Hearing in advanced age

Epidemiological, pathophysiological, and diagnostic perspectives from the Gothenburg H70 Birth Cohort Studies

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Gothenburg 2023

Cover illustration: Per-Olof Ekdahl

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ISBN 978-91-8069-387-5 (PRINT)
ISBN 978-91-8069-388-2 (PDF)

Printed in Borås, Sweden 2023
Printed by Stema Specialtryck AB

“Grey hair is a glorious crown…”

Proverbs 16:31

”Det finns inga syrsor längre, de fanns bara förr”

Morfar Holger

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ABSTRACT

The population aged 80 and above is expected to increase in the future resulting in an anticipated rise in health care demands. Age-related hearing loss (ARHL) is described as the third most common health condition associated with ageing. ARHL often results in communication difficulties and social isolation and is associated with cognitive decline. Ageing processes affect both the peripheral and the central auditory systems. Age-related deterioration in the central parts of the auditory pathways often results in severe communication difficulties. It is important to study the prevalence of ARHL, including age cohort differences, in order to assess rehabilitation needs. However, to gain a deeper understanding of ARHL and its associated care needs, it is essential to conduct studies that incorporate pathophysiological aspects of ageing in the auditory system. A limited amount of research has been carried out in this area in evolving populations 80 years and older. This thesis focuses on epidemiological, pathophysiological, as well as diagnostic perspectives of ARHL in 85-year-old men and women. The results are based on a prospective and epidemiological study, The Gothenburg H70 Birth Cohort Studies. The specific papers within this thesis explore different aspects of ARHL. **Paper I** presents pure-tone audiometry results, which predominantly reflect peripheral hearing. The findings indicate that men have better hearing at low frequencies but poorer hearing at high frequencies compared to women. Additionally, the study examines hearing decline longitudinally between the ages of 75 to 85, revealing a significant decline at mid-high frequencies for both sexes**. Paper II** also focuses on peripheral hearing loss and highlights differences in pure-tone hearing between two birth cohorts of 85-year-olds, born approximately 30 years apart. The prevalence of ARHL was found to have decreased over approximately three decades among 85-year-old men but remained unchanged in women. **Paper III** describes pathophysiological aspects of ARHL. Test results describe various validated and clinically utilized auditory measures, including speech audiometry, and suggest that sensorineural hearing loss, related to cochlear damage, is the most common subtype of auditory dysfunction in 85-year-olds. Only a few participants had conductive hearing loss (~6%), reflecting middle-ear pathologies. Additionally, almost one-fifth of the 85-year-olds had poor speech recognition in relation to a SII-based algorithm based on pure-tone thresholds as well as supra-threshold factors. Based on the criteria used in this study, poor speech recognition was only occasionally (~2%) attributed to auditory nerve dysfunction. **Paper IV** investigates central auditory function, specifically binaural listening skills in 70- and 85-year-olds. Central auditory function was studied using a simplified dichotic digit test (DDT) with the use of one-pair digits, which imposes a relatively low cognitive and linguistic load on participants. The results showed that older age was associated with poorer DDT scores. Furthermore, the outcome of the DDT was influenced by both peripheral hearing loss, including high frequency hearing loss, and cognitive abilities. This makes it difficult to identify isolated central auditory processing disorders using DDT in advanced age.

Keywords: Age-related hearing loss, Older adult, Hearing decline, Peripheral auditory function, Central auditory function, Audiological research

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SAMMANFATTNING PÅ SVENSKA

Globalt förväntas antalet personer över 80 år att öka i framtiden. Detta bidrar förmodligen till ett ökat vårdbehov av åldersrelaterade tillstånd och sjukdomar, varav åldersrelaterad hörselnedsättning (ARHL) rankas som den tredje vanligaste. Det finns ett påvisat samband mellan ARHL och kommunikationssvårigheter, social isolering och kognitiv svikt. I takt med stigande ålder sker försämringar i de perifera såväl som i de centrala hörselbanorna, det vill säga från öra till hjärna. Åldersrelaterade försämringar i centrala delar av hörselbanorna resulterar ofta i stora svårigheter att höra tal, speciellt i bullriga situationer. Genom att studera prevalensen för ARHL, inklusive åldersrelaterade kohortskillnader, kan man få en bättre översikt av behovet av hörselrehabilitering. För att uppnå en djupare kunskap om ARHL och dess rehabiliteringsbehov är det av betydelse att även studera patofysiologiska aspekter. Framför allt finns det ett behov av att studera detta på populationer över 80 år då tillgängliga data mestadels fokuserat på yngre åldrar. Denna doktorsavhandling beskriver epidemiologiska, patofysiologiska och diagnostiska perspektiv på ARHL hos 85-åriga män och kvinnor. Resultaten baseras på en prospektiv epidemiologisk studie som genomförs i Göteborg: H70 studierna. **Delarbete I** beskriver resultat från luftledd tonaudiometri som främst återspeglar perifer hörselfunktion. Resultatet visar att 85-åriga män har sämre hörsel vid höga frekvenser men bättre hörsel vid låga frekvenser jämfört med 85-åriga kvinnor. En longitudinell analys av hörselförändring mellan 75 och 85 års ålder visar på en betydande hörselförsämring i viktiga talfrekvenser för både män och kvinnor. **Delarbete II** fokuserar också på tonaudiometri och perifer hörselfunktion och presenterar skillnader i hörtrösklar för rena toner mellan två olika ålderkohorter med en åldersskillnad på ca 30 år. Prevalensen för ARHL minskade under cirka tre decennier för män, medan prevalensen var oförändrad för kvinnor. **Delarbete III** beskriver patofysiologiska aspekter av ARHL. Resultat från validerade och standardiserade kliniska testmetoder, inklusive talaudiometri, presenteras deskriptivt. Sensorineural hörselnedsättning relaterad till kokleär påverkan är den vanligaste sub-typen av auditiv dysfunktion hos 85-åringar. Endast ett fåtal deltagare (~6%) hade konduktiv hörselnedsättning. Cirka en femtedel av 85-åringarna hade sämre taluppfattning än förväntat utifrån tontrösklarna. Utifrån studiens specifika kriterier, kunde endast enstaka av dessa fall kopplas till dysfunktion i hörselnerven (~2%). I **delarbete IV** studeras central auditiv funktion, specifikt binaurala färdigheter, hos 70 och 85-åringar. Ett dikotiskt taltest med siffror används med låg kognitiv belastning. Resultatet påverkades av både perifer hörselnedsättning och kognitiv förmåga. Det är därmed svårt att identifiera isolerad central auditiv bearbetningsstörning med hjälp av DDT i denna åldersgrupp.

LIST OF PAPERS

This doctoral thesis is based on the following four studies, referred to in the text by their Roman numerals.

I. Göthberg H, Rosenhall U, Tengstrand T, Rydberg Sterner T, Wetterberg H, Zettergren A, Skoog I, Sadeghi A. (2019). *Cross-sectional assessment of hearing acuity of an unscreened 85-year-old cohort -Including a 10-year longitudinal study of a sub-sample.* Hearing Research 382:107797.

II. Göthberg H, Rosenhall U, Tengstrand T, Rydén L, Wetterberg H, Skoog I, Sadeghi A. (2020). *Prevalence of hearing loss and need for aural rehabilitation in 85-year-olds: a birth cohort comparison, almost three decades apart.* International Journal of Audiology 60(7):539-548.

III. Göthberg H, Skoog I, Tengstrand T, Magnusson L, Hoff M, Rosenhall U, Sadeghi A. (2023). *Pathophysiological and Clinical Aspects of Hearing Loss Among 85-Year-Olds.* American Journal of Audiology 17:1-13.

IV. Göthberg H, Skoog J, Tengstrand T, Hoff M, Hadarsson Bodin, T, Rosenhall U, Skoog I, Sadeghi A. (2023). *Results from a simplified dichotic listening test in younger and older olds.* Manuscript

CONTENTS

ABBREVIATIONS

AAA	American Academy of Audiology
ABR	Auditory Brainstem Responses
ANSD	Auditory Neuropathy Spectrum Disorders
ARHL	Age-Related Hearing loss
ASHA	American Speech- Language-Hearing Association
BSA	British Society of Audiology
CAD	Central Auditory Deficit
CAP	Central Auditory Processing
CAPD	Central Auditory Processing Disorders
CD	Cognitive Deficit
CHL	Conductive Hearing Loss
CVD	Cardiovascular Diseases
CI	Confidence Interval
dB HL	Decibel Hearing Level
dB nHL	dB HL calculated for a specific click stimulus used to elicit ABR-responses.
DDT	Dichotic Digit Test
DPOAE	Distortion Product Otoacoustic Emission
DR RE	Directed Reports Right Ear
DR LE	Directed Reports Left Ear
FR	Free Reports

GBD	Global Burden of Disease
ICF	International Classification of Functionality and Disability
IPL	Interpeak Latency
kHz	Kilohertz
Mmho	Millimho (1Mho is the inverse of 1 Ohm)
MS	MilliSecond
MMSE	Mini Mental State Exam
MOCA/MoCa	Montreal Cognitive Assessment
P	Probability (in statistics)
PARAN	Probably Age-Related auditory neuropathy
PTA	Pure-Tone Average
PTA 3	Pure-Tone Average for three frequencies 0.5, 1 and 2 kHz
PTA4	Pure-tone Average for four frequencies 0.5, 1, 2 and 4 kHz
PTAHF	Pure-Tone Average for High-Frequencies 4, 6 and 8 kHz
REA	Right Ear Advantage
SCB	Statistics Sweden
SII	Speech Intelligibility Index
SL	Sensation Level
SNR	Signal to Noise Ratio
UN	United Nations
WHO	World Health Organization

WRS	Word Recognition Score
WRS-N	Word Recognition Score in Noise
WRS-Q	Word Recognition score in Quite

INTRODUCTION

AGEING

There is no single definition of ageing, but it is often associated with declines in physiological and cognitive functions (Balcombe and Sinclair et al., 2001). At a biological level, ageing is associated with molecular and cellular damage over a long period. This leads to a gradual decrease in mental and physical capacity, and an increasing risk of disease. Ageing is most often framed in negative terms and old people are often assumed to be a burden to society. This ageist attitude may lead to discrimination and affect the possibilities of healthy ageing (Lloyd-Sherlock et al., 2012). Ageing is associated with positive factors, such as increased wisdom and life experience (Ardelt, 2010).

Biological changes are highly individual and there is no typical old person. Some 80-year-olds have physical and mental capacities like younger age-groups, while others experience significant declines in capacities at a much younger age. Several personal and environmental factors affect the lives of older individuals. Besides biological changes, other life factors such as social networks and the attitudinal environment affect the capacity of older individuals. According to the WHO, healthy ageing is about "developing and maintaining the functional ability that enables wellbeing in older age" (WHO, 2015). The public healthcare system must address the wide range of needs in this age group.

EPIDEMIOLOGY

Epidemiology is a field of research that focuses on studying different health conditions in populations. In epidemiology, cohort studies are commonly used to examine the association between exposure to certain factors and the development of specific health outcomes. Comparing different birth cohorts who share similar characteristics allows researchers to examine the effects of a birth year on the outcome. Time trends related to the prevalence and incidence of a disease can be influenced by both age effects, linked to individual age-related biological and social processes, and period effects, linked to variations caused by external factors, that affect all age groups at a particular historical time. Different risk and protective factors exist during different time periods and consequently, it is of interest to conduct repeated studies in the population, i.e., studying the same characteristic/condition but at different times (Blanchard et al., 1977). To ensure the validity of such comparisons, similar methodologies should be employed across the included cohorts. Cohort studies can be performed cross-sectionally and/or longitudinally. In cross-sectional studies, a specific condition is studied at a specific point in time (Wang et al, 2020). Descriptive cross-sectional studies aim to characterize the prevalence of a particular outcome in a defined population. Analytical cross-sectional studies collect data on both exposures and outcomes, allowing for the investigation of risk factors and/or protective factors which can be used to develop methods and interventions for disease prevention (Wang et al, 2020). Longitudinal studies are preferred for studying risk and protective factors as they offer a better understanding of changes over time. In a longitudinal study, the same individuals are followed over time, and a change in a specific health variable is influenced by both age-effects and period effects.

In epidemiology, it is of interest to describe a study sample using demographic data that is relevant to the specific health variable under investigation. Such demographic data may include factors such as education level, age, socioeconomic status, as well as various health-related factors. It is important to consider the geographical distribution of individuals in a study, as different regions exhibit distinct health conditions, functional levels, as well as specific risk and health factors that may affect a particular condition in participants within a specific geographical area (Diez Roux et al., 2001).

DEMOGRAPHY IN SWEDEN

An increase in life expectancy has been observed globally and has resulted in a growing proportion of individuals reaching advanced ages within populations. By 2050, the world's population of people aged 60 years and older will double, and the number of individuals aged 80 years or older is expected to triple between 2020 and 2050 (United Nation, 2019; WHO, 2015). Longevity is a good indicator of population health (Stiefel et al., 2010) and an increase in life expectancy is one of the factors that characterizes the 20th century. With an average life expectancy of 84 for women and 81 for men, Sweden ranks 13th (WHO, 2020) in the world in terms of life expectancy.

Sweden has from the middle of 1800s century undergone a significant transformation from an agricultural country to a predominantly urbanized one, with the majority of the population living in cities or urban areas. Gothenburg, the city where this study is based, is an industrial city with approximately 600 000 inhabitants (Statistics Sweden, 2023).

Swedish men born during the early 1900s, predominantly worked in industry and had a lower level of education compared to those born in later years. In terms of gender roles, during the early 1900s, a significant number of women in Sweden were housewives. However, between 1950 and 1980, many women started to work, often part-time, working in laundry and ironing companies or in sewing factories. In the 1970s, there was a shift towards more women working full-time, coinciding with increased access to preschool facilities for Swedish children (Statistics Sweden, 2018).

ANATOMY AND PHYSIOLOGY OF THE AUDITORY SYSTEM

Sound waves enter the outer ear and travel through the external ear canal causing the tympanic membrane (eardrum) to vibrate. The outer and middle ear conducts and amplifies these sound vibrations and transmits them to the cochlea by passing the oval window. The cochlea is divided into three parts (scala vestibuli, scala tympani and scala media) by two membranes. The lower membrane is known as the basilar membrane, which tapers from a wide (base) to a narrower (apex) part, and the upper membrane is called the tectorial membrane. On the top of the basilar membrane in the scala media are tiny hair cells arranged in rows. These hair cells include two types: inner hair cells (IHCs) and outer hair cells (OHCs). On the upper surface of the OHC there are projections, called sensory hairs or stereocilia. The stereocilia respond to the movement of cochlear fluid, and when the basilar membrane moves, they bend due to their connection with the overlying tectorial membrane. This bending leads to depolarization of the hair cells. The amplification caused by the depolarization of OHCs is most prominent at low input levels and at frequencies near the point of maximal basilar membrane movement (Rhode, 1971). The OHCs activate the IHCs, which transmit signals to cochlear neurons and onwards through the central auditory pathways in a frequency-specific manner, ultimately reaching higher auditory brain areas. The different nerve fibres consist of type I and type II fibres. Around 95% of afferent fibres are myelinated type I fibres that originate from the IHCs, and project to the brain. The unmyelinated type II afferent fibres only reach the OHCs and make up approximately 5% of the spiral ganglion neurons. Apart from afferent innervation, there is also efferent innervation of the OHCs, where signals are projected from the superior olivary complex to the cochlea. Stria vascularis is a highly vascular tissue in the outer wall of the cochlear duct, which maintains the ion balance of the endolymph and the endolymphatic potential (EP) (Gelfand, 2009).

From the cochlea, the auditory nerve projects to the brainstem and the cochlear nuclei. Approximately 90% of the projections reach the contralateral superior olivary complex and ascend through the lateral lemniscus pathway to the inferior colliculus, and to the medial geniculate nucleus where all fibres of the ascending auditory pathway synapse. The signal is finally projected to the auditory cortex, where much of the processing of auditory information occurs (Gelfand, 2009).

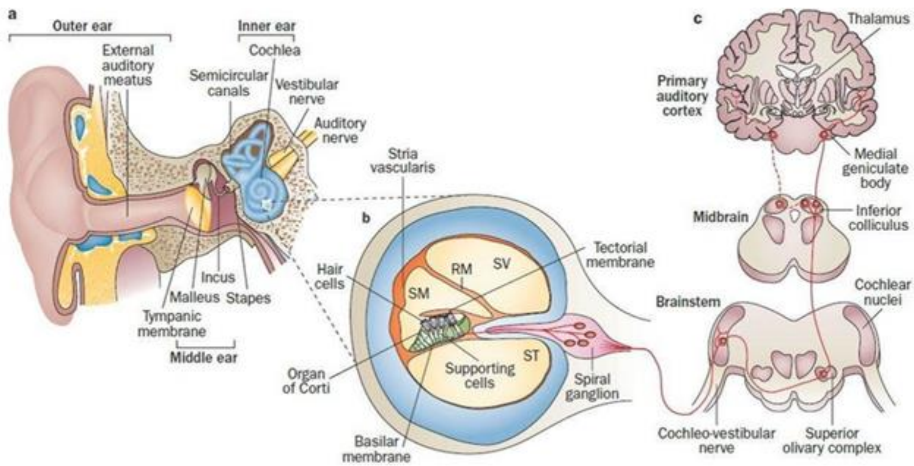


Figure 1. The auditory system. a. cross-section of the ear. b. Cross-section of the cochlear duct. c. Central auditory pathways.

Reprinted with permission from Springer Nature.: Ng L, Kelley MW, Forrest D. Making sense with thyroid hormone--the role of T(3) in auditory development. Nat Rev Endocrinol. 2013 May;9(5):296-307. doi: 10.1038/nrendo.2013.58. Epub 2013 Mar 26. PMID: 23529044. www.nature.com/articles/nrendo.2013.58

HEARING LOSS

Hearing loss is characterized by a reduction in hearing capacity and can be classified based on audiometric hearing thresholds. Hearing capacity is commonly assessed using pure-tone audiometry, and the results are documented in the audiogram. Typically, hearing thresholds are measured between 0.125-8 kHz. Although extended frequencies above 8 kHz (Best et al., 2005) can also be included in audiometry, they are not commonly used in clinical settings. Individuals with pure-tone hearing thresholds above a predefined threshold are considered to have a hearing loss. The severity of hearing losses can range from mild to profound (profound or deaf). The threshold used to define normal hearing varies among different classification systems, but a threshold of ≤20 dB hearing level (HL) is typically considered normal.

The impact of a hearing loss on an individual level is determined by its severity, and physiological type of hearing loss as well as by personal and environmental factors, such as environmental responsiveness to the individual's needs and the implementation of interventions (WHO, 2021).

CLASSIFICATION OF HEARING LOSS

The WHO introduced its first classification for hearing impairment in 1986, based on the recommendations of an expert group. Since then, this classification has undergone several modifications, and the most commonly used classification in population studies is presented in Table 1 (WHO, 1991). According to the WHO, adults (≥ 15 years) with a permanent unaided hearing impairment above 40 dB HL (pure-tone average at four frequencies, PTA4) in the better ear are considered to have a disabling hearing impairment.

Table 1. Classification of hearing impairment (WHO 1991).

Grade of hearing loss WHO	**PTA4*, Better ear**
No impairment	≤25 dB HL
Mild/slight	26-40 dB HL
Moderate	41-60 dB HL
Severe	61-80 dB HL
Profound	≥81 dB HL
"Disabling hearing loss"	>40 dB HL

*Mean PTA of 0.5,1,2 and 4 kHz in the better ear.

This classification has raised concern regarding its accuracy and appropriateness. The prescribed limit of 25 dB HL (PTA4) for defining normal hearing is not in agreement with several reports in the literature that highlight the functional experiences of individuals with slight hearing impairment

(≤ 25 dB HL). Moreover, there is no scientific basis for the uneven steps used to describe the different grades of hearing loss (Olusanya et al., 2019).

The International classification of functioning, disability and health (ICF) (WHO, 2001) is the framework established by WHO for defining and assessing health and disability from a biopsychosocial perspective at both individual and population levels. According to the ICF, a person's health status is defined by three dimensions (WHO, 2001):

- **Body function and structure** (impairment) refers to physiological and anatomical aspects of the body,

- **Activities** (limitations) refer to an individual's ability to carry out tasks and actions in their daily life.

- **Participation** (restriction) refers to an individual's involvement in life situations, including their social interactions, relationships, and engagement in community and societal activities.

The definition of disabling hearing impairment (WHO, 1991) excludes individuals with unilateral and mild hearing loss, which is inconsistent with the ICF.

In 2008, the Global Burden Disease (GBD) Expert Group on Hearing Loss addressed these concerns by reviewing the WHO classification for hearing impairment (Stevens et al, 2013) and proposed a revised classification, as shown in Table 2. A separate category for unilateral hearing impairment was introduced to align with the ICF's specific provisions for hearing problems related to localization and lateralization in challenging listening situations. The concept of disabling hearing impairment was thus expanded to include unilateral hearing loss. The GBD classification has demonstrated good validity based on evidence from large scale population and clinical studies, and the WHO has now adopted this new classification (Olusanya et al., 2019; WHO, 2021). However, it is important to note that this classification and its grades are intended for epidemiological use only and are applicable exclusively to adults.

Table 2. Classification of hearing impairment by (GBD, 2013)

Grade of hearing loss GBD	PTA4*, Better ear	Quiet environments	Noisy environments
No impairment	< 20 dB HL	Excellent/good hearing…	Good hearing/rarely difficulties…
Mild	20-34 dB HL	No problems…	May have difficulties…
Moderate	35-49 dB HL	May have difficulties…	Difficulties…
Moderately severe	50-64 dB HL	May have difficulties…	Great difficulties…
Severe	65-79 dB HL	Difficulties…	Very great difficulties…
Profound	80-94 dB HL	Great difficulties…	Cannot hear speech…
Complete or total	≥95 dB HL	Hears no speech	Cannot hear speech…
"Disabling hearing loss" **	≥35 dB HL		
Unilateral hearing loss	< 20 dB HL in better ear, ≥ 35 dB HL in worse ear	May have difficulties (speech in poorer ear) …	May have real difficulty…

*Mean PTA of 0.5,1,2 and 4 kHz in the better ear. ** The concept of disabling hearing loss is for epidemiological use and includes unilateral hearing loss. The World Report on Hearing by WHO (2021) provides detailed explanations of functional abilities in both quiet and noisy settings.

DISABLING HEARING LOSS

According to ICF, the term "disability" encompasses the various difficulties individuals with hearing loss may experience in their everyday lives, including impairments, limitations, and restrictions. Classifications based solely on pure-tone audiometry have limitations as individuals with similar audiograms may have different levels of hearing difficulties. The proposed GBD hearing loss categories, according to the ICF, should include the descriptions of functional performance that reflect activity limitations or participation restrictions in both noisy and quiet environments. Additionally, the disability experienced by individuals with hearing loss is influenced by the physical, social, and attitudinal environment in which they live. For example, a person with hearing loss who lacks access to hearing care is likely to experience a higher degree of disability (Granberg et al., 2014).

TYPES OF HEARING LOSS

There are different types of hearing loss, including *sensorineural hearing loss (i.e., sensory* and/or *neural hearing loss)*, *conductive hearing loss* (CHL), *mixed hearing loss*, and *central hearing loss.*

Sensorineural hearing loss involves damage to the cochlea (sensori-) and/or the auditory nerve (-neural). Sensorineural hearing loss is often used as an umbrella term since it is difficult to differentiate between sensory and neural sub-types using pure-tone audiometry. Damage to the OHCs is a common cause of sensorineural hearing loss. IHC damage may also be present, especially in individuals with severe hearing loss. Auditory neural dysfunction includes dysfunctions along the auditory nerve pathways, including changes or degenerations in afferent inner hair cell synapses, spiral ganglions, and damage or demyelination of auditory nerve fibres. Auditory neural dysfunction often leads to more significant hearing loss than expected based on the audiogram, a form of "hidden hearing loss". The term retrocochlear hearing loss is used to describe auditory nerve dysfunction and is often associated with the diagnosis of Auditory Neuropathy (AN). AN is typically diagnosed based on present otoacoustic emissions reflecting sustained cochlear function combined with abnormal auditory brainstem responses. The term Auditory Neuropathy Spectrum Disorders (ANSD) is more commonly used today since objective measures of AN have been limited in understanding the underlying etiologies (De Siati et al., 2020).

Conductive hearing loss (CHL) refers to structural changes in the external ear canal, or middle ear. Etiological factors such as otitis media, otosclerosis, disruption of the ossicular chain, or head trauma can cause CHL. In CHL, the transmission of air-conducted acoustic energy is partially or completely interrupted, resulting in attenuated air-conduction thresholds of up to 60 dB HL. If left untreated, CHL can lead to deprivation of central auditory pathways (Clarkson et al., 2016). Some individuals may have a combination of CHL and sensorineural hearing loss, known as *mixed hearing loss,* which often leads to a severe degree of hearing loss. In some cases, it may be possible to correct the conductive component, completely or partially, through treatment of the underlying cause (Gelfand, 2009).

Central hearing loss refers to deficits in the neural processing of auditory information in the Central Auditory Nervous System (CANS). However, it is difficult to separate the sensory and cognitive elements of central auditory function, and the status of Central Auditory Processing Disorders (CAPD) remains controversial. Research has shown a strong association between CAPD and peripheral hearing loss as well as between CAPD and language and cognitive abilities (Campbell et al., 2011). According to American Speech-Language-Hearing Association (ASHA, 2023), CAPD refers to dysfunctions in neural processing that are not attributable to higher order language or cognitive abilities. The British Society of Audiology (BSA) definition of Auditory Processing Disorders (APD) differs from ASHA´s definition and includes both efferent and afferent pathways in the auditory system, as well as higher level processing that facilitates top-down cognitive processes (Campbell et al., 2011).

CAPD is according to ASHA (2005) associated with poor performance in one or more central auditory processing (CAP) skills. Among these skills, auditory discrimination, temporal processing and binaural processing have received the most extensive research attention. However, criticism has been directed at the ASHA guidelines and there is major controversy in how to diagnose APD (Neijenhuis et al., 2019).

AGE-RELATED HEARING LOSS (ARHL)

Age-Related Hearing Loss (ARHL) is a multifactorial condition and most older adults experience progressive, symmetrical, sensorineural hearing loss, characterized by increased hearing thresholds. It primarily involves an increase in the hearing threshold in the high-frequency range (Gates and Mills, 2005). ARHL is mainly associated with dysfunctions in cochlear and neural structures, resulting in sensorineural hearing loss. However age-related degenerations occur in both peripheral and central auditory pathways and both peripheral and central hearing loss may be present in ARHL.

