003	0.004	0.02
Education (years)	139	94	9 ± 4	45	9 ± 3	0.92	0.19	0.27
Family history of hearing loss (%)	141	18	19.0	18	39.1	0.02	0.10	0.10
Number of years exposed to noise (years)	140	94	13 ± 16	46	23 ± 21	0.12	0.14	0.14
Body mass index (kg/m^2)	141	95	30.0 ± 6.8	46	27.7 ± 5.0	0.50	0.93	0.70
Nutritional Health Score [f]	140	94	5 ± 3	46	5 ± 3	0.92	0.61	0.60
Overall health [g]	141	95	1.7 ± 0.8	46	1.7 ± 0.7	0.75	0.99	0.79
Number of medications	141	95	6 ± 4	46	6 ± 3	0.66	0.81	0.96
Impaired cognition (%) [h]	141	23	24.2	15	32.6	0.88	0.26	0.15
Anemic (%) [i]	140	21	22.3	9	19.6	0.13	0.32	0.30
Serum vitamin B_{12} (pmol/L)	141	95	337.6 ± 132.4	46	365.3 ± 148.5	0.16	0.02	0.01
< 148 pmol/L (%)	141	7	7.4	4	8.7	0.83	0.53	0.60
< 185 pmol/L (%)	141	10	10.5	5	10.9	0.56	0.47	0.57
< 221 pmol/L (%)	141	18	19.0	8	17.4	0.81	0.69	0.70
< 258 pmol/L (%)	141	28	29.5	10	21.7	0.20	0.14	0.14
< 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid (%)	141	10	10.5	7	15.2	0.44	0.69	0.87
Serum methylmalonic acid (nmol/L)	141	95	237 ± 103	46	340 ± 341	0.45	0.81	0.75
> 271 nmol/L (%)	141	21	22.1	20	43.5	0.15	0.31	0.32
> 376 nmol/L (%)	141	9	9.5	8	17.4	0.95	0.46	0.45
Serum total homocysteine (µmol/L)	141	95	10.3 ± 3.4	46	11.4 ± 5.7	0.28	0.26	0.31
> 9.0 µmol/L (%)	141	55	57.9	28	60.9	0.17	0.25	0.35
> 11.0 µmol/L (%)	141	34	35.8	17	37.0	0.24	0.38	0.43
> 13.9 µmol/L (%)	141	10	10.5	9	19.6	0.93	0.79	0.63
Serum folate (nmol/L)	141	95	42.7 ± 23.2	46	48.2 ± 30.2	0.24	0.60	0.34
Cystathionine (nmol/L)	141	95	247 ± 127	46	274 ± 134	0.62	0.34	0.17
2-methylcitric acid (nmol/L)	141	95	184 ± 64	46	193 ± 75	0.39	0.13	0.12
Serum pepsinogen I (ng/mL)	139	93	96.4 ± 69.8	46	103.4 ± 73.3	0.79	0.91	0.84
≤ 20 ng/mL (%)	139	8	8.6	5	10.9	0.65	0.65	0.48
≤ 50 ng/mL (%)	139	24	25.8	8	17.4	0.11	0.20	0.28
Serum creatinine (µmol/L)	140	94	91.8 ± 40.0	46	103.2 ± 49.3	0.56	0.68	0.75

≥ 127 µmol/L (%)	140	9	9.6	8	17.4	0.88	0.89	0.92
Serum albumin (g/L)	140	94	4.1 ± 0.3	46	4.1 ± 0.3	0.84	0.36	0.34
Blood urea nitrogen (mmol/L)	140	94	18 ± 9	46	19 ± 7	0.90	0.64	0.53
Hemoglobin (g/dL)	140	94	13.1 ± 1.3	46	13.5 ± 1.4	0.11	0.36	0.34
Mean cell volume (fl)	140	94	90 ± 5	46	91 ± 5	0.99	0.53	0.51
S-adenosyl-methionine (nmol/L)	140	95	114 ± 62	45	118 ± 58	0.85	0.40	0.35
S-adenosyl-homocysteine (nmol/L)	141	95	34 ± 18	46	36 ± 26	0.14	0.06	0.06
SAM/SAH ratio	140	95	3.9 ± 2.0	45	4.1 ± 1.9	0.17	0.30	0.37
Multivitamin use (%)	141	35	36.8	21	45.7	0.22	0.57	0.66
Synthetic B_{12} intake (µg/d)	141	95	11.3 ± 61.7	46	9.6 ± 12.1	0.67	0.50	0.62
≥ 2.4 µg/d (%)	141	36	37.9	25	54.4	0.12	0.46	0.36
≥ 6 µg/d (%)	141	34	35.8	24	52.2	0.08	0.29	0.23
≥ 12 µg/d (%)	141	12	12.6	14	30.4	0.01	0.02	0.03
≥ 25 µg/d (%)	141	10	10.5	11	23.9	0.03	0.08	0.11
Synthetic folate intake (µg/d)	141	95	189.4 ± 216.5	46	267.2 ± 250.2	0.08	0.42	0.34
≥ 400 µg/d (%)	141	30	31.6	22	47.8	0.09	0.38	0.30
Worst ear								
n	137	78		59				
Hearing level (dB)	137	78	27 ± 7	59	53 ± 10			
Age (years)	137	78	73 ± 7	59	79 ± 8	<0.0001	<0.0001	<0.0001
Gender (% of female)	137	72	92.3	42	71.2	0.0003	0.0005	0.003
Race (% of Caucasian)	137	48	61.5	45	76.3	0.04	0.04	0.19
Education (years)	135	77	9 ± 3	58	9 ± 4	0.61	0.14	0.15
Family history of hearing loss (%)	137	13	16.7	21	35.6	0.01	0.03	0.03
Number of years exposed to noise (years)	136	77	13 ± 16	59	19 ±19	0.30	0.30	0.33
Body mass index (kg/m^2)	137	78	30.3 ± 7.0	59	28.1 ± 5.2	0.53	0.93	0.72
Nutritional Health Score [f]	136	78	5 ± 3	58	4 ± 3	0.34	0.58	0.56
Overall health [g]	137	78	1.6 ± 0.8	59	1.7 ± 0.7	0.82	0.91	0.95
Number of medications	137	78	6 ± 3	59	6 ± 4	0.60	0.85	0.68
Impaired cognition (%) [h]	137	17	21.8	20	33.9	0.50	0.20	0.08
Anemic (%) [i]	136	16	20.8	13	22.0	0.34	0.60	0.55
Serum vitamin B_{12} (pmol/L)	137	78	333.0 ± 128.2	59	362.9 ± 152.4	0.10	0.02	0.01
< 148 pmol/L (%)	137	4	5.1	7	11.9	0.33	0.50	0.41
< 185 pmol/L (%)	137	7	9.0	8	13.6	0.91	0.93	0.97
< 221 pmol/L (%)	137	15	19.2	11	18.6	0.83	0.65	0.62
< 258 pmol/L (%)	137	23	29.5	15	25.4	0.36	0.21	0.19
< 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid (%)	137	8	10.3	9	15.3	0.46	0.68	0.86
Serum methylmalonic acid (nmol/L)	137	78	233 ± 92	59	317 ± 312	0.84	0.65	0.59
> 271 nmol/L (%)	137	17	21.8	21	35.6	0.42	0.53	0.48
> 376 nmol/L (%)	137	7	9.0	9	15.3	0.84	0.59	0.60
Serum total homocysteine (µmol/L)	137	78	10.3 ± 3.2	59	11.1 ± 5.5	0.20	0.22	0.22

> 9.0 µmol/L (%)	137	44	56.4	36	61.0	0.24	0.33	0.37
> 11.0 µmol/L (%)	137	29	37.2	20	33.9	0.10	0.15	0.18
> 13.9 µmol/L (%)	137	8	10.3	9	15.3	0.75	0.99	0.80
Serum folate (nmol/L)	137	78	42.1 ± 24.0	59	47.2 ± 27.7	0.15	0.30	0.10
Cystathionine (nmol/L)	137	78	246 ± 130	59	270 ± 133	0.58	0.56	0.39
2-methylcitric acid (nmol/L)	137	78	184 ± 65	59	192 ± 72	0.21	0.10	0.08
Serum pepsinogen I (ng/mL)	135	76	99.7 ± 72.5	59	95.7 ± 68.8	0.58	0.54	0.36
≤ 20 ng/mL (%)	135	5	5.7	7	11.9	0.30	0.30	0.19
≤ 50 ng/mL (%)	135	17	22.4	14	23.7	0.87	0.92	0.70
Serum creatinine (µmol/L)	136	77	91.5 ± 43.2	59	100.1 ± 44.6	0.57	0.59	0.67
≥ 127 µmol/L (%)	136	7	9.1	9	15.3	0.86	0.85	0.85
Serum albumin (g/L)	136	77	4.1 ± 0.3	59	4.1 ± 0.3	0.73	0.42	0.35
Blood urea nitrogen (mmol/L)	136	77	18 ± 10	59	19 ± 7	0.96	0.99	0.94
Hemoglobin (g/dL)	136	77	13.1 ± 1.4	59	13.3 ± 1.4	0.65	0.89	0.89
Mean cell volume (fl)	136	77	90 ± 5	59	91 ± 5	0.44	0.74	0.72
S-adenosyl-methionine (nmol/L)	136	78	114 ± 66	58	117 ± 54	0.98	0.86	0.93
S-adenosyl-homocysteine (nmol/L)	137	78	33 ± 19	59	37 ± 24	0.98	0.86	0.84
SAM/SAH ratio	136	78	4.0 ± 2.0	58	3.9 ± 1.9	0.96	0.74	0.66
Multivitamin use (%)	137	26	33.3	28	47.5	0.03	0.10	0.10
Synthetic B_{12} intake (µg/d)	137	78	11.9 ± 68.0	59	9.9 ± 11.8	0.70	0.59	0.85
≥ 2.4 µg/d (%)	137	26	33.3	34	57.6	0.009	0.04	0.03
≥ 6 µg/d (%)	137	24	30.8	33	55.9	0.003	0.01	0.009
≥ 12 µg/d (%)	137	8	10.3	18	30.5	0.004	0.009	0.01
≥ 25 µg/d (%)	137	6	7.7	15	25.4	0.005	0.01	0.02
Synthetic folate intake (µg/d)	137	78	179.9 ± 213.7	59	266.2 ± 245.9	0.06	0.21	0.14
≥ 400 µg/d (%)	137	23	29.5	28	47.5	0.05	0.18	0.13

* PTA, pure-tone average threshold of 1, 2, and 4 kHz.
[a] Number of total participants.
[b] Number of participants with the condition.
[c] Logistic regression model adjusted for age and gender.
[d] Logistic regression model adjusted for age, gender, race, and creatinine.
[e] Logistic regression model adjusted for age, gender, race, creatinine, family history of hearing loss, and noise exposure.
[f] NHS: Nutritional Screening Initiative Questionnaire. Higher number indicates greater nutritional risk.
[g] 0 = poor, 1 = fair, 2 = good, and 3 = excellent. Higher number indicates better health status.
[h] Impaired cognition defined as ≥ 9 on Orientation Memory Concentration test.
[i] Anemic defined as hemoglobin ≤ 12 g/dL for females, ≤ 13 g/dL for males.

A POSSIBLE RELATIONSHIP OF HEARING IMPAIRMENT WITH MULTIPLE MEASURES OF VITAMIN B_{12} STATUS WAS EXAMINED IN OLDER ADULTS. PARTICIPANTS WITH ASYMMETRICAL HEARING LOSS WERE INCLUDED. PARTICIPANTS WITH CONDUCTIVE HEARING LOSS AND HIGH VITAMIN B_{12} CONCENTRATIONS (> 95 TH PERCENTILE) WERE EXCLUDED (TABLES C.13 - C.16).

Table C.13 Characteristics of participants at baseline *(Participants with high vitamin B_{12} concentrations and conductive hearing loss were excluded.)*

	N [a]	n [b]	Mean ± SD or %
Age (years)	104	104	74 ± 7 (58-92) [c]
Gender	104		
Female (%)		84	80.8
Male (%)		20	19.2
Race	104		
Caucasian (%)		71	68.3
African-American (%)		33	31.7
Hearing level in the best ear (dB)	104	104	32 ± 14 (8-73)
Hearing level in the worst ear (dB)	101	101	35 ± 14 (10-77)
Education (years)	102	102	9 ± 4 (0-16)
Family history of hearing loss (%)	104	24	23.1
Number of years exposed to noise (years)	103	103	16 ± 17 (0-62)
Body mass index (kg/m^2)	104	104	29.7 ± 7.0 (15.2-53.8)
Nutritional Health Score [d]	103	103	5 ± 4 (0-19)
Overall health [e]	104	104	1.6 ± 0.7 (0-3)
Number of medications	104	104	6 ± 3 (0-15)
Impaired cognition (%) [f]	104	28	26.9
Anemic (%) [g]	103	22	21.4
Serum vitamin B_{12} (pmol/L)	104	104	336.3 ± 132.5 (76.5-746.3)
< 148 pmol/L (%)	104	9	8.7
< 185 pmol/L (%)	104	11	10.6
< 221 pmol/L (%)	104	21	20.2
< 258 pmol/L (%)	104	29	27.9
< 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid (%)	104	15	14.4
Serum methylmalonic acid (nmol/L)	104	104	276 ± 240 (104-1972)
> 271 nmol/L (%)	104	32	30.8
> 376 nmol/L (%)	104	14	13.5
Serum total homocysteine (µmol/L)	104	104	10.3 ± 3.6 (5.1-27.0)
> 9.0 µmol/L (%)	104	56	53.9
> 11.0 µmol/L (%)	104	37	35.6
> 13.9 µmol/L (%)	104	11	10.6
Serum folate (nmol/L)	104	104	42.8 ± 25.4 (10.0-163.3)
Cystathionine (nmol/L)	104	104	252 ± 136 (89-968)
2-methylcitric acid (nmol/L)	104	104	182 ± 66 (58-453)

Serum pepsinogen I (ng/mL)	102	102	100.5 ± 73.9 (8.6-549.9)
≤ 20 ng/mL (%)	102	10	9.8
≤ 50 ng/mL (%)	102	24	23.5
Serum creatinine (μmol/L)	103	103	93.3 ± 38.9 (61.9-406.6)
≥ 127 μmol/L (%)	103	11	10.7
Serum albumin (g/L)	103	103	4.1 ± 0.3 (3.4-4.9)
Blood urea nitrogen (mmol/L)	103	103	18 ± 9 (8-79)
Hemoglobin (g/dL)	103	103	13.2 ± 1.4 (9.4-17.3)
Mean cell volume (fl)	103	103	90 ± 6 (68-101)
S-adenosyl-methionine (nmol/L)	103	103	114 ± 63 (42-511)
S-adenosyl-homocysteine (nmol/L)	104	104	33 ± 19 (10-144)
SAM/SAH ratio	103	103	4.0 ± 1.9 (0.9-9.4)
Multivitamin use (%)	104	35	33.7
Synthetic vitamin B_{12} intake (μg/d)	104	104	11.2 ± 59.2 (0.0-600.6)
≥ 2.4 μg/d (%)	104	38	36.5
≥ 6 μg/d (%)	104	35	33.7
≥ 12 μg/d (%)	104	14	13.5
≥ 25 μg/d (%)	104	13	12.5
Synthetic folate intake (μg/d)	104	104	183.5 ± 214.4 (0.0-1000.0)
≥ 400 μg/d (%)	104	29	27.9

[a] Number of total participants.
[b] Number of participants with the condition.
[c] Range in parentheses.
[d] NHS: Nutritional Screening Initiative Questionnaire. Higher number indicates greater nutritional risk.
[e] 0 = poor, 1 = fair, 2 = good, and 3 = excellent. Higher number indicates better health status.
[f] Impaired cognition defined as ≥ 9 on Orientation Memory Concentration test.
[g] Anemic defined as hemoglobin ≤ 12 g/dL for females, ≤ 13 g/dL for males.

Table C.14 Correlations of vitamin B_{12}, methylmalonic acid, and total homocysteine with pure-tone average (1, 2, and 4 kHz) in the best ear and the worst ear at baseline [a] *(Participants with high vitamin B_{12} concentrations and conductive hearing loss were excluded.)*

	Pure-tone average threshold in the best ear (N=102) [b]	**Pure-tone average threshold in the worst ear (N=99)** [b]
Vitamin B_{12}	r = 0.009	r = -0.04
	P = 0.93	*P* = 0.70
Methylmalonic acid	r = 0.12	r = 0.09
	P = 0.88	*P* = 0.38
Total homocysteine	r = -0.07	r = -0.09
	P = 0.47	*P* = 0.37

[a] Partial Spearman correlation coefficient from multivariable linear regression analysis; adjusted for age, gender, race, creatinine, family history of hearing loss, and noise exposure.
[b] Number of total participants.