RISK FACTORS IN ARHL

ARHL manifests due to a combination of both extrinsic and intrinsic factors. Some of these risk factors are partly or completely modifiable, and adopting preventive behaviors and maintaining a healthy lifestyle can help reduce the risk of hearing loss in older age (Zhan et al., 2010).

Genetic factors play an important role and probably interact with environmental factors (Gates et al., 1999; Newman et al., 2012). Heredity seems to be the most relevant factor in the etiology of ARHL, but it has been challenging to tease apart the genetic influences on ARHL (Tu and Friedman, 2018). However, the primary risk factor is age, and the incidence of hearing loss increases rapidly with advancing age (Corso, 1959; Gates et al., 1990; Pedersen et al., 1989; Cruickshank et al., 1998; Davis, 1989; Agrawal et al., 2008; Wiley et al., 2008; Gopinath et al., 2009). Men generally have a higher rate of hearing loss, particularly in high frequency ranges compared to women (Corso 1959; Homans et al., 2017). Noise exposure, including both occupational and leisure noise exposure, is widely recognized as one of the most important and extensively studied extrinsic risk factors for ARHL (Dobie 1994; Rosenhall et al., 1990). The site of damage in the auditory pathways may differ between age-related factors and risk factors, such as noise exposure. The existence of an interaction effect on hearing between excessive noise exposure and the ageing process remains a topic of controversy in the literature (Rosenhall et al.,1990; Fernandez et al., 2015; Kujawa & Lieberman, 2009; Cruickshanks et al., 2010; Hederstierna and Rosenhall, 2016) and to date, no consensus has been reached on this matter. Comorbidities, such as, diabetes mellitus (Samocha-Bonet et al., 2021) and cardiovascular disease (Gates et al. 1993; Helzner et al., 2005), have also been shown to associate with ARHL. Other environmental risk factors for ARHL include smoking and alcohol intake (Dawes et al., 2014), dietary habits (Rosenhall et al., 2015), and exposure to ototoxic medications or chemicals (Joo et al., 2018). Furthermore, increased body mass index (BMI) and obesity have been associated with hearing loss in adults (Hu et al., 2020). Socioeconomic status and education levels may influence the level of noise exposure and /or other negative environmental lifestyle factors, which in turn may be indirectly associated with an increased risk of ARHL Education level has been shown to increase and occupational noise exposure as well as ear infections have been shown to decrease in younger cohorts. (Cruickshanks et al., 2010; Lin et al., 2011a).

Table 3. Examples of intrinsic and extrinsic risk factors in ARHL.

Intrinsic factors	**Extrinsic factors**
Biological ageing	*Noise exposure*
Genetic factors	*Ototoxic drugs and chemical exposure*
Male sex	*Socioeconomic factors: income, education, occupation*
Comorbidities: *Cardiovascular diseases*	*Lifestyle factors: diet smoking, high BMI, alcohol consumption*
Inflammation	*Medication*

Table note: Partly or fully modifiable risk factors are in Italics.

PREVALENCE OF ARHL

The prevalence of hearing loss dramatically increases with age. In cross-sectional studies, the prevalence of ARHL can be measured at a specific point in time, providing an overview of the prevalence of ARHL within well-defined samples. The objective of a population-based study is to ensure that the sample accurately represents the population under investigation.

Numerous studies have investigated the prevalence of ARHL, primarily in high-income countries. Roth et al., (2011) attempted to examine the prevalence of ARHL in older individuals in Europe, by reviewing published literature, spanning from 1970 and onwards. Nevertheless, challenges arose as a result of discrepancies in the definitions of hearing loss employed in different studies. An estimation was made, suggesting that around 30% of men and 20% of women aged 70 and older had a hearing loss defined as 30 dB HL or more at frequencies between 0.5 and 4 kHz. Recommendations have been made to employ standardized procedures, including audiometric measures and the adherence to the WHO classification of hearing loss, in population-based studies of ARHL (Roth et al, 2011). Many studies have utilized the WHO criterion (WHO, 1991) of hearing loss; specifically, PTA4 > 25 dB HL in the better ear.

Lower average hearing thresholds reflecting better hearing and lower prevalence rates have been observed in more recent cohorts (Hoffman et al., 2010; Zhan et al., 2010; Engdahl et al., 2020: Hoff et al., 2018). Additionally, a notable observation is the "gender-reversal" phenomenon, whereby men tend to demonstrate better hearing at frequencies below 1 kHz and poorer hearing at frequencies above 2 kHz compared to women (Jerger et al., 1993). In general, all population-based studies of ARHL have reported a high prevalence of hearing loss at higher frequencies, a strong association/correlation with age, and with a greater impact on men than women.

HEARING DECLINE AND ARHL

Longitudinal studies, although more expensive and time-consuming than cross-sectional studies, are better suited for identifying changes in ARHL over time. Several contemporary studies have focused on the progression of hearing loss in older adults. Some notable longitudinal studies are The Epidemiology of Hearing Loss Study (EHLS) (Cruickshanks et al, 1998; 2003), the Framingham Heart Study (Gates et al., 1990), the Baltimore Longitudinal Study of Ageing (BLSA) (Brant and Fozard, 1990; Pearson et al., 1995), the Beaver Dam study (Cruickshanks et al, 1998), the National Health and Nutrition Examination Survey (NHANES) (Agrawal et al., 2008; Goman and Lin, 2016), the Rotterdam Study (Rigters et al., 2018), the Trondelag Health Study (HUNT) (Molaug et al., 2022), and the Gothenburg H70 Birth Cohort Studies (Jönsson and Rosenhall, 1998). Findings from studies focusing on individuals above the age of 80 have shown that pure-tone thresholds continue to increase with age (Gates, 1990; Wattamwar et al., 2017). However, an earlier study within the framework of the H70 studies showed a moderated decline in individuals above 80 years compared to younger old individuals (Jonsson et al., 1998), which may be attributed to methodological considerations discussed in the first paper of this thesis.

The rate of hearing decline has been found to be faster at lower frequencies in older olds, which can be attributed to pre-existing high frequency loss (Wiley et al., 2008), as well as ceiling effects observed at higher frequencies (Brant and Fozard 1990; Gates et al 2000). Moreover, the rate of decline appears to be influenced by baseline thresholds. A higher rate of decline has been observed in older women than in older men which is probably explained by a greater hearing loss at baseline among men (Gates 2000; Wiley et al., 2008; Lee et al., 2005).

PATHOPHYSIOLOGY OF ARHL

AUDITORY DEGENERATION

The most significant age-related changes in the peripheral auditory system occur in the organ of Corti. Pathologies associated with ARHL have been investigated through histological studies of temporal bones of older individuals (Schuknecht, 1955, 1964; Gacek and Schuknecht 1969; Ramadan and Schuknecht 1989). These findings have been correlated with audiogram configurations (Schuknecht and Gacek 1993), leading to the classification of ARHL into five categories, of which three are considered to be the most prevalent:

1) Sensory; Characterized by degeneration of the organ of Corti, primarily affecting the OHCs. It can also be caused by external factors, such as noise exposure, resulting in a rapid high-frequency sloping hearing loss.

2) Neural; Age-related neural loss is characterized by the decline of cochlear neurons, including spiral ganglion neurons loss. This is primarily associated with a poorer word discrimination that surpasses the predicted outcomes based on the audiogram (Schuknecht and Gacek 1993).

3) Strial (metabolic) pathology involves age-related degenerations of the stria vascularis, resulting in alterations to the endolymphatic potential (EP). The dysfunction due to EP changes, begins in the low-frequency apical region of the cochlea, potentially leading to a flat configuration with low-frequency hearing loss, which could be indicative of strial loss.

In fact, classifying ARHL into distinct categories based on audiogram configurations is challenging, particularly in older individuals, as it is difficult to separate contributing factors related to the ageing process (Schukneckt and Gacek, 1993). The possibility of forming distinct classes of ARHL, has been questioned, as there are no sharp delineations between categories, but rather a continuum of phenotypes (Allen and Eddins, 2010). Since many tissues showed pathological changes in several of the structures listed above, a "mixed" category was added. Subsequent studies have provided evidence suggesting that strial (metabolic) presbycusis is the primary etiology behind ARHL (Gates and Mills, 2005).

The process of ageing is also associated with affected middle ear transmission. A decline in elastic tissue within the ossicular chain has been observed among older individuals (Belal, 1975; Harty, 1953) and hearing loss due to middle ear stiffness may exacerbate ARHL (Gratton et al., 1998). However, the impact of age-related changes is primarily manifest within the cochlea rather than the external and middle ear structures (Schmiedt, 2010).

Auditory sensory dysfunction in this thesis is defined by changes and degenerations in the organ of Corti, primarily affecting the OHCs. It can be caused by both internal and external factors, such as age and noise exposure.

AUDITORY NEURAL DEGENERATION

Auditory nerve degeneration in older age is described as a combination of loss of nerve fibres and pathological changes in the spiral ganglion cells (Hinojosa and Nelson, 2011; White et al., 2000; Moser et al., 2013). It has been difficult to determine if age-related loss of spiral ganglion neurons is a primary or secondary degeneration. Loss of spiral ganglion neurons and nerve damage may occur as a secondary effect of IHC damage (Ohlemiller and Frisina, 2008). It has been suggested that a late stage of degeneration of spiral ganglion neurons is independent of age-related loss of hair cells (Bao and Ohlemiller, 2010). Moreover, deteriorated neural synaptic connections between the IHCs and afferents in the cochlea, known as cochlear synaptopathy, may also be a cause of auditory neural dysfunction in old age (Kujawa and Liberman, 2009; Gates and Mills, 2005). Cochlear neuropathy is proposed to result in compromised sound discrimination in noisy environments, regardless of pure-tone audiometric finding (Kujawa and Liberman, 2009). There has been a discussion regarding the potential role of excessive exposure to acoustic stimuli, such as noise-exposure, as a precipitating factor in the degeneration of IHCs synapses (Kujawa and Liberman, 2009). However, the concept of cochlear neuropathy has been a subject of discussion and inquiry, since research findings are primarily based on animal-studies (Dobie and Humes, 2017).

CENTRAL AUDITORY DEGENERATION

Ageing is also associated with an increased loss of neurons in more central structures of the brainstem and auditory cortex, leading to a decline in the perceptual processing of auditory information in the CANS. Longitudinal and cross-sectional studies have shown that the occurrence of deterioration in central auditory pathways increases with age in older individuals (Gates et al., 1996; Quaranta et al., 2014). Accordingly, it has also been defined as central presbycusis (Gates, 2012) or age-related Central Auditory Processing Disorders (CAPD) (ASHA, 2023).

CAPD in ARHL has been attributed to sensory deprivation, resulting from peripheral hearing loss (Panza et al., 2018b). It has also been debated whether CAPD is an independent form of neurodegeneration in older individuals. However, the causal pattern behind the alteration of CAPD has not yet been determined (Jayakody et al., 2018a; Nixon et al., 2019). Interestingly, evidence from animal studies suggests that there can be age-related pathophysiological changes in the central auditory pathways without any changes in peripheral pathways (Walton et al., 1998; Ouda and Syka, 2015). Additionally, epidemiological data (Gates et al., 2008b) suggest that central auditory function deteriorates faster than peripheral auditory function. However, age-related peripheral and central declines seem to manifest differently among different individuals. Since age-related degeneration of neurons occurs in both the peripheral and central auditory pathways, a combination of these subtypes of hearing loss is assumed to be common in older individuals. (Uchida et al., 2019).

SPEECH RECOGNITION IN ARHL

Speech recognition is affected by age-related declines in both peripheral (sensory/neural) and central auditory pathways, as well as in cognitive domains (Wong et al., 2009; Shinn-Cunningham and Best, 2008; Dubno et al., 1984). Real-life speech comprehension engages neural networks encompassing coordinated activity across various cortical and subcortical regions, including visual representations (Peelle and Wingfield 2016). However, speech audiometry conducted in the presence of background noise serves as a reflection of an individual's auditory representation during daily communication, (Davignon et al., 1986; Reynard et al., 2022).

Sensorineural hearing loss leads to deteriorated speech recognition, particularly in noisy conditions (Gates et al., 2003). Among the peripheral factors that impact speech understanding, poor audibility and distortion of the speech signal, mainly due to cochlear pathology (George et al., 2007) are significant contributors. Auditory neural hearing loss (ANSD) further impairs speech recognition due to impaired processing of temporal cues (Starr et al., 1996; Zeng et al., 2005). Gates et al. (2003) coined the term "Probable age-related auditory neuropathy" (PARAN), described as being linked to degenerations in spiral ganglion or other neural structures which occur in older individuals. One way of measuring the effects on speech recognition is the word recognition score (WRS) measurement. According to Gates et al. (2003), PARAN is associated with a poorer WRS than predicted from the articulation index (AI) (Gates and Popelka, 1992) and/or poorer WRS than predicted by the high-frequency pure-tone average (Yellin et al., 1989). It is therefore suggested that individuals with poor WRS should undergo further testing to determine the presence of AN (Gates et al., 2003). However, part of the difficulty seems to be associated with central deficits, such as temporal deficits in older adults (Gordon-Salant and Fitzgibbons, 1993; Tremblay et al., 2003) and with lower cognitive abilities, such as processing speed, memory, and reasoning (Moore et al., 2014).

CONSEQUENCES OF ARHL

ARHL often negatively affects communication, social interactions, and cognitive abilities (Samtani et al., 2022). It is also associated with an increased risk of loneliness (Pichora-Fuller et al., 2015), depression (Brewster et al., 2018), and low self-esteem (WHO, 2021). Furthermore, it has been shown to be associated with the risk of falls, which affects independence in old age (Lin and Ferrucci, 2012). According to the ICF, several factors can be affected by ARHL, such as the perception of speech, detection of sound sources such as alarms, and listening to TV and radio. In the absence of timely intervention, ARHL is associated with a reduced quality of life (Dalton et al., 2003). ARHL has also been associated with increased frailty based on an index of various deficits and cumulative burden (Panza et al., 2015). Socioeconomically, unaddressed ARHL leads to increased costs related to lost quality of life, social withdrawal, and lost productivity from early retirement (McDaid et al., 2021). The impact of a health condition, such as ARHL, can be measured in terms of DALYs (disability-adjusted life years), which takes both mortality and disability into account. The GBD has estimated ARHL to be among the ten leading causes of DALYs in the world. In conclusion, individuals, and their significant others as well as society are affected by the consequences of ARHL.

REHABILITATION AND ARHL

ARHL cannot be cured, but it can be partially compensated for. Audiological hearing rehabilitation includes the use of assistive hearing devices and hearing aids. Individual and group counseling are also important to meet social and emotional needs (Saunders et al., 2021; Timmer et al., 2023; Malmberg et al., 2017). Communication strategies can be employed to improve communication skills and, consequently, social interactions (Newton and Shah., 2013).

Rehabilitation in ARHL, including hearing aid use, is associated with decreased social isolation (Dawes et al., 2015) and reduced symptoms of depression (Acar, 2011; Castiglione et al., 2016). Hearing aids have also been linked to improved balance (Rumalla et al., 2014).

The brain requires time to adjust to hearing again, and the timing of intervention is crucial for the outcome. The longer a person waits, the more challenging it becomes to adapt to hearing aids and change communication patterns (Silman et al., 1992). One Swedish study within the H70 cohort showed that up to 20% of older individuals with hearing loss had considered obtaining a hearing aid but did not do so (Rosenhall and Espmark, 2003). There exist a number of barriers to the adoption of hearing aids, including the associated stigma, which adds to the stigma of ageing (Wallhagen, 2010). Another reason is that older individuals may normalize hearing loss in old age (Öberg et al., 2012).

In the management of CAPD, it is suggested to focus on the specific listening deficits that an individual experiences, determined by self-report and diagnostic test findings (ASHA, 2023). A comprehensive, multidisciplinary approach that includes both bottom-up and top-down approaches is recommended for the management of CAPD (Chermak and Musiek, 2002). The British Society of Audiology (Campbell et al., 2011) describes three main categories of current intervention strategies: 1. Auditory training, such as interactive training devices. 2. Modifying the listening environment, such as using remote microphone technology. 3. Compensatory strategies, such as training in self-regulation and problem-solving, as well as identifying individual listening strengths and limitations. Modifying the listening environment, including the use of remote microphone technology, has been shown to improve speech recognition in adults by increasing the signal-to-noise ratio (Chen et al., 2021). Auditory training and compensatory training have shown mixed results in studies (Moore et al., 2018).

AGEING AND COGNITION

The term cognition refers to the mental processes involved in the acquisition, storage, and retrieval of information (Harvey, 2019). There are many different types of cognitive processes or conceptual domains that overlap with each other. The origin of these domains is often linked to specific areas of the brain where these processes occur. They include:

- **Sensation:** Multisensory skills.
- **Motor skills and construction**: Praxic skills like drawing.
- **Attention and concentration**: A complex cognitive process that allows individuals to focus and concentrate on a specific stimulus in the environment.
- **Language:** The ability to understand and express thoughts through words and to communicate.
- **Executive functioning**: Reasoning and problem-solving. An intact frontal cortex is critical for the performance of executive functions.
- **Memory**: Memory allows individuals to encode, store, and retrieve information. Working memory and long-term memory are sub-domains. One cognitive measure for working memory is a digit span task, wherein the task is recalling longer series of digits in order.
- **Perception:** To perceive information through the senses and to use the information to interact with others.
- **Processing speed**: The time required to respond to or process information in the environment.

The cognitive skills most affected by normal ageing are those that rely on quick processing, such as working memory and executive function (Murman, 2015). Processing speed has been shown to slow dramatically in old age (Verhaeghen and Salthouse, 1997). Cognition has been associated with several health, lifestyle, and sociodemographic factors. Higher levels of education and an active lifestyle have been hypothesized to establish cognitive reserve, which protects against age-related cognitive decline and reduces the impacts of neuropathology and dementia (Scarmeas and Stern, 2003).

In clinical and research settings, psychometrically developed standardized instruments are employed to evaluate cognitive function at both global and domain-specific levels. Mild cognitive impairment (MCI) may constitute an early stage of cognitive ability loss and is defined as a worse subjective and objective decline in cognition than expected for an individual's age and education level, yet not meeting the diagnostic criteria for a dementia (Winblad et al., 2004). Older individuals with MCI constitute a high-risk population for developing dementia, especially Alzheimer’s disease (AD) (Lindbergh et al, 2016). Cognitive abilities are often assessed with test batteries, including several verbal and non-verbal tests. Domains of cognitive dysfunction are not completely separable, and tests of a specific domain should not be viewed as lacking validity if they are intercorrelated (Harvey, 2019). There are also some screening tests of global cognitive impairment, for example the Mini Mental State Exam (MMSE) (Folstein et al., 1975), and the Montreal Cognitive Assessment (MoCA). However, the validity of these tests has been debated. MMSE has a large ceiling effect, and it has been suggested that MoCA would be more adequate as a screening instrument for mild cognitive impairment (MCI) (Hoops et al., 2009). Both these screening instruments require additional neuropsychological assessments for a dementia diagnosis.

ARHL AND COGNITION

Earlier studies, both cross-sectional (Valentijn et al., 2005; Tay et al., 2006) and longitudinal (Lin et al., 2011b; Deal et al., 2015), have shown an association between peripheral hearing loss decline and cognitive decline in age-related hearing loss (ARHL).

An association between cognitive deficit and both untreated and treated peripheral ARHL has been demonstrated (Panza et al., 2018a; Taljaard et al., 2016). An association has also been shown between cognitive decline and central hearing loss in older individuals (Gates 2002; 2008; Idrizbegovic et al., 2011). ARHL has been shown to be associated with decreased global cognitive function, working memory skills, auditory and visual free recall tasks, language skills, executive function, processing speed, and memory (Wingfield and Grossman, 2006; Era et al., Lin et al., 2011; Harrisson Busch et al., 2015; Loughrey et al., 2020; Alattar et al., 2020; Loughrey et al., 2019; Brewster et al., 2021; Rönnberg et al., 2011). Moreover, an earlier study of 70-year-olds (H70 Study) showed an association between cognition and pure-tone thresholds as well as speech recognition scores in noise (Hoff et al., 2023).

ARHL has been recognized as an important risk factor for dementia and mild cognitive impairment (Livingston et al., 2020). Numerous attempts have been made to explain the association between ARHL and cognitive decline. However, the underlying causal relationships between auditory and cognitive decline have not yet reached a consensus. There are several hypotheses/theories explaining the relationship between ARHL and the decline in cognition, as listed below.

Cognitive Load Hypothesis

The cognitive load on perception hypothesis argues that the decline in cognitive capacity is related to an increase in cognitive load resulting from sensory loss. Hearing loss leads to degraded auditory information, and consequently, greater cognitive resources are required for auditory perceptual processing (Lindenberger and Baltes, 1995).

Sensory Deprivation Hypothesis

Hearing loss, or sensory deprivation, leads to reduced afferent input to CANS and, consequently, permanent deterioration in cognitive functions (Humes et al., 2013). Cortical reorganization in ARHL provides evidence to support the sensory deprivation hypothesis (Peelle et al., 2011).

Cascade Hypothesis

Social isolation followed by ARHL may generate sensory deprivation (Dawes et al., 2015), reducing the input to the CANS.

Common Cause Hypothesis

The Common cause hypothesis argues that general age-related neuropathological changes in the brain as well as in auditory domains explain the relationship between auditory and cognitive decline (Lindenberger and Baltes and Lindenberger, 1997).

Cognitive Reserve Hypothesis

Cognitive Reserve Hypothesis suggest that individuals with comparable neuropathological conditions, such as hearing loss, exhibit variations in their ability to use brain reserve during cognitive tasks (Scarmeas and Stern, 2003). Factors including education level, occupational level (Amieva et al., 2014; Garibotto et al., 2008), and social networking (Fratiglioni et al., 2000) are considered as contributing factors to cognitive reserve.

Overestimation

Evidence suggests that hearing loss could result in poorer outcomes in verbal cognitive measures, leading to an overestimation of cognitive impairments in participants with ARHL (Dupuis et al., 2015). However, studies using non-auditory cognitive tests still show an association between ARHL and cognitive impairment (Dupuis et al., 2015; Jayakody et al., 2018b).

No single theory or hypothesis has been able to completely explain the causal relationship between ARHL and cognitive impairment.

HEARING AIDS AND COGNITION

Hearing aid use has been shown to generate improvement in cognition (Acar et al., 2011; Dawes et al. (2015) showed that hearing aid use had a positive effect on cognition independently of social isolation and depression. However, previous systematic reviews do not find a definitive answer to whether hearing aids are beneficial for cognition (Sanders et al., 2021; Taljaard et al., 2016). Findings from a recent multicentre study suggest that a hearing intervention might reduce cognitive decline in populations of older adults with lower cognitive base-line scores, i.e. individuals at increased risk of cognitive decline and deficits (Lin et al., 2023).

AUDIOLOGICAL MEASUREMENTS

Precision in diagnosis and exploration of conductive, cochlear, neural, and/or central components within ARHL is imperative to provide accurate rehabilitative interventions for the elderly population. Hearing measurements are divided into behavioural and physiological test methods, and a combination of these tests is needed to describe different hearing functions accurately and to evaluate an individual's hearing ability.

Behavioural test methods, also known as psychoacoustic test methods, measure the reaction on various sounds and rely on a test person's active participation and ability to respond to various acoustic stimuli. These methods aim to describe how a person detects, identifies, and discriminates sounds. Two commonly used psychoacoustic tests are pure-tone audiometry and speech audiometry. Both threshold measurements and supra-threshold measurements are recommended for use in diagnostic hearing assessments.

Physiological measures of hearing offer an objective assessment of several hearing functions and are particularly useful with patients who cannot cooperate in behavioural hearing assessments, such as children or patients with cognitive decline and dementia. Several measures can be used in audiological diagnostics.

BEHAVIOURAL MEASUREMENTS

PURE-TONE AUDIOMETRY

Pure-tone audiometry is a valuable diagnostic measure for distinguishing between conductive and sensorineural hearing loss and, potentially, for differentiating between sensory, strial and neural loss using Schuknecht's taxonomy by analysing the audiogram configuration (Schuknecht and Gacek, 1993).

The assessment of monaural air-conducted hearing thresholds requires ear-specific transducers, such as headphones or insert phones. Different types of headphones with varying characteristics, such as noise dampening, can be used in pure-tone audiometry. Typically, pure-tone audiometry is conducted in a sound-proofed test booth, and supra-aural headphones are commonly used. However, if the test environment has less control over ambient noise levels, such as in patients' homes or home care units, headphones with greater noise dampening, like circum-aural headphones, are preferred. During pure-tone audiometry, an operator, usually an audiologist, administers the test, ensuring compliance with the test method, and the test person is instructed to press a button when the pure-tone is heard.

Bone-conducted hearing thresholds are assessed using an electromechanical earphone placed on the skull. This method stimulates the inner ear through mechanical vibrations of the skull, with minimal stimulation of the outer and middle ear. Both air-conducted and bone-conducted thresholds can be measured through pure-tone audiometry, and a combination of test results is necessary to assess the presence of CHL (Gelfand, 2009).

Several factors can influence the test results, such as environmental ambient noise levels, audiometer calibration, test instructions, operator skills, as well as the physiological health factors of the test person. The validity and reliability of pure-tone audiometry depend on all these factors. To minimize sources of error, international standards (International Organization for Standardization, ISO) have been established. ISO 7029:2017 presents and defines the distribution of hearing thresholds (0.125-8 kHz) for otologically normal populations of various ages (18-80 years) under monaural earphone listening conditions. This distribution is based on data from earlier large population studies and can be used as reference/normative data in epidemiological studies.

Pure-tone audiometry can also be performed using an automated method and is widely used in research as well as for screening purposes. Although automated audiometry has been validated in younger individuals, its application in older populations has not been extensively studied. Automated pure-tone audiometry has been available since 1947 (Békèsy, 1947) and was subsequently proposed for use in screening settings to allow audiologists to allocate their time to other advanced audiological tasks (Margolis and Morgan, 2008). The automated method is utilized, for example, in telehealth settings to reach populations in sparsely populated areas (Swanepoel et al., 2010a), and the criteria for normal hearing thresholds are typically set at 20 dB HL. Earlier studies demonstrated good agreement between audiometric results obtained from automated audiometry (using circum-aural headphones) and manual audiometry (using supra-aural headphones) in younger age groups (Swanepoel et al., 2010b; Margolis et al., 2011; Mahomed et al., 2013). However, older adults are an important target population for automated pure-tone audiometry.

SPEECH AUDIOMETRY

Speech audiometry encompasses a wide range of psychoacoustic tests that provide information about how the auditory system comprehends complex auditory stimuli. While pure-tone audiometry is valuable, additional auditory measures that assess different dimensions of hearing are necessary for comprehensive analysis (Bolonsya, 2019). Pure-tone audiometry often fails to accurately predict speech recognition, particularly in the presence of background noise (Beattie et al., 1997). Speech audiometry in the presence of simultaneous noise better reflects an individual's performance in communication and daily activities than speech audiometry without simultaneous noise (Davignon et al., 1986; Reynard et al., 2022).

Different speech tests have been described in the literature, and each test needs to be validated for a specific language. These tests include the assessment of supra-threshold speech performance such as word recognition tests conducted in quiet or in noise.

Speech audiometry employs various speech materials, such as words, syllables, and sentences, to assess how the auditory system processes complex auditory information. Speech perception involves both peripheral and central auditory pathways and it is difficult to distinguish between the sites of damage. Moreover, linguistic and cognitive skills can influence speech perception abilities, complicating diagnostic differentiation (Gordon-Salant and Fitzgibbons, 1993; van Rooij and Plomp (1990). However, specific speech materials can help differentiate between sites of damage in the auditory pathways. Performance in more complex speech audiometry tests, such as speech perception in competing backgrounds (Gates et al., 2008b) and timecompressed speech tests (Vaughan, 2008), relies on CAP abilities and cognitive skills in older individuals. On the other hand, speech recognition tests using monosyllabic words without linguistic context are less dependent on cognitive abilities (Wilson and McArdle et al., 2005; Magnusson et al., 1995) and can be useful for evaluating peripheral hearing function and for distinguishing between sensory and neural hearing dysfunction.

Predictions of speech intelligibility can be made using a measure called the Speech Intelligibility Index (SII, ANSI, 1997), initially known as the Articulation Index (AI). The SII considers both the audibility of the speech signal and the importance of different frequency bands involved. When these factors are included in the SII model, it correlates strongly with speech recognition performance, at least for individuals with normal hearing and mild hearing loss (ANSI 1997). To compensate for the impairment in speech recognition ability due to sensorineural hearing loss, i.e., supra-threshold components, a factor that is not solely attributed to audibility needed to be included. A frequency-dependent desensitization factor (Pavlovic, 1986, 1987) was incorporated to account for cochlear dysfunction, i.e., to compensate for cochlear distortion in each frequency band.

Magnusson (1996b) developed an SII-based algorithm using Swedish speech material, specifically phonemically balanced word lists (PB-lists), which are still used clinically in Sweden today. Magnusson (1996a) also included an age-related proficiency factor in the model to improve prediction accuracy for older individuals > 60 years of age. This updated algorithm can be utilized to predict speech performance in individuals with sensorineural hearing loss (Magnusson, 1996a). A worse score than the SII-predicted word score has been suggested to indicate auditory neural dysfunction (Gates et al., 2003; Grant et al., 2022). However, the effect of age and hearing sensitivity on predicted scores have been discussed and Kamm et al. (1985) implied that speech in noise scores could only be predicted correctly at normal hearing up to moderate hearing loss.

PHYSIOLOGICAL MEASUREMENTS

In addition to behavioural methods like pure-tone and speech audiometry, physiological tests can be used. Auditory brainstem response (ABR) and distortion product otoacoustic emissions (DPOAE) are important physiological test methods used to diagnose auditory neural dysfunction, particularly AN.

OTOACOUSTIC EMISSIONS

Otoacoustic Emissions, (OAEs) are used to assess the function of the cochlea, specifically the OHC function. OAEs are generated by the action of the OHCs.

A microphone is placed in the ear canal, and if the OHCs are intact, they produce a quiet sound (biproduct) that echoes back in the ear canal. Kemp (1980) first described OAEs, and the measurements have been developed for use in screening settings, such as newborn screening programmes. A healthy cochlea typically exhibits OAEs, but if the cochlea is damaged, emissions are diminished, indicating a sensory component of hearing loss (Torre et al., 2003; Uchida et al., 2006).

There are two main types of evoked OAEs: transient evoked otoacoustic emissions (TEOAEs), which are produced in response to click stimuli, and distortion product otoacoustic emissions (DPOAEs), which are evoked by two tones of different frequency (f1 and f2) at two different intensity levels (L1 and L2) to stimulate nonlinear elements in the cochlea (distortion products), (Hall, 2000). DPOAEs are more frequency specific than TEOAEs. Typically, the L1 level is lower than the L2 level, and an L1/L2 combination of 65/55 dB SPL is universally recommended in clinical guidelines for obtaining DPOAEs (Stover et al., 1996). Ageing affects DPOAEs by reducing the amplitude and narrowing the DPOAE response spectrum as the OHCs representing higher frequencies are gradually diminishing (Glavin et al., 2021). Higher intensity stimulus levels may elicit an OHC response from a wider range of the basilar membrane, consequently reducing the frequency-specificity of the test. L1/L2 combinations above 70/70 are discouraged to avoid response artefacts that can be mistaken for DPOAEs (Dhar & Hall, 2011).

AUDITORY BRAIN-STEM AUDIOMETRY

Auditory brainstem response (ABR) test is a physiological measurement used to identify pathologies in the nerve and brainstem. It can also be used to estimate hearing thresholds when individuals are unable to participate in psychoacoustic tests (Prosser & Arslan, 1987). ABR is an electrophysiologic measure in which electrical activity in the auditory nerve and brainstem is recorded through applied electrodes on the head. Jewett et al. (1970) first described ABR, which generates seven characteristic waves (Jewett waves I-VII) evoked by sound and originating in the nerve and brainstem. The amplitudes and latencies of these waves, most commonly waves I-V, can be analysed and interpreted. These potentials are also referred to as ABRs (auditory brainstem responses). Different test stimuli, such as clicks, chirps, or speech, can be used for different purposes. Click stimuli are the most used and have been well validated in both younger and older populations. Rosenhall et al. (1986) observed prolonged latencies in age-related hearing loss. However, ABR responses can be influenced by age-related peripheral hearing (Jerger and Hall, 1980), and it is difficult to separate contributing factors to decreased amplitudes or prolonged latencies in ABRs. Absent ABRs or prolongations of the absolute latency of Wave V and interaural latency differences (ILDs) in relation to age-appropriate normative values, combined with poor speech recognition, may indicate pathologies in the auditory nerve/brainstem (Starr et al., 1996).

Physiological measurements like ABR and DPOAE are proposed diagnostic tools for auditory neuropathy (Boettcher et al., 2002). However, the utility of these objective measures might be limited in discerning the specific sites of lesions along the auditory nerve, including inner hair cell synapses, particularly in older individuals with significant peripheral high-frequency hearing loss (Boettcher, 2002).

CENTRAL AUDITORY MEASUREMENTS

CAPD is described as the main cause of "hidden hearing loss," which refers to poorer speech recognition than expected from the audiogram (Hind et al., 2011). CAPD cannot be detected by conventional auditory measures such as pure-tone audiometry, OAEs, or click-evoked ABR. There is no reference standard for diagnosing CAPD and there is a lack of universal, standardized diagnostic criteria. (AAA, 2010; ASHA, 2023). Specific tests that reflect different central auditory pathway abilities have been developed to study various aspects of CAPD. Examples of CAPD tests include speech tests with low redundancy and dichotic tests. Since there is no absolute gold standard for comparison, it is challenging to report the sensitivity and specificity of a particular CAP test. These tests have primarily been validated in individuals with well-known impairments in the central auditory system (e.g., brainstem or temporal lobe tumors) (Bocca et al., 1954, 1955).

Several CAP tests have been described in the literature, and various test batteries have been suggested to assess CAPD (Emanuel DC, 2002). However, there is criticism of CAP test batteries because many of the tests involve cognitive and language skills. The complexity of neural processing and the involvement of both language and cognitive skills need to be considered when administering CAP tests (Moore et al., 2018). Abnormal performance in CAP tests has been shown to occur despite cognitive scores being within normal limits. Additionally, most APD tests only share a mild to moderate degree of variance with cognition, suggesting that CAP performance is not solely driven by cognition (Jerger et al., 1989; Rodriguez et al., 1990).

In addition to cognitive and language skills, the presence of peripheral hearing loss may affect the results of CAP tests (Miltenberger et al.,1978). Therefore, it is necessary to use a methodology with acoustic stimuli that are minimally affected by peripheral hearing loss (Musiek, Baran, & Pinheiro, 1990; Musiek, 1993). In cases of severe hearing loss, APD testing cannot yield reliable results (Fifer et al, 1983).

Both behavioural tests and electrophysiological tests are described as being used to assess CAP skills. According to Sardone et al. (2019), the most consistent clinical approach to detecting age-related CAP deficits is through auditory behavioural assessments, which aim to assess several functional abilities of the central auditory system.

According to ASHA (2005), CAPD is associated with poor performance in one or more CAP skills, including auditory discrimination, temporal processing, and binaural processing which are the three most studied skills.

- The ability to differentiate between acoustic stimuli that differ in frequency and/or intensity can be assessed with auditory discrimination tests.

- Auditory temporal processing tests assess the ability to analyse acoustic events over time, such as changes in stimulus duration, which is important for discriminating speech in noisy environments (Boettcher, 2002). However, temporal processes are strongly influenced by peripheral hearing loss and cognitive abilities, such as working memory and attention skills, in older individuals, making it difficult to separate the effects of ageing and cognitive impairment on test results (Humes and Dubno, 2012).

- Binaural processing can be assessed by dichotic speech tests which assess the ability to separate (binaural separation) or integrate (binaural integration) different auditory stimuli presented simultaneously to each ear. Both bottom-up (perceptual or sensory processing) and top-down (cognitive processing) processes are involved, and the test method and the test stimuli used for a specific purpose needs to be carefully considered (Chermak, 2007)

Electrophysiological measurements, such as middle latency response (MLR), late cortical response, P300, and mismatch negativity, may be useful when behavioural procedures are not feasible (Sardone et al., 2019). Speech-evoked ABR has been studied, and an abnormal response has been associated with deficits in central auditory pathways. However, investigations into electrophysiological tests have been predominantly focused on experimental studies conducted with relatively limited sample sizes (Iliadou and Iakovides 2003), Sardone et al., 2019) resulting in a lack of reference data pertaining to older populations.

Since APD test scores can be affected by cognitive or language processing deficits, the BSA (2018) highlights the importance of a multidisciplinary diagnostic approach, including cognitive assessment.

SUMMARY AND RATIONALE

Age-related hearing loss (ARHL) has been consistently documented in many cross-sectional and longitudinal studies. Continuous population-based research is necessary to evaluate the changing needs of hearing rehabilitation due to evolving environmental and lifestyle factors. With the increase in life expectancy, it becomes crucial to concentrate on the oldest age group (individuals above 80 years), which has received relatively less attention in research. Moreover, existing population-based studies on ARHL primarily rely on results from pure-tone audiometry, which mainly assesses peripheral hearing function. However, it is recognized that individuals with identical audiograms may experience varying degrees of hearing difficulties, highlighting the necessity for a more sophisticated test protocol to elucidate these disparities. To achieve a more comprehensive understanding of age-related hearing deterioration, it is essential to integrate behavioural and physiological auditory measures.

The assessment of speech perception can be accomplished through speech audiometry, which, when combined with other physiological measures, enables the characterization of specific types of hearing loss, particularly auditory neural dysfunction. Given that advanced age is associated with declines in both peripheral and central auditory pathways, as well as in cognitive function, it is essential to comprehensively investigate these interrelated aspects. While extensive research on CAP function has been conducted in experimental settings, population-based studies, particularly among older individuals, have been comparatively limited. The primary objective of the papers included in this thesis was to examine both peripheral and central auditory functions in an age-homogeneous birth cohort of individuals aged 85. Another aim was to study the associations between auditory data and cognitive measures. Each paper within this study aims to describe different aspects of ARHL in advanced age. The rationale for this thesis stems from the necessity for current population-based research focusing on the oldest age group, which holds significant importance for several reasons:

1. ARHL is a prevalent condition that affects a significant proportion of the older population.
2. The global population is rapidly ageing, with a substantial increase expected in the number of individuals over 80 years of age.

3. By focusing on the oldest age group, researchers can gain a better understanding of the specific characteristics of ARHL in this population, providing insights into the unique challenges faced by this group.

4. This knowledge can contribute to the development of targeted interventions and treatment strategies to improve the quality of life for individuals in advanced age with ARHL.

AIMS

The overall aim was to investigate the peripheral and central auditory function of an age-homogenous birth cohort of 85-year-olds and to study the association between auditory data and data related to cognition.

The specific aims for each paper were as follow:

I

To determine pure-tone hearing thresholds in an unscreened birth cohort of 85-year-olds (born in 1930), in Gothenburg, Sweden. Moreover, to study hearing decline between the ages 75 and 85 years for both sexes.

II

To determine results from pure-tone audiometry, including the prevalence of hearing loss, in unscreened 85-year-olds (born in 1930). A secondary aim was to identify differences in audiometric results between two 85-year-old birth cohorts examined ~30 years apart (cohorts born in 1901-02 and 1930).

III

To study the prevalence of CHL or mixed hearing loss, and sensorineural hearing loss, with an attempt to differentiate between sensory and neural components.

IV

To investigate the performance of 70 and 85-year-olds on the Dichotic Digits Test (DDT) with one-pair digits. Secondly, to examine the potential of the DDT test to differentiate between a primarily central auditory deficit and a primarily cognitive deficit compared to a normal profile in 85-year-olds.

PARTICIPANTS AND METHODS

The results included in this thesis are part of the Gothenburg H70 birth cohort studies (H70 Study), which is a large epidemiological study, conducted in Gothenburg, Sweden. The H70 Study is a population-based study that focuses on normative ageing (from 70 years of age) and encompasses both medical and cognitive domains. H70 was initiated in 1971 and age-homogeneous birth cohorts, representative of the city of Gothenburg, have been examined since then using both cross-sectional and longitudinal designs. Various trends in mental and physical health have been identified across multiple birth cohorts.

The coordination of the H70 Study involves several research groups, primarily in geriatrics, general medicine, and epidemiology. The study protocol has been maintained as identical as possible over the years. Participants were invited to take part in the study and offered a comprehensive health check, which included among others a medical examination, blood and urine tests, electrocardiogram (ECG), and vision as well as hearing assessments. Participants were also asked to complete a questionnaire covering various health parameters. The examinations for the main target group in this thesis, 85-year-olds born in 1930, were conducted over 1-2 days at the Neuropsychatric outpatient department at Wallinsgatan, Mölndal, or through home visits/nursing home visits, depending on the participants' abilities.

The study protocol comprised the following components:

- Interviews regarding general health, functional ability, family history, and social factors.
- Self-rating questionnaires (face-to face interview with a research nurse).
- Physical examinations, including a hearing test using computerised automated pure-tone audiometry.
- Blood samples and measurements of weight and height.
- Clinical and psychometric cognitive examinations.

Trained nurses primarily conducted most of the tests and interviews. However, for certain assessments, such as extended tests or specialized examinations (e.g., dietary assessments, MRI, CT, and more comprehensive audiological examinations), medical doctors, physiotherapists, psychiatrists, audiologists and other professionals were involved, as required.

The main target cohort studied in this thesis consists of 85-year-olds (at the time of invitation for this study) born in 1930, residing in Gothenburg and adjacent municipalities, including Ale, Kungsbacka, Kungälv, Lerum, and Mölndal at the first time of invitation (namely, 70, 75 and 85 years of age). Participants were identified through information from the Swedish tax agency and selected based on specific birth dates. To be included, participants needed to have sufficient Swedish language skills to understand test instructions and the written information to give a consent in Swedish. The effective sample of 85-year-olds consisted of 767 participants. Some participants were only able to participate in certain parts of the test protocol due to test fatigue or other health issues, and examinations were conducted either at the research clinic or through home visits/nursing home.

In the H70 studies, several birth cohorts underwent hearing assessments using pure-tone audiometry at the age of 70, and some cohorts were longitudinally followed with pure-tone audiometry. For an over-view of the H70 birth cohorts included in this thesis, see Table 4.

*Table 4. Specific H70 birth cohorts included **in this thesis** being assessed with pure-tone audiometry at 70, 75 and/or at 85 years of age. Cohorts included in Paper I-IV are marked in pink.*

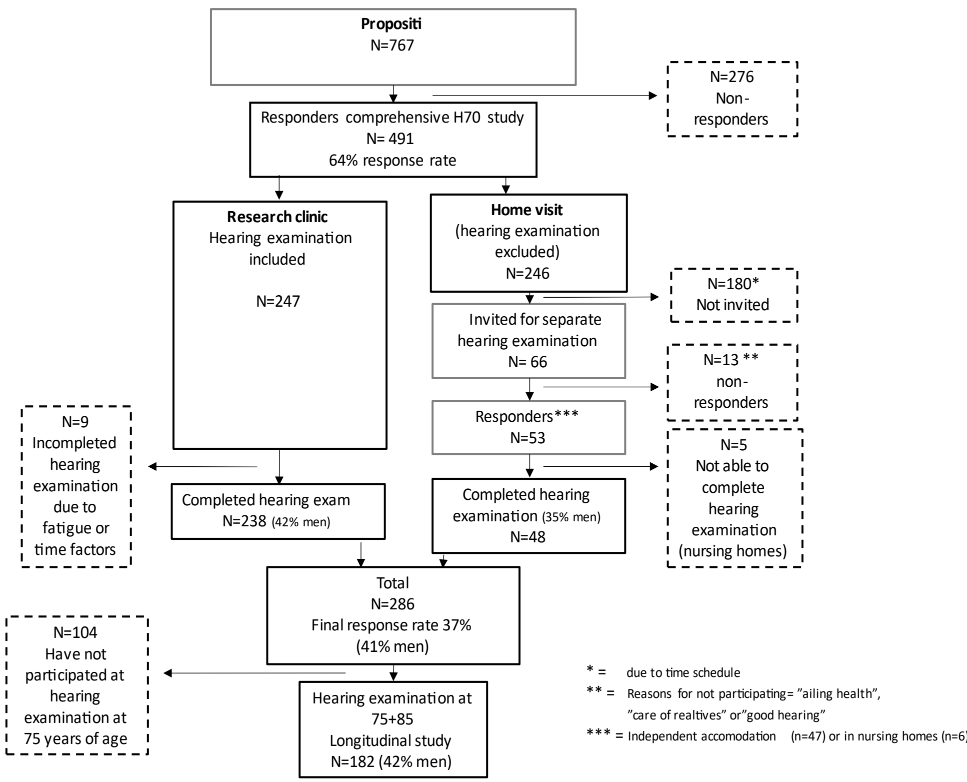
Birth Cohort	70 y	75 y	80 y	85 y
1901–02	X	X	X	X
1930	X	X		X
1944	X	X		

Table note: Gothenburg H70 birth cohort studies from the beginning (1971) until 2019. The longitudinal study in Paper I included participants born in 1930 that were hearing tested at 75 and 85 years of age. The Cohort study in Paper II included 85-year-olds born in 1901-02- and 85-year-olds born in 1930. Paper III included 85-year-olds born in 1930. Paper IV included 70-year-olds born 1944 and 85-year-olds born in 1930.

AUDIOLOGICAL EXAMINATIONS

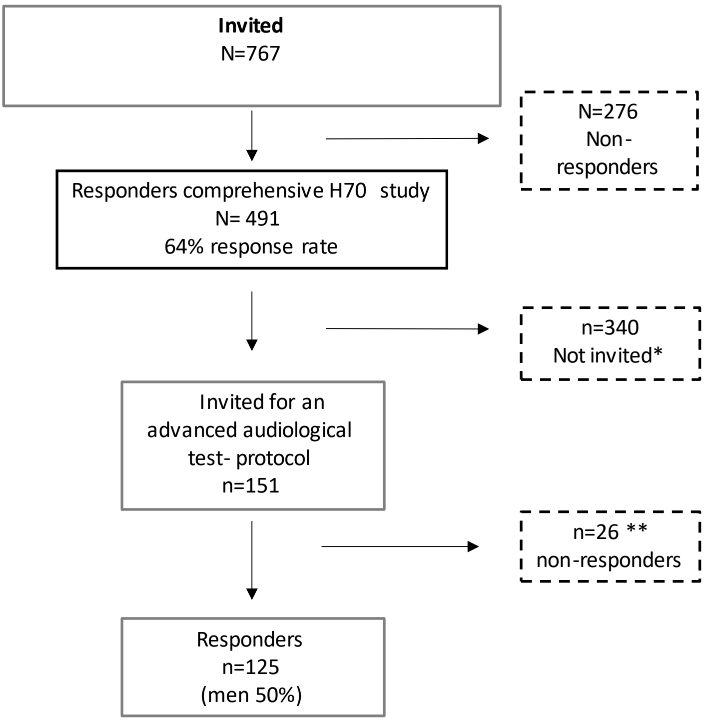
The 85-year-olds, born in 1930 were assessed in a **main audiological examination,** which included otoscopy, a self-rating questionnaire, including hearing-related items, and automated pure-tone audiometry, which were conducted either at the research clinic or through home visits/nursing home visits. Almost all participants investigated at the research clinic underwent automated pure-tone audiometry, administered by research nurses (2015-2017). However, participants examined during home visits or in nursing homes were not assessed by the research nurses. Instead, audiologists conducted separate home visits or nursing home visits to perform automated pure-tone audiometry on a subgroup. In total, 286 85-year-olds underwent the main audiological examination. A proportion of these (n=182) had been hearing tested previously, at age 75, and were therefore also studied longitudinally (**Paper I**). The selection procedure for the cohort born 1930 in **Paper I and II** is illustrated in Figure 2A. Additionally, an **extended audiological examination** was conducted on a selected group of 85-year-olds (n=125) to study both the peripheral and the central hearing function in this age group (**Paper III and IV**). An overview of the selection procedure for **Paper III and IV** is illustrated in Figure 2 B-C.

2A. Flow chart, cohort born in 1930, Paper I and II



Reprinted with permission from Hearing Research.: Göthberg H, Rosenhall U, Tengstrand T, Rydberg Sterner T, Wetterberg H, Zettergren A, Skoog I, Sadeghi A. Cross-sectional assessment of hearing acuity of an unscreened 85-year-old cohort - Including a 10-year longitudinal study of a sub-sample. Hear Res. 2019 Oct;382:107797, doi: 10.1016/j.heares.2019.107797. Epub 2019 Sep 5. PMID: 31525615.

2B. Flowchart Paper III



* due to time constraints (n=274) or difficulties to participate (care home, or other health issues) at the comprehensive H70 study (n=66).
** = Reasons for not participating= "ailing health" n=6, "good hearing" n=7, busy or undefined reason n=10, deceased n=3.

Reprinted with permission from American Journal of Audiology: Göthberg H, Skoog I, Tengstrand T, Magnusson L, Hoff M, Rosenhall U, Sadeghi A. Pathophysiological and Clinical Aspects of Hearing Loss Among 85-Year-Olds. Am J Audiol. 2023 Jun;32(2):440-452. doi: 10.1044/2023_AJA-22-00214. Epub 2023 May 17. PMID: 37195321.

2C. Flow chart manuscript IV

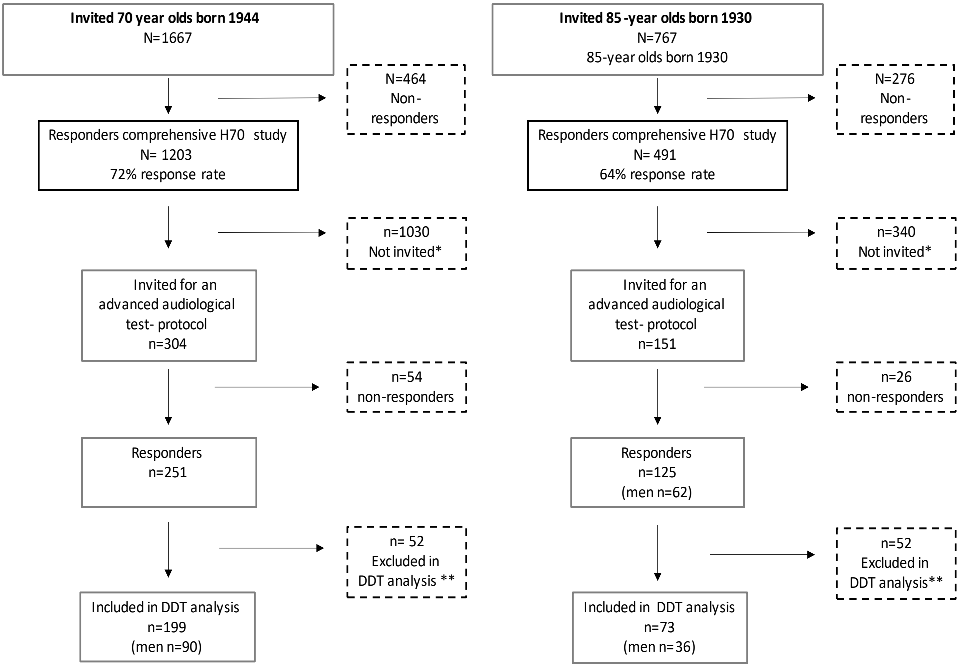


Figure 2 A-C. Selection procedure in Paper I, II (A) III (B) and IV (C)

Cohorts in the H70 Study which had been studied previously, were included in **Papers I and II** to investigate longitudinal findings as well as birth-cohort differences. In **Paper II**, hearing thresholds in 85-year-olds born in 1930 (n=286) were compared with a sample of 85-year-olds born in 1901-02 (n=249). An overview of all the samples included in **Papers I and II** is illustrated in Table 5 (**Paper I**) and in Table 6 (**Paper II**).

*Table 5. **Paper I**, Cross-sectional and longitudinal study. Number of propositi and respondents of the birth cohort born in 1930 at ages 75 and 85 years.*

Age	Invited (n)	Respondents Comprehensive sample (n)	Response-rate (%)	Hearing exam. Subsample (n)	Response-rate (%)	Longitudinal study 75-85 (n)
75	1255	768	61	570 (41%men)	45	181
85	767	491	64	286 (41% men)	37	(41% men)

*Table 6. **Paper II**, Birth-cohort study. Number of propositi and responders aged 85 in the birth cohorts born in 1930 and 1901-02.*

Birth cohort born	Sex	Invited (n)	Respondents Comprehensive sample (n)	Response-rate (%)	Hearing exam. Subsample (n)	Response-rate (%)
1930	Men	272	175		116	
	Women	494	316		170	
	Total	767	491	64	286	37
1901-02	Men	444	302		95	
	Women	1070	672		154	
	Total	1514	974	64	249	16

HEARING QUESTIONNAIRE

Several self-rating questionnaires were used in the main H70 investigation, which included questions related to education level, overall health, and specific questions concerning the participants' hearing ability. The specific hearing questionnaire, consisting of eight questions, was developed for the H70 birth cohort studies in the early 1970s and has remained largely unchanged since then. The questionnaire was administered by research nurses with a face-to-face interview at the clinic or in their home/nursing home.