Table C.15 Demographics, nutrition and auditory function in the best ear and the worst ear at baseline ***(PTA ≤ 25 vs. > 25 dB hearing level;*** *Participants with high vitamin B_{12} concentrations and conductive hearing loss were excluded.)**

		Hearing						
		Normal (PTA ≤ 25 dB HL)		Impaired (PTA >25 dB HL)				
	N [a]	n [b]	Mean ± SD or %	n [b]	Mean ± SD or %	P value[c]	P value[d]	P value[e]
Best ear								
n	104	48		56				
Hearing level (dB)	104	48	19 ± 4	56	42 ± 11			
Age (years)	104	48	71 ± 6	56	77 ± 8	<0.0001	<0.0001	<0.0001
Gender (% of female)	104	45	93.8	39	69.6	0.002	0.002	0.007
Race (% of Caucasian)	104	29	60.4	42	75.0	0.18	0.19	0.19
Education (years)	102	48	9 ± 3	54	9 ± 4	0.64	0.84	0.75
Family history of hearing loss (%)	104	11	22.9	13	23.2	0.66	0.52	0.47
Number of years exposed to noise (years)	103	47	12 ± 14	56	19 ± 19	0.33	0.32	0.30
Body mass index (kg/m^2)	104	48	30.7 ± 7.9	56	28.9 ± 6.0	0.99	0.59	0.54
Nutritional Health Score [f]	103	48	6 ± 4	55	5 ± 3	0.09	0.14	0.11
Overall health [g]	104	48	1.5 ± 0.7	56	1.7 ± 0.7	0.40	0.59	0.54
Number of medications	104	48	6 ± 3	56	5 ± 3	0.60	0.66	0.53
Impaired cognition (%) [h]	104	10	20.8	18	32.1	0.57	0.40	0.35
Anemic (%) [i]	103	10	21.3	12	21.4	0.26	0.48	0.40
Serum vitamin B_{12} (pmol/L)	104	48	361.4 ± 134.8	56	314.7 ± 127.8	0.19	0.36	0.29
< 148 pmol/L (%)	104	2	4.2	7	12.5	0.40	0.51	0.52
< 185 pmol/L (%)	104	2	4.2	9	16.1	0.17	0.23	0.22
< 221 pmol/L (%)	104	7	14.6	14	25.0	0.22	0.30	0.33
< 258 pmol/L (%)	104	10	20.8	19	33.9	0.18	0.31	0.31
< 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid (%)	104	5	10.4	10	17.9	0.37	0.58	0.65
Serum methylmalonic acid (nmol/L)	104	48	219 ± 94	56	326 ± 308	0.22	0.30	0.28
> 271 nmol/L (%)	104	11	22.9	21	37.5	0.75	0.86	0.81
> 376 nmol/L (%)	104	4	8.3	10	17.9	0.97	0.94	0.83
Serum total homocysteine (µmol/L)	104	48	9.8 ± 3.2	56	10.8 ± 4.0	0.89	0.85	0.73
> 9.0 µmol/L (%)	104	24	50.0	32	57.1	0.63	0.75	0.85
> 11.0 µmol/L (%)	104	14	29.2	23	41.1	0.72	0.46	0.50
> 13.9 µmol/L (%)	104	4	8.3	7	12.5	0.82	0.79	0.72
Serum folate (nmol/L)	104	48	40.2 ± 22.9	56	45.0 ± 27.3	0.23	0.32	0.35
Cystathionine (nmol/L)	104	48	248 ± 149	56	255 ± 125	0.36	0.50	0.50
2-methylcitric acid (nmol/L)	104	48	176 ± 65	56	187 ± 67	0.63	0.57	0.57
Serum pepsinogen I (ng/mL)	102	46	103.4 ± 82.5	56	98.0 ± 66.7	0.26	0.29	0.26
≤ 20 ng/mL (%)	102	2	4.4	8	14.3	0.13	0.17	0.14

≤ 50 ng/mL (%)	102	10	21.7	14	25.0	0.75	0.64	0.59
Serum creatinine (µmol/L)	103	47	91.5 ± 51.8	56	94.9 ± 23.7	0.61	0.56	0.53
≥ 127 µmol/L (%)	103	4	8.5	7	12.5	0.68	0.69	0.73
Serum albumin (g/L)	103	47	4.1 ± 0.3	56	4.1 ± 0.3	0.69	0.93	0.94
Blood urea nitrogen (mmol/L)	103	47	17 ± 11	56	18 ± 7	0.52	0.17	0.14
Hemoglobin (g/dL)	103	47	13.0 ± 1.4	56	13.3 ± 1.4	0.32	0.58	0.46
Mean cell volume (fl)	103	47	90 ± 5	56	90 ± 6	0.94	0.78	0.76
S-adenosyl-methionine (nmol/L)	103	48	114 ± 73	55	113 ± 55	0.98	0.95	0.92
S-adenosyl-homocysteine (nmol/L)	104	48	33 ± 22	56	34 ± 16	0.95	0.80	0.85
SAM/SAH ratio	103	48	4.0 ± 1.8	55	4.0 ± 2.0	0.61	0.73	0.68
Multivitamin use (%)	104	15	31.3	20	35.7	0.19	0.35	0.34
Synthetic B_{12} intake (µg/d)	104	48	15.7 ± 86.4	56	7.4 ± 12.3	0.90	0.98	0.86
≥ 2.4 µg/d (%)	104	16	33.3	22	39.3	0.52	0.86	0.87
≥ 6 µg/d (%)	104	14	29.3	21	37.5	0.18	0.35	0.33
≥ 12 µg/d (%)	104	4	8.3	10	17.9	0.06	0.08	0.07
≥ 25 µg/d (%)	104	3	6.3	10	17.9	0.04	0.06	0.05
Synthetic folate intake (µg/d)	104	48	181.8 ± 221.3	56	184.9 ± 210.2	0.95	0.56	0.61
≥ 400 µg/d (%)	104	13	27.1	16	28.6	0.76	0.84	0.85
Worst ear								
n	101	35		66				
Hearing level (dB)	101	35	21 ± 4	66	43 ± 12			
Age (years)	101	35	70 ± 5	66	76 ± 8	0.0003	0.008	0.0003
Gender (% of female)	101	33	94.3	50	75.8	0.01	0.01	0.05
Race (% of Caucasian)	101	20	57.1	48	72.7	0.13	0.15	0.28
Education (years)	99	35	9 ± 3	64	9 ± 4	0.65	0.82	0.80
Family history of hearing loss (%)	101	6	17.1	17	25.8	0.44	0.42	0.51
Number of years exposed to noise (years)	100	34	10 ± 13	66	18 ± 18	0.17	0.17	0.19
Body mass index (kg/m^2)	101	35	31.0 ± 8.1	66	29.4 ± 6.3	0.84	0.61	0.65
Nutritional Health Score [f]	100	35	6 ± 4	65	5 ± 4	0.39	0.54	0.47
Overall health [g]	101	35	1.6 ± 0.7	66	1.6 ± 0.8	0.81	0.89	0.99
Number of medications	101	35	6 ± 3	66	5 ± 3	0.43	0.49	0.41
Impaired cognition (%) [h]	101	7	20.0	20	30.3	0.64	0.50	0.24
Anemic (%) [i]	100	6	17.7	15	22.7	0.78	0.79	0.98
Serum vitamin B_{12} (pmol/L)	101	35	371.2 ± 131.8	66	316.7 ± 131.9	0.14	0.31	0.36
< 148 pmol/L (%)	101	1	2.9	8	12.1	0.34	0.46	0.51
< 185 pmol/L (%)	101	1	2.9	10	15.2	0.20	0.28	0.34
< 221 pmol/L (%)	101	4	11.4	17	25.8	0.13	0.20	0.26
< 258 pmol/L (%)	101	6	17.1	23	34.9	0.10	0.20	0.22
< 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid (%)	101	1	2.9	14	21.2	0.04	0.07	0.10
Serum methylmalonic acid (nmol/L)	101	35	202 ± 80	66	314 ± 288	0.06	0.08	0.07
> 271 nmol/L (%)	101	5	14.3	25	37.9	0.11	0.12	0.07

> 376 nmol/L (%)	101	2	5.7	11	16.7	0.61	0.52	0.51
Serum total homocysteine (µmol/L)	101	35	9.9 ± 3.5	66	10.5 ± 3.7	0.79	0.91	0.96
> 9.0 µmol/L (%)	101	16	45.7	38	57.6	0.83	0.64	0.68
> 11.0 µmol/L (%)	101	12	34.3	24	36.4	0.47	0.62	0.53
> 13.9 µmol/L (%)	101	4	11.4	6	9.1	0.25	0.44	0.64
Serum folate (nmol/L)	101	35	42.0 ± 24.3	66	42.6 ± 25.8	0.94	0.76	0.94
Cystathionine (nmol/L)	101	35	253 ± 163	66	252 ± 124	0.28	0.47	0.55
2-methylcitric acid (nmol/L)	101	35	176 ± 71	66	186 ± 65	0.67	0.62	0.68
Serum pepsinogen I (ng/mL)	99	34	106.3 ± 93.0	65	96.7 ± 61.8	0.41	0.46	0.31
≤ 20 ng/mL (%)	99	1	2.9	8	12.3	0.18	0.23	-
≤ 50 ng/mL (%)	99	9	26.5	14	21.5	0.44	0.55	0.72
Serum creatinine (µmol/L)	100	34	92.6 ± 59.3	66	93.5 ± 24.1	0.61	0.56	0.53
≥ 127 µmol/L (%)	100	3	8.8	8	12.1	0.66	0.70	0.67
Serum albumin (g/L)	100	34	4.1 ± 0.2	66	4.1 ± 0.3	0.92	0.70	0.60
Blood urea nitrogen (mmol/L)	100	34	18 ± 12	66	18 ± 6	0.90	0.61	0.52
Hemoglobin (g/dL)	100	34	13.2 ± 1.3	66	13.2 ± 1.4	0.98	0.51	0.71
Mean cell volume (fl)	100	34	90 ± 4	66	90 ± 6	0.95	0.65	0.69
S-adenosyl-methionine (nmol/L)	100	35	117 ± 84	65	112 ± 51	0.96	0.91	0.91
S-adenosyl-homocysteine (nmol/L)	101	35	33 ± 25	66	33 ± 15	0.65	0.47	0.56
SAM/SAH ratio	100	35	4.1 ± 1.8	65	3.9 ± 2.0	0.99	0.86	0.94
Multivitamin use (%)	101	12	34.3	22	33.3	0.55	0.92	0.90
Synthetic B_{12} intake (µg/d)	101	35	20.7 ± 101.1	66	6.6 ± 11.5	0.61	0.68	0.62
≥ 2.4 µg/d (%)	101	11	31.4	26	39.4	0.35	0.69	0.63
≥ 6 µg/d (%)	101	11	31.4	23	34.9	0.44	0.81	0.75
≥ 12 µg/d (%)	101	4	11.4	10	15.2	0.42	0.52	0.56
≥ 25 µg/d (%)	101	3	8.6	10	15.2	0.27	0.38	0.43
Synthetic folate intake (µg/d)	101	35	187.6 ± 236.8	66	181.9 ± 205.0	0.86	0.34	0.42
≥ 400 µg/d (%)	101	10	28.6	18	27.3	0.99	0.54	0.65

* PTA, pure-tone average threshold of 1, 2, and 4 kHz.
[a] Number of total participants.
[b] Number of participants with the condition.
[c] Logistic regression model adjusted for age and gender.
[d] Logistic regression model adjusted for age, gender, race, and creatinine.
[e] Logistic regression model adjusted for age, gender, race, creatinine, family history of hearing loss, and noise exposure.
[f] NHS: Nutritional Screening Initiative Questionnaire. Higher number indicates greater nutritional risk.
[g] 0 = poor, 1 = fair, 2 = good, and 3 = excellent. Higher number indicates better health status.
[h] Impaired cognition defined as ≥ 9 on Orientation Memory Concentration test.
[i] Anemic defined as hemoglobin ≤ 12 g/dL for females, ≤ 13 g/dL for males.
- Not applicable. There was possibly a quasi-complete separation of data points.

Table C.16 Demographics, nutrition and auditory function in the best ear and the worst ear at baseline ***(PTA ≤ 40 vs. > 40 dB hearing level;*** *Participants with high vitamin B_{12} level and conductive hearing loss were excluded.)**

		Hearing						
		PTA ≤ 40 dB HL		PTA > 40 dB HL				
	N [a]	n [b]	Mean ± SD or %	n [b]	Mean ± SD or %	P value[c]	P value[d]	P value[e]
Best ear								
n	104	77		27				
Hearing level (dB)	104	77	25 ± 8	27	52 ± 8			
Age (years)	104	77	73 ± 7	27	78 ± 8	0.003	0.002	0.002
Gender (% of female)	104	70	90.9	14	51.9	<0.0001	0.0002	0.002
Race (% of Caucasian)	104	48	62.3	23	85.2	0.06	0.05	0.14
Education (years)	102	76	9 ± 4	26	9 ± 4	0.82	0.50	0.73
Family history of hearing loss (%)	104	14	18.2	10	37.0	0.10	0.23	0.22
Number of years exposed to noise (years)	103	76	12 ± 14	27	26 ± 21	0.03	0.03	0.03
Body mass index (kg/m^2)	104	77	30.1 ± 7.3	27	28.7 ± 5.8	0.65	0.39	0.49
Nutritional Health Score [f]	103	76	5 ± 4	27	5 ± 4	0.65	0.97	0.80
Overall health [g]	104	77	1.6 ± 0.8	27	1.6 ± 0.7	0.75	0.82	0.96
Number of medications	104	77	6 ± 3	27	6 ± 3	0.61	0.50	0.58
Impaired cognition (%) [h]	104	19	24.7	9	33.3	0.67	0.28	0.17
Anemic (%) [i]	103	17	22.4	5	18.5	0.16	0.36	0.19
Serum vitamin B_{12} (pmol/L)	104	77	341.4 ± 131.9	27	321.6 ± 135.6	0.79	0.71	0.58
< 148 pmol/L (%)	104	6	7.8	3	11.1	0.72	0.64	0.69
< 185 pmol/L (%)	104	7	9.1	4	14.8	0.98	0.99	0.99
< 221 pmol/L (%)	104	14	18.2	7	25.9	0.55	0.70	0.77
< 258 pmol/L (%)	104	20	26.0	9	33.3	0.71	0.93	0.95
< 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid (%)	104	9	11.7	6	22.2	0.19	0.33	0.64
Serum methylmalonic acid (nmol/L)	104	77	237 ± 108	27	387 ± 420	0.32	0.40	0.54
> 271 nmol/L (%)	104	19	24.7	13	48.2	0.23	0.25	0.32
> 376 nmol/L (%)	104	8	10.4	6	22.2	0.91	0.63	0.45
Serum total homocysteine (µmol/L)	104	77	10.2 ± 3.5	27	10.9 ± 4.1	0.42	0.79	0.83
> 9.0 µmol/L (%)	104	39	50.7	17	63.0	0.83	0.73	0.63
> 11.0 µmol/L (%)	104	27	35.1	10	37.0	0.28	0.74	0.62
> 13.9 µmol/L (%)	104	8	10.4	3	11.1	0.31	0.55	0.85
Serum folate (nmol/L)	104	77	41.9 ± 22.8	27	45.2 ± 31.9	0.51	0.94	0.68
Cystathionine (nmol/L)	104	77	249 ± 135	27	260 ± 142	0.23	0.28	0.14
2-methylcitric acid (nmol/L)	104	77	182 ± 65	27	181 ± 70	0.19	0.14	0.11
Serum pepsinogen I (ng/mL)	102	75	100.0 ± 73.7	27	101.8 ± 75.8	0.50	0.54	0.24
≤ 20 ng/mL (%)	102	7	9.3	3	11.1	0.74	0.83	0.68
≤ 50 ng/mL (%)	102	18	24.0	6	22.2	0.76	0.83	0.83

Serum creatinine (µmol/L)	103	76	92.0 ± 43.5	27	96.9 ± 21.6	0.39	0.31	0.31
≥ 127 µmol/L (%)	103	8	10.5	3	11.1	0.07	0.06	0.05
Serum albumin (g/L)	103	76	4.1 ± 0.3	27	4.1 ± 0.3	0.95	0.48	0.41
Blood urea nitrogen (mmol/L)	103	76	18 ± 10	27	18 ± 6	0.97	0.51	0.65
Hemoglobin (g/dL)	103	76	13.1 ± 1.3	27	13.6 ± 1.5	0.26	0.49	0.34
Mean cell volume (fl)	103	76	90 ± 5	27	90 ± 7	0.88	0.44	0.44
S-adenosyl-methionine (nmol/L)	103	77	113 ± 65	26	115 ± 61	0.88	0.96	0.90
S-adenosyl-homocysteine (nmol/L)	104	77	34 ± 20	27	31 ± 16	0.15	0.14	0.12
SAM/SAH ratio	103	77	3.9 ± 2.0	26	4.2 ± 1.7	0.14	0.25	0.32
Multivitamin use (%)	104	26	33.8	9	33.3	0.55	0.99	0.86
Synthetic B_{12} intake (µg/d)	104	77	12.2 ± 68.5	27	8.5 ± 12.9	0.78	0.64	0.66
≥ 2.4 µg/d (%)	104	26	33.8	12	44.4	0.48	0.98	0.88
≥ 6 µg/d (%)	104	24	31.2	11	40.7	0.37	0.82	0.66
≥ 12 µg/d (%)	104	8	10.4	6	22.2	0.04	0.08	0.10
≥ 25 µg/d (%)	104	7	9.1	6	22.2	0.04	0.08	0.09
Synthetic folate intake (µg/d)	104	77	175.6 ± 216.5	27	206.0 ± 210.6	0.42	0.95	0.88
≥ 400 µg/d (%)	104	20	26.0	9	33.3	0.48	0.99	0.77
Worst ear								
n	101	65		36				
Hearing level (dB)	101	65	26 ± 7	36	52 ± 9			
Age (years)	101	65	72 ± 6	36	77 ± 8	0.0004	0.0004	0.0004
Gender (% of female)	101	61	93.9	22	61.1	<0.0001	0.0002	0.0008
Race (% of Caucasian)	101	41	63.1	27	75.0	0.31	0.30	0.49
Education (years)	99	64	10 ± 3	35	9 ± 4	0.55	0.30	0.32
Family history of hearing loss (%)	101	12	18.5	11	30.6	0.25	0.33	0.34
Number of years exposed to noise (years)	100	64	12 ± 14	36	20 ± 20	0.33	0.33	0.34
Body mass index (kg/m^2)	101	65	30.4 ± 7.4	36	29.1 ± 6.0	0.82	0.58	0.67
Nutritional Health Score [f]	100	65	5 ± 4	35	4 ± 4	0.18	0.26	0.28
Overall health [g]	101	65	1.6 ± 0.8	36	1.6 ± 0.7	0.77	0.99	0.99
Number of medications	101	65	6 ± 3	36	6 ± 3	0.78	0.86	0.87
Impaired cognition (%) [h]	101	14	21.5	13	36.1	0.24	0.14	0.08
Anemic (%) [i]	100	13	20.3	8	22.2	0.53	0.80	0.64
Serum vitamin B_{12} (pmol/L)	101	65	342.6 ± 127.4	36	323.0 ± 145.5	0.94	0.76	0.60
< 148 pmol/L (%)	101	3	4.6	6	16.7	0.21	0.24	0.25
< 185 pmol/L (%)	101	4	6.2	7	19.4	0.20	0.23	0.26
< 221 pmol/L (%)	101	11	16.9	10	27.8	0.34	0.41	0.49
< 258 pmol/L (%)	101	16	24.6	13	36.1	0.45	0.60	0.69
< 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid (%)	101	7	10.8	8	22.2	0.15	0.22	0.35
Serum methylmalonic acid (nmol/L)	101	65	229 ± 93	36	358 ± 377	0.35	0.36	0.44
> 271 nmol/L (%)	101	15	23.1	15	41.7	0.25	0.24	0.23
> 376 nmol/L (%)	101	6	9.2	7	19.4	0.95	0.98	0.93