The hearing questionnaire examined general hearing acuity as well as hearing acuity in specific situations, such as traffic or group conversations. It also included questions about tinnitus and the use of hearing aids. Results from the questionnaire, i.e., self-reported data, were used to describe sub-samples in **Papers III and IV**. However, the self-reported data was not presented in **Papers I and II** since the data from the questionnaires had not yet been processed at the time of publication. A subsequent analysis was done and an overview of sample characteristics for all samples included in this thesis (**Papers I-IV**) are summarized in Table 7. This overview includes results from self-reported data, i.e., education level, overall health, noise exposure, and prevalence of perceived hearing loss. Higher education levels in Gothenburg and Sweden were obtained from Statistics Sweden by Wetterberg et al., 2022.

Table 7. Sample-characteristics (self-reported variables) for all 85-year-old respondents (born in 1930) in the comprehensive study (n=491) as well as for sub-samples included in Paper I-II (n=286), Paper III (n=125) and Paper IV (n=73) as well as for 85-year-olds living in Gothenburg respectively living in Sweden.

Self-reported variables (%)	**Paper I and II**		**Paper III**		**Paper IV**	**Comprehensive H85 cohort**		**Gothen-burg**	**Sweden**
	M	W	M	W	Overall	M	W	Overall	Overall
	n=116	n=170	n=63	n=62	n=73	n=175	n=316	N=1 808	N=40316
Higher Education * (%)	26	10	29	23	26	27	13	19	16
Occupational noise (yes) (%)	52	23	57	18	n/a	52	20	n/a	n/a
“Poor health” (%)	11	14	6	12	8	13	19	n/a	n/a
“Having hearing loss” (%)	70	69	81	73	63	69	68	n/a	n/a

Table note: Self-reported variables were reported at 75 or at 85 years of age. * Higher education: university studies. Hearing loss: “yes”, mild - poor. n/a: not available

TEST PROTOCOL

MAIN AUDIOLOGICAL EXAMINATION

Paper I and II:

The main audiological examination was conducted by nurses at a research clinic. The following examinations were performed:

- Otoscopy
- Automated pure-tone audiometry: Air conduction thresholds were determined using standardized measurement methodology.
- Self-rating questionnaires including hearing-related questions.

EXTENDED AUDIOLOGICAL EXAMINATION

Papers III and IV:

An extended audiological examination was conducted by qualified and experienced audiologists in a sound-treated booth, following international standards for the respective measurement method. The following examinations were performed:

- Otoscopy
- Conventional pure-tone audiometry: Air and bone conduction thresholds were determined.
- Speech audiometry with monosyllabic words (Word Recognition in Noise (S/N+4) or in Quiet (Magnusson 1995).
- Dichotic Digits Test (DDT) with one-pair digits (Hällgren et al., 2001).
- Auditory Brainstem Responses (ABR)
- Otoacoustic emissions (DPOAE)

The test protocol had a duration of approximately 90 minutes, and prior to testing, a brief medical interview was conducted.

Wideband tympanometry was included in the test protocol. However, due to methodological issues, such as a high proportion of participants with invalid tympanometry results (due to a leaking probe), this data was not analysed or published.

STUDY VARIABLES

MAIN AUDIOLOGICAL EXAMINATION

Paper I and II

Automated computerised pure-tone audiometry

Automated computerised pure-tone audiometry was performed in a quiet office by research nurses or during home visits/nursing home visits by audiologists. The nurses also conducted an otoscopy and noted the presence of cerumen, but no removal of cerumen was performed during the testing session. Air conduction thresholds were measured at frequencies of 0.25, 0.5, 1, 2, 3, 4, 6, and 8 kHz, with a measurement range spanning from 0 to 90 dB HL. Participants were instructed to press a button when they heard a tone. The nurse placed the headphones on the participants and initiated the automatic test by pressing the start button on the audiometer. The test method followed a modified Houston-Westlake procedure (Carhart and Jerger, 1959), combining descending and ascending series of test stimuli. Thresholds were accepted if two correct responses were obtained in an ascending sequence at a specific frequency. The assessment always began at 1 kHz and in the right ear.

Equipment: Entomed SA 2021V with circum-aural Sennheiser HDA200 Headphones.

EXTENDED AUDIOLOGICAL EXAMINATION

Paper III and Paper IV

Conventional pure-tone audiometry

Air and bone conduction thresholds were measured in a soundproof test environment following standardized methodology according to ISO 8253-1. This examination was conducted by qualified audiologists. Frequencies 0.25, 0.5, 1, 2, 3, 4, 6, and 8 kHz were tested for air conduction, and frequencies of 0.5, 1, 2, 3, and 4 kHz were tested for bone conduction. The measurement range for air conduction was from -10 to 110 dB HL, and for bone conduction, it was from -10 to 70 dB HL. Participants were instructed to press a button each time they heard a tone, and the threshold was defined as three out of five correct responses during an ascending sequence. The test started in the better hearing ear at 1 kHz. Masking was applied when necessary following standardized methodology (ISO 8253-1; Almqvist, 2004).

Equipment: Equinox 440 with headphones (TDH-39). Bone-conductor: Radioear B71.

Speech audiometry

Speech audiometry, specifically the assessment of word recognition in quiet or noisy environments, was conducted following the guidelines of ISO-standard 8253-3 (ISO, 2010). The word list was monaurally presented in both the right and left ears at the individual's most comfortable level, starting at a speech level (speech level according to IEC 645-2) of ~50 dB above the pure-tone average at three frequencies (0.5, 1, and 2 kHz). In Swedish clinical praxis this level is described as 35 dB above PTA3 (0.5, 1 and 2 kHz) which is related to the dB HL value that is visualized at the audiometer. For words presented in noise, a pre-mixed speech-weighted noise was added at a signal-to-noise ratio of +4 dB (Magnusson, 1995). Participants who failed all of the first 10 words in Word Recognition in Noise were categorised as test failures and were subsequently tested with Word Recognition in Quiet, without speech-weighted noise. Contralateral masking was applied if the speech presentation level exceeded the air or bone conducted hearing thresholds in the contralateral ear by 40 dB or more.

A predicted word recognition score in noise (WRS-N) was calculated using a Speech Intelligibility Index (SII)-based algorithm (Magnusson, 1996b), which incorporated audiometric hearing thresholds between 0.25-8 kHz, presentation level, and age. Corrections were also implemented for the sensorineural component, i.e., the desensitization factor (Pavlovic et al., 1986) and for the age and the presentation level. Using the same algorithm, a predicted word recognition score in a quiet condition (WRS-Q) was also calculated. A conservative threshold of 16 p.p. was adopted. for significant score differences between two measured scores, such as the predicted score and the measured score (Hagerman, 1976; Magnusson et al., 2001). Scores surpassing this threshold were deemed indicative of abnormal word recognition performance. Moreover, ears classified as test failures during word recognition in a quiet condition were also classified as having abnormal word recognition scores.

Equipment: Equinox 440 with headphones (TDH-39).

Distortion Products (DPOAE)

DPOAEs were measured using a 70/70 stimulus with a fixed ratio f2/f1=1.22 at six discrete test frequencies: 1, 1.5, 2, 3, 4, and 6 kHz. Emissions were recorded at 2f1-f2. The test participant was seated in a comfortable chair and instructed to remain still during the procedure. A reference measurement of the test ear cavity was conducted daily to ensure the absence of system artefacts. Additionally, a check fit procedure was performed to verify the correct position of the probe. The measurement was conducted by an audiologist, and a measuring probe was placed in the participants ear canal.

Equipment: Otodynamics Echoport ILO 292-II ILO version 6 software on a PC laptop.

Dichotic Digits Test (DDT)

A dichotic listening test with one-pair digits, was administered by an audiologist. Digits were simultaneously presented to each ear. The test material consisted of monosyllabic digits (1, 2, 3, 5, 6, and 7) based on the method described by Hällgren et al. (1998; 2001). Each session started with training stimuli to ensure the participant understood the instructions and to determine a comfortable level for both ears via headphones, starting at the same intensity level as used in the speech audiometry measurement (see above). Participants were asked to verbally repeat the test stimulus and to guess if necessary. One digit was presented in each ear. Three different types of reporting were used: free reports (FR), directed reports in right ear (DR RE), and directed reports in left ear (DR LE). In FR, the stimuli were combined into 20 dichotic pairs with a pause in between. In the DR test, there were 40 dichotic pairs (20 for each ear), and the test took approximately 10 minutes.

Equipment: Equinox 440 with headphones (TDH-39).

Auditory Brainstem Responses (ABR)

ABR were obtained monaurally for both ears at up to six stimulus levels in the range of 80-30 dB nHL with an alternating polarity (22.1 clicks/second) and 2000 clicks were incorporated. The electrode impedance limit was set to 3 kΩ. Standard electrodes were applied to the ipsilateral mastoids and forehead, while an electrode on the cheek served as the ground. Participants were seated comfortably during the assessment. The signal was filtered with a 0.1-3 kHz bandpass filter. The analysis of ABRs was performed by two experienced audiologists who were blinded to the results of pure-tone audiometry. The latencies of Jewett waves I, III, and V were recorded.

Equipment: Interacoustics Eclipse (equivalent to EP 25) with EAR insert earphones

Cognitive assessment

The cognitive test battery was designed to assess a wide range of cognitive abilities. Most of the tests were selected from the Dureman and Sälde (1959) test battery, which was widely used in Sweden at the start of the H70 Study in 1971-72. Additional tests were chosen from the Alzheimer's Disease Assessment Scale-Cognitive (ADAS-COG) (Rosen et al., 1984). Verbal instructions were provided, and participants were encouraged to use hearing aids and spectacles as needed. A practice round was included to ensure that the participants understood the instructions. The examination was conducted by research staff members who had received training by a psychologist. Several tests were administered to evaluate different cognitive abilities, including memory abilities. Working memory was assessed using a supra-span memory test (BUS), involving the repetition of a list of items of clothing (Buschke and Fuld, 1974). Mental Speed was measured using a figure identification test (PSIF), (Wechsler, 1991), where participants identified which one of five symbols was a copy of another. Visual memory was assessed with Thurstone's Picture Memory (Thurstone 1939), where participants distinguished previously shown images from distractors. Logical reasoning was assessed using the Figure Logic test (Dureman et al., 1971), where participants identified which figure, out of five, differed from the rest. Semantic fluency (Kertesz, 1982) was measured by a task in which participants generated as many items as possible in a given category. Phonemic fluency was measured using Controlled Oral Word Association (Benton and Hamsher, 1983), where participants generated as many words as possible beginning with a specific phoneme, such as /F/. Visuospatial construction was tested using the Block Design test (Koh's Block Test) (Wechsler, 1991), where participants produced a block design that matched a given model. Further information about the validity and scoring procedures of the tests is available in Rydberg Sterner et al. (2019).

Raw test scores for all the tests described above were z-transformed, and global cognitive function was defined as the average of these scores, provided valid scores were available in at least four domains. The internal consistency of the global index has been shown to be acceptable (Cronbach's alpha = 0.72) (Hoff et al., 2023).

ANALYSIS

For Papers I and II, statistical analysis was performed using a local software called GIDSS (Geriatric Departments Interactive Database and Statistical System). In Papers III and VI, statistical analysis was primarily conducted using IBM SPSS for Windows version 25.

Paper I and II

Medians and quartiles of hearing thresholds in dB HL, obtained from automated pure-tone audiometry, were analysed for the right and left ears. As the lower and upper limits of the audiometer were set at 0 dB HL and 90 dB HL, respectively, the 10th and 90th percentiles were excluded and not applied in the analysis. Since hearing thresholds were measured in 5-dB steps, medians were interpolated and presented separately for men and women at each frequency, following the same methodology used in earlier studies within the H70 cohort (Jonsson & Rosenhall, 1998; Jonsson et al., 1998; Hoff et al., 2018).

Since the test range, i.e., the lowest and highest used stimulus levels, differed between the various cohorts that were compared in **Papers I and II**, all thresholds were capped at 0 and 90 dB HL respectively.

In Paper I, non-parametric statistics were primarily used due to the non-normally distributed data. Longitudinal changes in pure-tone thresholds (0.25-8 kHz) between the ages of 75 and 85 years, as well as differences between ears, were calculated using the Wilcoxon Signed-Rank Test. Sex differences in longitudinal changes were analysed using the Mann-Whitney U Test. Differences in hearing thresholds between participants tested at the research clinic and participants tested during home visits were analysed using an independent-samples T-test (but also tested with the non-parametric Mann-Whitney U Test, although unpublished). Consideration was given to adjusting for multiple statistical tests. However, such tests, e.g., the Bonferroni correction, have been described as overly conservative (KJ Rothman, 1990) and could increase the risk of a type II error. Therefore, a compromise of $p < .01$ was used as the threshold for significance in **Paper I** and **Paper II**.

In **Paper II**, hearing loss prevalence was defined according to the WHO definition, which is a four-frequency pure-tone average (PTA 0.5, 1, 2, 4 kHz) greater than 25 dB HL in the better ear. The prevalence of disabling hearing loss was also analysed based on the WHO definition (PTA4 > 40 dB HL in the better ear) and the GBD criterion (PTA4 ≥35 dB HL in the better ear) (Stevens et al., 2013). Different grades of hearing loss were classified using the WHO criteria for mild (>25–40 dB HL), moderate (>40–60 dB HL), and severe-profound (>60 dB HL). Unilateral hearing loss was analysed according to the WHO definition (1991), (PTA4 ≤25 dB HL in the better ear and PTA4 >25 dB HL in the worse ear). The better ear, as defined by WHO and GBD, was the ear with the better PTA4, and this definition was used in all analyses of hearing loss prevalence and grades of hearing loss. Birth cohort comparisons **in Paper II** were made using two different audiometric methods: computerised automated audiometry using circum-aural headphones (cohort 1930) and manual audiometry using supra-aural headphones (cohort 1901-1902). Due to the non-normal distribution of the data, differences between birth cohorts in median pure-tone thresholds were analysed using the non-parametric Mann-Whitney U test. Changes between sexes in prevalence figures within the respective cohort were analysed with a Fishers exact test.

An overview of sampling and methodologies (pure-tone audiometry) of samples included in **Papers I and II** are illustrated in Figure 4.

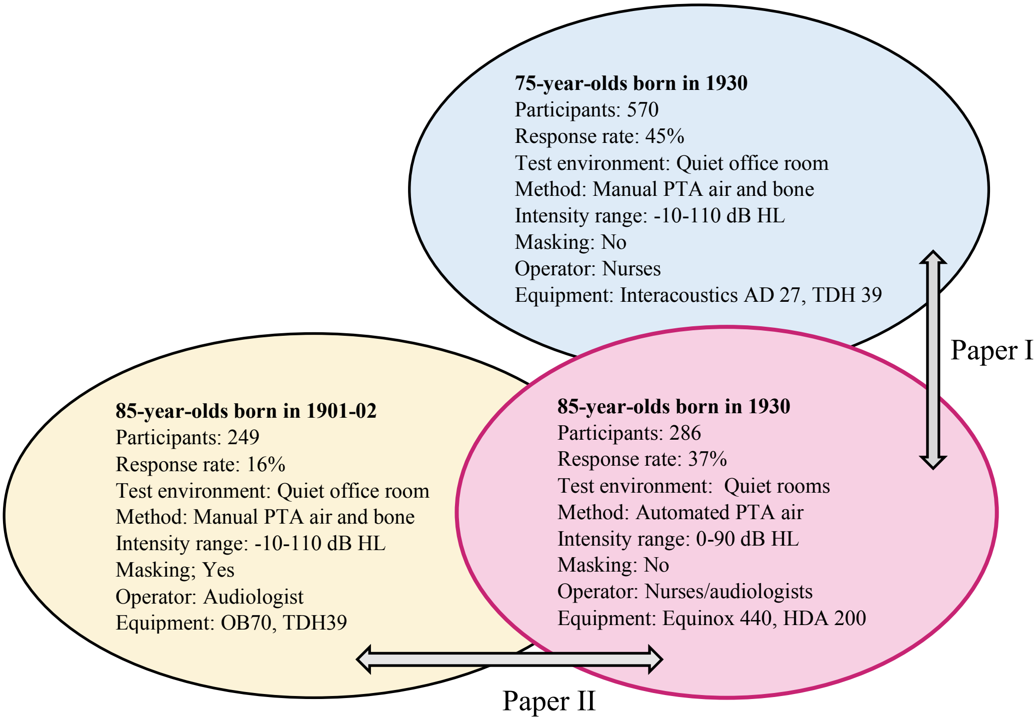


Figure 4. Overview of test methodologies (pure-tone audiometry) used in the samples included in Papers I and II.

Paper III

To assess significant differences between participants and non-participants in self-reported variables Fisher's exact test and Pearson chi-square were used and reported in the papers. Due to sufficient normally distributed data, parametric descriptive statistics (mean and SD) were used to present ABR latencies, as well as measured and predicted word recognition scores in men and women, and in the right and left ears. Sex differences in WRS-N were examined using independent-samples t-tests, with a p-value < 0.05 considered significant. To avoid bias, ears with CHL and/or severe hearing loss were excluded in the analysis of abnormal word recognition scores and auditory neural dysfunction.

The presence of DPOAE was analysed at single frequencies using specific signal-to-noise ratio criteria: 6 dB signal-to-noise ratio (SNR) at 1.5-6 kHz which according to the manufacturer gives a 99.9 confidence level. Only present emissions (≥6 dB SNR) with accepted amplitudes (Vinck et al., 1996) were classified as present DPOAEs. The test frequency of 1 kHz was excluded to avoid false positive results due to high noise levels. Auditory neural dysfunction was defined as abnormal word recognition scores in combination with absent or abnormal ABRs, characterized by prolongation of the interaural latency difference (ILDs) and/or the absolute latency for Wave V. Abnormal ABRs were considered if absolute latency of wave V was prolonged, i.e., >6.2 ms for women and >6.6 for men or if ILDs for wave V were >0.4 ms. These limits were based on normative data from a study of 70-year-olds with normal hearing defined as a pure-tone average at 0.5-4 kHz (PTA4) of ≤25 dB HL (n=155), which utilized the same methodology and equipment (Hoff et al., 2020).

Sensorineural hearing loss was defined as PTA > 25 dB HL in one or both ears, with air- and bone-conducted thresholds ≥ 25 dB HL without any air-bone gaps. Auditory sensory dysfunction was defined by absent DPOAE´s. Auditory neural dysfunction (related to the degenerative processes in the auditory nerve or at more central neural position) was defined as abnormal word recognition scores in combinations with absent or abnormal ABR latency wave V latencies. CHL was defined as an air-bone gap equal to or greater than 15 dB at two or more frequencies, while mixed HL was defined as an air-bone gap equal to or greater than 15 dB at two or more frequencies in combination with sensorineural HL. To avoid bias due to collapsing ear canals caused by the headphones, an isolated air-bone-gap at 3-4 kHz was not accepted. (Rosenhall et al., 2011).

Paper IV

Medians and quartiles (% correct repeated digits) of free reports (FR), directed reports in right ear (DR RE), and directed reports in left ear (DR LE) were calculated for 70- and 85-year-olds. Non-parametric descriptive statistics were used due to skewed data and ceiling effects. The threshold for a normal score in the DDT with one-pair digits in both FR and DR conditions was set at ≥90% (Musiek, 1983; Hällgren, 2001). The test methodology was inspired by the results from Jerger and Martin (2006). Normal and abnormal test results in FR and DR were attributed to differences in cognitive load between FR and DR conditions and to hemispheric asymmetry. Combinations of FR and DR test results were used to classify participants into four different profiles: a normal profile, a primarily cognitive deficit profile, a primarily central auditory deficit profile, and an "undetermined" profile. Boxplots were used to display the distribution of PTAs and Global cognition results across the specific profiles for 85-year-old participants. To test if it is empirical support for the DDT-profile model, the association between DDT profiles and cognitive performance and peripheral hearing was examined in 85-year-olds using a multinomial regression model. Each DDT profile was compared against a reference group, namely the normal profile. The DDT profile was predicted based on specific predictor variables, including the sex of the participant, PTA 3, PTA4, or PTA HF in the left ear, and the Global cognition score. PTA 3, PTA4, and PTA HF were included one by one as predictors in separate regression models (three different models).

ETHICAL CONSIDERATIONS

The project obtained approval from the Regional Ethics Review Board in Gothenburg, with Diary numbers 131-15 and 513-15. Ethical considerations were carefully considered throughout all aspects of the project, as outlined in the attached ethical applications. There are two separate ethical approvals associated with this study. The first approval (Diary no. 131-15) covers the comprehensive H70 examination, conducted at the neuropsychiatric outpatient department at Sahlgrenska Hospital (research clinic), including the main audiological examination. The second approval (Diary no. 513-15) pertains to the extended audiological examination, conducted at the research clinic at the University of Gothenburg.

Research ethics involves assessing the risks and benefits of a study. Ethical considerations are relevant to every stage of the research process, such as project design, research questions formulation, securing funding, participant selection, publication of results, and dissemination of knowledge to the public. Important aspects include informed consent, privacy, and confidentiality (Cooper and McNair, 2015). Epidemiological research involves screening the general population to determine the prevalence of health conditions. For participants, involvement in such studies has advantages, including receiving a comprehensive health examination free of charge. However, it may also lead to the identification of previously undetected health conditions and the presence of risk factors for serious diseases. Ethically, it is crucial to provide participants with information on how to interpret the test results and guidance on when and how to seek further medical care. Ethical approvals were obtained for the studies included in this thesis through separate applications (Salerno et al., 2019).

Papers I and II

Ethical approval I, the main audiological examination, diary no: 131-15

Information letters and consent forms were sent out by the H70 group. To address all research questions in the comprehensive H70 Study, it was not possible to exclude individuals with cognitive impairment and dementia. In cases where a person was unable to provide consent independently, consent from a relative was obtained and documented. All participants underwent examinations either at a clinic or through home visits, with the main audiological examination (automated pure-tone audiometry) included as part of the test protocol. Following the audiological examinations for all participants, written information regarding the interpretation of audiograms was provided. For participants who opted for a home visit, they were initially contacted by telephone to obtain consent and schedule an appointment. If a participant with dementia in a nursing home was unable to provide consent independently, a relative or care staff member from the nursing home was contacted for consent, and the details were documented, including the relative's name and date. If any participant with dementia in a nursing home experienced even slight discomfort during the hearing test, the test was immediately discontinued.

Paper III and IV

Ethical approvement II, the extended audiological examination, diary no. 513-15

Information letters and consent forms were sent, and participants were contacted via phone calls to provide information about the study's structure, potential risks, and benefits, as well as to address any questions they may have had. If consent was possible, an appointment (approximately 120 minutes long) was scheduled for the audiological examination, including breaks. For participants who were unable to travel to the clinic on their own, compensation in the form of taxi fare was offered for transportation to and from the research clinic. Consent forms were obtained upon arrival at the research clinic, and participants were clearly informed of their right to withdraw from the study at any time. After the examination, information regarding the test results was provided, and copies of the audiogram and consent form were given to the participants. Participants who received test results indicating requirement for additional medical assessment were given the option of being referred to either an Ear Nose and Throat specialist or an audiologist (Masic et al., 2014). Those requiring hearing rehabilitation were offered appointments at

Hörselverksamheten, Västra Götalandsregionen. All test methods used in the study were standardized, and no associated risks were documented in relation to the tests. In Paper IV, audiometric results from an earlier studied cohort of 70-year-olds (Hoff et al., 2020) were reported. Ethical approval has been obtained for the 70-year-olds, with Diary no 976-13 (Hoff et al., 2020).

RESULTS

PAPER I

CROSS-SECTIONAL RESULTS

Median air conduction pure-tone thresholds are presented for both sexes in the right and left ear in Figure 5A-B. The 85-year-old women had significantly poorer hearing thresholds at lower frequencies (0.25-1 kHz) and significantly better hearing thresholds at higher frequencies (3-8 kHz) compared to the 85-year-old men.

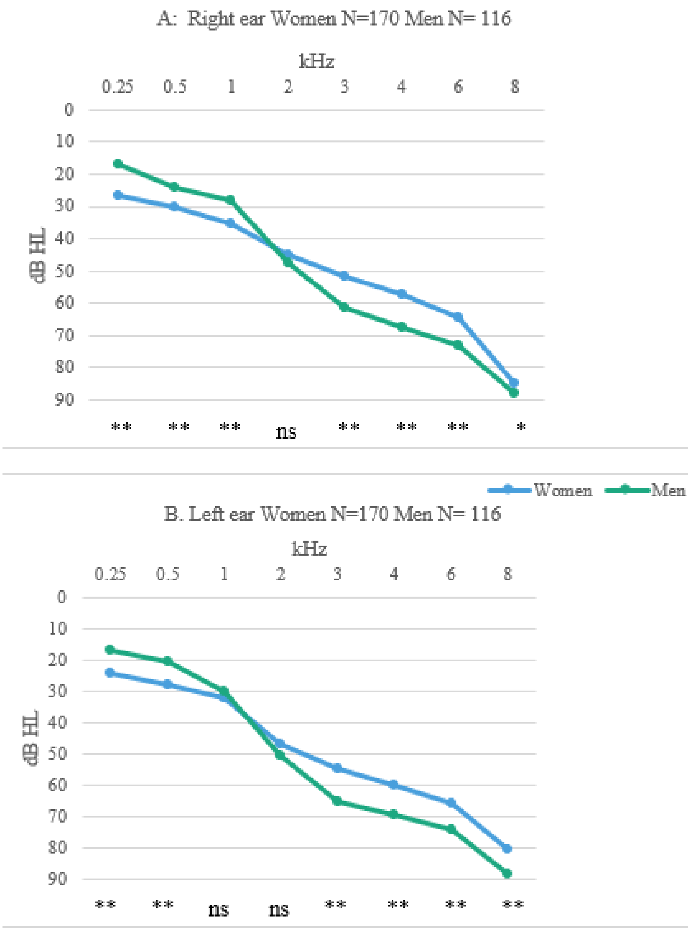


*Figure 5 A-B. Cross-sectional result of pure-tone hearing thresholds **= p<0.001*

LONGITUDINAL RESULTS

The longitudinal study in **Paper I** shows a statistically significant decline between the age of 75 and 85 years at mid-high frequencies (>1 kHz) for both sexes and in both ears. The most pronounced decline occurred at 2-4 kHz and 8 kHz for both men and women, and in both ears (Figure 6). There was no significant difference in hearing decline between sexes at any frequency.

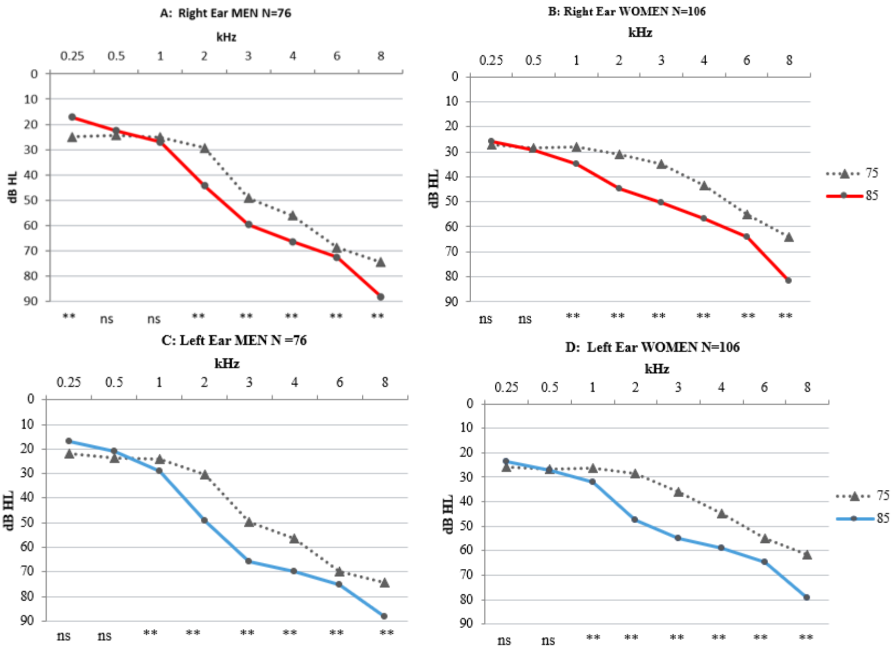


*Figure 6 A-D. Decline in pure-tone hearing thresholds in right (A-B) and left (C-D) ears for men and women between 75–85-year-olds in 85-year-olds. **= p<0.001*

PAPER II

PREVALENCE OF HEARING LOSS

The overall prevalence of hearing loss for 85-year-olds born in 1930 was 83% according to the WHO definition (1991). Among them, 38% had mild hearing loss, 39% had moderate hearing loss, and 6% had severe to profound hearing loss. Additionally, the prevalence of unilateral hearing loss (WHO definition) was 6% for both men and women.

COHORT DIFFERENCES

In the later born birth cohort (b. 1930), men had significantly better hearing thresholds ($p<.01$) at frequencies of 0.25–1 kHz in the right ear and at 0.5–4 kHz in the left ear compared to the earlier born birth cohort (b. 1901-02). However, women in the later born cohort only showed significantly better hearing ($p<.01$) at single frequencies of 0.25 kHz (right and left ear), 0.5 kHz (left ear), and 8 kHz (right ear) compared to women in the earlier born cohort. Consequently, this led to the PTA4 (average of 0.5, 1, 2, and 4 kHz) in the better ear being more similar in men and women in the later born cohort compared to the earlier born cohort (Figure 7).

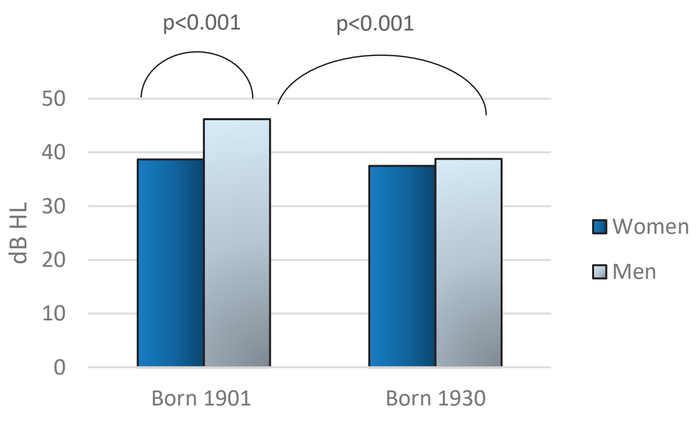


Figure 7. Pure-tone average at four frequencies (0.5-4 kHz) in 85-year-old men and women born 1901-02 and 1930. p= p-value

The prevalence of disabling hearing loss (Table 8) and the proportions of different grades of hearing loss (Figure 8) presented in **Paper II** are also based on PTA4, thus resulting in the same trend of reduced sex differences observed in the later born birth cohort. Men showed a significant higher prevalence of disabling hearing loss (WHO) than women in Cohort 1901-02 while no significant sex-difference was observed in Cohort 1930. See Table 8 for the prevalence of disabling hearing loss among 85-year-olds born in 1930 and in 1901-02. Both WHO and GBD criteria of disabling hearing loss are listed.

Table 8. Prevalence of disabling hearing loss for 85-year-olds born in 1930

Disabling HL	Men 1930	Women 1930	Men 1901-02	Women 1901-02
WHO	43 %	45 %	67 %	47 %
GBD	61 %	63 %	80 %	60 %

Table note: WHO= PTA4>40 dB HL in the better ear. GBD=PTA4 ≥35 dB HL in the better ear.

The distribution of different grades of hearing loss according to WHO definition (1991) are illustrated below for both men and women and for both birth cohorts (Figure 8).

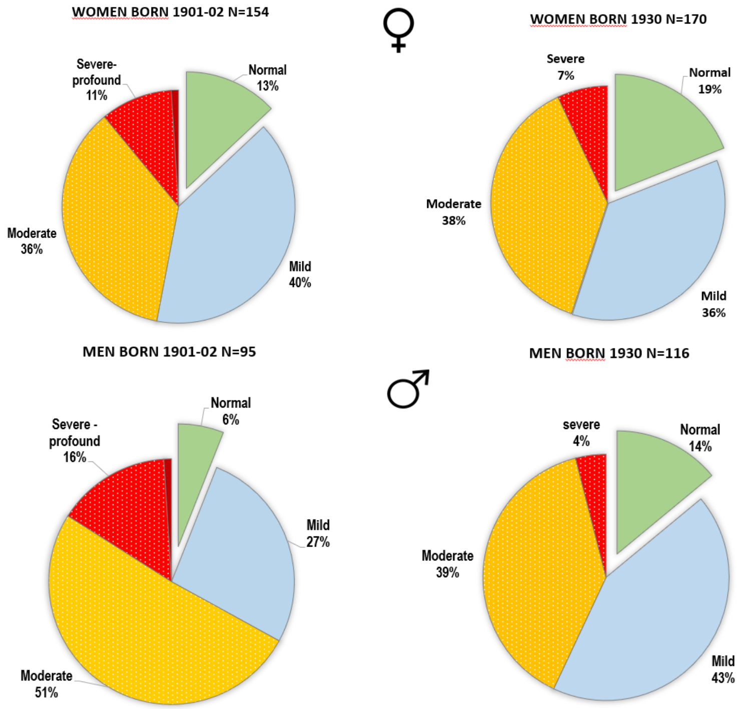


Figure 8. Distribution of hearing loss grades (WHO, 1991) in 85-year-old men and women born 1901-02 and 1930.

Adapted from International Journal of audiology: Göthberg H, Rosenhall U, Tengstrand T, Rydén L, Wetterberg H, Skoog I & Sadeghi A (2021) Prevalence of hearing loss and need for aural rehabilitation in 85-year-olds: a birth cohort comparison, almost three decades apart, Int J Audiol, 60:7, 539548, doi:10.1080/14992027.2020.1734878. Epub 2020 Mar 4.

PAPER III

SPEECH AUDIOMETRY

Based on manual pure-tone audiometry, approximately 98% of the participants included in **Paper III** had sensorineural or mixed HL in one or both ears. The majority of the 85-year-old participants (81%) took part in the Word Recognition in Noise test (WRN), with valid results being obtained in at least one ear. After excluding participants with another native language than Swedish and ears with CHL and severe hearing loss, approximately 20% of the participants (15 men and 4 women) showed abnormal word recognition scores in one or both ears according to the definition used in this paper (16 p.p. lower score than the SII- predicted score).

DISTORTION PRODUCT OTOACOUSTIC EMISSIONS

Only 11-17% had DPOAEs at 1.5 and/or 2 kHz, and 5% had DPOAEs at 3 and/or 4 and/or 6 kHz, according to the criteria in this study. Participants with DPOAEs at two or more adjacent frequencies in the right and/or left ear (~14%) had a PTA4 of ≤ 45 dB HL in that ear. The majority, around 70%, of 85-year-olds had absent DPOAEs at 70/70 intensity level in both ears and for all frequencies.

AUDITORY BRAINSTEM RESPONSES

Wave V latencies were identified in 96% of the participants in the right and/or left ear. However, approximately 90% of the subjects had absent or unidentified Wave I, and around 45% of the subjects had absent or unidentified Wave III. All participants/ears with profound hearing loss (n=3) (PTA4 > 80 dB HL) had absent absolute wave V latency. Twelve participants (10%) had prolonged ILDs. Six of these participants showed CHL and/or severe HL in the worse ear, which could explain the asymmetry. The remaining six participants had word recognition scores within predicted scores bilaterally and no obvious explanation was found for the large ILDs. Moreover, five women and three men had a unilateral prolonged absolute Wave V latency with word recognition scores within predicted scores and were consequently not classified as having auditory neural dysfunction (unpublished data).

TYPES OF HEARING LOSS

Approximately 98% of the participants had sensorineural hearing loss in one or both ears. The vast majority of participants with sensorineural hearing loss had absent DPOAEs, probably indicating sensory dysfunction (OHC loss). Based on the definition used in this study (using air and bone conduction thresholds), approximately 6% had CHL, all in combination with sensorineural hearing loss (mixed HL). After excluding participants with another native language than Swedish, CHL and/or severe hearing loss, approximately 20% showed abnormal word recognition scores (WRS-N or WRS-Q). Among these subjects, the majority were men (79%). Only two subjects had abnormal wave V ABR latencies based on the criteria used in this study. Consequently, 1.6% of the sample met the criteria for auditory neural dysfunction.

PAPER IV

Almost all (~99%) 70- and 85-year-old participants (PTA3 ≤50 dB HL) had valid (participated) test results in DDT. A considerable ceiling effect was observed for all test conditions in 70-year-olds. The ceiling effect was not as obvious for 85-year-olds, at least not for men in the FR and DR LE conditions. Approximately 90% of 70-year-olds and 35% of 85-year-olds had normal DDT results. Only a few 70-year-olds were categorised with a primary central auditory deficit or a primarily cognitive deficit, while almost one third of 85-year-olds fell into these categories (see Paper IV). Additionally, a substantial proportion of the 85-year-olds fell into the undetermined profile, i.e., abnormal DDT score across all attention modes. Both peripheral hearing loss and global cognition emerged as significant predictors for the DDT categorization.

RESULTS IN MEN AND WOMEN

PAPERS I-IV

- At age 85, women had significantly poorer pure-tone hearing thresholds than men at low frequencies but significantly better hearing thresholds at higher frequencies.
- There was no significant sex difference in hearing decline between the ages of 75 and 85 years at any frequency.
- The prevalence of disabling hearing loss (according to the WHO definition) was significantly lower among men in Cohort 1930

compared to men in Cohort 1901–1902. On the contrary, women did not show a significant cohort difference in disabling hearing loss.

- For 85-year-old women, there was an almost equal distribution of different grades of hearing loss in the two birth cohorts (1901-02 vs 1930), while for men, the distribution between the cohorts differed.
- Women had a significantly better mean word recognition score in noise (WRS-N) compared to men.
- The majority of participants with abnormal speech recognition scores were men.
- Both men and women aged 70 and 85 showed ceiling effects in dichotic digit test (DDT) results. The ceiling effects were less prominent for 85-year-old men than for 85-year-old women.

DISCUSSION

STUDY DESIGN AND METHODOLOGIES

The study design of the papers included in this thesis was primarily cross-sectional, providing information on hearing function at a single point in time. The use of cross-sectional data allowed for the calculation of hearing loss prevalence. Cross-sectional data was used to compare birth cohorts, in this case born approximately 30 years apart (time-lag design). **Paper I** utilized a longitudinal design to study hearing decline over time.

The methodologies and sampling strategies within the H70 Study were kept as consistent as possible, ensuring comparability of research data across different age groups and birth cohorts. However, it is important to consider certain methodological discrepancies when interpreting test results. The comparisons of hearing thresholds between the samples in **Papers I and II** were based on two different audiological methods: manual audiometry using supra-aural headphones versus computerised automated audiometry using circum-aural headphones.

Automated audiometry has been demonstrated to provide reliable and accurate measurements of hearing thresholds (Swanepoel et al., 2010b), and a good agreement has been reported between these methods (Margolis et al., 2011). The accuracy of the method used in **Paper I and II**, i.e., automated audiometry with circum-aural headphones, was recently reported in a paper by Hoff et al (2023). In relation to manual audiometry, automated audiometry was found to produce accurate assessments of hearing sensitivity in the majority of older adults (70- and 85-year-olds). Roughly 90% of all thresholds measured with automated audiometry corresponded within ± 10 dB of the equivalent PTTs determined with manual audiometry, and the mean differences were close to zero at most test frequencies. The mean difference for PTA4 of which the prevalence figures were based on was -1.6 dB. The accuracy of automated audiometry was not affected by relevant factors associated with old age, such as test frequency, age, sex, PTA 4, and cognitive status (Hoff et al., 2023).

The use of circum-aural headphones attenuates more background noise compared to supra-aural headphones, which probably have influenced the longitudinal result at low frequencies in **Paper I.** At age 75, pure-tone audiometry was assessed by nurses in an office room with supra-aural headphones, with a risk of ambient noise affecting the result. At age 85, circum-aural headphones were used. This probably explains why participants had better hearing thresholds at low frequencies at age 85 than at age 75.

Furthermore, in **Paper II**, masking was used in Cohort 1901–1902 but not in Cohort 1930, which may have affected the result. The absence of appropriate contralateral masking may generate better hearing thresholds than what is true, specifically for asymmetric hearing losses. However, the majority of the participants had symmetric air-conducted thresholds, and the lack of masking probably only had a minor impact.

Finally, the restricted upper level of 90 dB HL in the cohort born in 1930 was used to avoid discomfort in participants. However, this may have affected the results due to a ceiling effect, particularly at high frequencies. Consequently, the results at 6-8 kHz need to be interpreted with caution. Medians were used in the analyses to minimize these effects.

In **Paper III**, several audiological measurements were utilized to reflect different functions in the auditory system. CHL was defined in terms of air-bone gaps. To comprehensively characterize middle ear pathologies, additional data, such as medical records and tympanometry, are required. This information was not available for the study participants and middle ear pathologies could not be identified.

In this study, abnormal word recognition scores in older individuals were only occasionally linked to abnormal Wave V latencies. Earlier wave latencies, IPL I-V and amplitude ratios (wave I/V) would possibly have been more suitable for the assessment of auditory neural function. However, a relatively fast ABR stimulation rate was used to reduce the test duration, which may result in a lower rate of visibility of Wave I amplitudes than if a slower rate would have been used. However, the visibility of wave I is described to not improve much with decreased stimulate rates at advanced age (Bramhall, 2021).

The use of DDT with one-pair digits in **Paper IV** was chosen since it is not overly complicated and is therefore considered to perceive appropriateness for a sample drawn from the general population with older participants with varying health and cognition. However, one-pair digits resulted in large ceiling effects, especially for the 70-year-olds. The inclusion of two- or three-pair digits would probably result in a more balanced distribution among 70-year-olds but at the expense of increasing cognitive demand, mainly impacting the

85-year-olds. Since there is no gold standard procedure for diagnosing CAPD, determining the validity of test methods used to study central auditory abilities is challenging. The validity of DDT in reflecting CAPD is discussed in the literature. DDT has been validated based on studies involving participants with known lesions in central auditory pathways (Bocca et al., 1954, 1955; Kimura 1967).

An interpretation model, inspired by results from Jerger and Martin (2006), was used to distinguish between participants with a primarily central auditory deficit and participants with a primarily cognitive deficit, as well as those with a normal profile. Abnormal Free Reports (FR) and Directed Reports in left ear (DR LE) in combination with a normal Directed Reports in right ear (DR RE) were interpreted as indicating a primarily central auditory deficit, while an abnormal test result on only FR was interpreted as a primarily cognitive deficit. A dichotomous variable was used in categorizing DDT profiles and was based on a strict limit for normal vs. abnormal DDT results (≥90%). A 90% cut-off score has been shown to be slightly greater than two standard deviations below the mean for an earlier studied normal-hearing group (Museik 1983). Moreover, this cut-off score has been shown to be valid for DDT with one-pair digits in adults (42-66 years) with peripheral hearing loss (hearing-aid users) (Hällgren, 2001). Variations in test scores below 90% in FR and DR were not reflected in the classification of profiles, which should be taken into consideration when interpreting the results.

PARTICIPANTS

An epidemiological approach was used with the aim of achieving a sample that is representative of the general population of 85-year-olds. In population-based studies, there is an ambition to generalize the results to the populations from which the study samples were drawn. The H70 Study utilized a systematic sampling methodology based on birth dates (day of birth). The participation rate in the comprehensive H70 investigation was relatively high (64%), which is favorable for the representativeness of the sample. However, sub-samples were used in the audiological assessments in **Papers I-IV**, resulting in decreased participation rates that likely affected the generalizability of the results. To maintain the representativeness of the 85-year-old sample as far as possible, home visits or nursing home visits were offered (**Papers I and II**). However, due to practical limitations, it was not feasible to conduct a separate hearing test on all participants who opted for a home visit, and the sample may have been biased towards healthier individuals. Nevertheless, within the home visit group, there were no significant differences in self-reported health, hearing-related variables, or education level between participants who underwent audiological examination and those who did not. Therefore, the excluded home visits should not have significantly impacted the overall representativeness of the sample.

In **Papers III-IV**, a consecutive sampling method was applied, and an extended test protocol was used, including both psychoacoustic and physiological assessments. Participants were asked to visit the research clinic, and no home visits were offered. It is important to consider that individuals with poor health may have been less likely to participate (**Paper III and IV**), and this may have resulted in lower generalizability of the results in the extended audiological investigation compared to the main audiological investigation used in **Papers I and II**. However, efforts were made to minimize this bias by offering transportation assistance and including participants who opted for a home visit in the main investigation. Despite this effort, the subsequent report of self-reported data (Table 7 in this thesis) indicates that men included in **Papers III and IV** were generally healthier than men included in **Papers I and II**. Additionally, a generally higher education level was indicated in women in **Paper III** than in women in **Paper I and II**. Moreover, the resulting sub-sample in **Paper III** had a sex distribution (more men) that did not reflect the general population of 85-year-olds in Gothenburg at the time of the study. This was partly due to a higher number of non-responding women compared to men and practical limitations such as the availability of the research clinic during a specific time period. To minimize bias in test results, most of the results in **Paper III** were presented separately for men and women. In **Paper IV**, only participants with relatively well-preserved peripheral hearing (PTA3 < 50 dB HL) were included, and therefore, the result cannot be generalized to the general population of 85-year-olds.

It is important to note that the participants in this thesis were from a single geographical region in Sweden, which may limit the generalizability of the test results to other populations (Wetterberg et al., 2022). Gothenburg, being an industrial city with many industrial workers, primarily men, who may have been exposed to occupational noise earlier in life, could have influenced the results.

In this thesis, age- homogeneous samples were used, which had both advantages and disadvantages. Many population-based gerontological studies include participants within broader age ranges, often with an overrepresentation of younger individuals, due to health factors. An advantage of age-homogeneous samples is that there is no need for age adjustments in the analyses. However, age- homogeneous samples only provide hearing data at a specific stage of ageing and may not be representative of a wider range of ages, which could be a limiting factor. In **Paper III**, it would have been interesting to have included a wider range of ages to provide data for older individuals in general. However, audiological test results from a previously published study within the H70 project, which included 70-year-olds (Hoff et al., 2020), using the same study design and test protocol, allowed us to discuss age differences in audiometric results (70- and 85-year-olds) in **Paper III**. Moreover, DDT data from both 70-year-olds and 85-year-olds were included in **Paper IV**, and age differences in DDT were reported descriptively in the results.

CROSS-SECTIONAL FINDINGS

Age-related hearing loss is commonly associated with high-frequency hearing loss, which was also observed for both sexes in **Paper I**. However, men exhibited better hearing at low frequencies and worse hearing at high frequencies compared to women. This finding is consistent with earlier studies (Gates et al., 1990; Jerger et al., 1993; Morell et al., 1996). It has been suggested that noise exposure in men, which primarily affects the high frequencies, and a more pronounced stria vascularis atrophy in women could potentially explain this sex difference (Gates et al., 1993; Jerger et al., 1993). Given that Gothenburg is an industrial city, it is likely that men born in 1930 have had greater exposure to noise over their lifetime compared to women. To validate the findings in **Paper I**, the hearing thresholds of the 85-year-olds were compared with data from ISO 7029 (2017), which presents a formula from which the expected median values of hearing thresholds can be calculated. This formula is based on data from earlier population-based studies. However, ISO 7029 only provides data up to 80 years of age, which probably contributes to the poorer hearing thresholds observed in **Paper I**. The observed poorer thresholds in the 85-year-old sample in **Paper I** can also be attributed to the fact that the ISO 7029 data only included otologically screened samples, while the H70 Study utilized unscreened samples.

The prevalence of hearing loss in 85-year-olds, born in 1930, was presented in **Paper II**. Earlier population-based studies have reported various prevalence figures for older individuals, which can be attributed to differences in methodologies, including equipment used, sampling methods, age brackets of participants, geographical factors, and test years. Table 9 summarizes the prevalence of disabling hearing loss (GBD) from a few earlier European population-based studies, including the current H70 Study (see table 9).

Table 9. Prevalence figures (%) of disabling hearing loss (GBD) from European population-based studies including the H70 samples included in Paper II (marked in red).

Country	**Study group**	**Subjects (n)**	**Study year**	**Age**	**Prevalence % (PTA4 ≥35 dB)**	
					Men	**Women**
Sweden	H70	249	1986–87	85	80	60
Sweden	H70	286	2014–15	85	61	63
Norway	HUNT	n/a*	2017–19	~85	~62*	~42*
Germany	HÖRSTAT	220	2010–12	75–84	42	34
Netherlands	Rotterdam	235	2011–15	80–84	~54	~52
Netherlands	Rotterdam	141	2011–15	85+	~81	~73

*HUNT n=28339>19 years. All normative data in the HUNT study are presented related to the median HT levels of otologically normal subjects included in HUNT, aged 19 to 23 as a reference. HUNT study: Engdahl et al., 2020; HÖRSTAT study: von Gablenz et al., 2020; Rotterdam Study: Homan et al., 2017

LONGITUDINAL FINDINGS

The longitudinal study in **Paper I** demonstrated a significant decline in hearing between 75 and 85 years of age, with a decline measuring 10-20 dB at 2-4 kHz for both men and women. Population-based data from Wiley et al. (2008), conducted between 1998 and 2005, also show a considerable decline in older individuals (70-89 years) of approximately 1-2 dB per year, although the largest decline was in the low and mid frequencies (0.5-2 kHz). Other population-based studies have shown that the rate of hearing decline increases for low frequencies and decreases for high frequencies in older age groups compared to younger age groups. This pattern has partly been attributed to a ceiling effect at high frequencies (Glorig and Nixon, 1962; Brant and Fozard, 1990; Lee et al., 2005; Wiley et al., 2008). Moreover, Wattamwar et al. (2017) observed a significantly faster decline at low frequencies (0.25-1 kHz) in individuals above 90 years of age compared to earlier stages of life. Again, the lack of decline at low frequencies in **Paper I** may be potentially biased due to utilization of different headphones and different test environments for the 75- and 85-year-old participants. Comparing the rate of decline between studies is challenging due to differences in sample ages, years of assessment, the time over which thresholds were compared, and methodologies employed, all of which can impact the outcomes.

Earlier studies of ARHL have presented varying results regarding sex differences in hearing decline. Møller (1981) observed a larger decline in pure-tone thresholds in women than in men between 70-75 years of age. Pearson et al. (1995) concluded that hearing decreases twice as fast in men compared to older women at most frequencies and ages (>30y) (age). However, at 80, the rate of hearing loss was more equal between sexes. Gates et al. (1990) found no sex difference at any frequency between the ages of 70 and 89, which aligns with the findings in **Paper I**. Additionally, Wattamwar et al. (2018) demonstrated that the difference in auditory function between sexes is minimal above 80 years of age. Discrepancies in test results regarding sex differences in hearing decline may be attributed to variations in the age ranges included in the samples, baseline hearing thresholds and differences in methodologies across studies. However, our results support the concept of a similar decline in men and women in increasing age.

BIRTH-COHORT DIFFERENCES

Paper II presents significantly better hearing thresholds in 85-year-old men born 1930 than in 85-year-old men born in 1901-02, particularly at low to mid frequencies. The improvement in hearing thresholds in later-born men led to a lower PTA4 score and consequently a decreased prevalence of hearing loss (according to both WHO and GBD criteria), compared to the earlier-born men. Furthermore, a notable change in the distribution of grades of hearing loss was observed in men born in 1930 compared to those born in 1901-02. However, these changes were not observed in women. Earlier studies also reported better hearing in later-born cohorts, although with various results for specific ages and for men and women (Homans et al., 2017; Hoffman et al., 2010; Zhan et al., 2010; Hoff et al., 2018; Engdahl et al., 2020).

Minor differences in mean PTA can result in large differences in prevalence figures, particularly when a significant proportion of the cohort has PTA values close to the cut-off for defining normal hearing. However, this bias is likely more pronounced when comparing samples with a large proportion of participants with thresholds close to the normal hearing cut-off, such as younger participants rather than older participants. However, it is important to consider that older individuals typically have PTAs that are closer to the cut-off score for mild and moderate hearing loss when interpreting the proportion of different grades of hearing loss as well as the proportion of disabling hearing loss in **Paper II.**

Methodological factors, as for example ambient noise levels, may bias test results. However, the fact that a cut-off score of 40 dB HL was used for analyzing sex and cohort differences of disabling hearing loss, reduces the risk for bias stemming from ambient noise levels. Other methodological factors retaining the potential to influence test outcomes are discussed in **Paper II** and are not considered to explain the cohort difference. Instead, various risk factors affecting participants differently in the respective cohorts, such as occupational noise exposure, demographic variations, and health-related factors have been discussed as potential explanations for the improvement in hearing acuity observed in men of the later-born cohort. Better treatment of middle-ear disorders in the later-born cohort may also contribute to the result. Higher education level, less occupational noise exposure, as well as decreased ear infections contributed to better hearing the last 20 years in Norway (Engdahl et al., 2021). Moreover, considering Gothenburg being an industrial city, the absence of hearing improvement in women born 1930 may partly be related to more women exposed to occupational noise in the later-born cohort than in the earlier-born cohort. However, further research is warranted to fully understand the factors contributing to the improvement in hearing acuity in later-born men, as well as the absence of improvement in women in the present study.