Serum total homocysteine (µmol/L)	101	65	10.0 ± 3.2	36	10.9 ± 4.3	0.54	0.79	0.71
> 9.0 µmol/L (%)	101	32	49.2	22	61.1	0.74	0.96	0.93
> 11.0 µmol/L (%)	101	22	33.9	14	38.9	0.44	0.71	0.66
> 13.9 µmol/L (%)	101	6	9.2	4	11.1	0.54	0.86	0.96
Serum folate (nmol/L)	101	65	41.0 ± 23.1	36	44.9 ± 28.7	0.17	0.25	0.14
Cystathionine (nmol/L)	101	65	247 ± 135	36	262 ± 144	0.23	0.28	0.24
2-methylcitric acid (nmol/L)	101	65	182 ± 66	36	185 ± 69	0.16	0.11	0.09
Serum pepsinogen I (ng/mL)	99	63	104.1 ± 75.6	36	92.9 ± 70.6	0.09	0.10	0.06
≤ 20 ng/mL (%)	99	4	6.4	5	13.9	0.17	0.20	0.17
≤ 50 ng/mL (%)	99	13	20.6	10	27.8	0.42	0.36	0.29
Serum creatinine (µmol/L)	100	64	91.2 ± 46.4	36	96.7 ± 22.4	0.63	0.58	0.61
≥ 127 µmol/L (%)	100	6	9.4	5	13.9	0.23	0.22	0.21
Serum albumin (g/L)	100	64	4.1 ± 0.3	36	4.1 ± 0.3	0.55	0.36	0.34
Blood urea nitrogen (mmol/L)	100	64	18 ± 10	36	18 ± 6	0.98	0.60	0.62
Hemoglobin (g/dL)	100	64	13.1 ± 1.4	36	13.3 ± 1.4	0.49	0.28	0.37
Mean cell volume (fl)	100	64	90 ± 5	36	90 ± 6	0.81	0.94	0.95
S-adenosyl-methionine (nmol/L)	100	65	114 ± 69	35	114 ± 56	0.72	0.60	0.65
S-adenosyl-homocysteine (nmol/L)	101	65	33 ± 20	36	34 ± 17	0.69	0.47	0.44
SAM/SAH ratio	100	65	4.0 ± 2.0	35	3.9 ± 1.7	0.89	0.74	0.63
Multivitamin use (%)	101	21	32.3	13	36.1	0.18	0.32	0.35
Synthetic B_{12} intake (µg/d)	101	65	12.8 ± 74.4	36	9.1 ± 12.7	0.75	0.68	0.78
≥ 2.4 µg/d (%)	101	20	30.8	17	47.2	0.09	0.18	0.14
≥ 6 µg/d (%)	101	18	27.7	16	44.4	0.03	0.07	0.05
≥ 12 µg/d (%)	101	5	7.7	9	25.0	0.005	0.008	0.008
≥ 25 µg/d (%)	101	4	6.2	9	25.0	0.004	0.006	0.007
Synthetic folate intake (µg/d)	101	65	173.0 ± 213.0	36	203.5 ± 221.2	0.37	0.67	0.59
≥ 400 µg/d (%)	101	17	26.2	11	30.6	0.50	0.78	0.66

* PTA, pure-tone average threshold of 1, 2, and 4 kHz.
[a] Number of total participants.
[b] Number of participants with the condition.
[c] Logistic regression model adjusted for age and gender.
[d] Logistic regression model adjusted for age, gender, race, and creatinine.
[e] Logistic regression model adjusted for age, gender, race, creatinine, family history of hearing loss, and noise exposure.
[f] NHS: Nutritional Screening Initiative Questionnaire. Higher number indicates greater nutritional risk.
[g] 0 = poor, 1 = fair, 2 = good, and 3 = excellent. Higher number indicates better health status.
[h] Impaired cognition defined as ≥ 9 on Orientation Memory Concentration test.
[i] Anemic defined as hemoglobin ≤ 12 g/dL for females, ≤ 13 g/dL for males.

A POSSIBLE RELATIONSHIP OF AGE-RELATED HEARING LOSS WITH MULTIPLE MEASURES OF VITAMIN B_{12} STATUS WAS EXAMINED IN CAUCASIANS (TABLES C.17 – C.19).

Table C.17 Characteristics of participants at baseline in Caucasians

	N [a]	**n** [b]	**Mean ± SD or %**
Age (years)	60	60	75 ± 7 (58-92) [c]
Gender	60		
Female (%)		48	80.0
Male (%)		12	20.0
Hearing level in the best ear (dB)	60	60	34 ± 15 (15-73)
Hearing level in the worst ear (dB)	57	57	36 ± 15 (17-77)
Education (years)	58	58	10 ± 3 (0-16)
Family history of hearing loss (%)	60	15	25.0
Number of years exposed to noise (years)	60	60	16 ± 18 (0-62)
Number of medications	60	60	6 ± 3 (0-13)
Anemic (%) [d]	60	10	16.7
Serum vitamin B_{12} (pmol/L)	60	60	308.1 ± 113.1 (76.5-559.6)
< 185 pmol/L (%)	60	8	13.3
< 258 pmol/L (%)	60	20	33.3
< 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid (%)	60	12	20.0
Serum MMA (nmol/L)	60	60	328.0 ± 298.7 (138-1972)
> 271 nmol/L (%)	60	25	41.7
Serum tHcy (µmol/L)	60	60	10.8 ± 4.1 (5.1-27.0)
Serum folate (nmol/L)	60	60	48.6 ± 28.9 (13.6-163.3)
Serum pepsinogen I (ng/mL)	59	59	110.3 ± 86.1 (8.6-549.9)
≤ 20 ng/mL (%)	59	6	10.2
Serum creatinine (µmol/L)	60	60	97.2 ± 46.7 (61.9-406.6)
≥ 127 µmol/L (%)	60	7	11.7
Serum albumin (g/L)	60	60	4.2 ± 0.3 (3.6-4.9)
Hemoglobin (g/dL)	60	60	13.3 ± 1.3 (9.4-16.8)
Mean cell volume (fl)	60	60	90 ± 6 (68-100)
Multivitamin use (%)	60	23	38.3
Synthetic vitamin B_{12} intake (µg/d)	60	60	6.7 ± 11.3 (0.0-50.4)
≥ 2.4 µg/d (%)	60	27	45.0
Synthetic folate intake (µg/d)	60	60	230.6 ± 234.0 (0.0-1000.0)
≥ 400 µg/d (%)	60	22	36.7

[a] Number of total participants.
[b] Number of participants with the condition.
[c] Range in parentheses.
[d] Anemic defined as hemoglobin ≤ 12 g/dL for females, ≤ 13 g/dL for males.

Table C.18 Correlations of vitamin B_{12}, methylmalonic acid, and total homocysteine with pure-tone average threshold (1, 2, and 4 kHz) in the best ear and the worst ear at baseline in Caucasians [a]

	Pure-tone average threshold in the best ear (N = 60) [b]	**Pure-tone average threshold in the worst ear (N = 57)** [b]
Vitamin B_{12}	r = -0.10 *P* = 0.48	r = -0.20 *P* = 0.15
Methylmalonic acid	r = 0.15 *P* = 0.28	r = 0.23 *P* = 0.10
Total homocysteine	r = -0.06 *P* = 0.66	r = -0.06 *P* = 0.69

[a] Partial Spearman correlation coefficient, controlled for age, race, creatinine, family history of hearing loss, and noise exposure.
[b] Number of total participants.

Table C.19 Demographics, nutrition and auditory function in the best ear at baseline in Caucasians

Best ear	N [c]	Hearing: Normal (PTA [a] ≤ 25 dB HL[b]) n [d]	Mean ± SD or %	Hearing: Impaired (PTA >25 dB HL) n [d]	Mean ± SD or %	P value[e]	P value[f]	P value[g]
n	60	24		36				
Hearing level (dB)	60	24	20 ± 3	36	43 ± 12			
Age (years)	60	24	72 ± 6	36	77 ± 8	0.01	0.01	0.009
Gender (% of female)	60	23	95.8	25	69.4	0.03	0.03	0.03
Education (years)	58	24	10 ± 3	34	10 ± 4	0.36	0.37	0.41
Family history of hearing loss (%)	60	6	25.0	9	25.0	0.61	0.56	0.61
Number of years exposed to noise (years)	60	24	14 ± 16	36	18 ± 19	0.63	0.60	0.66
Number of medications	60	24	7 ± 3	36	6 ± 4	0.28	0.30	0.31
Anemic (%) [h]	60	5	20.8	5	13.9	0.22	0.32	0.34
Serum vitamin B_{12} (pmol/L)	60	24	321.2 ± 92.7	36	299.5 ± 125.4	0.43	0.50	0.38
< 185 pmol/L (%)	60	1	4.2	7	19.4	0.20	0.21	0.15
< 258 pmol/L (%)	60	7	29.2	13	36.1	0.45	0.51	0.45
< 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid (%)	60	4	16.7	8	22.2	0.68	0.70	0.56
Serum MMA (nmol/L)	60	24	244 ± 99	36	384 ± 369	0.28	0.15	0.14
> 271 nmol/L (%)	60	8	33.3	17	47.2	0.86	0.64	0.61
Serum tHcy (µmol/L)	60	24	9.8 ± 3.5	36	11.4 ± 4.5	0.52	0.17	0.14
Serum folate (nmol/L)	60	24	48.4 ± 24.8	36	48.8 ± 31.7	0.89	0.77	0.93
Serum pepsinogen I (ng/mL)	59	23	126.0 ± 104.8	36	100.3 ± 71.6	0.09	0.13	0.13
≤ 20 ng/mL (%)	59	0	0.0	6	16.7	0.07[i]	-	-
Serum creatinine (µmol/L)	60	24	98.0 ± 68.8	36	96.7 ± 23.8	0.59	0.56	0.58
≥ 127 µmol/L (%)	60	2	8.3	5	13.9	0.54	0.99	0.99
Serum albumin (g/L)	60	24	4.2 ± 0.3	36	4.1 ± 0.3	0.84	0.83	0.81
Hemoglobin (g/dL)	60	24	13.2 ± 1.5	36	13.4 ± 1.1	0.52	0.70	0.82
Mean cell volume (fl)	60	24	90 ± 6	36	90 ± 6	0.60	0.60	0.56
Multivitamin use (%)	60	10	41.7	13	36.1	0.57	0.67	0.66
Synthetic B_{12} intake (µg/d)	60	24	5.0 ± 6.8	36	7.8 ± 13.5	0.17	0.19	0.19
≥ 2.4 µg/d (%)	60	12	50.0	15	41.7	0.68	0.58	0.51
Synthetic folate intake (µg/d)	60	24	271.0 ± 245.3	36	203.6 ± 225.7	0.32	0.24	0.19
≥ 400 µg/d (%)	60	10	41.7	12	33.3	0.63	0.54	0.47

[a] PTA, pure-tone average threshold of 1, 2, and 4 kHz.
[b] HL, hearing level.
[c] Number of total participants.
[d] Number of participants with the condition.
[e] Logistic regression model controlled for age and gender.
[f] Logistic regression model controlled for age, gender, and creatinine.
[g] Logistic regression model controlled for age, gender, creatinine, family history of hearing loss, and noise exposure.
[h] Anemic defined as hemoglobin ≤ 12 g/dL for females, ≤ 13 g/dL for males.
[i] Chi-square analyses.
- Not applicable. There was possibly a quasi-complete separation of data points.

A POSSIBLE RELATIONSHIP OF AGE-RELATED HEARING LOSS WITH MULTIPLE MEASURES OF VITAMIN B_{12} STATUS WAS EXAMINED IN AFRICAN-AMERICANS (TABLES C.20 – C.23).

Table C.20 Characteristics of participants at baseline in African-Americans

	N [a]	n [b]	Mean ± SD or %
Age (years)	33	33	74 ± 8 (65-90) [c]
Gender	33		
Female (%)		29	87.9
Male (%)		4	12.1
Hearing level in the best ear (dB)	33	33	27 ± 11 (8-50)
Hearing level in the worst ear (dB)	33	33	30 ± 11 (10-53)
Education (years)	33	33	8 ± 4 (0-14)
Family history of hearing loss (%)	33	4	12.1
Number of years exposed to noise (years)	32	32	12 ± 15 (0-57)
Number of medications	33	33	5 ± 3 (0-15)
Anemic (%) [d]	32	11	34.4
Serum vitamin B_{12} (pmol/L)	33	33	397.7 ± 155.2 (139-746.3)
< 185 pmol/L (%)	33	2	6.1
< 258 pmol/L (%)	33	6	18.2
< 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid (%)	33	1	3.0
Serum MMA (nmol/L)	33	33	192.9 ± 65.1 (104.0-366.0)
> 271 nmol/L (%)	33	4	12.1
Serum tHcy (μmol/L)	33	33	9.9 ± 2.9 (6.1-16.1)
Serum folate (nmol/L)	33	33	33.3 ± 16.7 (10.0-79.1)
Serum pepsinogen I (ng/mL)	33	33	84.1 ± 51.7 (11.5-212.2)
≤ 20 ng/mL (%)	33	3	9.1
Serum creatinine (μmol/L)	32	32	87.8 ± 22.7 (61.9-141.4)
≥ 127 μmol/L (%)	33	3	9.1
Serum albumin (g/L)	32	32	4.0 ± 0.3 (3.4-4.5)
Hemoglobin (g/dL)	32	32	12.6 ± 1.1 (9.9-16.1)
Mean cell volume (fl)	32	32	88 ± 5 (74-96)
Multivitamin use (%)	33	7	21.2
Synthetic vitamin B_{12} intake (μg/d)	33	33	20.4 ± 104.3 (0.0-600.6)
≥ 2.4 μg/d (%)	33	6	18.2
Synthetic folate intake (μg/d)	33	33	84.2 ± 135.6 (0.0-520.0)
≥ 400 μg/d (%)	33	3	9.1

[a] Number of total participants.
[b] Number of participants with the condition.
[c] Range in parentheses.
[d] Anemic defined as hemoglobin ≤ 12 g/dL for females, ≤ 13 g/dL for males.

Table C.21 Correlations of vitamin B_{12}, methylmalonic acid, and total homocysteine with pure-tone average threshold (1, 2, and 4 kHz) in the best ear and the worst ear at baseline in African-Americans [a]

	Pure-tone average threshold in the best ear (N = 31) [b]	**Pure-tone average threshold in the worst ear (N = 31)** [b]
Vitamin B_{12}	r = -0.10 *P* = 0.64	r = 0.11 *P* = 0.58
Methylmalonic acid	r = 0.22 *P* = 0.27	r = 0.22 *P* = 0.28
Total homocysteine	r = 0.02 *P* = 0.90	r = -0.03 *P* = 0.89

[a] Partial Spearman correlation coefficient, controlled for age, race, creatinine, family history of hearing loss, and noise exposure in African-American.
[b] Number of total participants.

Table C.22 Demographics, nutrition and auditory function in the best ear at baseline in African-Americans

Best ear	N [c]	Normal (PTA [a] ≤ 25 dB HL[b]) n [d]	Normal Mean ± SD or %	Impaired (PTA >25 dB HL) n [d]	Impaired Mean ± SD or %	P value[e]	P value[f]	P value[g]
n	33	19		14				
Hearing level (dB)	33	19	19 ± 4	14	37 ± 4			
Age (years)	33	19	70 ± 5	14	80 ± 7	0.003	0.004	0.01
Gender (% of female)	33	18	94.7	11	78.6	0.04	0.06	0.21
Education (years)	33	19	9 ± 3	14	6 ± 4	0.70	0.67	1.0
Family history of hearing loss (%)	33	3	15.8	1	7.1	0.31	0.21	0.14
Number of years exposed to noise (years)	32	18	7 ± 11	14	19 ± 18	0.07	0.06	0.05
Number of medications	33	19	6 ± 4	14	5 ± 2	0.46	0.33	0.39
Anemic (%) [h]	32	5	27.8	6	42.9	0.43	0.44	0.20
Serum vitamin B_{12} (pmol/L)	33	19	437.1 ± 151.6	14	344.2 ± 148.8	0.41	0.39	0.43
< 185 pmol/L (%)	33	0	0.0	2	14.3	0.17[i]	-	-
< 258 pmol/L (%)	33	2	10.5	4	28.6	0.59	0.59	0.21
< 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid (%)	33	0	0.0	1	7.1	0.42[i]	-	-
Serum MMA (nmol/L)	33	19	166 ± 54	14	230 ± 62	0.16	0.19	0.66
> 271 nmol/L (%)	33	1	5.3	3	21.4	0.61	0.57	-
Serum tHcy (µmol/L)	33	19	9.8 ± 3.0	14	10.0 ± 2.9	0.20	0.08	-
Serum folate (nmol/L)	33	19	31.6 ± 19.3	14	35.7 ± 12.7	0.13	0.09	0.09
Serum pepsinogen I (ng/mL)	33	19	76.5 ± 40.2	14	94.5 ± 64.4	0.55	0.65	0.23
≤ 20 ng/mL (%)	33	1	5.3	2	14.3	0.76	0.75	-
Serum creatinine (µmol/L)	32	18	84.0 ± 20.2	14	92.8 ± 25.4	0.81	0.28	0.32
≥ 127 µmol/L (%)	33	1	5.3	2	14.3	0.15	0.11	0.51
Serum albumin (g/L)	32	18	4.1 ± 0.2	14	3.9 ± 0.3	0.79	0.87	0.84
Hemoglobin (g/dL)	32	18	12.6 ± 1.0	14	12.7 ± 1.4	0.41	0.42	-
Mean cell volume (fl)	32	18	88 ± 5	14	87 ± 5	0.54	0.60	0.92
Multivitamin use (%)	33	4	21.1	3	21.4	0.86	0.81	0.35
Synthetic B_{12} intake (µg/d)	33	19	32.9 ± 137.5	14	3.5 ± 6.9	0.87	0.87	0.82
≥ 2.4 µg/d (%)	33	3	15.8	3	21.4	0.67	0.61	0.32
Synthetic folate intake (µg/d)	33	19	85.1 ± 151.7	14	83.0 ± 115.8	0.89	0.82	0.73
≥ 400 µg/d (%)	33	2	10.5	1	7.1	0.87	0.90	0.93

[a] PTA, pure-tone average threshold of 1, 2, and 4 kHz.
[b] HL, hearing level.
[c] Number of total participants.
[d] Number of participants with the condition.
[e] Logistic regression model controlled for age and gender.
[f] Logistic regression model controlled for age, gender, and creatinine.
[g] Logistic regression model controlled for age, gender, creatinine, family history of hearing loss, and noise exposure.
[h] Anemic defined as hemoglobin ≤ 12 g/dL for females, ≤ 13 g/dL for males.
[i] Chi-square analyses.
- Not applicable. There was possibly a quasi-complete separation of data points.