SUB-TYPES OF ARHL

In **Paper III** a comprehensive test protocol was employed to study the sub-types of hearing loss. Only 6% of participants had CHL, which was always accompanied by sensorineural hearing loss, resulting in a mixed type of hearing loss. Almost all 85-year-old participants exhibited sensorineural hearing loss as determined by pure-tone audiometry. The sensory sub-type was considered the most common due to a large proportion of participants with absent DPOAEs and with word recognition scores within predicted values. Atrophy of the stria vascularis is recognized as a major age-related component of hearing loss (Schuknecht and Gacek 1993). However, multiple factors contribute to ARHL, making it difficult to isolate the biological ageing factor from other contributing factors. The strial type of ARHL (Schuknecht's typography) is characterized by a flat sensorineural configuration (Schuknecht and Gacek 1993). However, an isolated flat configuration was not observed in the 85-year-old sample included in **Paper III.** All ears with hearing loss exhibited pure-tone thresholds that fell toward the high frequencies, indicating a mix of age-related and environmental factors contributing to the hearing loss. Noise exposure is associated with considerable high-frequency loss, which likely contributes to the large proportion of falling audiograms observed in **Paper III.**

One-fifth of the participants had word recognition scores poorer than expected from the audiogram, indicating auditory dysfunctions central to sensory dysfunction. The criteria used to define auditory neural dysfunction, such as prolonged wave V latency, were relatively strict and only two individuals were identified with auditory neural dysfunction. These two individuals likely have a combination of sensory and neural dysfunction, as both their ABR and DPOAE results were abnormal. Participants with severe hearing loss were excluded from the analyses, which may have led to a lower rate of auditory neural dysfunction observed in the 85-year-old cohort. It is important to note that damage to peripheral axons or synapses in the IHCs (synaptopathy) may not be detected by analysing wave V latencies. Therefore, it is possible that a larger proportion than the reported 1.6 % of 85-year-olds with poor speech recognition may have auditory neural dysfunction.

Causes of poor speech recognition were not studied further in this thesis, but several potential factors are discussed in **Paper III.** Poor speech recognition scores were more frequently observed in men than in women, which may be attributed to sex differences in occupational noise exposure earlier in life. Noise exposure has been associated with cochlear synaptopathy in animal models (Liberman and Kujawa, 2017). Theoretical reasoning suggests that synaptopathy affects the neural coding of speech in noise and, consequently, speech intelligibility in noisy environments (Lopez-Poveda and Barrios, 2013). IHC degeneration could also be an important factor in poor speech recognition (Bredberg, 1968; Hoben et al., 2017).

Other important contributing factors to poor speech recognition include deterioration in central auditory pathways and cognitive domains (Humes, 1996). It is possible that peripheral dysfunction coexists with central auditory dysfunctions and cognitive decline. Central auditory function was assessed using DDT in **Paper IV**, but no further analysis was conducted to explore the association between poor word recognition scores and DDT results.

Further studies are needed to investigate the association between speech audiometry results and central auditory function, and also cognitive scores. Test fatigue and tiredness may also contribute to poor speech recognition scores. However, participants were offered breaks between hearing measurements, and the audiologist observed the participants during the procedure.

CENTRAL AUDITORY DEFICIT AND COGNITION

Several behavioural assessments have been suggested to assess central auditory function, whereas only DDT is used in this thesis. Employing the interpretation model of DDT used in Paper IV, the differentiation between central auditory deficit and both peripheral hearing loss and cognitive decline posed challenges, necessitating careful consideration when interpreting the outcome of DDT results in advanced age.

Regarding sex differences, there was a tendency of men having lower DDT scores than women. However, in the regression analysis, sex was not a significant predictor for DDT profiles (i.e., central auditory deficit profile, cognitive deficit profile, undetermined profile against the normal profile) when pure-tone average was included in the analysis. This suggests that the observed sex difference in DDT scores may be explained by peripheral hearing loss. Global cognition played a significant role in evaluating DDT profiles in 85-year-olds (Paper IV). This finding is consistent with other studies that have demonstrated an association between APD tests and cognition in ARHL (Panza et al., 2018b; Jayakody et al., 2018b). Global cognition did not predict the central auditory deficit profile against the normal profile. However, the use of other cognitive measures, particularly focusing on executive functions, may have generated another result. It also needs to be considered that a few observations in each profile may have affected the outcome of the multinomial logistic regression analysis.

ARHL IN YOUNGER AND OLDER OLDS

A younger sample of older individuals, aged 70 (born 1944), was studied with a similar design related to auditory function in 2014 (Hoff et al., 2018; 2021). Both the 70- and 85-year-olds were assessed using the extended audiological test protocol described in this thesis. The 85-year-olds born in 1930 and the

70-year-olds born in 1944 were tested during the same period (2014-2017). This led to an opportunity to discuss some test results for the two age groups in **Paper III**. For an overview, test results for 70- and 85-year-olds are summarized in Table 10. Data for the 70-year-olds were collected from Hoff et al. (2020), and the data for the 85-year-olds are presented in **Paper III**. The proportions of different types of hearing loss in 70-year-olds (Hoff et al., 2020) and 85-year-olds have been analysed using similar definitions and are illustrated in Table 11. However, when comparing the results between the different age-groups, it is important to take the representativeness of the two samples into account, i.e., the older sample probably constitutes a less representative sample (due to health factors) than the younger sample.

Table 10. Audiological test results in 70-year-olds born 1944 (Hoff et al, 2020) and in 85-year-olds born in 1930 (Göthberg et al., 2023) studied/analysed between 2014-2017. Similar methodologies were used.

Age	**WRS-N* Mean (SD)**		**Present DPOAE, 2 kHz**		**ABR Wave V (ms) Mean, SD**		**Proportion with normal DDT****	
	M	W	M	W	M	W	Men	Women
70	R60 (17) L59 (16)	R69 (13) L66 (14)	44%	45%	R6.1, 0.5 L6.0, 0.4	R5.7, 0.4 L5.8, 0.4	FR 83% DRR 96% DRL 90%	FR 92% DRR 97% DRL 94%
85	R37 (18) L35 (16)	R51 (17) L49 (16)	11%	17%	R6.2, 0.4 L6.3, 0.5	R5.9, 0.3 L6.0, 0.4	FR 17% DRR 56% DRL 47%	FR 47% DRR 70% DRL 64%

Table note: Data for 70-year-olds is collected from Hoff et al., 2020. Similar methodologies are used in 70- and 85-year-olds. WRS-N and DDT: Subjects with another native language than Swedish are excluded. Abnormal WRS-N*: Worse than the predicted SII score or failed WRS-N in one or two ears. DPOAE: Distortion Product Otoacoustic Emissions, DPOAE stimuli: 70/70. ABR: Auditory Brainstem Responses, SD: Standard Deviation, **Normal DDT: ≥ 90% correct repeated digits. R: Right ear, L: Left ear, FR: Free reports, DRR. Directed reports in the right ear, DRL: Directed reports in the left ear.

Table 11. Proportion of participants with various types of hearing losses in 70-year-olds (Hoff et al, 2020) and 85-year-olds (Göthberg et al., 2023).

Age	Normal hearing	CHL/mixed HL	Sensorineural HL	Auditory neural dysfunction*
70	~50%	~2%	~49%	~2%
85	~2%	~6%	~98%	~2%

Table note: These cases are not mutually exclusive. Normal hearing: Pure-tone average at four frequencies (0.5, 1, 2, 4 kHz) ≤25 dB HL in both ears. Prevalence data for 70-year-olds is collected from Hoff et al., 2020. Similar methodologies, including definition of hearing loss types, are used in 70- and 85-year-olds. *= based on poor word recognition scores and absent or abnormal ABR´s including an abnormal wave I-V latency (70-year-olds) or an abnormal wave V latency (85-year-olds). Participants/ears with PTA4>60 dB HL are excluded in the analysis of auditory neural dysfunction.

STRENGTHS AND LIMITATIONS

PARTICIPANTS AND SAMPLING METHODOLOGY

One strength of this thesis was the use of a relatively large sample of participants above the age of 80, which is rare in population-based studies of advanced age. The inclusion of age-homogenous samples in the H70 studies provides a valuable complement to studies that include samples spanning a wide age range. By including participants born in single years, the need for age adjustment in analyses is eliminated, which is an advantage. However, it is important to note that the results are specific to the particular age group studied and may not fully represent a broader age range.

Another strength was the inclusion of various audiological measures beyond pure-tone audiometry, encompassing both behavioural and physiological assessments. Most of the tests included in the protocol are widely used with documented validity and reliability. This comprehensive approach makes it possible to describe different auditory functions across the auditory pathways, rather than solely focusing on results from pure-tone audiometry, as commonly done in other population-based studies.

It should be noted that using a test protocol with a wide range of measures performed at the same occasion also has its limitations. Consideration was given to the fact that some 85-year-old individuals can only sustain attention for a relatively short period of time. As a result, the speech recognition test in quiet was not performed on all participants, which limited the information that could be obtained.

The use of an extensive test-protocol results in a large amount of data and only a part of this can be published within the framework of a doctoral thesis. The descriptive reporting of results in **Paper III** was due to the inclusion of multiple variables and hearing measures, which constrained the opportunity for extensive analysis within the given page limits. Consequently, many research questions arose from the findings and should be explored in future research within the H70 Study. Much of the remaining data will be analysed in future studies.

METHODOLOGIES AND TEST VARIABLES

There are some discrepancies in audiometric assessments between the study samples included in **Paper I** (75- and 85-year-olds) and in **Paper II** (85-year-olds born in 1930 vs 1901-02), which may have affected the validity of the test results. Factors such as headphones, masking, restricted ranges in decibels, and different operators (nurses or audiologists) need to be considered. The implications of these methodological factors are discussed in **Papers I and II**, as well as in earlier chapters of this thesis.

It is important to note that since self-reported variables and other health variables collected in the main H70 investigation were not processed at the time of publication of **Papers I and II**, explanatory factors for hearing decline or differences between birth cohorts could not be studied, which is a limitation of the studies. Moreover, the representativeness of cohort 1901-02 was not presented in **Paper II**. However, participants and non-participants in cohort 1901-02 were similar regarding sex, three years mortality rate, cardiovascular disorders, stroke, and depression (Wetterberg et al., 2021).

In Paper IV, central auditory function in 85-year-olds was studied. However, it should be noted that a dichotic test is just one of several behavioural APD tests described in the literature. DDT mainly reflects the ability to process binaural information. Other aspects of APD abilities were not studied, which is a limitation.

An index variable based on several domain-specific cognitive measures was used to assess global cognitive ability in **Paper IV**. This provides better information about individual differences in cognition compared to screening instruments such as the Mini-Mental State Examination (MMSE) or the Montreal Cognitive Assessment (MOCA), which are commonly used to assess cognition in studies of CAPD. However, other specific cognitive measures, targeting working memory and executive functions, may yield different results.

Another limitation in **Paper IV** was the administration of the FR attention mode, which only assessed binaural information and did not consider ear-specific information which was considered in Jerger and Martin (2006). With this procedure, a considered REA in FR, could not be validated. However, a failed FR has earlier been described to be associated with cognitive decline, since one digit needs to be remembered while repeating the other digit (Hällgren et al.,1998).

IMPLICATIONS

This thesis primarily utilizes cross-sectional analyses to provide an overview of how the auditory functions are affected in advanced age, specifically in 85-year-olds. The findings of this thesis also generate new hypotheses for future research on ARHL.

Paper I:

The longitudinal study in Paper I demonstrated a significant decline in hearing between 75 and 85 years of age for both men and women, particularly at frequencies important for speech recognition. The continued decline in older age underscores the significance of seeking help for hearing loss in the early stages of old age. The substantial decline in hearing at frequencies crucial for speech perception, coupled with increased life expectancy, emphasizes the importance of identifying individuals with hearing loss at a younger age and motivating them to seek hearing rehabilitation.

It was observed that 85-year-old men had poorer pure-tone hearing thresholds than women, particularly at frequencies critical for speech perception (>2 kHz). This finding suggests that men may face greater challenges in recognizing speech compared to women at a population level. However, it is important to note the wide range of hearing thresholds (interquartile range) observed in both men and women, indicates significant individual differences that should be considered in healthcare planning.

Paper II

Prevalence figures for disabling hearing loss were calculated based on cross-sectional findings in Paper II, providing an initial estimate of rehabilitation and care needs in ARHL for epidemiological purposes. Hearing rehabilitation has been shown to be beneficial for individuals with disabling hearing loss (Stevens et al., 2013). However, it is important to note that pure-tone hearing thresholds alone are not sufficient to accurately determine rehabilitation needs in clinical settings. Factors such as unilateral and mild hearing loss, as well as various individual considerations, must be taken into account to evaluate the specific rehabilitation needs of individuals. To plan for effective individualised rehabilitation programs, both individual factors and environmental considerations (ICF), as well as results from other audiological measures, must be taken into account for both men and women when calculating expected rehabilitation needs.

The improved hearing in 85-year-old men, born in 1930, compared to earlier born men, born in 1901-02, suggests that modifiable environmental factors are important for the development of ARHL. It is worth noting that this improvement was observed not only at the typical frequencies affected by noise exposure but also at low-mid frequencies. The cohort born 1930 was provided with noise conservation programmes during the latter part of their working lives, which may explain the improvement, especially at high frequencies. However, it is possible that other health-related factors have influenced the outcome, and further research is needed to explore these factors. Notably, if these factors have selectively impacted men and not women, it raises interesting questions for future research. The prevalence of cardiovascular diseases (CVD) has been shown to be associated with low-frequency hearing loss (Gates et al., 1993) and it may constitute such a factor. Interestingly, a decrease in CVD prevalence has been observed in older men but not in older women in another population-based study (Wattamwar et al., 2018). Exploring potential explanatory factors, such as CVD, for the improved hearing in men but not in women warrants further investigation.

Paper III

Many previous population-based studies on individuals of advanced age have primarily focused on pure-tone audiometry, which mainly assesses peripheral hearing function. However, to gain a more comprehensive understanding of the pathophysiological aspects of ARHL, it is necessary to perform additional audiological tests. The findings in Paper III, which include behavioural and physiological measures, contribute to the evaluation of care needs and planning of more targeted rehabilitation strategies, in advanced age. A large proportion of the participants in Paper III had word recognition scores poorer than expected from the audiogram/ the SII-algorithm (20%). Considering that the 85-year-old sample in Paper III is most likely healthier than the general population of advanced age, it is reasonable to expect a higher proportion of individuals with abnormal speech recognition in clinical settings. A significant difference in speech recognition scores was observed between men and women, and various factors contributing to this sex difference have been discussed in Paper III. However, considering the large individual discrepancies in speech audiometry results among both men and women, sex should not significantly influence clinical practice when evaluating hearing loss in advanced age.

In Paper III, only 1.6 % were identified with auditory neural dysfunction with use of ABR wave V latencies. However, it is possible that other electrophysiological tests would have identified deficits along the auditory neural pathway. Central auditory dysfunction and/or cognitive decline may also be possible factors in poor speech recognition.

It is important to note that hearing aids primarily provide amplification and compression, but they may not fully address speech discrimination and temporal deficits. Therefore, it is crucial to explore other rehabilitation strategies beyond hearing aids for this age-group. Assistive listening devices and communication strategy training and auditory training, whether individually or in a group setting, web-based or at the clinic, may enhance the overall outcomes of hearing rehabilitation for older individuals (Lesner, 2003; Bennett et al., 2021; Malmberg et al., 2017; Anderson and Kraus., 2013).

Paper IV

ARHL is associated with declines in both peripheral and central auditory functions. In this study, DDT was used to assess central auditory function.

However, it is important to note that dichotic tests only evaluate binaural listening function and do not assess other central auditory abilities, such as temporal listening skills. The significant difference in DDT test results between 70- and 85-year-olds has clinical implications, suggesting that younger and older individuals may require different assessment approaches. Despite the use of a relatively simple test stimulus, many 85-year-olds demonstrated poor DDT results, indicating that additional rehabilitation strategies, such as assistive listening devices or communication strategies, may be necessary alongside hearing aids. Furthermore, distinguishing central auditory dysfunction from peripheral hearing loss and cognitive decline using the DDT test proved challenging. Although the one-pair digit test material was designed to minimize the influence of peripheral hearing and cognitive decline, these factors still had a significant impact on the results. The presence of ceiling effects also limited the utility of the DDT with one-pair digits as a screening or routine measurement in clinical settings. However, in cases where older individuals experience significant self-reported communication difficulties that cannot be explained by peripheral hearing loss or cognitive decline, a poor DDT result with a right ear advantage in FR and DR may indicate central auditory dysfunction, specifically a decline in binaural listening abilities. However, additional CAPD tests need to be included for the diagnosis of central auditory dysfunction in older individuals, and a multidisciplinary approach should be implemented, including cognitive assessments. Awareness among clinicians of the association between peripheral hearing, central auditory dysfunction, and cognitive decline in ARHL should be increased.

Diagnostic implications

In the present thesis, automated audiometry was used to assess hearing thresholds. Since the accuracy of automated pure-tone audiometry in older individuals has been demonstrated to be acceptable (Hoff et al., 2023), it may be possible to use it in primary care units. Those who do not pass the screening should be referred for further evaluation, including speech audiometry. It is worth noting that many 85-year-old participants in this study were able to complete speech audiometry in noise with valid test results. However, in clinical settings it is important to consider the impact of tiredness and reduced concentration associated with old age on test performance.

At the age of 85, DPOAE does not seem to give any further clinical information beyond what is already known from the audiogram.

When individuals report significant communication difficulties which cannot be attributed to peripheral hearing loss or cognitive decline, assessment of central auditory function in ARHL may be recommended. However, a comprehensive evaluation of central auditory function requires the use of both electrophysiological and psychoacoustic audiological measures, along with cognitive assessments, necessitating a multidisciplinary approach. Moreover, reference data from such CAP tests need to be available before implementation.

In summary, a combination of peripheral dysfunctions, including degeneration in synaptic afferents and central auditory dysfunction, as well as cognitive decline, may contribute to hearing difficulties, including poor speech recognition, in advanced age. Given the complexity of differentiating between these pathophysiological components in advanced age, it is crucial to consider self-reported communication difficulties when assessing hearing rehabilitation needs. This requires adequately trained professionals who possess a comprehensive understanding of the complexity of ARHL, and who have access to sufficient time to conduct thorough individual assessments.

CONCLUSIONS

This thesis provides insights into different aspects of age-related hearing loss (ARHL) in a cohort of unscreened 85-year-olds born in 1930 from an industrialized city in Sweden. The following conclusions can be drawn from the results presented in Papers I-V of this thesis.

Paper I:

- 85-year-old men born in 1930 have better hearing at low frequencies but poorer hearing at high frequencies compared to women.
- Both men and women show a significant decline in hearing at mid-high frequencies, which are crucial for speech intelligibility.

Paper II

- The prevalence of hearing loss according to the WHO definition is high (> 80%) in 85-year-old men and women living in an urban city.
- Pure-tone hearing thresholds at low and mid frequencies have significantly improved in 85-year-old men born in 1930 compared to those born in 1901-02.
- The prevalence of disabling hearing loss (WHO criteria) has decreased significantly in 85-year-old men over approximately three decades, but no significant cohort difference was observed in women.
- Pure-tone hearing thresholds became more similar between the sexes in Cohort 1930 compared to Cohort 1901-02.

Paper III

- Sensorineural hearing loss is very common, and the sensory type seems to be the most common type of hearing loss in the 85-year-old population and is likely related to significant OHC loss.
- Conductive hearing loss based on pure-tone audiometry and air-bone gaps is relatively rare in 85-year-olds and is often combined with sensorineural hearing loss, i.e., mixed hearing loss.
- Poor word recognition scores are common in 85-year-olds, especially in men. One-fifth of the sample had word recognition scores poorer than the predicted scores. 85-year-old men had significantly worse word recognition score than women.

- ❖ Auditory neural dysfunction based on abnormal word recognition and auditory brainstem wave V latency were observed in only two participants, suggesting a limited prevalence in this cohort.
- ❖ Differentiating between sensory and neural types of hearing loss is challenging due to extensive cochlear pathology in advanced age, and further studies are needed to address the underlying factors affecting speech recognition.

Paper IV

- ❖ DDT with one-pair digits shows significant ceiling effects, particularly in 70-year-olds.
- ❖ Interpreting DDT results in older adults with ARHL is complex, and caution must be exercised when interpreting results based on differences in Free Reported (FR) and Directed Reported (DR) scores.
- ❖ Peripheral hearing loss (including high-frequency loss > 3 kHz) and cognitive decline need to be considered in the assessment of DDT in older age-groups.

FUTURE PERSPECTIVES

The findings presented in this thesis underscore the importance of further research in the field of ARHL to expand upon our current knowledge. To this end, several recommendations for future research are put forward:

1. **Explanatory factors**: Further research should explore potential contributing risk and health factors to the improved hearing observed in later-born men. Health variables such as cardiovascular disease (CVD), diabetes, cognitive decline, as well as demographic variables like education level, noise exposure, and measures of social interaction should be carefully considered. Longitudinal studies with more than two test occasions are preferred to track changes over time.

2. **Understanding the underlying factors for poor speech recognition:** Future research should include investigation of underlying physiological factors that contribute to poor speech recognition in ARHL. Variables associated with auditory neural dysfunction, listening effort, and cognition should be included in such analyses to explain the challenges observed in word recognition. Furthermore, the impact of noise exposure and audiometric configuration on speech recognition scores should be evaluated.

3. **Central auditory function studies:** Further research is recommended in central auditory function in the context of ARHL. Both peripheral hearing and cognitive abilities need to be considered. These studies should incorporate data on hearing difficulties, hearing aid usage, and validated tests targeting working memory and executive functions. Such an approach will facilitate a better understanding of the mechanisms involved in CAP disorders.

4. **Association between auditory function and cognition:** Further exploration of the association between peripheral and central auditory function and cognition is needed in the elderly, preferably through longitudinal studies.

5. **Rehabilitation outcomes and hearing loss types:** It is important to explore whether rehabilitative outcomes improve when different hearing loss types and cognitive abilities are considered in ARHL. This will contribute to a deeper understanding of ARHL, its underlying mechanisms, and to the development of individualized interventions and rehabilitation strategies for individuals with ARHL.

ACKNOWLEDGEMENTS

I wish to express my deepest appreciation to my supervisors, **André Sadeghi, Ulf Rosenhall and Ingmar Skoog. André,** thank you for your guidance and support throughout this journey. I appreciate your ability to look ahead and to put things in a wider perspective. I got my "drivers' licence" in research, as you said. **Ulf,** thank you for your valuable support and guidance! I deeply respect your broad knowledge of the field of ARHL, your humble personality, and your respectful character. I really appreciate our countless research discussions in real life and by e-mail. **Ingmar,** thank you for letting me join H70 and for insightful comments on the manuscripts. I am thankful to the commitment you show to the field of the ageing research.

I will always remember the encouragement, support, laughs and friendship of my past and fellow graduate students within H70. I´ve got friends in you! **Maria Hoff**, you have been my rock during this period, always so generous, caring, and competent! I really appreciate your respectful and genuine personality, as well as your insightfulness. **Åsa Winzell Juhlin**, I am so happy for you being my colleague and roommate. Thank you for always being encouraging, engaged, helpful, and willing to give valuable feedback. **Mona Eng**, thank you for your encouragement. I look forward to following your PhD project.

I would like to thank the members of the Hearing research group of H70. **Tomas Tengstrand**, my colleague for many years, thank you for the great cooperation with the data collection and for co-authorship. Your knowledge and genuine interest in audiology, as well as your clinical experience, have been so important during this journey. **Inger Wikström**, my inspiring past "diagnostic teacher", profound thanks for your thorough coordination of the data collection. **Gunilla Jansson**, thank you for introducing me to the H70 project and to the research group. Thank you for the practical guidance and support at the beginning of my PhD.

My past and present colleagues at the Department of Audiology; **Lennart Magnusson**, my former teacher, colleague and now also co-writer, thank you for your guidance throughout the narrow field of speech audiometry and for always being calm, listening and encouraging. **Milijana Malmberg**, thank you for your encouragement, friendship and for being inspiring and helpful. **Sofie Fredriksson**, thank you for your support, and willingness to discuss research questions, always with great interest. **Andreas Björsne**, thank you for always being helpful, insightful and for a lot of laughs. **Eva Andersson**, my colleague, and friend, thank you for being honest and caring. **Jonas Fogels**, thank you for interesting discussions and for great input. **Ann-Charlotte Persson**, thanks for nice lunch meetings, sharing experiences…soon it is your turn**!** Thank you **Kim Kähäri** for being inspiring and encouraging, **Daniel Landälv** for your valuable feedback**, Anita Niiström** for all the practical help and for being there, **Andreas Thulin,** for your inventiveness and for many laughs**.** Thank you all for your generosity and for the encouragement when I doubted myself. It is so great to have you all around, I could not be happier with all my colleagues; we are a great team!

I would also like to acknowledge the **members of the H70 Study** for their co-operation. **Johan Skoog** and **Timothy Hadarson-Bodin**, thank you for sharing your expertise in psychology and for being co-authors in Paper III. Thank you, **Therese Rydberg Sterner, Lina Rydén, Hanna Wetterberg,** and **Anna Zettergren**, for the valuable co-authorship in paper I and II, **Valter Sundh**, for statistical support, **Tina Jacobsson** for all your help, and the **nurses** for carrying out the audiometric tests.

Thank you, co-workers, and fellow graduate students, in the **Speech and Language Pathology Division** for being supportive, friendly and helpful. Let's keep on discussing and developing research questions in the field of communication.

Radi Jönsson and **Ylva Dahlin-Redfors,** thank you so much for great feedback!

To my colleagues and friends at the clinic, including the **pediatric audiologists**. I really appreciate our conversations in the lunchroom. **Emma Lidman**, my colleague for many years, thank you for being helpful and flexible when it comes to scheduling.

Thank you **Habilitering and Hälsa** for funding and support. I would like to give special thanks to the head of Hörselverksamheten, **Mattias Johansson**, for putting research as an important area and for letting me perform my PhD studies and for being supportive.

Thank you to further funding agencies: **Agneta Prytz-Folkes and Gösta Folkes Stiftelse, Rune and Ulla Almlövs Stiftelse, Göteborgs Läkarsällskap, Hörselforskningsfonden, Sahlgrenska Universitetssjukhusets forskningsstiftelser** and **Felix Neuberghs stiftelse.**

My uncle **Per-Olof Ekdahl**, thank you for the nice picture on the front page, illustrating my 85-year-old parents looking out from the oval window, communicating with younger generations (Gothenburg profiles).