Table C.23 Demographics, nutrition and auditory function in the worst ear at baseline in African-Americans

		Hearing						
		Normal (PTA[a] ≤ 25 dB HL[b])		Impaired (PTA > 25 dB HL)				
Worst ear	N [c]	n [d]	Mean ± SD or %	n [d]	Mean ± SD or %	P value[e]	P value[f]	P value[g]
n	33	15		18				
Hearing level (dB)	33	15	21 ± 5	18	38 ± 8			
Age (years)	33	15	70 ± 6	18	78 ± 7	0.01	0.01	0.01
Gender (% of female)	33	14	93.3	15	83.3	0.24	0.25	0.41
Education (years)	33	15	9 ± 3	18	6 ± 4	0.25	0.32	0.22
Family history of hearing loss (%)	33	2	13.3	2	11.1	0.38	0.12	0.12
Number of years exposed to noise (years)	32	14	9 ± 12	18	15 ± 17	0.55	0.33	0.27
Number of medications	33	15	6 ± 4	18	5 ± 3	0.36	0.45	0.87
Anemic (%) [h]	32	4	28.6	7	38.9	0.62	0.61	0.18
Serum vitamin B_{12} (pmol/L)	33	15	416.0 ± 164.8	18	382.4 ± 149.8	0.77	0.90	0.98
< 185 pmol/L (%)	33	0	0.0	2	11.1	0.49[i]	-	-
< 258 pmol/L (%)	33	2	13.3	4	22.2	0.97	0.98	0.76
< 258 pmol/L, MMA > 271 nmol/L, and MMA > 2-methylcitric acid (%)	33	0	0.0	1	5.6	1.0[i]	-	-
Serum MMA (nmol/L)	33	15	169 ± 57	18	213 ± 66	0.49	0.54	0.70
> 271 nmol/L (%)	33	1	6.7	3	16.7	0.89	0.95	-
Serum tHcy (µmol/L)	33	15	10.1 ± 3.3	18	9.6 ± 2.7	0.23	0.18	0.26
Serum folate (nmol/L)	33	15	30.4 ± 16.1	18	35.8 ± 17.3	0.52	0.65	0.68
Serum pepsinogen I (ng/mL)	33	15	73.7 ± 43.1	18	92.8 ± 57.7	0.36	0.31	0.49
≤ 20 ng/mL (%)	33	1	6.7	2	11.1	0.95	0.90	-
Serum creatinine (µmol/L)	32	14	85.9 ± 22.6	18	89.4 ± 23.3	0.77	0.85	0.86
≥ 127 µmol/L (%)	33	1	6.7	2	11.1	0.52	0.21	0.19
Serum albumin (g/L)	32	14	4.2 ± 0.3	18	4.0 ± 0.3	0.86	0.82	0.95
Hemoglobin (g/dL)	32	14	12.6 ± 1.1	18	12.6 ± 1.2	0.98	0.97	0.19
Mean cell volume (fl)	32	14	88 ± 5	18	88 ± 5	0.93	0.99	0.89
Multivitamin use (%)	33	3	20.0	4	22.2	0.85	0.95	0.92
Synthetic B_{12} intake (µg/d)	33	15	41.1± 154.8	18	3.2 ± 6.2	0.70	0.70	0.46
≥ 2.4 µg/d (%)	33	2	13.3	4	22.2	0.51	0.58	0.61
Synthetic folate intake (µg/d)	33	15	69.3 ± 121.3	18	96.6 ± 148.8	0.48	0.57	0.60
≥ 400 µg/d (%)	33	1	6.7	2	11.1	0.50	0.54	0.28

[a] PTA, pure-tone average threshold of 1, 2, and 4 kHz.
[b] HL, hearing level.
[c] Number of total participants.
[d] Number of participants with the condition.
[e] Logistic regression model controlled for age and gender.
[f] Logistic regression model controlled for age, gender, and creatinine.
[g] Logistic regression model controlled for age, gender, creatinine, family history of hearing loss, and noise exposure.
h Anemic defined as hemoglobin ≤ 12 g/dL for females, ≤ 13 g/dL for males.
[i] Chi-square analyses.
- Not applicable. There was possibly a quasi-complete separation of data points.

APPENDIX D

NUTRITION, HEARING AND MEMORY AMONG SENIOR CENTER IN NORTHEAST GEORGIA CONSENT FORM AND TEST BOOK

NUTRITION, HEARING, AND MEMORY AMONG SENIOR CENTERS IN NORTHEAST GEORGIA

2001

FORM B

NUTRITION, HEARING, AND MEMORY STUDY
CONSENT FORM

I,______________________________agree to participate in the research titled "NUTRITION, HEARING, AND MEMORY" conducted by Drs. Mary Ann Johnson, Albert DeChicchis, and L. Stephen Miller in the Departments of Foods and Nutrition, Communication Sciences and Disorders, and Psychology at the University of Georgia.

I understand that I do not have to take part if I do not want to. I can stop taking part without giving any reason, and without penalty. I can ask to have all of the information about me returned to me, removed from the research records, or destroyed. My decision to participate will not affect the services that I receive at the Senior Center.

The reason for this study is to learn more about nutrition and health, and to determine if taking a vitamin B-12 supplement will help me hear better and improve my memory. If I volunteer to take part in this study, I will be asked to do the following things:

1) **Answer questions about my food, nutrition, and health.**
2) **Have my hearing tested.**
3) **Have my memory and thinking tested with a computer based test.**
4) **A medical technologist will take 4 7-10 ml tubes of blood to measure my blood sugar, cholesterol, vitamins and minerals. My blood sample will be destroyed within 10 years.**
5) **Have my blood pressure taken.**
6) **I will take a vitamin B-12 supplement (up to 1,000 mcg/day) or a placebo (a pill without vitamin B-12) for 4 months to see if it helps me hear and think better.**
7) **After 4 months, all of the questions and tests related to health, food, nutrition, hearing, and memory, and the blood tests will be repeated.**
8) **If my tests show that I have depression, I will be notified and referred for treatment.**
9) **Someone from the study may call me to clarify my information.**

If I am found to have vitamin B-12 deficiency, my physician and I will be notified. I will give vitamin B-12 (1,000 mcg/day as a tablet) as part of this study. If my doctor treats me with vitamin B-12 (pill or shots) I can still continue in this study, and will not need to take the vitamin B-12 supplement provided by this study.

I will receive $25 after completing all the test the first time, and another $25 after taking vitamin B-12 (or the placebo) for 4 months and repeating the tests a second time.

My blood will not be tested for HIV-AIDS. I understand that these questions and blood tests are not for diagnostic purposes. If I have questions about my test results I should see a physician. The benefits for me are that the study may help me understand and improve my health.

No risk is expected but I may experience some discomfort or stress when my hearing is tested (because of the ear plugs), when my blood is drawn or when the researchers ask me questions about my health, memory and nutrition. The risks of drawing blood from my arm include the unlikely possibilities of a small bruise or localized infection, bleeding, and fainting. These risks will be reduced in the following ways: my blood will be drawn only by a qualified and experienced person who will follow standard sterile techniques, who will observe me after the needle is withdrawn, and who will apply pressure to the blood draw-site. In the event that I have any health problems associated with the blood draws, my insurance or I will be responsible for any related medical expenses.

No information about me, or provided by me during the research, will be shared with others without my written permission, except if it is necessary to protect my welfare (for example, if I need physician care) or if required by law. I will be assigned an identifying number and this number will be used on all of forms I fill out.

If I have any further questions about the study, now or during the course of the project I can call Mrs. Nikki Hawthorne 706-542-4838 or Dr. Mary Ann Johnson 706-542-2292.

I give my permission for you to release my blood analysis information to my health care providers.
Circle one: YES / NO. Initial _____.

I give my permission for you to release my hearing results to my health care providers.
Circle one: YES / NO. Initial _____.

I give my permission for you to release my memory test results to my primary physician.
Circle one: YES / NO. Initial _____.

I will allow the staff to take my picture, videotape or record me while participating in the study. I can verbally refuse at anytime and my wishes will be upheld. My pictures will only be used to promote this nutrition, hearing, and memory study.
Circle one: YES / NO. Initial _____.

I understand that I am agreeing by my signature on this form to take part in this project and understand that I will receive a signed copy of this consent form for my records.

____

Project Coordinator Date Signature of Participant Date

____

Phone Number Address

Questions or problems regarding your rights as a participant should be addressed to Ms. Julia Alexander; Institutional Review Board; Office of V.P. for Research; The University of Georgia; 604A Graduate Studies Research Center; Athens, GA 30602-7411; Telephone 706-542-6514.

revised 00/13/12

UGA project number:H1998-10501-4
DHR project number: 000904

FORM D

NUTRITION, HEARING, AND MEMORY STUDY
CONSENT FORM

I,______________________________agree to participate in a continuation to the research titled "NUTRITION, HEARING, AND MEMORY" conducted by Drs. Mary Ann Johnson, Albert DeChicchis, and L. Stephen Miller in the Departments of Foods and Nutrition, Communication Sciences and Disorders, and Psychology at the University of Georgia.

I understand that I do not have to take part if I do not want to. I can stop taking part without giving any reason, and without penalty. I can ask to have all of the information about me returned to me, removed from the research records, or destroyed. My decision to participate will not affect the services that I receive at the Senior Center.

The reason for this continuation to this study is to learn more about nutrition and health, and to determine if taking a vitamin B-12 supplement will help improve my memory. If I volunteer to take part in this study, I will be asked to do the following things:

10) Answer questions about my food, nutrition, and health.
11) Have my memory and thinking tested with a computer based test.
12) A medical technologist will take 2 7-10 ml tubes of blood to measure my vitamin B-12 status. My blood sample will be destroyed within 10 years.
13) Have my blood pressure taken.
14) I will take a vitamin B-12 supplement (up to 1,000 mcg/day) or a placebo (a pill without vitamin B-12) for 6 months to see if it helps me think better.
15) If my tests show that I have depression, I will be notified and referred for treatment.
16) Someone from the study may call me to clarify my information.

I will receive $25 after completing all of the testing.
My blood will not be tested for HIV-AIDS. I understand that these questions and blood tests are not for diagnostic purposes. If I have questions about my

test results I should see a physician. The benefits for me are that the study may help me understand and improve my health.

No risk is expected but I may experience some discomfort or stress when my blood is drawn or when the researchers ask me questions about my health, memory and nutrition. The risks of drawing blood from my arm include the unlikely possibilities of a small bruise or localized infection, bleeding, and fainting. These risks will be reduced in the following ways: my blood will be drawn only by a qualified and experienced person who will follow standard sterile techniques, who will observe me after the needle is withdrawn, and who will apply pressure to the blood draw-site. In the event that I have any health problems associated with the blood draws, my insurance or I will be responsible for any related medical expenses.

No information about me, or provided by me during the research, will be shared with others without my written permission, except if it is necessary to protect my welfare (for example, if I need physician care) or if required by law. I will be assigned an identifying number and this number will be used on all forms I fill out.

If I have any further questions about the study, now or during the course of the project I can call Mrs. Nikki Hawthorne 706-542-4838 or Dr. Mary Ann Johnson 706-542-2292.

I give my permission for you to release my blood analysis information to my health care providers.
Circle one: YES / NO. Initial _____.

I give my permission for you to release my memory test results to my primary physician.
Circle one: YES / NO. Initial _____.

I will allow the staff to take my picture, videotape or record me while participating in the study. I can verbally refuse at anytime and my wishes will be upheld. My pictures will only be used to promote this nutrition, hearing, and memory study.
Circle one: YES / NO. Initial _____.

I understand that I am agreeing by my signature on this form to take part in this project and understand that I will receive a signed copy of this consent form for my records.

____

Project Coordinator   Date   Signature of Participant   Date

____

Phone Number   Address

Questions or problems regarding your rights as a participant should be addressed to Dr. Chris Joseph; Institutional Review Board; Office of V.P. for Research; The University of Georgia; 604A Graduate Studies Research Center; Athens, GA 30602-7411; Telephone 706-542-6514.

UGA project number:H1998-10501-4
DHR project number: 000904

5/16/01

Department of Foods and Nutrition
University of Georgia
390 Dawson Hall
Athens, GA 30602

Date: __________

Dear __________________________:

We are so pleased that you are participating in our study "Vitamin B-12 Deficiency in Elderly Nutrition Programs." We look forward to seeing you again in four months to repeat the hearing tests, memory tests, blood tests, and nutrition questions. As a service to our participants we are sending you a copy of your blood work and nutritional status report. These tests are not for diagnostic purposes. If you have any questions about your results, you should call your physician. Your physician will also receive a copy of your blood work, hearing tests, and memory tests.

If you have any questions, please contact me at 706-542-4838.

Sincerely,

Nikki Hawthorne, MS, RD, LD.
Research Coordinator

Enc.

Department of Foods and Nutrition
University of Georgia
390 Dawson Hall
Athens, GA 30602

Date: __________

Dear ___________________________:

We are so pleased that you are participating in our study "Vitamin B-12 Deficiency in Elderly Nutrition Programs." We look forward to seeing you again in four months to repeat the hearing tests, memory tests, blood tests, and nutrition questions. As a service to our participants, we are sending you a copy of your blood work and nutritional status report.

These tests are not for diagnostic purposes. However, the methylmalonic acid test of your blood indicates that you might be deficient in vitamin B-12. As part of this study, we are giving you a daily supplement of vitamin B-12 (1 milligram) which should improve your vitamin B-12 status if taken daily. Your physician will also receive a copy of your blood work, hearing tests, and memory tests. Your physician may decide to give you vitamin B-12 which will not in any way interfere with this study. If you have any questions about your results, please call your physician and please follow your physicians' advice.

If you have any questions, please contact me at 706-542-4838.

Sincerely,

Nikki Hawthorne, MS, RD, LD.
Research Coordinator
Enc.

Department of Foods and Nutrition
University of Georgia
390 Dawson Hall
Athens, GA 30602

Date: _______

Dear Physician:

Your patient, ______________________, has recently enrolled in the research study titled "Vitamin B-12 Deficiency in Elderly Nutrition Programs" with the Department of Foods and Nutrition at the University of Georgia. As a service to our participants, we are providing their physicians with copies of blood work, nutrition status report, hearing tests, and memory tests. Any critical values have been reported previously to your office. We do not provide a diagnosis based on the results of their blood work. However, based on the serum methylmalonic acid, it is possible that this patient is vitamin B-12 deficient (> 271 nmol/L indicates possible vitamin B-12 deficiency). Your patient's serum methylmalonic acid is _________nmol/L. These analyses were performed by Dr. Sally P. Stabler, MD, Co-Director of Hematology, University of Colorado Health Sciences Center, Denver, CO. As part of this research study, we have given your patient an oral supplement of vitamin B-12 (1 mg) to be taken daily. Oral vitamin B-12 has been shown to reverse vitamin B-12 deficiency (see enclosure). Your follow-up and treatment of possible vitamin B-12 deficiency in this patient is welcome and will not in any way interfere with this ongoing study.

If you have any questions, please contact me at 706-542-2292.

Sincerely,

Mary Ann Johnson, Ph.D.
Professor of Foods and Nutrition
& Faculty of Gerontology

Enc.

Department of Foods and Nutrition
University of Georgia
390 Dawson Hall
Athens, GA 30602

Date: _______

Dear Physician:

Your patient, ______________________, has recently enrolled in the research study titled "Vitamin B-12 Deficiency in Elderly Nutrition Programs" with the Department of Foods and Nutrition at the University of Georgia. As a service to our participants, we are providing their physicians with copies of blood work, nutrition status report, hearing tests, and memory tests. Any critical values have been previously reported to your office. We do not provide a diagnosis based on the results of their blood work.

If you have any questions, please contact me at 706-542-2292.

Sincerely,

Mary Ann Johnson, Ph.D.
Professor of Foods and Nutrition
& Faculty of Gerontology

Enc.

Department of Foods and Nutrition
University of Georgia
390 Dawson Hall
Athens, GA 30602-3622

June 2, 2001

Dear ___________________________:

We would like to congratulate and thank you for participating in our study "Vitamin B-12 Deficiency in Elderly Nutrition Programs." More than 220 people had their ears examined and 150 people enrolled in the study and are taking a supplement.

As a service to our participants we are sending you a copy of your nutritional status report and two copies of your blood work. The extra copy can be given to your physician. These tests are not for diagnostic purposes. If you have any questions about your results, you should contact your physician.

Please continue to take your vitamins. We plan to continue the study. It is possible you might qualify and be given more supplements, so please continue to take your remaining vitamins.

We will let you know what supplement you were taking and issue the results of the study in the year 2002. Again, we thank you for participating and look forward to seeing you at the senior center soon. If you have any questions please feel free to contact us at 706-542-4838.

Sincerely,

Nikki Hawthorne, MS, RD, LD.

Enc.

October 23, 2001

Dear Physician:

Your patient, ________________________, has enrolled in the research study titled "Vitamin B-12 Deficiency in Elderly Nutrition Programs" with the Department of Foods and Nutrition at the University of Georgia. As a service to our participants, we are providing their physicians with copies of blood work. Any critical values have been previously reported to your office. We do not provide a diagnosis based on the results of their blood work. We gave your patient vitamin B-12 supplements (1000mcg) for 3 months, but their methylmalonic acid is still indicating a vitamin B-12 deficiency
(> 271 nmol/L indicates possible vitamin B-12 deficiency). Your patient's methylmalonic acid is _________nmol/L. These analyses were performed by Dr. Sally P. Stabler, MD, Hematologist at the University of Colorado. We are encouraging them to continue taking the supplements however, your treatment of possible vitamin B-12 deficiency in this patient is welcome and will not in any way interfere with this ongoing study.

If you have any questions, please feel free to contact me at 706-542-2292.

Sincerely,

Mary Ann Johnson, Ph.D.
Professor of Foods and Nutrition
& Faculty of Gerontology

Enc.