Importantly, my family and beloved ones. My love **Mathias**, thank you for encouraging me to do my PhD and for being patient, understanding, supportive and caring (I made it like you said ;). Our adorable children, **Clara Alice, and Edvard**, you are the best and the most important to me. Love you! You have all been patient during hard work and a lot of computer work at home, especially during the pandemic.

Thank you, my amazing mother and father, **Owe and Ann-Mari**, for your encouragement, support and love. You are my role-models! My gratitude also for a wonderful family situation encompassing three sisters as best friends: **Eva, Mona, and Lena**, you keep me on track with a lot of laughs. Love you! Thank you **Solweig and Lennart and families** for being there for us and for your support. **My friends on Öckerö, in V. Frölunda, and Cathrine**, I am happy for breaks, fika, discussions and boat trips in between my studies!

Last but not least, I want to express my gratitude to **all the participants** for their invaluable participation in the H70 Birth Cohort Studies! Without you it would not have been possible.

REFERENCES

Acar, B., Yurekli, M. F., Babademez, M. A., Karabulut, H., & Karasen, R. M. (2011). Effects of hearing aids on cognitive functions and depressive signs in elderly people. Arch Gerontol and Geriatr, 52(3), 250-252.

Agrawal, Y., Platz, E. A., & Niparko, J. K. (2008). Prevalence of hearing loss and differences by demographic characteristics among us adults: Data from the national health and nutrition examination survey, 1999-2004. Arch inten med, 168(14), 1522-1530.

Alattar, A. A., Bergstrom, J., Laughlin, G. A., Kritz-Silverstein, D., Richard, E. L., Reas, E. T., Harris, J. P., Barrett-Connor, E., & McEvoy, L. K. (2020). Hearing Impairment and Cognitive Decline in Older, Community-Dwelling Adults. J Gerontol A Biol Sci Med Sci, 75(3), 567-573.

Allen PD, Eddins DA. (2010, June). Presbycusis phenotypes form a heterogeneous continuum when ordered by degree and configuration of hearing loss. Hear Res, 1;264(1–2):10-20.

Almqvist, B. Svenska audiologiska metodboksgruppen [SAME]. (2004). Metodbok i praktisk hörselmätning. C-A Tegnér. Amieva, H., Ouvrard, C., Giulioli, C., Meillon, C., Rullier, L., & Dartigues, J.- F. (2015). Self-Reported Hearing Loss, Hearing Aids, and Cognitive Decline in Elderly Adults: A 25-Year Study. J. Am. Geriatr. Soc, 63(10), 2099-2104.

American Academy of Audiology. (2010). Clinical practice guidelines: Diagnosis, treatment, and management of children and adults with central auditory processing disorder. Retrieved June 1, 2023, from https://audiology-web.s3.amazonaws.com/migrated/CAPD%20Guidelines%208-2010.pdf_539952af956c79.73897613.pdf

American National Standards Institute. (1997) S3. 5-1997, Methods for the calculation of the speech intelligibility index. New York: American National Standards Institute, 19, 90-119.

American Speech-Language-Hearing Association. (2005). (Central) auditory processing disorders—the role of the audiologist [Position Statement]. Available from www.asha.org/policy/.

American Speech-Language-Hearing Association. (n.d.). Central Auditory 08012023, Processing Disorder. (Practice Portal). Retrieved June 1, 2023 from www.asha.org/Practice-Portal/Clinical-Topics/Central-Auditory-Processing-Disorder/.

Amieva H, Mokri H, Le Goff M, Meillon C, Jacqmin-Gadda H, Foubert-Samier A, Orgogozo JM, Stern Y, Dartigues JF. (2014, April) Compensatory mechanisms in higher-educated subjects with Alzheimer's disease: a study of 20 years of cognitive decline. Brain, 137(Pt 4):1167-75.

Anderson S, Kraus N. (2013, May.) Auditory Training: Evidence for Neural Plasticity in Older Adults. Perspect Hear Hear Disord Res Res Diagn. 17:37-

Ardelt, M. (2010) Are older adults wiser than college students? A comparison of two age cohorts. J Adult Dev, 17(4), 193–207

Balcombe, N. R., & Sinclair, A. (2001). Ageing: definitions, mechanisms and the magnitude of the problem. Best Pract Res Clin Gastroenterol, 15(6), 835-849.

Baltes, P. B., & Lindenberger, U. (1997). Emergence of a powerful connection between sensory and cognitive functions across the adult life span: a new window to the study of cognitive ageing? Psychol Ageing, 12(1), 12.

Bao, J., & Ohlemiller, K. K. (2010). Age-related loss of spiral ganglion neurons. Hearing research, 264(1-2), 93-97.

Beattie RC, Barr T, Roup C. (1997). Normal and hearing-impaired word recognition scores for monosyllabic words in quiet and noise. Br J Audiol, Jun;31(3):153-64.

Belal A. (1975). Presbyacusis: physiological or pathological. J Laryngol Otol, (89), 1011–25.

Benton, Benton, A. L., Hamsher, d. S. K., & Sivan, A. B. (1983). Controlled Oral Word Association Test (COWAT) [Database record]. APA PsycTests. A. L., deS, K., & Sivan, A. B. (1994). Multilingual aphasia examination. AJA associates.

Bennett RJ, Barr C, Cortis A, Eikelboom RH, Ferguson M, Gerace D, Heffernan E, Hickson L, van Leeuwen L, Montano J, Preminger JE, Pronk M, Saunders GH, Singh G, Timmer BHB, Weinstein B, Bellekom S. (2021). Audiological approaches to address the psychosocial needs of adults with hearing loss: perceived benefit and likelihood of use. Int J Audiol.60(sup2):12-19.

Best V, Carlile S, Jin C, van Schaik A. (2005, July) The role of high frequencies in speech localization. J Acoust Soc Am, 2005 118(1):353–63.

Blanchard, R. D., Bunker, J. B., & Wachs, M. (1977). Distinguishing ageing, period and cohort effects in longitudinal studies of elderly populations. Socio-Econ. Plan. Sci, 11(3):137–146

Bocca E, Calero C, Cassinari V. (1954 May-June). A new method for testing hearing in temporal lobe tumours; preliminary report. Acta Otolaryngol.;44(3):219-21.

Bocca E, Calero C, Cassinari V, Migliavacca F. (1955 Jul-Aug). Testing "cortical" hearing in temporal lobe tumours. Acta Otolaryngol. 45(4):289-304.

Bramhall NF. (2021, Dec) Use of the auditory brainstem response for assessment of cochlear synaptopathy in humans. J Acoust Soc Am 150(6):4440. doi: 10.1121/10.0007484. PMID: 34972291.

Brant, L. J., & Fozard, J. L. (1990). Age changes in pure-tone hearing thresholds in a longitudinal study of normal human ageing. J Acoust Soc Am, 88(2), 813-820.

Bredberg G. (1968). Cellular pattern and nerve supply of the human organ of Corti. Acta Otolaryngology, Suppl 236:1+. PMID: 4886545.

Brewster, K. K., Ciarleglio, A., Brown, P. J., Chen, C., Kim, H.-O., Roose, S. P., Golub, J. S., & Rutherford, B. R. (2018). Age-Related Hearing Loss and Its Association with Depression in Later Life. Am J Geriatr Psychiatry 26(7), 788-796.

Brewster KK, Hu MC, Wall MM, Brown PJ, Zilcha-Mano S, Roose SP, Stein A, Golub JS, Rutherford BR. (2021). Age-Related Hearing Loss, Neuropsychological Performance, and Incident Dementia in Older Adults. J Alzheimers Dis, 80(2):855-864.

Buschke H, Fuld PA. (1974). Evaluating storage, retention, and retrieval in disordered memory and learning. Neurology, Nov;24(11):1019-25.

Campbell, N.G. (Lead Author), Alles, R., Bamiou, D., Batchelor, L., Canning, D., Grant, P., Luxon, L., Moore, D., Murray, P., Nairn, S., Rosen, S., Sirimanna, T., Treharne, D. and Wakeham, K. (2011). BSA Practice guidance: an overview of current management of auditory processing disorder (APD) British Society of Audiology 60pp.

Carhart, R., & Jerger, J. (1959). Preferred method for clinical determination of pure-tone thresholds. J. speech hear. disord, 24, 330-345.

Castiglione A, Benatti A, Velardita C, Favaro D, Padoan E, Severi D, Pagliaro M, Bovo R, Vallesi A, Gabelli C, Martini A. (2016). Ageing, Cognitive Decline and Hearing Loss: Effects of Auditory Rehabilitation and Training with Hearing Aids and Cochlear Implants on Cognitive Function and Depression among Older Adults. Audiol Neurootol, 21 Suppl 1:21-28

Chen J, Wang Z, Dong R, Fu X, Wang Y, Wang S. (2021, Apr). Effects of Wireless Remote Microphone on Speech Recognition in Noise for Hearing Aid Users in China. Front Neurosci, 12; 15:643205.

Chermak, G.D., & Musiek, F.E. (2002). Auditory Training: Principles and Approaches for Remediating and Manageing Auditory Processing Disorders. Seminars in Hearing, 23, 297-308.

Chermak, G. D. (2007). Central resources training: Cognitive, metacognitive, and metalinguistic skills and strategies. In G. D. Chermak & F. E. Musiek (Eds.), Handbook of (central) auditory processing disorder. Volume II: Comprehensive intervention (pp. 107–166). San Diego, CA: Plural

Clarkson C, Antunes FM, Rubio ME. (2016). Conductive Hearing Loss Has Long-Lasting Structural and Molecular Effects on Presynaptic and Postsynaptic Structures of Auditory Nerve Synapses in the Cochlear Nucleus. J Neurosci, Sep 28;36(39):10214-27.

Corso, J. F. (1959). Age and sex differences in pure-tone thresholds. J Acoust Soc Am, 31(4), 498-507.

Cooper JA, McNair L. (2015, Feb). Simplifying the complexity of confidentiality in research. J Empir Res Hum Res Ethics. 10(1):100-2.

Coughlin, S. S. (2006). Ethical issues in epidemiologic research and public health practice. Emerg. Themes Epidemiology, 3(1), 16.

Cruickshanks, K. J., Nondahl, D. M., Tweed, T. S., Wiley, T. L., Klein, B. E. K., Klein, R., Chappell, R., Dalton, D. S., & Nash, S. D. (2010). Education, occupation, noise exposure history and the 10-yr cumulative incidence of hearing impairment in older adults. Hear Res, 264(1-2), 3-9.

Cruickshanks, K. J., Wiley, T. L., Tweed, T. S., Klein, B. E. K., Klein, R., Mares-Perlman, J. A., & Nondahl, D. M. (1998). Prevalence of Hearing Loss in Older Adults in Beaver Dam, Wisconsin: The Epidemiology of Hearing Loss Study. Am. J. Epidemiol, 148(9), 879-886.

Cruickshanks KJ, Tweed TS, Wiley TL, Klein BE, Klein R, Chappell R, Nondahl DM, Dalton DS. (2003, Oct) The 5-year incidence and progression of hearing loss: the epidemiology of hearing loss study. Arch Otolaryngol Head Neck Surg, 129(10):1041-6.

Dalton, D. S., Cruickshanks, K. J., Klein, B. E. K., Klein, R., Wiley, T. L., & Nondahl, D. M. (2003). The Impact of Hearing Loss on Quality of Life in Older Adults. Gerontol, 43(5), 661-668.

Davignon DD, Leshowitz BH. (1986). The Speech-In-Noise test: a new approach to the assessment of communication capability of elderly persons. Int J Ageing Hum Dev, 23(2):149-60.

Dawes, P., Cruickshanks, K. J., Moore, D. R., Edmondson-Jones, M., McCormack, A., Fortnum, H., & Munro, K. J. (2014). Cigarette smoking, passive smoking, alcohol consumption, and hearing loss. J Assoc Res Otolaryngol, 15(4), 663-674.

Dawes, P., Emsley, R., Cruickshanks, K. J., Moore, D. R., Fortnum, H., Edmondson-Jones, M., McCormack, A., & Munro, K. J. (2015). Hearing Loss and Cognition: The Role of Hearing Aids, Social Isolation and Depression. PloS one, 10(3), e0119616.

Davis, A. (1989) The Prevalence of Hearing Impairment and Reported Hearing Disability among Adults in Great Britain. Int J Epidemiol, 18(4), 911-917.

Dhar, S., & Hall, J. W. (2011). Otoacoustic emissions: Principles, procedures, and protocols. San Diego, CA: Plural Publishing.

De Siati RD, Rosenzweig F, Gersdorff G, Gregoire A, Rombaux P, Deggouj N. (2020, Apr). Auditory Neuropathy Spectrum Disorders: From Diagnosis to Treatment: Literature Review and Case Reports. J Clin Med. 10;9(4):1074.

Deal, J. A., Sharrett, A. R., Albert, M. S., Coresh, J., Mosley, T. H., Knopman, D., Wruck, L. M., & Lin, F. R. (2015). Hearing Impairment and Cognitive Decline: A Pilot Study Conducted Within the Atherosclerosis Risk in Communities Neurocogntive Study. Am. J. Epidemiol, 181(9), 680-690.

Diez Roux AV. (2001, Nov). Investigating neighborhood and area effects on health. Am J Public Health, 91(11):1783-9.

Dobie, R. A. (1994). Separating noise-induced from age-related hearing loss. West J Med, 160(6), 564-565.

Dobie RA, Humes LE. (2017). Commentary on the regulatory implications of noise-induced cochlear neuropathy. Int J Audiol, 56(sup1):74-78.

Dubno JR, Dirks DD, Morgan DE. (1984, Jul). Effects of age and mild hearing loss on speech recognition in noise. J Acoust Soc Am. 76(1):87-96.

Dupuis, K., Pichora-Fuller, M. K., Chasteen, A. L., Marchuk, V., Singh, G., & Smith, S. L. (2015). Effects of hearing and vision impairments on the Montreal Cognitive Assessment. Neuropsychol Dev Cogn B Ageing Neuropsychol Cogn, 22(4), 413-437.

Dureman I, Kebbon L, Osterberg E. Manual till DS-batteriet [Manual of the DS-battery] (1971). Stockholm: Psykologiförlaget AB

Dureman, I., & Sälde, H. (1959). Psychometric and experimental psychological methods for clinical application. Stockholm, Sweden: Almquist & Wiksell.

Engdahl B, Strand BH, Aarhus L. (2020, Jan-Feb) Better Hearing in Norway: A Comparison of Two HUNT Cohorts 20 Years Apart. Ear Hear. 42(1):42-52.

Engdahl, B., Stigum, H., & Aarhus, L. (2021) Explaining better hearing in Norway: A comparison of two HUNT cohorts 20 years apart. BMC Public Health, Jan 28;21(1):242.

Era P, Jokela J, Qvarnberg Y, Heikkinen E. (1986). Pure-tone thresholds, speech understanding, and their correlates in samples of men of different ages. Audiology;25(6):338-352.

Fernandez, K. A., Jeffers, P. W. C., Lall, K., Liberman, M. C., & Kujawa, S. G. (2015). Ageing after Noise Exposure: Acceleration of Cochlear Synaptopathy in "Recovered" Ears Journ Neurosci, 35(19), 7509-7520.

Fifer, R. C., Jerger, J. F., Berlin, C. I., Tobey, E. A., & Campbell, J. C. (1983). Development of a dichotic sentence identification test for hearing-impaired adults. Ear Hear, 4(6), 300-305.

Folstein, M., Folstein, S., & McHugh, P. (1975). Mini-mental state (MMSE) J Psychiatr Res, 12.

Fratiglioni L, Wang HX, Ericsson K, Maytan M, Winblad B. (2000, Apr) Influence of social network on occurrence of dementia: a community-based longitudinal study. Lancet. 15;355(9212):1315-9

Gacek, R. R., & Schuknecht, H. F. (1969). Pathology of presbycusis. International Audiology, 8(2-3), 199-209.

Garibotto V, Borroni B, Kalbe E, Herholz K, Salmon E, Holtoff V, Sorbi S, Cappa S, Padovani A, Fazio F, Perani D. (2008). Education and occupation as proxies for reserve in a MCI converters and AD: FDG-PET evidence. Neurol 71: 1342–1349.

Gates GA, Popelka GR. Neural presbycusis: a diagnostic dilemma. (1992). Am J Otol. Jul;13(4):313-7. PMID: 1415492.

Gates, G. A., Cobb, J. L., D'Agostino, R. B., & Wolf, P. A. (1993). The relation of hearing in the elderly to the presence of cardiovascular disease and cardiovascular risk factors. Arch. Otorhinolaryngol, 119 (2), 156-161.

Gates, G. A. (2012). Central presbycusis: an emerging view. Otolaryngol Head Neck Surg, 147(1), 1-2.

Gates, G. A., Beiser, A., Rees, T. S., D'Agostino, R. B., & Wolf, P. A. (2002). Central Auditory Dysfunction May Precede the Onset of Clinical Dementia in People with Probable Alzheimer's Disease. J Am Geriatr Soc, 50(3), 482-488.

Gates, G. A., Cobb, J. L., Linn, R. T., Rees, T., Wolf, P. A., & D'Agostino, R. B. (1996). Central auditory dysfunction, cognitive dysfunction, and dementia in older people. Arch. otorhinolaryngol, 122(2), 161-167.

Gates, G. A., P. M. Feeney, and R. J. Higdon. (2003). Word Recognition and the Articulation Index in Older Listeners with Probable Age-Related Auditory Neuropathy. J Am Acad Audiol, 14 (10): 574–581.

Gates, G. A., Cooper Jr, J., Kannel, W. B., & Miller, N. J. (1990). Hearing in the Elderly: The Framingham Cohort, 1983-1985Part 1. Basic Audiometric Test Results. Ear and Hear, 11(4), 247-256.

Gates, G. A., Couropmitree, N. N., & Myers, R. H. (1999). Genetic associations in age-related hearing thresholds. Arch Otolaryngol Head Neck Surg, 125(6), 654-659.

Gates, G. A., & Mills, J. H. (2005) Presbycusis. The Lancet, 366(9491), 1111-1120.

Gates GA, Anderson ML, Feeney MP, McCurry SM, Larson EB. (2008, Jul). Central auditory dysfunction in older persons with memory impairment or Alzheimer dementia. Arch Otolaryngol Head Neck Surg, 134(7):771-7.

Gates GA, Feeney MP, Mills D. (2008, Dec) Cross-sectional age-changes of hearing in the elderly. Ear Hear. 29(6):865-74.

Gelfand, S. A. (2009). Essentials of audiology. New York: Thieme.

Glavin CC, Siegel J, Dhar S. (2021, Dec). Distortion Product Otoacoustic Emission (DPOAE) Growth in Ageing Ears with Clinically Normal Behavioural Thresholds. J Assoc Res Otolaryngol. 22(6):659-680.

Glorig, A., & Nixon, J. (1962). Hearing loss as a function of age. The Laryngoscope, 72(11), 1596-1610.

Goman, A. M., & Lin, F. R. (2016). Prevalence of Hearing Loss by Severity in the United States. American journal of public health, 106(10), 1820- 1822.

Gopinath, B., Rochtchina, E., Wang, J., Schneider, J., Leeder, S. R., & Mitchell, P. (2009). Prevalence of age-related hearing loss in older adults: Blue mountains study. Arch. Intern Med, 169(4), 415-418.

Gordon-Salant, S., & Fitzgibbons, P. J. (1993) Temporal factors and speech recognition performance in young and elderly listeners. J. Speech Lang Hear Res, 36(6), 1276-1285

Granberg S, Swanepoel de W, Englund U, Möller C, Danermark B. (2014, Aug) The ICF core sets for hearing loss project: International expert survey on functioning and disability of adults with hearing loss using the international classification of functioning, disability, and health (ICF). Int J Audiol,53(8):497-506.

Grant KJ, Parthasarathy A, Vasilkov V, Caswell-Midwinter B, Freitas ME, de Gruttola V, Polley DB, Liberman MC, Maison SF. (2022, Jun) Predicting neural deficits in sensorineural hearing loss from word recognition scores. Sci Rep, 23;12(1):8929.

Gratton MA, Bateman K, Cannuscio JF, Saunders JC. (2008). Outer- and middle-ear contributions to presbycusis in the Brown Norway rat. Audiol Neurootol, 13(1):37-52.

Göthberg H, Rosenhall U, Tengstrand T, Rydberg Sterner T, Wetterberg H, Zettergren A, Skoog I, Sadeghi A. (2019). Cross-sectional assessment of hearing acuity of an unscreened 85-year-old cohort - Including a 10-year longitudinal study of a sub-sample. Hear Res, 382:107797.

Göthberg H, Rosenhall U, Tengstrand T, Rydén L, Wetterberg H, Skoog I, Sadeghi A. (2021, Jul). Prevalence of hearing loss and need for aural rehabilitation in 85-year-olds: a birth cohort comparison, almost three decades apart. Int J Audiol. 60(7):539-548.

Göthberg H, Skoog I, Tengstrand T, Magnusson L, Hoff M, Rosenhall U, Sadeghi A. (2023, May). Pathophysiological and Clinical Aspects of Hearing Loss Among 85-Year-Olds. Am J Audiol, 17:1-13.

Hall, J. W. (2000) Handbook of otoacoustic emissions. Cengage Learning. Hall, J. W., & Swanepoel, D. W. (2009). Objective assessment of hearing. Plural Publishing. 91

Harrison Bush AL, Lister JJ, Lin FR, Betz J, Edwards JD. (2015, Jul-Aug). Peripheral Hearing and Cognition: Evidence From the Staying Keen in Later Life (SKILL) Study. Ear Hear. 36(4):395-407.

Harty M. (1953.) Elastic tissue in the middle-ear cavity. J Laryngol Otol, Dec;67(12):723-9.

Harvey, P. D. (2019). Domains of cognition and their assessment. Dialogues Clin, 21(3), 227-237.

Hayflick, L. (2000). New approaches to old age. Nature, 403(6768), 365-365.

Hederstierna, C., Hultcrantz, M., Collins, A., & Rosenhall, U. (2007). Hearing in women at menopause. Prevalence of hearing loss, audiometric configuration and relation to hormone replacement therapy. Acta otolaryngol, 127(2), 149-155.

Hederstierna, C., & Rosenhall, U. (2016) Age-related hearing decline in individuals with and without occupational noise exposure. Noise Health, 18(80), 21-25.

Helzner, E. P., Cauley, J. A., Pratt, S. R., Wisniewski, S. R., Zmuda, J. M., Talbott, E. O., Rekeneire, N., Harris, T. B., Rubin, S. M., & Simonsick, E. M.

(2005). Race and sex differences in age-related hearing loss: The Health, Ageing and Body Composition Study. J Am Geriatr Soc, 53(12), 2119-2127.

Hind, S. E., Haines-Bazrafshan, R., Benton, C. L., Brassington, W., Towle, B., & Moore, D. R. (2011). Prevalence of clinical referrals having hearing thresholds within normal limits. Int J Audiol, 50(10), 708-716.

Hinojosa R, Nelson EG. (2011, Dec). Cochlear nucleus neuron analysis in individuals with presbycusis. Laryngoscope 121(12):2641-8.

Hoben R, Easow G, Pevzner S, Parker MA. (2017) Outer Hair Cell and Auditory Nerve Function in Speech Recognition in Quiet and in Background Noise. Front Neurosci, April 7; 11:157.

Hoff M, Tengstrand T, Sadeghi A, Skoog I, Rosenhall U. (2018, May). Improved hearing in Swedish 70-year olds-a cohort comparison over more than four decades (1971-2014). Age Ageing, 1;47(3):437-444.

Hoff M., T. Tengstrand, A. Sadeghi, I. Skoog & U. Rosenhall. (2020). Auditory function and prevalence of specific ear and hearing related pathologies in the general population at age 70. Int J Audiol, 59:9: 682-693,

Hoff M, Skoog J, Bodin TH, Tengstrand T, Rosenhall U, Skoog I, Sadeghi A. (2023). Hearing Loss and Cognitive Function in Early Old Age: Comparing Subjective and Objective Hearing Measures. Gerontol.;69(6):694-705.

Hoff M, Göthberg H, Tengstrand T, Rosenhall U, Skoog I, Sadeghi A. (2023, jun). Accuracy of automated pure-tone audiometry in population-based samples of older adults. Int J Audiol, 19:1-9.

Hoffman, H. J., Dobie, R. A., Ko, C. W., Themann, C. L., & Murphy, W. J. (2010). Americans hear as well or better today compared with 40 years ago: hearing threshold levels in the unscreened adult population of the United States, 1959-1962 and 1999-2004. Ear Hear, 31(6), 725-734.

Homans, N. C., Metselaar, R. M., Dingemanse, J. G., van der Schroeff, M. P., Brocaar, M. P., Wieringa, M. H., Baatenburg de Jong, R. J., Hofman, A., & Goedegebure, A. (2017). Prevalence of age-related hearing loss, including sex differences, in older adults in a large cohort study. Laryngoscope, 127(3), 725-730.

Hoops S, Nazem S, Siderowf AD, Duda JE, Xie SX, Stern MB, Weintraub D. (2009, Nov) Validity of the MoCA and MMSE in the detection of MCI and dementia in Parkinson disease. Neurology, 24;73(21):1738-45.

Hu H, Tomita K, Kuwahara K, Yamamoto M, Uehara A, Kochi T, Eguchi M, Okazaki H, Hori A, Sasaki N, Ogasawara T, Honda T, Yamamoto S, Nakagawa T, Miyamoto T, Imai T, Nishihara A, Nagahama S, Murakami T, Shimizu M, Akter S, Kashino I, Yamaguchi M, Kabe I, Mizoue T, Sone T, Dohi S; (2020) Japan Epidemiology Collaboration on Occupational Health Study Group. Obesity and risk of hearing loss: A prospective cohort study. Clin Nutr. Mar;39(3):870-875.

Humes, L. E. (1996). Speech understanding in the elderly. J Acoust Soc Am, 161–167.

Humes L.E. and Dubmo, J. R., (2012). Central presbyacusis: a review and evaluation of the evidence. J Am Acad Audiol, 23, 635-666.

Humes LE, Busey TA, Craig J, Kewley-Port D. (2013, Apr). Are age-related changes in cognitive function driven by age-related changes in sensory processing? Atten Percept Psychophys, 75(3):508-24.

Hällgren, M., Johansson, M., Larsby, B., and Arlinger, S (1998). Dichotic speech tests. Scand Audiol, Supplement, 49, 35

Hällgren M, Larsby B, Lyxell B, Arlinger S (2001, Apr). Cognitive effects in dichotic speech testing in elderly persons. Ear Hear,22(2):120-9.