Vitamin B-12 Study Checklist
ID:_______________

Questionnaire	PRE TEST		POST TEST		Flagged-Explain
	Date Completed	Initials	Date Completed	Initials	
Consent Form					
Blood Drawn					
General Information					
Sun Exposure					
Blood Pressure (Gave Blood Pressure Form to participant)					
Orientation/ Memory Test					
Nutritional Screening Initiative					
MNA					
Nutrition Questions					
Illnesses					
Medications					
Supplements: Explained & Date Started					
Supplements: Stopped					
Nutritional Status Report - Sent to Individual					
Hearing History Questionnaire (HHQ)			**(E) ONLY**		
Hearing Handicap Inventory for adults (HHIA)					
Noise Exposure History					
Hearing Evaluation					
Cognition/computer -prompted test					
Geriatric Depression Scale					
Irritability and Agitation questions					

7
Flagged Notes:

Revised 00/09/13

GENERAL INFORMATION **ID: ______ ______**
(1-3)

_ _ _ _ _ _ (10-15) **1. Today's date: ___ / ____ / ____** ***Month/Day/Year***

__ (16) **2. This information was obtained from:**
0 _____ Client
1 _____ Senior center staff person
2 _____ Family member of client
3 _____ Caregiver for client
4 _____ Other: ________________

__ __ . __ (17-20) **3. How long has the client been using the services of the senior center?**
___ ___.___ years *Code as years (xx.x years)*

_ _ _ _ _ _ _ _ (21-28) **4. Date of birth: ___ / ____ / ____** ***Month/Day/Year***

__ __ __ (29-31) **5. Current age:** __________ years *Example: age 75 is 075*

__ (32) **6. Gender:** ______ Male (0) ______ Female (1)

__ (33) **7. Ethnicity:** ______ Caucasian (0) ______ Black (1) ______ Hispanic (2)
______ Asian (3) ______ Other (4)

__ __ (34-35) **8. Years completed in school?** ______ Years

__ (36) **9. Do you take a multiple-vitamin/mineral supplement?** ______ No (0) ____ Yes (1)

__ (37) **10. Do you take any other nutritional supplements that contain vitamins or minerals?**
_____ No (0) _____ Yes (1)

*** Health Care Provider** ____

Address____

____

Phone____

*** Care giver/ Next of Kin**

(1) ____________________________________ **Phone**_______________________________

Address____

(2) ____________________________________ **Phone**_______________________________

Address____

__ __ 38-39 **11. How many hours ago did you last eat? _________** (code number of hours ago).

__ 40 **12. Fasting status (coded by medical technologist).**

0 Not fasted, food in the last 4 hours
1 Fasted, food not eaten in the past 4 hours

__ 41 **13. How would you rate your overall health at the present time -- excellent, good, fair, or poor?**

3 Excellent
2 Good
1 Fair
0 Poor
9 Not answered

__ 42 **14. Is your health now better, about the same, or worse than it was five years ago?**

2 Better
1 About the same
0 Worse
9 Not answered

__ 43 **15. How much do your health troubles stand in the way of your doing things you want to -- not at all, a little (some), or a great deal?**

2 Not at all
1 A little (some)
0 A great deal
9 Not answered

__ __ 44-45 **16. County of residence 00-12**

00= Madison	03= Jackson	06= Greene	09= Elbert	12=Franklin
01= Morgan	04= Newton	07= Clark	10= Oconee	
02= Walton	05= Barrow	08= Oglethorpe	11= Jasper	

__ 46 **18. Did you participate in our vitamin supplement study during spring and summer 1999?** ***(ASK ONLY IN GREENE AND MORGAN COUNTY)***

1= YES
0= NO

SUN EXPOSURE

__
47 **19. How many minutes of sun exposure do you get each week?**
__ (0) < 9 minutes/week
__ (1) 10-30 minutes/week
__ (2) 30-59 minutes/week
__ (3) 60-89 minutes/week
__ (4) 90-119 minutes/week
__ (5) 120 (2 hours) or more minutes/week
__ (8) do not know
__ (9) missing

__
48 **20. How often do you use sunscreen when you go outside?**
__ (0) Rarely/Never
__ (1) Sometimes
__ (2) Always
__ (8) Not applicable; does not go outside
__ (9) Missing

__
49 **21. If you use sunscreen, what level do you use?**
__ (0) Don't know
__ (1) SPF 4 or less
__ (2) SPF 6 or 8
__ (3) SPF 10
__ (4) SPF 15
__ (5) SPF 30 and up
__ (8) Doesn't use
__ (9) Missing

BLOOD PRESSURE

(NOTE: RECORD RESULTS ON "BLOOD PRESSURE FORM" AND GIVE TO PARTICIPANT)

__ __ __
50-52 **22. Blood Pressure**
Systolic (mmHg)
__ (0) < 120 Optimal
__ (1) < 130 Normal
__ (2) 130-139 High-normal
__ (3) 140-159 Mild Hypertension (Stage 1)
__ (4) 160-179 Moderate Hypertension (Stage 2)
__ (5) > 180 Severe Hypertension (Stage 3)
__ (999) Missing

Diastolic (mmHg)
__ __ __ __ (0) < 80 Optimal
53-55 __ (1) < 85 Normal
__ (2) 85-95 High-normal
__ (3) 90-99 Mild Hypertension (Stage 1)
__ (4) 100-109 Moderate Hypertension (Stage 2)
__ (5) > 110 Severe Hypertension (Stage 3)

ORIENTATION-MEMORY-CONCENTRATION TEST

Read all questions to the participant. Tell them that some of the questions may be easy and some may be hard -- just do the best you can.

	Resp onse	# of Errors	Max. Errors	Weight Factor	Total
1) What is the year now?			**1**	**4**	
2) What month is it now?			**1**	**3**	
Please repeat this phrase after me: **JOHN BROWN, 42 MARKET STREET, CHICAGO** *No score for this -- it is a memory phrase for Item # 6. Allow the person up to three trials for learning (repeating) the phrase. If the subject has not learned the phrase after three trials, record the value of "0" as the total score for Item #6, and proceed to Item #3.*					
3) Without looking at your watch or a clock, tell me about what time is it? *Note: score is correct if within one hour of actual time.*			**1**	**3**	
4) Count backwards from 20 to 1. *20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1*			**2**	**2**	
5) Say the months of the year in reverse order. *DEC, NOV, OCT, SEPT, AUG, JULY, JUNE, MAY, APR, MAR, FEB, JAN*			**2**	**2**	
6) Please repeat the name and address I asked you to remember. *Count the number of items (5) in memory phrase recalled incorrectly. An answer of either Market or Market Street is acceptable.* John / Brown / 42 / Market Street / Chicago			**5**	**2**	
(10-11) **TOTAL SCORE**					

Interpretation of corrected scores:

≤ 8	Normal or minimal impairment
9-19	Moderate impairment
≥ 20	Severe impairment

Source: Katzman, R., Brown, T., Fuld, P., Peck, A., Schechter, R., Schimmel, H. Validation of a short orientation-memory-concentration test of cognitive impairment. *American Journal of Psychiatry* 140: 734-739, 1983.

NUTRITIONAL HEALTH: Nutritional Screening Initiative Questionnaire

ID: _________

No=0
Yes=

____ NH1. I have an illness or condition that made me change the kind and/or
(10) amount of food I eat..Yes / No (2)

____ NH2. I eat fewer than 2 meals per day...Yes / No (3)
(11)

____ NH3. I eat few fruits or vegetables, or milk products....................................Yes / No (2)
(12)

____ NH4. I have 3 or more drinks of beer, liquor or wine almost every day..........Yes / No (2)
(13)

____ NH5. I have tooth or mouth problems that make it hard for me to eat ....Yes / No (2)
(14)

____ NH6. I don't' always have enough money to buy the food I need...................Yes / No (4)
(15)

____ NH7. I eat alone most of the time..Yes / No (1)
(16)

____ NH8. I take 3 or more different prescribed or over-the-counter drugs a day....Yes / No (1)
(17)

____ NH9. Without wanting to, I have lost or gained 10 pounds in the last
(18) 6 months...Yes / No (2)

____ NH10. I am not always physically able to shop, cook, and/or feed myself..........Yes/No (2)
(19)

Your Nutritional Score is: __________. If it's:
(20-21)

0-2 **Good.** Recheck your nutritional score in 6 months.

3-5 **You are at moderate nutritional risk.** See what can be done to improve your eating habits and lifestyle. Your office on aging, senior nutrition program, senior citizens center or health department can help. Recheck your nutritional score in 3 months.

6 or more. **You are at high nutritional risk.** Bring this checklist the next time you see your doctor, dietitian or other qualified health or social service professional. Talk with them about any problems you may have. Ask for help to improve

MINI-NUTRITIONAL ASSESSMENT

ID# ____________
(1-3)

Name: First name: Sex: Date:
Age:

04 *** enter decimal points*
(4-5)

TSF. Triceps skin fold (mm): __ __.__
(6-9)

Kneeht. Knee Height (cm): __ __.__
(10-13)

I. ANTHROPOMETRIC ASSESSMENT

____ MNA1. BMI (weight/(height)^2 in kg/m^2); weight = ____ lbs. / 2.205 = __ __ __ . __kg (15-19)kg
(14) *0 = BMI < 19* height = ____ in. * .0254 = __ __ __ . __ meters (20-24)m
1 = 19 ≤ BMI < 21 BMI = __ __ . __ (25-28) BMI
2 = 21 ≤ BMI < 23
3 = BMI ≥ 23

_____ MNA2. Mid arm circumference (MAC in cm.): __ __ . __ cm. (30-33)cm
(29) *0.0 = MAC < 21*
0.5 = 21 ≤ MAC ≤ 22
1.0 = MAC > 22

_____ MNA3. Calf circumference (CC in cm.): __ __ . __cm. (35-38)cm
(34) *0 = CC < 31*
1 = CC ≥ 31

_____ MNA4. Weight loss during last 3 months: _________ lbs. / 2.205 = __ __ __ . __ kg (40-44)kg
(39) *0 = weight loss > 3 kg*
1 = does not know
2 = weight loss between 1 and 3 kg
3 = no weight loss

_____ MNA12A. How many servings of <u>milk, yogurt, or cheese</u> does the individual consume?
(45)

0 ____ *Less than one per week*	3 ____ *3 per week*	6 ____ *6 per week*
1 ____ *1 per week*	4 ____ *4 per week*	7 ____ *At least one per day*
2 ____ *2 per week*	5 ____ *5 per week*	8 ____ *2 or more per day*
		9 ____ *Missing/don't know*

_____ MNA12D. How many servings of <u>meat, fish, or poultry</u> does the individual consume?
(46)

0 ____ *Less than one per week*	3 ____ *3 per week*	6 ____ *6 per week*
1 ____ *1 per week*	4 ____ *4 per week*	7 ____ *At least one per day*
2 ____ *2 per week*	5 ____ *5 per week*	8 ____ *2 or more per day*
		9 ____ *Missing/don't know*

NUTRITION QUESTIONS

__ **1. Have you ever received home delivered meals?**
47 0 = Yes
1 = No

__ __ **2. If you receive home delivered meals, for how long have you been receiving them? __ __**
48-49 ***years***
Code as whole years (xx years)

__
50 **3. How many times a week do you eat at the senior center?**

0 ____ Less than one per week	3 ____ 3 per week	6 ____ 6 per week
1 ____ 1 per week	4 ____ 4 per week	7 ____ At least one per day
2 ____ 2 per week	5 ____ 5 per week	8 ____ 2 or more per day
		9 ____ Missing/don't know

__ **4. How many servings of green vegetables do you eat?**
51

0 ____ Less than one per week	3 ____ 3 per week	6 ____ 6 per week
1 ____ 1 per week	4 ____ 4 per week	7 ____ At least one per day
2 ____ 2 per week	5 ____ 5 per week	8 ____ 2 or more per day
		9 ____ Missing/don't know

__ **5. How many servings of orange or yellow vegetable do you eat?**
52

0 ____ Less than one per week	3 ____ 3 per week	6 ____ 6 per week
1 ____ 1 per week	4 ____ 4 per week	7 ____ At least one per day
2 ____ 2 per week	5 ____ 5 per week	8 ____ 2 or more per day
		9 ____ Missing/don't know

__ **6. How many servings of citrus fruit or citrus juice do you eat (e.g., orange, grapefruit)?**
53

0 ____ Less than one per week	3 ____ 3 per week	6 ____ 6 per week
1 ____ 1 per week	4 ____ 4 per week	7 ____ At least one per day
2 ____ 2 per week	5 ____ 5 per week	8 ____ 2 or more per day
		9 ____ Missing/don't know

__ **7. How many servings of other non-citrus fruit or juice do you consume?**
54

0 ____ Less than one per week	3 ____ 3 per week	6 ____ 6 per week
1 ____ 1 per week	4 ____ 4 per week	7 ____ At least one per day
2 ____ 2 per week	5 ____ 5 per week	8 ____ 2 or more per day
		9 ____ Missing/don't know

__ **8. How many servings of liver (eg., beef, chicken,pork) do you consume?**
55

0 ____ Less than one per week	3 ____ 3 per week	6 ____ 6 per week
1 ____ 1 per week	4 ____ 4 per week	7 ____ At least one per day
2 ____ 2 per week	5 ____ 5 per week	8 ____ 2 or more per day
		9 ____ Missing/don't know

FOODS FORTIFIED WITH B-VITAMINS

We would like to know if you eat any of the following foods that may be fortified with B-vitamins

				Code daily intake of vit. B12 from each source.	Code daily intake of folate from each source.	Code daily intake of vit. B6 from each source.
8. Breakfast cereals, such as, Just Right w/ fruits & nuts, Product 19, Nutri-Grain, Total, Special K	**0 = No 1 = Yes**	**If yes, what BRAND(s) do you usually eat?**	**If yes, how often do you eat breakfast cereal?**			
9. Breakfast or energy bars, such as, Nutri-Grain, power bar,	**0 = No 1 = Yes**	**If yes, what BRAND(s) do you usually eat?**	**If yes, how often do you eat breakfast bars?**			
10. Liquid meal replacements, such as, carnation, ensure plus	**0 = No 1 = Yes**	**If yes, what BRAND(s) do you usually drink?**	**If yes, how often do you drink ensure, or boost etc.?**			
Other	**0 = No 1 = Yes**	**If yes, what BRAND(s) do you usually eat?**	**If yes, how often do you eat this food?**			
Other	**0 = No 1 = Yes**	**If yes, what BRAND(s) do you usually eat?**	**If yes, how often do you eat this food and in what quantity?**			

Are You at Risk for Osteoporosis?

Complete the following questionnaire to find out your risk for developing osteoporosis.

Question	Yes	No
1. Are you a postmenopausal women?		
2. If you are a postmenopausal woman, did you have an early (before 50 years old) menopause or surgically induced menopause?		
3. If you are a postmenopausal women, are you taking Hormone Replacement Therapy such as Raloxifene, Draloxifene, Premarin, Prempo?		
4. Do you have a small, thin frame?		
5. Has anyone in your family (father, mother, sister, brother) ever had a fracture or broken bone after age 50?		
6. Have you had a fall within the past 1 year?		
7. Have you had a fracture or broken bone after age 50?		
8. Do you eat at least 2 servings of dairy products such as milk, yogurt, or cheese everyday?		
9. Do you eat salmon at least twice a week?		
10. Do you eat calcium-rich green vegetables such as mustard, turnip, or collard greens everyday?		
11. Do you drink calcium-fortified juice everyday?		
12. Do you eat calcium-fortified cereals (such as Total, Kellogg's K) everyday?		
13. Do you take a calcium and vitamin D supplement everyday?		
14. Have you been taking excessive thyroid medication or high or prolonged doses of cortisone-like drugs for asthma, arthritis, or cancer?		
15. Do you currently or did you ever smoke cigarettes, pipes, cigars or chew tobacco on a daily basis?		
16. Do you exercise at least 30 minutes everyday?		

(NOTE: COPY THIS INFORMATION FROM PREVIOUS QUESTIONS)

17. Age : _____ years old
18. Gender : Male Female (please circle)
19. Ethnicity : White Black Hispanic Asian Others (please circle)
20. County : _______________
21. Height : ______ feet ______ inches OR ______ cm
22. Weight : _____ pounds OR _______ kg

Is height and weight measured or self-reported?

The more times you answer in the shaded boxes, the greater your risk for developing osteoporosis. See your physician.

MEDICATIONS AND ILLNESSES

NAME/ID: _______________

Obtain information from reliable source. This information was provided by: client, caretaker, other___?

	YES (1)	NO (0)	DON'T KNOW	Space
Total number of PRESCRIPTION medications				10-11
Total number of NON -PRESCRIPTION medications, not counting vitamins and minerals				12-13
Multiple vitamin mineral supplement? 0 = no, 1 = yes				14
Number of other nutritional supplements?				15
Total number of illnesses - fill in when finished below.				16-17
1) Anemia in the past year				18
2) Alzheimer's: Kind________________; Dx date_________________				19
3) Other dementias: Kind_______________; Dx date _______________				20
4) Cancer: Kind_____________; Dx date__________; Status________				21
5) Circulatory problems in the past year				22
6) Congestive heart failure in the past year				23
7) Constipation in the past year				24
8) Diabetes: Kind_________________; Dx date ________________				25
9) Diarrhea in the past year				26
10) Glaucoma in the past year				27
11) Hearing problems in the past year				28
12) Heart disease in the past year				29
13) Hypertension in the past year				30
14) Legally blind in the past year				31
15) Liver disease in the past year				32
16) Mental illness: Kind________________; Dx date_______________				33
17) Osteoporosis in the past year				34
18) Hip fracture in the past year				35
19) Have you every had a pace maker				36
20) Parkinson's disease: Dx date_____________________				37
21) Renal disease in the past year				38
22) Respiratory disease in the past year				39
23) Seizures: 1st date_____________; last date______________				40
24) Skin rashes, bed sores in the past year				41
25) Stroke: Number______; Dates______________________________				42
26) Thyroid problems: Kind_____________; Dx date______________				43
27) Visual disturbances in the past year				44
28) Cataracts in the past year				45
29) Have you used any type of tobacco in the past year				46
30) Have you every had stomach surgery				47
31) Emergency room visit in the past year				48
32) Other				49
33) Arthritis in the past year				50
34) Pneumonia in the past year				51
35) Dizziness in the past year				52
36) Gout in the past year				53
37)				54

MEDICATIONS *(NOTE: ASK EVERY MEDICATION QUESTION THEN RECORD MEDS ON THE NEXT FORM)*			
1)	Are you currently taking aspirin?	1 = Yes 0 = No	10
2)	Are you currently taking ibuprofen such as Advil, Motrin, Nuprin?	1 = Yes 0 = No	11
3)	Are you currently taking Aleve?	1 = Yes 0 = No	12
4)	Are you currently taking Acetaminophen such as Tylenol or similar medication?	1 = Yes 0 = No	13
5)	Are you currently taking antacids or medications for heartburn or indigestion such as maalox, mylanta, alka aid (alka-seltzer) gaviscon, propulsid, zantac, pepcid, axid, cyotec, tums, tagamet, proton pump inhibitors such as prevacid, prevapac,prilosec, or other medication? **CIRCLE ALL THAT APPLY**	1 = Yes 0 = No	14
6)	Are you currently taking laxatives such as milk of magnesia, fiber tablets, metamucil or other laxative medication? **CIRCLE ALL THAT APPLY**	1 = Yes 0 = No	15
7)	Are you currently taking a cough suppressant such as humibid, robitussin, entrex or other medication?	1 = Yes 0 = No	16
8)	Are you currently taking allergy, sinus, or cold medication such as chlorpheniramine, relief, allerfed, seldane, sudafed, sine aid, Tylenol allergy sinus, contac, tylenol cold formulas, methypred dose, claritin, phenylprop, guaif, bromfed, tavist-d, actifed, benadryl, equate allergy sinus or other medication?	1 = Yes 0 = No	17
9)	Are you currently using nasal spray for allergy or sinus, such as aerobid, flonase, beconase, Nasalcrom or other medication?	1 = Yes 0 = No	18
10)	Are you currently taking a non-steroidal anti-inflammatory drug (NSAID) such as voltaren, diclofenac, naprosyn, naproxyn, sulindac, lodine, relafen, daypro, oruvail or similar medication?	1 = Yes 0 = No	19
11)	Are you currently taking a pain medication such as ultram, darvocet-N-100, fiorinal or similar medication?	1 = Yes 0 = No	20
12)	Are you currently taking an arthritis medication such as prednisone, rheumatrex methotrexate, orasone, deltasone or other medication?	1 = Yes 0 = No	21
13)	Are you currently taking antibiotics such as zithromax, amoxicillin or other antibiotic medication?	1 = Yes 0 = No	22
14)	Are you currently taking a sleeping aid such as Tylenol PM or other medication?	1 = Yes 0 = No	23

MEDICATIONS			
15)	Are you currently taking migraine medication such as mepergan fortis, imitrex, ercaf, Forbal-S or other migraine medication?	1 = Yes 0 = No	24
	# 16 and #18 - important for cognitive tests - so probe carefully		
16)	Are you currently taking anti-anxiety medication such as Alprazolam (xanax), Buspirone (Buspar), Chlordiaxepoxide (Librium), Clonazepam (klonopin), Clorazepate (tranxene), Diazepam (Valium), Hydroxyzine (Vistaril), Lorazepam (Ativan), Oxazepam (Serax), Propanolol (Inderal) or other anti-anxiety medication? **Circle all that apply**	1 = Yes 0 = No	25
17)	Are you currently taking anti-depressant medication such as Amitriptyline (Elavil), Citalopram (Celexa), Clomipramine (Anafranil), Desipramine (Norpramin), Doxepin (Sinequan), Fluoxetine (Prozac), Fluvoxamine (Luvox), Imipramine (Tofranil), Maprotiline (Ludiomil), Nortriptyline (Pamelor), Paroxetine (Paxil), Sertraline (zoloft), Trazadone (Desyrel), Venlafaxine (Effexor) or other anti-depressant medication? **Circle all that apply**	1 = Yes 0 = No	26
	#41 & 42 - important for cognitive tests - so probe carefully		
41)	Are you currently taking any drugs to help or enhance your thinking such as Chlorpromazine (Thorazine), Thioridazine (Mellaril), Fluphenazine (Prolixin), Trifluoperazine (Stelazine), Haloperidol (Haldol), Thiothixene (Navane), Loxapine (Loxitane), Molindone (Moban), Clozapine (Clozaril), Risperidone (Risperdal), Quetiapine (Seroquel), Olanzapine (Zyprexa) or other neuroleptic medications? **Circle all that apply**	1 = Yes 0 = No	27
42)	Are you currently taking any drugs to help or enhance your memory such as Tacrine (Cognex) or Donepezil hydrochloride (Aricept)? **Circle all that apply**	1 = Yes 0 = No	28
43)	List any other medications currently taken:	1 = Yes 0 = No	29
45)	Are you currently receiving Vitamin B-12 injections/shots? Last Vitamin B-12 shot (date) : _______________ How often? _______________(*example: once a year, twice a year, every other month, once a month) 762* ***(NOTE: IF YES, THEY NEED TO HAVE HAD A SHOT 6 MONTHS AGO OR LATER AND AGREE NOT TO RECEIVE A SHOT FOR THE NEXT FOUR MONTHS TO PARTICIPATE IN THIS STUDY)***	1 = Yes 0 = No	30
	Total number of prescription medications *(total of prescription meds)*		31-32
	Total number of non-prescription medications *(total of nonprescription meds)*		33-34

RESIDENT MEDICATION RECORDS:
Include prescription, non-prescription, and vitamins/minerals

ID _________

Medication	Dosage	Schedule	Route of Administration	*How Long have you been taking medication	DOCUMENTATION (Check all that apply)		
					Bottle only	Cardex Record	Signature Administration Record

	______ SUPP # __	______ SUPP # __	______ SUPP # __	______ SUPP # __	______ SUPP # __	TOTAL
	__ # pills per D, W, M WRITE IN AMOUNT /PILL & CIRCLE UNIT	__ # pills per D, W, M WRITE IN AMOUNT /PILL & CIRCLE UNIT	__ # pills per D, W, M WRITE IN AMOUNT /PILL & CIRCLE UNIT	__ # pills per D, W, M WRITE IN AMOUNT /PILL & CIRCLE UNIT	__ # pills per D, W, M WRITE IN AMOUNT /PILL & CIRCLE UNIT	
For how long?	**_____mo/yrs**	**_____mo/yrs**	**_____mo/yrs**	**_____mo/yrs**	**_____mo/yrs**	
Vitamin A	IU RE	IU RE	IU RE	IU RE	IU RE	
Vitamin C	mg	mg	mg	mg	mg	
Vitamin D	IU mg	IU mg	IU mg	IU mg	IU mg	
Vitamin E	IU mg	IU mg	IU mg	IU mg	IU mg	
Thiamin (B1)	mg	mg	mg	mg	mg	
Riboflavin (B2)	mg	mg	mg	mg	mg	
Niacin or Niacinamide or Vit. B3	mg	mg	mg	mg	mg	
Pyridoxine or Vitamin B6	mg	mg	mg	mg	mg	
Folic acid or Folate	mcg mg	mcg mg	mcg mg	mcg mg	mcg mg	
Vitamin B-12	mg mcg	mg mcg	mg mcg	mg mcg	mg mcg	
Biotin	mg mcg	mg mcg	mg mcg	mg mcg	mg mcg	
Pantothenic Acid	mg	mg	mg	mg	mg	
Vitamin K	mcg	mcg	mcg	mcg	mcg	
Calcium	mg	mg	mg	mg	mg	
Iron	mg	mg	mg	mg	mg	
Phosphorus	mg	mg	mg	mg	mg	
Iodine	mcg	mcg	mcg	mcg	mcg	
Magnesium	mg	mg	mg	mg	mg	
Zinc	mg	mg	mg	mg	mg	
Copper	mg	mg	mg	mg	mg	
Potassium	mg	mg	mg	mg	mg	
Manganese	mg	mg	mg	mg	mg	
Chromium	mcg	mcg	mcg	mcg	mcg	
Molybdenum	mcg	mcg	mcg	mcg	mcg	
Chloride	mg	mg	mg	mg	mg	
Nickel	mcg	mcg	mcg	mcg	mcg	
Silicon	mg mcg	mg mcg	mg mcg	mg mcg	mg mcg	
Vanadium	mcg	mcg	mcg	mcg	mcg	
Boron	mg mcg	mg mcg	mg mcg	mg mcg	mg mcg	
Fluoride	mg	mg	mg	mg	mg	
Selenium	mcg	mcg	mcg	mcg	mcg	
Other						
	______	______	______	______	______	

	SUPP # __	*SUPP # __*	*SUPP # __*	*SUPP # __*	*SUPP # __*	*TOTAL*
	__ # pills per D, W, M **WRITE IN AMOUNT /PILL & CIRCLE UNIT**	**__ # pills per D, W, M** **WRITE IN AMOUNT /PILL & CIRCLE UNIT**	**__ # pills per D, W, M** **WRITE IN AMOUNT /PILL & CIRCLE UNIT**	**__ # pills per D, W, M** **WRITE IN AMOUNT /PILL & CIRCLE UNIT**	**__ # pills per D, W, M** **WRITE IN AMOUNT /PILL & CIRCLE UNIT**	
For how long?	**_____mo/yrs**	**_____mo/yrs**	**_____mo/yrs**	**_____mo/yrs**	**_____mo/yrs**	
Vitamin A	IU RE	IU RE	IU RE	IU RE	IU RE	
Vitamin C	mg	mg	mg	mg	mg	
Vitamin D	IU mg	IU mg	IU mg	IU mg	IU mg	
Vitamin E	IU mg	IU mg	IU mg	IU mg	IU mg	
Thiamin (B1)	mg	mg	mg	mg	mg	
Riboflavin (B2)	mg	mg	mg	mg	mg	
Niacin or Niacinamide or Vit. B3	mg	mg	mg	mg	mg	
Pyridoxine or Vitamin B6	mg	mg	mg	mg	mg	
Folic acid or Folate	mcg mg	mcg mg	mcg mg	mcg mg	mcg mg	
Vitamin B-12	mg mcg	mg mcg	mg mcg	mg mcg	mg mcg	
Biotin	mg mcg	mg mcg	mg mcg	mg mcg	mg mcg	
Pantothenic Acid	mg	mg	mg	mg	mg	
Vitamin K	mcg	mcg	mcg	mcg	mcg	
Calcium	mg	mg	mg	mg	mg	
Iron	mg	mg	mg	mg	mg	
Phosphorus	mg	mg	mg	mg	mg	
Iodine	mcg	mcg	mcg	mcg	mcg	
Magnesium	mg	mg	mg	mg	mg	
Zinc	mg	mg	mg	mg	mg	
Copper	mg	mg	mg	mg	mg	
Potassium	mg	mg	mg	mg	mg	
Manganese	mg	mg	mg	mg	mg	
Chromium	mcg	mcg	mcg	mcg	mcg	
Molybdenum	mcg	mcg	mcg	mcg	mcg	
Chloride	mg	mg	mg	mg	mg	
Nickel	mcg	mcg	mcg	mcg	mcg	
Silicon	mg mcg	mg mcg	mg mcg	mg mcg	mg mcg	
Vanadium	mcg	mcg	mcg	mcg	mcg	
Boron	mg mcg	mg mcg	mg mcg	mg mcg	mg mcg	
Fluoride	mg	mg	mg	mg	mg	
Selenium	mcg	mcg	mcg	mcg	mcg	
Other						

HEARING HANDICAP INVENTORY FOR ADULTS (HHIA)

Date: ______ ID: ______

The purpose of these questions is to identify any problems your hearing loss may be causing you. Please do not skip any questions. Even if you feel you do not have a hearing loss, please answer all of the questions. For each question, circle one response: No, Sometimes, or Yes.

		0	2	4	Line Space Line # 4-5
S1	Does a hearing problem cause you to use the phone less often than you would like?	No	Sometimes	Yes	10
E2*	Does a hearing problem cause you to feel embarrassed when meeting new people?	No	Sometimes	Yes	11
S3	Does a hearing problem cause you to avoid groups of people?	No	Sometimes	Yes	12
E4	Does a hearing problem make you irritable?	No	Sometimes	Yes	13
E5*	Does a hearing problem cause you to feel frustrated when talking to members of your family?	No	Sometimes	Yes	14
S6	Does a hearing problem cause you difficulty when attending a party?	No	Sometimes	Yes	15
S7	Does a hearing problem cause you difficulty hearing/understanding coworkers, clients, or customers?	No	Sometimes	Yes	16
E8*	Do you feel handicapped by a hearing problem?	No	Sometimes	Yes	17
S9*	Does a hearing problem cause you difficulty when visiting friends, relatives, or neighbors?	No	Sometimes	Yes	18
E10	Does a hearing problem cause you to feel frustrated when talking to coworkers, clients, or customers?	No	Sometimes	Yes	19
S11*	Does a hearing problem cause you difficulty in the movies or theater?	No	Sometimes	Yes	20
E12	Does a hearing problem cause you to be nervous?	No	Sometimes	Yes	21
S13	Does a hearing problem cause you to visit friends, relatives, or neighbors less often than you would like?	No	Sometimes	Yes	22
E14*	Does a hearing problem cause you to have arguments with family members?	No	Sometimes	Yes	23
S15*	Does a hearing problem cause you difficulty when listening to the TV or radio?	No	Sometimes	Yes	24
E16	Does a hearing problem cause you to go shopping less often than you would like?	No	Sometimes	Yes	25
E17	Does any problem or difficulty with your hearing upset you at all?	No	Sometimes	Yes	26
E18	Does a hearing problem cause you to want to be by yourself?	No	Sometimes	Yes	27
S19	Does a hearing problem cause you to talk to family members less often than you would like?	No	Sometimes	Yes	28
E20*	Do you feel that any difficulty with your hearing limits or hampers your personal or social life?	No	Sometimes	Yes	29
S 21*	Does a hearing problem cause you difficulty when	No	Sometimes	Yes	30

	in a restaurant with relatives or friends?				
E 22	Does a hearing problem cause you to feel depressed?	No	Sometimes	Yes	31
S 23	Does a hearing problem cause you to listen to TV or radio less often than you would like?	No	Sometimes	Yes	32
E 24	Does a hearing problem cause you to feel uncomfortable when talking to friends?	No	Sometimes	Yes	33
E 25	Does a hearing problem cause you to feel left out when you are with a group of people?	No	Sometimes	Yes	34
E 26	Does a hearing problem cause you to feel "stupid" or "dumb"?	No	Sometimes	Yes	35
S 27	Do you have difficulty hearing when someone speaks in a whisper?	No	Sometimes	Yes	36
S 28	Does a hearing problem cause you to attend religious services less often than you would like?	No	Sometimes	Yes	37

* Items comprising the HHIA-S.
From: Newman, C.W., Weinstein, B.E., Jacobson, G.P., and Hug, G.A. Test-retest reliability of the Hearing Handicap Inventory for Adults, Ear and Hearing, 1991;12(5): 355-357.

NOISE EXPOSURE HISTORY

We need to know about noise exposure in your past, even as a child. An example of a loud noise is a noise that makes it hard to talk or hear another person, or makes your ears ring after exposure.

NOISE AT YOUR WORK **1. Have you had any of these jobs?**			**Date Started**	**Date Ended**	**How often did you use hearing protection?** Never	Sometimes	Always
A. Cannery	No	Yes	19____	_____	1	2	3
B. Construction	No	Yes	19____	_____	1	2	3
C. Factory: _______________ *(type of factory)*	No	Yes	19____	_____	1	2	3
D. Farming	No	Yes	19____	_____	1	2	3
E. Logging, Lumber industry	No	Yes	19____	_____	1	2	3
F. Loud music (performing)	No	Yes	19____	_____	1	2	3
G. Mining	No	Yes	19____	_____	1	2	3
H. Police, Fire, Dept.	No	Yes	19____	_____	1	2	3
I. Printing	No	Yes	19____	_____	1	2	3
J. Transportation *(truck, boat, plane...)*	No	Yes	19____	_____	1	2	3
K. Any other types of noisy jobs Describe______________________	No	Yes	19____	_____	1	2	3

NOISE DURING MILITARY SERVICE **2. Were you exposed to noise during military service (including basic training and reserves)?**			**Date Started**	**Date Ended**	**How often did you use hearing protection?** Never	Sometimes	Always
A. Artillery	No	Yes	19___	_______	1	2	3
B. Explosion	No	Yes	19___	_______	1	2	3
C. Planes, helicopters	No	Yes	19___	_______	1	2	3
D. Small arms	No	Yes	19___	_______	1	2	3
E. Tanks, other heavy equipment	No	Yes	19___	_______	1	2	3
F. Other types of noise: Describe_____________________	No	Yes	19___	_______	1	2	3

NOISE DURING RECREATION **3. Have you been exposed to noise during recreational or leisure-time activities?**			**Date Started**	**Date Ended**	**How often did you use hearing protection?** Never	Sometimes	Always
A. Gunfire	No	Yes	19____	_____	1	2	3
B. Loud Engines *(boat, auto, plane, motorcycle, skimobile)*	No	Yes	19____	_____	1	2	3
C. Loud Music	No	Yes	19____	_____	1	2	3
D. Power Tools	No	Yes	19____	_____	1	2	3
E. Other types of noise: Describe______________________	No	Yes	19____	_____	1	2	3

Have you ever undergone any accidental exposure to sudden intense noise?

No	1		Which ear or side?			
Yes	2	Type of noise__________________________	LEFT ear	1	BOTH ears	3
		Your age then_________________________	Right ear	2	Not sure	4

Adapted fom Meikle, Griest & Press (1986)

Geriatric Depression Scale (GDS) Short form

Choose the best answer for how you felt over the past week. Please answer the following questions "YES" or "NO there are no right or wrong answers, only what best applies to you.

		1	0	Space
1)	Are you basically satisfied with your life?	Yes	*NO	10
2)	Have you dropped many of your activities and interests?	*YES	No	11
3)	Do you feel that your life is empty?	*YES	No	12
4)	Do you often get bored?	*YES	No	13
5)	Are you in good spirits most of the time?	Yes	*NO	14
6)	Are you afraid that something bad is going to happen to you?	*YES	No	15
7)	Do you feel happy most of the time?	Yes	*NO	16
8)	Do you often feel helpless?	*YES	No	17
9)	Do you prefer to stay at home, rather than going out and doing new things?	*YES	No	18
10)	Do you feel you have more problems with memory than most people?	*YES	No	19
11)	Do you think it is wonderful to be alive now?	Yes	*NO	20
12)	Do you feel pretty worthless the way you are now?	*YES	No	21
13)	Do you feel full of energy?	Yes	*NO	22
14)	Do you feel that your situation is hopeless?	*YES	No	22
15)	Do you think that most people are better off than you are?	*YES	No	23

*** = 1 point. If * score is 10 or greater, or if (Nos. 1,5,7,11,13) were answered with * then the participant may be depressed. Proceed with referral plan.**

In the last few weeks have you found things to be easily disturbing or annoying (e.g., have other people, objects or situations been getting on your nerves or causing you frustration?)

1 2 3 4 5 6 7

Not at all all of the time

In the last few weeks have you felt restless or experienced difficulty with activities such as sleeping, following instructions, keeping your mind on what you are doing?

1 2 3 4 5 6 7

Not at all all of the time

NUTRITION AND DEPRESSION STATUS REPORT

NAME: ____________________________
COUNTY: _________________________

NUTRITION SCREENING INITIATIVE - 10 ITEM QUESTIONNAIRE:

This questionnaire screens for nutritional problems.

_____	0-2	Good
_____	3-5	Moderate nutritional risk
_____	6 or more.	High nutritional risk; recommend nutrition consult

BODY MASS INDEX (KG/M2) - INDEX OF WEIGHT FOR HEIGHT:

This is an index of underweight, normal weight, overweight and obesity.

_____ Greater than 30 Obese; recommend nutrition consult

_____ 25-29 Overweight; At risk for nutrition problems; recommend nutrition consult

_____ 21-24.9 Normal Range

_____ Less than 19.9; At risk for nutrition problems; recommend nutrition consult

WEIGHT LOSS (> 3 KG or 7 POUNDS IN PREVIOUS 3 MONTHS): ______

Unintentional weight loss is an indicator of low food intake or illness. However, some people need to lose weight if they are overweight and their weight is contributing to health problems.

_____ No weight loss Good

_____ Weight loss > 7 lb At risk for nutrition problems; recommend nutrition consult

PLEASE FEEL FREE TO CONTACT NIKKI HAWTHORNETO MAKE AN APPOINTMENT FOR A NUTRITIONAL CONSULT: 706-542-4838

GERIATRIC DEPRESSION SCALE- 15 ITEM QUESTIONNAIRE:___________

This questionnaire measures depression.

_____ 9 or less; probably not depressed

_____ 10 or more; at risk for depression - contact senior center director

POST TEST

GENERAL INFORMATION **ID:** ____________
(1-3)

_ _ _ _ _ _ (10-15) **1. Today's date: ___ / ____ / ____** ***Month/Day/Year***

__ (16) **2. This information was obtained from:**
0 _____ Client
1 _____ Senior center staff person
2 _____ Family member of client
3 _____ Caregiver for client
4 _____ Other: ________________

__ __ . __ (17-20) **3. How long has the client been using the services of the senior center?**
___ ___.___ years *Code as years (xx.x years)*

_ _ _ _ _ _ _ _ (21-28) **4. Date of birth: ___ / ____ / ____** ***Month/Day/Year***

__ __ __ (29-31) **5. Current age:** __________ years *Example: age 75 is 075*

__ (32) **6. Gender:** ______ Male (0) ______ Female (1)

__ (33) **7. Ethnicity:** ______ Caucasian (0) ______ Black (1) ______ Hispanic (2) ______ Asian (3) ______ Other (4)

__ __ (34-35) **8. Years completed in school?** ______ Years

__ (36) **9. Do you take a multiple-vitamin/mineral supplement?** ______ No (0) ____ Yes (1)

__ (37) **10. Do you take any other nutritional supplements that contain vitamins or minerals?**
_____ No (0) _____ Yes (1)

*** Health Care Provider** ____

Address____

____

Phone____

*** Care giver/ Next of Kin**

(1) ___________________________________ **Phone**______________________________

Address____

____

(2) ___________________________________ **Phone**______________________________

Address____

__ __ 38-39

11. How many hours ago did you last eat? __________ (code number of hours ago).

__ 40

12. Fasting status (coded by medical technologist).

0 Not fasted, food in the last 4 hours
1 Fasted, food not eaten in the past 4 hours

__ 41

13. How would you rate your overall health at the present time -- excellent, good, fair, or poor?

3 Excellent
2 Good
1 Fair
0 Poor
9 Not answered

__ 42

14. Is your health now better, about the same, or worse than it was five years ago?

2 Better
1 About the same
0 Worse
9 Not answered

__ 43

15. How much do your health troubles stand in the way of your doing things you want to -- not at all, a little (some), or a great deal?

2 Not at all
1 A little (some)
0 A great deal
9 Not answered

__ __ 44-45

16. County of residence 00-12

00= Madison	**03= Jackson**	**06= Greene**	09= Elbert	**12=Franklin**
01= Morgan	**04= Newton**	**07= Clark**	10= Oconee	
02= Walton	**05= Barrow**	08= Oglethorpe	11= Jasper	

__ 46

18. Did you participate in our vitamin supplement study during spring and summer 1999?
(ASK ONLY IN GREENE AND MORGAN COUNTY)

1= YES
0= NO

BLOOD PRESSURE

(NOTE: RECORD RESULTS ON "BLOOD PRESSURE FORM" AND GIVE TO PARTICIPANT)

__ __ __
50-52 **22. Blood Pressure**
Systolic (mmHg)
__ (0) < 120 Optimal
__ (1) < 130 Normal
__ (2) 130-139 High-normal
__ (3) 140-159 Mild Hypertension (Stage 1)
__ (4) 160-179 Moderate Hypertension (Stage 2)
__ (5) > 180 Severe Hypertension (Stage 3)
__ (999) Missing

Diastolic (mmHg)

__ __ __
53-55
__ (0) < 80 Optimal
__ (1) < 85 Normal
__ (2) 85-95 High-normal
__ (3) 90-99 Mild Hypertension (Stage 1)
__ (4) 100-109 Moderate Hypertension (Stage 2)
__ (5) > 110 Severe Hypertension (Stage 3)
__ (999) Missing

ORIENTATION-MEMORY-CONCENTRATION TEST

Read all questions to the participant. Tell them that some of the questions may be easy and some may be hard -- just do the best you can.

	Response	# of Errors	Max. Errors	Weight Factor	Total
1) What is the year now?			1	4	
2) What month is it now?			1	3	
Please repeat this phrase after me: **JOHN BROWN, 42 MARKET STREET, CHICAGO** *No score for this -- it is a memory phrase for Item # 6. Allow the person up to three trials for learning (repeating) the phrase. If the subject has not learned the phrase after three trials, record the value of "0" as the total score for Item #6, and proceed to Item #3.*					
3) Without looking at your watch or a clock, tell me about what time is it? *Note: score is correct if within one hour of actual time.*			1	3	
4) Count backwards from 20 to 1. *20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1*			2	2	
5) Say the months of the year in reverse order. *DEC, NOV, OCT, SEPT, AUG, JULY, JUNE, MAY, APR, MAR, FEB, JAN*			2	2	
6) Please repeat the name and address I asked you to remember. *Count the number of items (5) in memory phrase recalled incorrectly. An answer of either Market or Market Street is acceptable.* John / Brown / 42 / Market Street / Chicago			5	2	
(10-11) **TOTAL SCORE**					

Interpretation of corrected scores:	≤ 8	Normal or minimal impairment
	9-19	Moderate impairment
	≥ 20	Severe impairment

Source: Katzman, R., Brown, T., Fuld, P., Peck, A., Schechter, R., Schimmel, H. Validation of a short orientation-memory-concentration test of cognitive impairment. *American Journal of Psychiatry* 140: 734-739, 1983.

MINI-NUTRITIONAL ASSESSMENT

ID# ____________
(1-3)

Name: First name: Sex: Date:
Age:

04 ** *enter decimal points*
(4-5)

TSF. Triceps skin fold (mm): __ __.__
(6-9)

Kneeht. Knee Height (cm): __ __.__
(10-13)

I. ANTHROPOMETRIC ASSESSMENT

____ MNA1. BMI (weight/(height)^2 in kg/m^2); weight = ___ lbs. / 2.205 = __ __ __ . __kg (15-19)kg
(14)
0 = BMI < 19 height = ____ in. * .0254 = __ __ __ . __ meters (20-24)m
1 = 19 ≤ BMI < 21 BMI = __ __ . __ (25-28) BMI
2 = 21 ≤ BMI < 23
3 = BMI ≥ 23

_____ MNA2. Mid arm circumference (MAC in cm.): __ __ . __ cm. (30-33)cm
(29)
0.0 = MAC < 21
0.5 = 21 ≤ MAC ≤ 22
1.0 = MAC > 22

_____ MNA3. Calf circumference (CC in cm.): __ __ . __cm. (35-38)cm
(34)
0 = CC < 31
1 = CC ≥ 31

_____ MNA4. Weight loss during last 3 months: _________ lbs. / 2.205 = __ __ __ . __ kg (40-44)kg
(39)
0 = weight loss > 3 kg
1 = does not know
2 = weight loss between 1 and 3 kg
3 = no weight loss

_____ MNA12A. How many servings of <u>milk, yogurt, or cheese</u> does the individual consume?
(45)

0 ____ *Less than one per week*	3 ____ *3 per week*	6 ____ *6 per week*
1 ____ *1 per week*	4 ____ *4 per week*	7 ____ *At least one per day*
2 ____ *2 per week*	5 ____ *5 per week*	8 ____ *2 or more per day*
		9 ____ *Missing/don't know*

_____ MNA12D. How many servings of <u>meat, fish, or poultry</u> does the individual consume?
(46)

0 ____ *Less than one per week*	3 ____ *3 per week*	6 ____ *6 per week*
1 ____ *1 per week*	4 ____ *4 per week*	7 ____ *At least one per day*
2 ____ *2 per week*	5 ____ *5 per week*	8 ____ *2 or more per day*
		9 ____ *Missing/don't know*

NUTRITION QUESTIONS

__ 47 **1. Have you ever received home delivered meals?**
0 = Yes
1 = No

__ __ 48-49 **2. If you receive home delivered meals, for how long have you been receiving them? __ __ *years***
Code as whole years (xx years)

__ 50 **3. How many times a week do you eat at the senior center?**

0 ____ Less than one per week	3 ____ 3 per week	6 ____ 6 per week
1 ____ 1 per week	4 ____ 4 per week	7 ____ At least one per day
2 ____ 2 per week	5 ____ 5 per week	8 ____ 2 or more per day
		9 ____ Missing/don't know

__ 51 **4. How many servings of green vegetables do you eat?**

0 ____ Less than one per week	3 ____ 3 per week	6 ____ 6 per week
1 ____ 1 per week	4 ____ 4 per week	7 ____ At least one per day
2 ____ 2 per week	5 ____ 5 per week	8 ____ 2 or more per day
		9 ____ Missing/don't know

__ 52 **5. How many servings of orange or yellow vegetable do you eat?**

0 ____ Less than one per week	3 ____ 3 per week	6 ____ 6 per week
1 ____ 1 per week	4 ____ 4 per week	7 ____ At least one per day
2 ____ 2 per week	5 ____ 5 per week	8 ____ 2 or more per day
		9 ____ Missing/don't know

__ 53 **6. How many servings of citrus fruit or citrus juice do you eat (e.g., orange, grapefruit)?**

0 ____ Less than one per week	3 ____ 3 per week	6 ____ 6 per week
1 ____ 1 per week	4 ____ 4 per week	7 ____ At least one per day
2 ____ 2 per week	5 ____ 5 per week	8 ____ 2 or more per day
		9 ____ Missing/don't know

__ 54 **7. How many servings of other non-citrus fruit or juice do you consume?**

0 ____ Less than one per week	3 ____ 3 per week	6 ____ 6 per week
1 ____ 1 per week	4 ____ 4 per week	7 ____ At least one per day
2 ____ 2 per week	5 ____ 5 per week	8 ____ 2 or more per day
		9 ____ Missing/don't know

__ 55 **8. How many servings of liver (eg., beef, chicken,pork) do you consume?**

0 ____ Less than one per week	3 ____ 3 per week	6 ____ 6 per week
1 ____ 1 per week	4 ____ 4 per week	7 ____ At least one per day
2 ____ 2 per week	5 ____ 5 per week	8 ____ 2 or more per day
		9 ____ Missing/don't know

FOODS FORTIFIED WITH B-VITAMINS

We would like to know if you eat any of the following foods that may be fortified with B-vitamins

				Code daily intake of vit. B12 from each source.	Code daily intake of folate from each source.	Code daily intake of vit. B6 from each source.
8. Breakfast cereals, such as, Just Right w/ fruits & nuts, Product 19, Nutri-Grain, Total, Special K	**0 = No 1 = Yes**	**If yes, what BRAND(s) do you usually eat?**	**If yes, how often do you eat breakfast cereal?**			
9. Breakfast or energy bars, such as, Nutri-Grain, power bar,	**0 = No 1 = Yes**	**If yes, what BRAND(s) do you usually eat?**	**If yes, how often do you eat breakfast bars?**			
10. Liquid meal replacements, such as, carnation, ensure plus	**0 = No 1 = Yes**	**If yes, what BRAND(s) do you usually drink?**	**If yes, how often do you drink ensure, or boost etc.?**			
Other	**0 = No 1 = Yes**	**If yes, what BRAND(s) do you usually eat?**	**If yes, how often do you eat this food?**			
Other	**0 = No 1 = Yes**	**If yes, what BRAND(s) do you usually eat?**	**If yes, how often do you eat this food and in what quantity?**			

MEDICATIONS AND ILLNESSES
NAME/ID: _______________

Obtain information from reliable source. This information was provided by: client, caretaker, other___?

	YES (1)	NO (0)	DON'T KNOW	Space
Total number of PRESCRIPTION medications				10-11
Total number of NON -PRESCRIPTION medications, not counting vitamins and minerals				12-13
Multiple vitamin mineral supplement? 0 = no, 1 = yes				14
Number of other nutritional supplements?				15
Total number of illnesses - fill in when finished below.				16-17
1) Anemia in the past year				18
2) Alzheimer's: Kind________________; Dx date_____________				19
3) Other dementias: Kind__________________; Dx date __________				20
4) Cancer: Kind_____________; Dx date____________; Status_____				21
5) Circulatory problems in the past year				22
6) Congestive heart failure in the past year				23
7) Constipation in the past year				24
8) Diabetes: Kind_________________; Dx date ________________				25
9) Diarrhea in the past year				26
10) Glaucoma in the past year				27
11) Hearing problems in the past year				28
12) Heart disease in the past year				29
13) Hypertension in the past year				30
14) Legally blind in the past year				31
15) Liver disease in the past year				32
16) Mental illness: Kind___________________; Dx date___________				33
17) Osteoporosis in the past year				34
18) Hip fracture in the past year				35
19) Have you every had a pace maker				36
20) Parkinson's disease: Dx date____________________				37
21) Renal disease in the past year				38
22) Respiratory disease in the past year				39
23) Seizures: 1st date_____________; last date______________				40
24) Skin rashes, bed sores in the past year				41
25) Stroke: Number______; Dates______________________________				42
26) Thyroid problems: Kind____________; Dx date______________				43
27) Visual disturbances in the past year				44
28) Cataracts in the past year				45
29) Have you used any type of tobacco in the past year				46
30) Have you every had stomach surgery				47
31) Emergency room visit in the past year				48
32) Other				49
33) Arthritis in the past year				50
34) Pneumonia in the past year				51
35) Dizziness in the past year				52
36) Gout in the past year				53
37)				54

MEDICATIONS ***(NOTE: ASK EVERY MEDICATION QUESTION THEN RECORD MEDS ON THE NEXT FORM)***			
1)	Are you currently taking aspirin?	1 = Yes 0 = No	10
2)	Are you currently taking ibuprofen such as Advil, Motrin, Nuprin?	1 = Yes 0 = No	11
3)	Are you currently taking Aleve?	1 = Yes 0 = No	12
4)	Are you currently taking Acetaminophen such as Tylenol or similar medication?	1 = Yes 0 = No	13
5)	Are you currently taking antacids or medications for heartburn or indigestion such as maalox, mylanta, alka aid (alka-seltzer) gaviscon, propulsid, zantac, pepcid, axid, cyotec, tums, tagamet, proton pump inhibitors such as prevacid, prevapac,prilosec, or other medication? **CIRCLE ALL THAT APPLY**	1 = Yes 0 = No	14
6)	Are you currently taking laxatives such as milk of magnesia, fiber tablets, metamucil or other laxative medication? **CIRCLE ALL THAT APPLY**	1 = Yes 0 = No	15
7)	Are you currently taking a cough suppressant such as humibid, robitussin, entrex or other medication?	1 = Yes 0 = No	16
8)	Are you currently taking allergy, sinus, or cold medication such as chlorpheniramine, relief, allerfed, seldane, sudafed, sine aid, Tylenol allergy sinus, contac, tylenol cold formulas, methypred dose, claritin, phenylprop, guaif, bromfed, tavist-d, actifed, benadryl, equate allergy sinus or other medication?	1 = Yes 0 = No	17
9)	Are you currently using nasal spray for allergy or sinus, such as aerobid, flonase, beconase, Nasalcrom or other medication?	1 = Yes 0 = No	18
10)	Are you currently taking a non-steroidal anti-inflammatory drug (NSAID) such as voltaren, diclofenac, naprosyn, naproxyn, sulindac, lodine, relafen, daypro, oruvail or similar medication?	1 = Yes 0 = No	19
11)	Are you currently taking a pain medication such as ultram, darvocet-N-100, fiorinal or similar medication?	1 = Yes 0 = No	20
12)	Are you currently taking an arthritis medication such as prednisone, rheumatrex methotrexate, orasone, deltasone or other medication?	1 = Yes 0 = No	21
13)	Are you currently taking antibiotics such as zithromax, amoxicillin or other antibiotic medication?	1 = Yes 0 = No	22
14)	Are you currently taking a sleeping aid such as Tylenol PM or other medication?	1 = Yes 0 = No	23

MEDICATIONS			
15)	Are you currently taking migraine medication such as mepergan fortis, imitrex, ercaf, Forbal-S or other migraine medication?	1 = Yes 0 = No	24
	# 16 and #18 - important for cognitive tests - so probe carefully		
16)	Are you currently taking anti-anxiety medication such as Alprazolam (xanax), Buspirone (Buspar), Chlordiaxepoxide (Librium), Clonazepam (klonopin), Clorazepate (tranxene), Diazepam (Valium), Hydroxyzine (Vistaril), Lorazepam (Ativan), Oxazepam (Serax), Propanolol (Inderal) or other anti-anxiety medication? **Circle all that apply**	1 = Yes 0 = No	25
17)	Are you currently taking anti-depressant medication such as Amitriptyline (Elavil), Citalopram (Celexa), Clomipramine (Anafranil), Desipramine (Norpramin), Doxepin (Sinequan), Fluoxetine (Prozac), Fluvoxamine (Luvox), Imipramine (Tofranil), Maprotiline (Ludiomil), Nortriptyline (Pamelor), Paroxetine (Paxil), Sertraline (zoloft), Trazadone (Desyrel), Venlafaxine (Effexor) or other anti-depressant medication? **Circle all that apply**	1 = Yes 0 = No	26
	#41 & 42 - important for cognitive tests - so probe carefully		
41)	Are you currently taking any drugs to help or enhance your thinking such as Chlorpromazine (Thorazine), Thioridazine (Mellaril), Fluphenazine (Prolixin), Trifluoperazine (Stelazine), Haloperidol (Haldol), Thiothixene (Navane), Loxapine (Loxitane), Molindone (Moban), Clozapine (Clozaril), Risperidone (Risperdal), Quetiapine (Seroquel), Olanzapine (Zyprexa) or other neuroleptic medications? **Circle all that apply**	1 = Yes 0 = No	27
42)	Are you currently taking any drugs to help or enhance your memory such as Tacrine (Cognex) or Donepezil hydrochloride (Aricept)? **Circle all that apply**	1 = Yes 0 = No	28
43)	List any other medications currently taken:	1 = Yes 0 = No	29
45)	Are you currently receiving Vitamin B-12 injections/shots? Last Vitamin B-12 shot (date) : _______________ How often? ________________*(example: once a year, twice a year, every other month, once a month) 762* ***(NOTE: IF YES, THEY NEED TO HAVE HAD A SHOT 6 MONTHS AGO OR LATER AND AGREE NOT TO RECEIVE A SHOT FOR THE NEXT FOUR MONTHS TO PARTICIPATE IN THIS STUDY)***	1 = Yes 0 = No	30
	Total number of prescription medications *(total of prescription meds)*		31-32
	Total number of non-prescription medications *(total of nonprescription meds)*		33-34

RESIDENT MEDICATION RECORDS:
Include prescription, non-prescription, and vitamins/minerals

ID _________

Medication	Dosage	Schedule	Route of Administration	*How Long have you been taking medication	DOCUMENTATION (Check all that apply)		
					Bottle only	Cardex Record	Signature Administration Record

	______ *SUPP # __*	________ *SUPP # __*	________ *SUPP # __*	________ *SUPP # __*	________ *SUPP # __*	*TOTAL*
	__ # pills per D, W, M **WRITE IN AMOUNT /PILL & CIRCLE UNIT**	**__ # pills per D, W, M** **WRITE IN AMOUNT /PILL & CIRCLE UNIT**	**__ # pills per D, W, M** **WRITE IN AMOUNT /PILL & CIRCLE UNIT**	**__ # pills per D, W, M** **WRITE IN AMOUNT /PILL & CIRCLE UNIT**	**__ # pills per D, W, M** **WRITE IN AMOUNT /PILL & CIRCLE UNIT**	
For how long?	**_____mo/yrs**	**_____mo/yrs**	**_____mo/yrs**	**_____mo/yrs**	**_____mo/yrs**	
Vitamin A	IU RE	IU RE	IU RE	IU RE	IU RE	
Vitamin C	mg	mg	mg	mg	mg	
Vitamin D	IU mg	IU mg	IU mg	IU mg	IU mg	
Vitamin E	IU mg	IU mg	IU mg	IU mg	IU mg	
Thiamin (B1)	mg	mg	mg	mg	mg	
Riboflavin (B2)	mg	mg	mg	mg	mg	
Niacin or Niacinamide or Vit. B3	mg	mg	mg	mg	mg	
Pyridoxine or Vitamin B6	mg	mg	mg	mg	mg	
Folic acid or Folate	mcg mg	mcg mg	mcg mg	mcg mg	mcg mg	
Vitamin B-12	mg mcg	mg mcg	mg mcg	mg mcg	mg mcg	
Biotin	mg mcg	mg mcg	mg mcg	mg mcg	mg mcg	
Pantothenic Acid	mg	mg	mg	mg	mg	
Vitamin K	mcg	mcg	mcg	mcg	mcg	
Calcium	mg	mg	mg	mg	mg	
Iron	mg	mg	mg	mg	mg	
Phosphorus	mg	mg	mg	mg	mg	
Iodine	mcg	mcg	mcg	mcg	mcg	
Magnesium	mg	mg	mg	mg	mg	
Zinc	mg	mg	mg	mg	mg	
Copper	mg	mg	mg	mg	mg	
Potassium	mg	mg	mg	mg	mg	
Manganese	mg	mg	mg	mg	mg	
Chromium	mcg	mcg	mcg	mcg	mcg	
Molybdenum	mcg	mcg	mcg	mcg	mcg	
Chloride	mg	mg	mg	mg	mg	
Nickel	mcg	mcg	mcg	mcg	mcg	
Silicon	mg mcg	mg mcg	mg mcg	mg mcg	mg mcg	
Vanadium	mcg	mcg	mcg	mcg	mcg	
Boron	mg mcg	mg mcg	mg mcg	mg mcg	mg mcg	
Fluoride	mg	mg	mg	mg	mg	
Selenium	mcg	mcg	mcg	mcg	mcg	
Other						

	________ *SUPP # __*	________ *SUPP # __*	________ *SUPP # __*	________ *SUPP # __*	________ *SUPP # __*	***TOTAL***
	__ # pills per D, W, M **WRITE IN AMOUNT /PILL & CIRCLE UNIT**	**__ # pills per D, W, M** **WRITE IN AMOUNT /PILL & CIRCLE UNIT**	**__ # pills per D, W, M** **WRITE IN AMOUNT /PILL & CIRCLE UNIT**	**__ # pills per D, W, M** **WRITE IN AMOUNT /PILL & CIRCLE UNIT**	**__ # pills per D, W, M** **WRITE IN AMOUNT /PILL & CIRCLE UNIT**	
For how long?	**_____mo/yrs**	**_____mo/yrs**	**_____mo/yrs**	**_____mo/yrs**	**_____mo/yrs**	
Vitamin A	IU RE	IU RE	IU RE	IU RE	IU RE	
Vitamin C	mg	mg	mg	mg	mg	
Vitamin D	IU mg	IU mg	IU mg	IU mg	IU mg	
Vitamin E	IU mg	IU mg	IU mg	IU mg	IU mg	
Thiamin (B1)	mg	mg	mg	mg	mg	
Riboflavin (B2)	mg	mg	mg	mg	mg	
Niacin or Niacinamide or Vit. B3	mg	mg	mg	mg	mg	
Pyridoxine or Vitamin B6	mg	mg	mg	mg	mg	
Folic acid or Folate	mcg mg	mcg mg	mcg mg	mcg mg	mcg mg	
Vitamin B-12	mg mcg	mg mcg	mg mcg	mg mcg	mg mcg	
Biotin	mg mcg	mg mcg	mg mcg	mg mcg	mg mcg	
Pantothenic Acid	mg	mg	mg	mg	mg	
Vitamin K	mcg	mcg	mcg	mcg	mcg	
Calcium	mg	mg	mg	mg	mg	
Iron	mg	mg	mg	mg	mg	
Phosphorus	mg	mg	mg	mg	mg	
Iodine	mcg	mcg	mcg	mcg	mcg	
Magnesium	mg	mg	mg	mg	mg	
Zinc	mg	mg	mg	mg	mg	
Copper	mg	mg	mg	mg	mg	
Potassium	mg	mg	mg	mg	mg	
Manganese	mg	mg	mg	mg	mg	
Chromium	mcg	mcg	mcg	mcg	mcg	
Molybdenum	mcg	mcg	mcg	mcg	mcg	
Chloride	mg	mg	mg	mg	mg	
Nickel	mcg	mcg	mcg	mcg	mcg	
Silicon	mg mcg	mg mcg	mg mcg	mg mcg	mg mcg	
Vanadium	mcg	mcg	mcg	mcg	mcg	
Boron	mg mcg	mg mcg	mg mcg	mg mcg	mg mcg	
Fluoride	mg	mg	mg	mg	mg	
Selenium	mcg	mcg	mcg	mcg	mcg	
Other						

HEARING HANDICAP INVENTORY FOR ADULTS (HHIA)

Date: ______ ID: ______

The purpose of these questions is to identify any problems your hearing loss may be causing you. Please do not skip any questions. Even if you feel you do not have a hearing loss, please answer all of the questions. For each question, circle one response: No, Sometimes, or Yes.

		0	2	4	Line Space Line # 4-5
S1	Does a hearing problem cause you to use the phone less often than you would like?	No	Sometimes	Yes	10
E2*	Does a hearing problem cause you to feel embarrassed when meeting new people?	No	Sometimes	Yes	11
S3	Does a hearing problem cause you to avoid groups of people?	No	Sometimes	Yes	12
E4	Does a hearing problem make you irritable?	No	Sometimes	Yes	13
E5*	Does a hearing problem cause you to feel frustrated when talking to members of your family?	No	Sometimes	Yes	14
S6	Does a hearing problem cause you difficulty when attending a party?	No	Sometimes	Yes	15
S7	Does a hearing problem cause you difficulty hearing/understanding coworkers, clients, or customers?	No	Sometimes	Yes	16
E8*	Do you feel handicapped by a hearing problem?	No	Sometimes	Yes	17
S9*	Does a hearing problem cause you difficulty when visiting friends, relatives, or neighbors?	No	Sometimes	Yes	18
E10	Does a hearing problem cause you to feel frustrated when talking to coworkers, clients, or customers?	No	Sometimes	Yes	19
S11*	Does a hearing problem cause you difficulty in the movies or theater?	No	Sometimes	Yes	20
E12	Does a hearing problem cause you to be nervous?	No	Sometimes	Yes	21
S13	Does a hearing problem cause you to visit friends, relatives, or neighbors less often than you would like?	No	Sometimes	Yes	22
E14*	Does a hearing problem cause you to have arguments with family members?	No	Sometimes	Yes	23
S15*	Does a hearing problem cause you difficulty when listening to the TV or radio?	No	Sometimes	Yes	24
E16	Does a hearing problem cause you to go shopping less often than you would like?	No	Sometimes	Yes	25
E17	Does any problem or difficulty with your hearing upset you at all?	No	Sometimes	Yes	26

E18	Does a hearing problem cause you to want to be by yourself?	No	Sometimes	Yes	27
S19	Does a hearing problem cause you to talk to family members less often than you would like?	No	Sometimes	Yes	28
E20*	Do you feel that any difficulty with your hearing limits or hampers your personal or social life?	No	Sometimes	Yes	29
S 21*	Does a hearing problem cause you difficulty when in a restaurant with relatives or friends?	No	Sometimes	Yes	30
E 22	Does a hearing problem cause you to feel depressed?	No	Sometimes	Yes	31
S 23	Does a hearing problem cause you to listen to TV or radio less often than you would like?	No	Sometimes	Yes	32
E 24	Does a hearing problem cause you to feel uncomfortable when talking to friends?	No	Sometimes	Yes	33
E 25	Does a hearing problem cause you to feel left out when you are with a group of people?	No	Sometimes	Yes	34
E 26	Does a hearing problem cause you to feel “stupid” or “dumb”?	No	Sometimes	Yes	35
S 27	Do you have difficulty hearing when someone speaks in a whisper?	No	Sometimes	Yes	36
S 28	Does a hearing problem cause you to attend religious services less often than you would like?	No	Sometimes	Yes	37

* Items comprising the HHIA-S.
From: Newman, C.W., Weinstein, B.E., Jacobson, G.P., and Hug, G.A. Test-retest reliability of the Hearing Handicap Inventory for Adults, Ear and Hearing, 1991;12(5): 355-357

Geriatric Depression Scale (GDS) Short form

Choose the best answer for how you felt over the past week. Please answer the following questions "YES" or "NO there are no right or wrong answers, only what best applies to you.

		1	0	Space
1)	Are you basically satisfied with your life?	Yes	*NO	10
2)	Have you dropped many of your activities and interests?	*YES	No	11
3)	Do you feel that your life is empty?	*YES	No	12
4)	Do you often get bored?	*YES	No	13
5)	Are you in good spirits most of the time?	Yes	*NO	14
6)	Are you afraid that something bad is going to happen to you?	*YES	No	15
7)	Do you feel happy most of the time?	Yes	*NO	16
8)	Do you often feel helpless?	*YES	No	17
9)	Do you prefer to stay at home, rather than going out and doing new things?	*YES	No	18
10)	Do you feel you have more problems with memory than most people?	*YES	No	19
11)	Do you think it is wonderful to be alive now?	Yes	*NO	20
12)	Do you feel pretty worthless the way you are now?	*YES	No	21
13)	Do you feel full of energy?	Yes	*NO	22
14)	Do you feel that your situation is hopeless?	*YES	No	22
15)	Do you think that most people are better off than you are?	*YES	No	23

*** = 1 point. If * score is 10 or greater, or if (Nos. 1,5,7,11,13) were answered with * then the participant may be depressed. Proceed with referral plan.**

In the last few weeks have you found things to be easily disturbing or annoying (e.g., have other people, objects or situations been getting on your nerves or causing you frustration?)

1 2 3 4 5 6 7

Not at all all of the time

In the last few weeks have you felt restless or experienced difficulty with activities such as sleeping, following instructions, keeping your mind on what you are doing?

1 2 3 4 5 6 7

Not at all all of the time

NUTRITION AND DEPRESSION STATUS REPORT

NAME: ______________________________
COUNTY: __________________________
DATE:___________________

NUTRITION SCREENING INITIATIVE - 10 ITEM QUESTIONNAIRE:

This questionnaire screens for nutritional problems.

_____	0-2	Good
_____	3-5	Moderate nutritional risk
_____	6 or more.	High nutritional risk; recommend nutrition consult

BODY MASS INDEX (KG/M2) - INDEX OF WEIGHT FOR HEIGHT:

This is an index of underweight, normal weight, overweight and obesity.

_____ Greater than 30 Obese; recommend nutrition consult

_____ 25-29 Overweight; At risk for nutrition problems; recommend nutrition consult

_____ 21-24.9 Normal Range

_____ Less than 19.9; At risk for nutrition problems; recommend nutrition consult

WEIGHT LOSS (> 3 KG or 7 POUNDS IN PREVIOUS 3 MONTHS): ___________

Unintentional weight loss is an indicator of low food intake or illness. However, some people need to lose weight if they are overweight and their weight is contributing to health problems.

_____ No weight loss Good

_____ Weight loss > 7 lb At risk for nutrition problems; recommend nutrition consult

PLEASE FEEL FREE TO CONTACT NIKKI HAWTHORNETO MAKE AN APPOINTMENT FOR A NUTRITIONAL CONSULT: 706-542-4838

GERIATRIC DEPRESSION SCALE- 15 ITEM QUESTIONNAIRE:____________

This questionnaire measures depression.

_____ 9 or less; probably not depressed

_____ 10 or more; at risk for depression - contact senior center director

PRE TEST

Hearing History Questionnaire (HHQ)

Please fill out this form as completely as possible, even if you do not have a hearing problem.

I. IDENTIFICATION

ID/Name:______________________________________ Date:_____________________

Date of Birth:__________ Age:___

Telephone #:________________

II. HISTORY INFORMATION

A. Communication

Do you feel you have a hearing loss? Explain:

____

____

If yes:

Describe any changes in your hearing since it began:

____

____

Describe any variations in the nature or severity of your problem:

____

____

State your opinion of the cause of your problem:

____

____

B. Family

Do any of the following family members have a hearing loss?

If yes, please indicate at what age their hearing loss began and the cause.

Mother	YES	NO	____
Father	YES	NO	____
Brother	YES	NO	____
Sister	YES	NO	____
Grandparent	YES	NO	____

C. Previous Evaluations and Treatment

List any individual or agency who has evaluated your hearing. Include dates and a description of the results:

____

Have you ever worn a hearing aid? ___________When? _________________

If yes, indicate: Make ________ Model ____________ Ear ________________

D. Medical

List any physicians who have provided medical care related to your hearing:

____

Have you ever experienced any of the following:

If yes, explain:

Ear Pain	YES	NO	________________
Ear Discharge	YES	NO	________________
Fullness or pressure in ears	YES	NO	________________
Ear, Nose or Throat surgery	YES	NO	________________
Dizziness	YES	NO	________________

Have you ever had any major surgeries? ______________________________

If yes, were you given any specific medications at that time? (Please list, especially antibiotics)
____

Have you ever had chemotherapy?
____

E. Tinnitus

Do you have ringing or noises (tinnitus) in your ears? YES NO

If yes, about how long have you been aware of having tinnitus?

(1) _____ Less than a year
(2) _____ 1 to 2 years
(3) _____ 3 to 5 years
(4) _____ 6 to 10 years
(5) _____ 11 to 20 years
(6) _____ 20 or more years

Which one of the statements below best describes your current tinnitus?

(1) _____ Tinnitus usually lasts a few minutes at most
(2) _____ Tinnitus usually lasts up to several hours
(3) _____ Tinnitus usually lasts up to several days
(4) _____ Tinnitus is always there

If your tinnitus is not present all of the time, how much of the time does it seem to be present?

(1) _____ Less than half the time (2) _____ Half the time or more

Does your tinnitus interfere with your...

(1)	SLEEP	YES	NO
(2)	HEARING	YES	NO
(3)	DAY TO DAY LIVING	YES	NO

III. ADDITIONAL COMMENTS

____
____
____

POST TEST

Hearing History Questionnaire (HHQ)

E. Tinnitus

Do you have ringing or noises (tinnitus) in your ears? YES NO

If yes, about how long have you been aware of having tinnitus?

(1) _____ Less than a year	(4) _____ 6 to 10 years
(2) _____ 1 to 2 years	(5) _____ 11 to 20 years
(3) _____ 3 to 5 years	(6) _____ 20 or more years

Which one of the statements below best describes your current tinnitus?

(1) _____ Tinnitus usually lasts a few minutes at most
(2) _____ Tinnitus usually lasts up to several hours
(3) _____ Tinnitus usually lasts up to several days
(4) _____ Tinnitus is always there

If your tinnitus is not present all of the time, how much of the time does it seem to be present?

(1) _____ Less than half the time (2) _____ Half the time or more

Does your tinnitus interfere with your...

(1)	SLEEP	YES	NO
(2)	HEARING	YES	NO
(3)	DAY TO DAY LIVING	YES	NO

III. ADDITIONAL COMMENTS

____
____
____