Idrizbegovic E, Hederstierna C, Dahlquist M, Kämpfe Nordström C, Jelic V, Rosenhall U. (2011, Mar) Central auditory function in early Alzheimer's disease and in mild cognitive impairment. Age Ageing. 40(2):249-54.

Iliadou V, Iakovides S. (2003, May). Contribution of psychoacoustics and neuroaudiology in revealing correlation of mental disorders with central auditory processing disorders. Ann Gen Hosp Psychiatry, 20;2(1):5.

International Organization for Standardization. (2010). Acoustics-Audiometric Test Methods-Part 1: Pure-Tone Air and Bone Conduction Audiometry (ISO 8253-1:2010).

International Organization for Standardization. (2010). Acoustics-Audiometric Test Methods-Part 3: Speech audiometry (ISO 8253-3:2010).

International Organization for Standardization. (2017). Acoustics — Statistical distribution of hearing thresholds related to age and gender (ISO 7029:2017).

International Organization for Standardization. (2010). Acoustics – audiometric test methods - Part 1: Pure-tone air and bone conduction audiometry (ISO 8253-1:2010).

Jayakody, D. M., Friedland, P. L., Martins, R. N., and Sohrabi, H. R. (2018a) Impact of ageing on the auditory system and related cognitive functions: a narrative review. Front. Neurosci. 12:125.

Jayakody, D. M. P., Friedland, P. L., Eikelboom, R. H., Martins, R. N., & Sohrabi, H. R. (2018b) A novel study on association between untreated hearing loss and cognitive functions of older adults: Baseline non-verbal cognitive assessment results. Clin Otolaryngol, 43(1), 182- 191.

Jerger, J., Jerger, S., Oliver, T., & Pirozzolo, F. (1989). Speech understanding in the elderly. Ear Hear, 10, 79–89.

Jerger, J. & Martin, J. (2006). Dichotic listening tests in the assessment of auditory processing disorders. Audiol Med, 4, 25–34

Jerger, J., Chmiel, R., Stach, B., & Spretnjak, M. (1993). Gender affects audiometric shape in presbyacusis. J Am Acad Audiol, 4(1), 42-49.

Jerger, J., & Hall, J. (1980). Effects of age and sex on auditory brainstem response. Arch. Otolaryngol, 106(7), 387-391.

Jonsson, R., & Rosenhall, U. (1998). Hearing in advanced age. A study of presbyacusis in 85-, 88- and 90-year-old people. Audiol, 37(4), 207-218.

Joo Y, Cruickshanks KJ, Klein BEK, Klein R, Hong O, Wallhagen M. (2018, Jan) Prevalence of ototoxic medication use among older adults in Beaver Dam, Wisconsin. J Am Assoc Nurse Pract, 30(1):27-34.

Jönsson R, Rosenhall U. (1998). Hearing in advanced age. A study of presbyacusis in 85-, 88- and 90-year-old people. Audiology. 1998 Jul-Aug;37(4):207-18. Kamm CA, Dircks DD, Bell TS. (1985) Speech recognition and the articulation index for normal and hearing-impaired listeners. J. Acoust Soc Am, 77:281-8.

Kemp, D. (1980) The significance of otoacoustic emissions. Psychophysical, Physiological and Behavioural Studies in Hearing, Delft University Press, Delft, the Netherlands, 75-76.

Kertesz, A. (1982). Western Aphasia Battery. San Antonio, TX. The Psychological Corporation.

Kimura, D. (1967). Functional asymmetry of the brain in dichotic listening. Cortex 3,163–178

Kricos, P. B. (2006). Audiologic management of older adults with hearing loss and compromised cognitive/psychoacoustic auditory processing capabilities. Trends Amplif, 10(1), 1-28.

Kujawa, S. G., & Liberman, M. C. (2009). Adding insult to injury: cochlear nerve degeneration after "temporary" noise-induced hearing loss. Journal of Neuroscience, 29(45), 14077-14085. Laplante-Lévesque, A., Hickson, L., & Worrall, L. (2010). Rehabilitation of Older Adults with Hearing Impairment: A Critical Review. J Ageing Health., 22(2), 143-153.

Lee, F. S., Matthews, L. J., Dubno, J. R., & Mills, J. H. (2005). Longitudinal study of pure-tone thresholds in older persons. Ear Hear, 26(1), 1-11.

Lesner SA. Candidacy and management of assistive listening devices: special needs of the elderly. Int J Audiol. 2003 Jul;42 Suppl 2:2S68-76. PMID: 12918632.

Liberman MC, Kujawa SG. (2017, Jun) Cochlear synaptopathy in acquired sensorineural hearing loss: Manifestations and mechanisms. Hear Res, 2017 349:138-147.

Lin, F. R., & Ferrucci, L. (2012). Hearing loss and falls among older adults in the United States. Archives of internal medicine, 172(4), 369-371.

Lin, F. R., Thorpe, R., Gordon-Salant, S., & Ferrucci, L. (2011a), Hearing Loss Prevalence and Risk Factors Among Older Adults in the United States. J Gerontol A Biol Sci Med, 66A (5), 582-590.

Lin, F. R., Ferrucci, L., Metter, E. J., An, Y., Zonderman, A. B., & Resnick, S. M. (2011b). Hearing loss and cognition in the Baltimore Longitudinal Study of Ageing. Neuropsychology, 25(6), 763-770.

Lin, F. R., Yaffe, K., Xia, J., Xue, Q. L., Harris, T. B., Purchase-Helzner, E., Satterfield, S., Ayonayon, H. N., Ferrucci, L., & Simonsick, E. M. (2013). Hearing loss and cognitive decline in older adults. JAMA Intern Med, 173(4), 293-299.

Lin FR, Pike JR, Albert MS, Arnold M, Burgard S, Chisolm T, Couper D, Deal JA, Goman AM, Glynn NW, Gmelin T, Gravens-Mueller L, Hayden KM, Huang AR, Knopman D, Mitchell CM, Mosley T, Pankow JS, Reed NS, Sanchez V, Schrack JA, Windham BG, Coresh J; (2023, Jul) ACHIEVE Collaborative Research Group. Hearing intervention versus health education control to reduce cognitive decline in older adults with hearing loss in the USA (ACHIEVE): a multicentre, randomised controlled trial. Lancet. 17:S0140-6736(23)01406-X.

*Lindbergh, C.A., Dishman, R.K. & Miller, L.S. (2016). Functional Disability in Mild Cognitive Impairment: A Systematic Review and Meta-Analysis. Neuropsychol Rev **26**, 129–159 (2016).*

Lindenberger, U., & Baltes, P. (1995). Cognitive capacity in advanced age: initial results of the Berlin Ageing Study. Z Psychol Z Angew Psychol, 203(4), 283.

Livingston G, Huntley J, Sommerlad A, Ames D, Ballard C, Banerjee S, Brayne C, Burns A, Cohen-Mansfield J, Cooper C, Costafreda SG, Dias A, Fox N, Gitlin LN, Howard R, Kales HC, Kivimäki M, Larson EB, Ogunniyi A, Orgeta V, Ritchie K, Rockwood K, Sampson EL, Samus Q, Schneider LS, Selbæk G, Teri L, Mukadam N. (2020, Aug) Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. Lancet. 8;396(10248):413-446.

Lloyd-Sherlock P, McKee M, Ebrahim S, Gorman M, Greengross S, Prince M, Pruchno R, Gutman G, Kirkwood T, O'Neill D, Ferrucci L, Kritchevsky SB, Vellas B. (2012, Apr) Population ageing and health. Lancet, 7;379(9823):1295-6.

Lopez-Poveda EA, Barrios P. (2013, Jul) Perception of stochastically undersampled sound waveforms: a model of auditory deafferentation. Front. Neurosci, 16; 7:124.

Loughrey DG, Parra MA, Lawlor BA. (2019, Aug) Visual short-term memory binding deficit with age-related hearing loss in cognitively normal older adults. Sci Rep. 29;9(1):12600.

Loughrey DG, Pakhomov SVS, Lawlor BA. (2020, Feb) Altered verbal fluency processes in older adults with age-related hearing loss. Exp Gerontol, 130:110794. doi: 10.1016/j.exger.2019.110794.

Magnusson, L. (1995). Reliable Clinical Determination of Speech Recognition Scores Using Swedish PB Words in Speech-weighted Noise. Scand. Audiol 24(4), 217-223.

Magnusson, L. (1996a). Predicting the Speech Recognition Performance of Elderly Individuals with Sensorineural Hearing Impairment A Procedure Based on the Speech Intelligibility Index. Scand. n Audiol, 25(4), 215-222.

Magnusson, L. (1996b). Speech intelligibility index transfer functions and speech spectra for two Swedish speech recognition tests. Scand Audiol, 25(1), 59-67.

Magnusson L, Karlsson M, Leijon A. (2001). Predicted and measured speech recognition performance in noise with linear amplification. Ear Hear, 22(1):46-57.

Malmberg, M., Lunner, T., Kähäri, K., & Andersson, G. (2017). Evaluating the short-term and long-term effects of an internet-based aural rehabilitation programme for hearing aid users in general clinical practice: a randomised controlled trial. BMJ open, 7(5).

Margolis, R. H., & Morgan, D. E. (2008). Automated Pure-Tone Audiometry: An Analysis of Capacity, Need, and Benefit. Am J Audiol, 17(2), 109- 113.

Margolis, R. H., Frisina, R., & Walton, J.P. (2011). AMTAS: Automated method for testing auditory sensitivity: II. Air conduction audiograms in children and adults. Int J Audiol, 50: 434-439

Masic I, Hodzic A, Mulic S. (2014). Ethics in medical research and publication. Int J Prev Med, Sep;5(9):1073-82. PMID: 25317288; PMCID: PMC4192767.

Mathers, C. D., Stevens, G. A., Boerma, T., White, R. A., & Tobias, M. I. (2015) Causes of international increases in older age life expectancy. The Lancet, 385(9967), 540-548.

McArdle RA, Wilson RH, Burks CA. (2005, Oct) Speech recognition in multitalker babble using digits, words, and sentences. J Am Acad Audiol, 16(9):726-39; quiz 763-4.

McDaid D, Park AL, (2021). Chadha S. Estimating the global costs of hearing loss. Int J Audiol. 2021;60(3):162-170.

Miltenberger GE, Dawson GJ, Raica AN. (1978, Jan). Central auditory testing with peripheral hearing loss. Arch Otolaryngol, 104(1):11-5.

Murman DL. (2015, Aug). The Impact of Age on Cognition. Semin Hear, 36(3):111-21.

Musiek, F.E., Shinn, J.B., Jirsa, R., Bamiou, D.E., Baran, J.A, & Zaidan, E. (2005). The GIN (Gaps-in-Noise) Test performance in subjects with and without confirmed central auditory nervous system involvement, Ear and Hear, 26(6), 608-618

Musiek, F.E., Baran, J.A., & Pinheiro, M. (1990). Duration pattern recognition in normal subjects and in patients with cerebral and cochlear lesions. Audiology, 29(6), 304-313.

Musiek FE. (1983 Mar-Apr). Assessment of central auditory dysfunction: the dichotic digit test revisited. Ear and Hear, 4(2):79-83.

Molaug I, Engdahl B, Degerud E, Mehlum IS, Aarhus L. (Dec 2022). Occupation and 20-year hearing decline: findings from The HUNT Study. Occup Med (Lond). 31;72(9):622-628.

Moore, D. R., Edmondson-Jones, M., Dawes, P., Fortnum, H., McCormack, A., Pierzycki, R. H., et al. (2014). Relation between speech-in-noise threshold, hearing loss and cognition from 40–69 years of age. PLoS One 9: e107720.

Moore, David & Campbell, Nicole & Rosen, Stuart & Bamiou, Doris-Eva & Sirimanna, Tony & Grant, Pauline & Wakeham, Kelvin. (2018). Position Statement and Practice Guidance Auditory Processing Disorder (APD).

Moser T, Predoehl F, Starr A. (2013, Aug) Review of hair cell synapse defects in sensorineural hearing impairment. Otol Neurotol, 34(6):995-1004.

Møller MB. Hearing in 70 and 75 year old people: results from a cross sectional and longitudinal population study. (1981 Feb), Am J Otolaryngol.;2(1):22-9.

Ng L, Kelley MW, Forrest D. (2013, May) Making sense with thyroid hormone--the role of T (3) in auditory development. Nat Rev Endocrinol, 9(5):296-307.

Neijenhuis K, Campbell NG, Cromb M, Luinge MR, Moore DR, Rosen S, de Wit E. (2019, Mar). An Evidence-Based Perspective on "Misconceptions" Regarding Pediatric Auditory Processing Disorder. Front Neurol. 26;10:287.

Newman, D. L., Fisher, L. M., Ohmen, J., Parody, R., Fong, C. T., Frisina, S. T., Mapes, F., Eddins, D. A., Robert Frisina, D., Frisina, R. D., & Friedman, R. A. (2012). GRM7 variants associated with age-related hearing loss based on auditory perception. Hearing Res, 294(1- 2), 125-132.

Newton VE, Shah SR. (2013) Improving communication with patients with a hearing impairment. Community Eye Health J. 26(81):6-7.

Nixon G, Sarant JZ, Tomlin D, Dowell R. (2019, Dec). The relationship between peripheral hearing loss and higher order listening function on cognition in older Australians. Int J Audiol, Dec;58(12):933-944.

Ohlemiller, K.K., Frisina, R.D. (2008). Age-Related Hearing Loss and Its Cellular and Molecular Bases. In: Schacht, J., Popper, A.N., Fay, R.R. (eds) Auditory Trauma, Protection, and Repair. Springer Handbook of Auditory Research, vol 31. Springer, Boston, MA.

Olusanya, B. O., Davis, A. C., & Hoffman, H. J. (2019). Hearing loss grades and the International classification of functioning, disability and health. Bulletin of the World Health Organization, 97(10), 725.

Ouda L, Profant O, Syka J. (2015, Jul) Age-related changes in the central auditory system. Cell Tissue Res, 361(1):337-58.

Panza F, Solfrizzi V, Logroscino G. (2015, Mar) Age-related hearing impairment-a risk factor and frailty marker for dementia and AD. Nat Rev Neurol, 11(3):166-75.

Panza F, Lozupone M, Sardone R, Battista P, Piccininni M, Dibello V, La Montagna M, Stallone R, Venezia P, Liguori A, Giannelli G, Bellomo A, Greco A, Daniele A, Seripa D, Quaranta N, Logroscino G. (2018a, Nov) Sensorial frailty: age-related hearing loss and the risk of cognitive impairment and dementia in later life. Ther Adv Chronic Dis, 9; 10:2040

Panza, F., Quaranta, N., and Logroscino, G. (2018b). Sensory changes and the hearing loss–cognition link: the cognitive ear. JAMA Otolaryngol. Head Neck Surg. 144, 127–128.

Pavlovic CV, Studebaker GA, Sherbecoe RL. (1986). An articulation index-based procedure for predicting the speech recognition performance of hearing-impaired individuals. Journal Acoustic Society Am. Jul;80(1):50-7.

Pearson, J. D., Morrell, C. H., Gordon-Salant, S., Brant, L. J., Metter, E. J., Klein, L. L., & Fozard, J. L. (1995). Gender differences in a longitudinal study of age-associated hearing loss. J Acoust, 97 (2), 1196-1205.

Pedersen, K. E., Rosenhall, U., & Moller, M. B. (1989). Changes in pure-tone thresholds in individuals aged 70-81: results from a longitudinal study. Audiology, 28(4), 194-204.

Peelle JE, Troiani V, Grossman M, Wingfield A. (2011,Aug). Hearing loss in older adults affects neural systems supporting speech comprehension. J Neurosci, 31;31(35):12638-43.

Peelle JE, Wingfield A. (2016, Jul). The Neural Consequences of Age-Related Hearing Loss. Trends Neurosci. 39(7):486–497.

Pichora-Fuller, M. K., Mick, P., & Reed, M. (2015). Hearing, Cognition, and Healthy Ageing: Social and Public Health Implications of the Links between Age-Related Declines in Hearing and Cognition. Semin Hear, 36(3), 122-139.

Prosser, S., & Arslan, E. (1987). Prediction of auditory brainstem wave V latency as a diagnostic tool of sensorineural hearing loss. Audiology, 26(3), 179-187.

Quaranta, N., Coppola, F., Casulli, M., Barulli, O., Lanza, F., Tortelli, R., Capozzo, R., Leo, A., Tursi, M., Grasso, A., Solfrizzi, V., Sobbà, C., & Logroscino, G. (2014) The Prevalence of Peripheral and Central Hearing Impairment and Its Relation to Cognition in Older Adults. Audiol. Neurotol., 19(suppl 1) (Suppl. 1), 10-14.

Ramadan, H. H., & Schuknecht, H. F. (1989). Is there a conductive type of presbycusis? Otolaryngol, 100(1), 30- 34.

Reynard P, Lagacé J, Joly CA, Dodelé L, Veuillet E, Thai-Van H. (2022). Speech-in-Noise Audiometry in Adults: A Review of the Available Tests for French Speakers. Audiol Neurootol. 27(3):185-199.

Rigters SC, van der Schroeff MP, Papageorgiou G, Baatenburg de Jong RJ, Goedegebure A. (2018) Progression of Hearing Loss in the Aging Population: Repeated Auditory Measurements in the Rotterdam Study. Audiol Neurootol. 23(5):290-297.

Rhode WS. (1971, Apr). Observations of the vibration of the basilar membrane in squirrel monkeys using the Mössbauer technique. J Acoust Soc Am, 49(4): Suppl 2:1218

Rosen, W. G., Mohs, R. C., & Davis, K. L. (1984). A new rating scale for Alzheimer's disease. The American journal of psychiatry.

Rosenhall, U., Hederstierna, C., & Idrizbegovic, E. (2011, Sep). Otological diagnoses and probable age-related auditory neuropathy in "younger" and "older" elderly persons. Int J Audiol, 50(9), 578-581.

Rosenhall, U., Idrizbegovic, E., Hederstierna, C., & Rothenberg, E. (2015). Dietary habits and hearing. Int J Audiol, 54 Suppl 1, S53-56.

Rosenhall, U., Pedersen, K., & Dotevall, M. (1986). Effects of presbycusis and other types of hearing loss on auditory brainstem responses. Scand Audiol, 15(4), 179-185.

Rosenhall, U., Pedersen, K., & Svanborg, A. (1990). Presbycusis and noise induced hearing loss. Ear and Hear, 11(4), 257-263.

Rosenhall U, Karlsson Espmark AK. (2003). Hearing aid rehabilitation: what do older people want, and what does the audiogram tell? Int J Audiol, Jul;42 Suppl 2:2S53-7. PMID: 12918629.

Roth, T. N., Hanebuth, D., & Probst, R. (2011). Prevalence of age-related hearing loss in Europe: a review. Eur Arch Otorhinolaryngol, 268(8), 1101-1107.

Rodriguez GP, DiSarno NJ, Hardiman CJ. Central auditory processing in normal-hearing elderly adults. Audiology. 1990;29(2):85-92. doi: 10.3109/00206099009081649. PMID: 2350306.

Rumalla, K., Karim Adham, M., & Hullar Timothy, E. (2014). The effect of hearing aids on postural stability. The Laryngoscope, 125(3), 720-723.

Rydberg Sterner T, Ahlner F, Blennow K, Dahlin-Ivanoff S, Falk H, Havstam Johansson L, Hoff M, Holm M, Hörder H, Jacobsson T, Johansson B, Johansson L, Kern J, Kern S, Machado A, Mellqvist Fässberg M, Nilsson J, Ribbe M, Rothenberg E, Rydén L, Sadeghi A, Sacuiu S, Samuelsson J, Sigström R, Skoog J, Thorvaldsson V, Waern M, Westman E, Wetterberg H, Zetterberg H, Zetterberg M, Zettergren A, Östling S, Skoog I. (2019, Feb). The Gothenburg H70 Birth cohort study. 16: design, methods and study population. Eur J Epidemiol, 34(2):191-209.

Rönnberg J, Danielsson H, Rudner M, Arlinger S, Sternäng O, Wahlin A, Nilsson LG. (2011, April). Hearing loss is negatively related to episodic and semantic long-term memory but not to short-term memory. J Speech Lang Hear Res, Apr;54(2):705-26.

Salerno J, Peters ES, Pinney SM, Morain S, Hlaing WM. (2019, June). Untangling the ethical intersection of epidemiology, human subjects research, and public health. Ann Epidemiol. 34:1-5.

Samocha-Bonet D, Wu B, Ryugo DK. (2021). Diabetes mellitus and hearing loss: A review. Ageing Res Rev. Nov;71:101423.

Sanders ME, Kant E, Smit AL, Stegeman I. (2021, Dec) The effect of hearing aids on cognitive function: A systematic review. PLoS One, 31;16(12): e0261207.

Samtani S, Mahalingam G, Lam BCP, Lipnicki DM, Lima-Costa MF, Blay SL, Castro-Costa E, Shifu X, Guerchet M, Preux PM, Gbessemehlan A, Skoog I, Najar J, Rydberg Sterner T, Scarmeas N, Kim KW, Riedel-Heller S, Röhr S, Pabst A, Shahar S, Numbers K, Ganguli M, Jacobsen E, Hughes TF, Crowe M, Ng TP, Maddock J, Marseglia A, Mélis R, Szcześniak D, Wiegelmann H, Vernooij-Dassen M, Jeon YH, Sachdev PS, Brodaty H; (2022, Nov). SHARED consortium for the Cohort Studies of Memory in an International Consortium (COSMIC). Associations between social connections and cognition: a global collaborative individual participant data meta-analysis. Lancet Healthy Longev. Nov;3(11):e740-e753.

Sardone, R., Battista, P., Panza, F., Lozupone, M., Griseta, C., Castellana, F., Capozzo, R., Ruccia, M., Resta, E., Seripa, D., Logroscino, G., & Quaranta, N. (2019). The Age-Related Central Auditory Processing Disorder: Silent Impairment of the Cognitive Ear [Mini Review]. Front, 13(619).

Sardone R, Castellana F, Bortone I, Lampignano L, Zupo R, Lozupone M, Griseta C, Dibello V, Seripa D, Guerra V, Donghia R, Logroscino G, Solfrizzi V, Quaranta N, Ferrucci L, Giannelli G, Panza F. (2021) Association Between Central and Peripheral Age-Related Hearing Loss and Different Frailty Phenotypes in an Older Population in Southern Italy. JAMA Otolaryngol Head Neck Surg, Jun 1;147(6):561-571.

*Saunders, G.H., C. Vercammen, B. H.
B. Timmer, G. Singh, A. Pelosi, M. Meis, S. Launer, S. E. Kramer, J.-P. Gagné, and A. E. Bott. (2021). "Changing the narrative for hearing health in the broader context of healthy living: A call to action." Intern Journ of Audiol 1905892.*

Scarmeas N, Stern Y. (2003, Aug) Cognitive reserve and lifestyle. J Clin Exp Neuropsychol, 25(5):625-33.

Schmiedt RA (2010). The physiology of cochlear Presbycusis. In: Gordon-Salant S, Frisina R, Popper A, Fay R (eds) The ageing auditory system. Springer handbook of auditory research. Springer, New York, USA, pp 9–38

Sininger, Y. S., Hood, L. J., Starr, A., Berlin, C. T., Picton, T. W. (1995). Hearing loss due to auditory neuropathy. Audiology Today, 7, 16–18.

Statistics Sweden (SCB), (2018). The future population of Sweden 2012–2060. Retrieved 2018 May 12 from https://www.scb.se/statistik/_publikationer/BE0401_2012I60_BR_BE51BR1202ENG.pdf

Schuknecht, H. F. (1955). Presbycusis. The Laryngoscope, 65(6), 402-419.

Schuknecht, H. F. (1964). Further observations on the pathology of presbycusis. Arch Otolaryngol, 80(4), 369-382.

Schuknecht, H. F., & Gacek, M. R. (1993). Cochlear pathology in presbycusis. Ann Otol Rhinol Laryngol, 102(1 Pt 2), 1-16.

Shinn-Cunningham BG, Best V. (2008, Dec). Selective attention in normal and impaired hearing. Trends Amplif, 12(4):283-99.

Silman S, Silverman CA, Emmer MB, Gelfand SA. (1992, Nov). Adult-onset auditory deprivation. J Am Acad Audiol, 3(6):390-6.

Starr A, Picton TW, Sininger Y, Hood LJ, Berlin CI. (1996). Auditory neuropathy. Brain, 119(Pt 3):741-53.

Statistics Sweden (SCB) 2020. The future population of Sweden 2020-2070

Stevens, G., Flaxman, S., Brunskill, E., Mascarenhas, M., Mathers CD, Finucane M; on behalf of the Global Burden of Disease Hearing Loss Expert Group (2013). Global and regional hearing impairment prevalence: an analysis of 42 studies in 29 countries. Eur J Public Health, 23 (1), 146-152.

Stiefel MC, Perla RJ, Zell BL. (2010, Mar). A healthy bottom line: healthy life expectancy as an outcome measure for health improvement efforts. Milbank Q, 88(1):30-53.

Stover L, Gorga MP, Neely ST, Montoya D. (1996, Aug) Toward optimizing the clinical utility of distortion product otoacoustic emission measurements. J Acoust Soc Am, 100(2 Pt 1):956-67.

Swanepoel, D. W., Clark, J. L., Koekemoer, D., Hall Iii, J. W., Krumm, M., Ferrari, D. V., McPherson, B., Olusanya, B. O., Mars, M., Russo, I., & Barajas, J. J. (2010a). Telehealth in audiology: The need and potential to reach underserved communities. Int J Audiol, 49(3), 195-202.

Swanepoel de W, Mngemane S, Molemong S, Mkwanazi H, Tutshini S. (2010b, Jun) Hearing assessment-reliability, accuracy, and efficiency of automated audiometry. Telemed J E Health. 16(5):557-63.

Taljaard DS, Olaithe M, Brennan-Jones CG, Eikelboom RH, Bucks RS. (2016, Dec) The relationship between hearing impairment and cognitive function: a meta-analysis in adults. Clin Otolaryngol. 41(6):718–729.

Tay T, Kifley A, Lindley R, Landau P, Ingham N, Mitchell P, Wang JJ. (2006, Apr) Are sensory and cognitive declines associated in older persons seeking aged care services? Findings from a pilot study. Ann Acad Med Singap. 35(4):254-9.

Timmer BHB, Bennett RJ, Montano J, Hickson L, Weinstein B, Wild J, Ferguson M, Holman JA, LeBeau V, Dyre L. (2023, Mar). Social-emotional well-being and adult hearing loss: clinical recommendations. Int J Audiol. 24:1-12.

Thurstone, L. L. (1938). Primary mental abilities (Vol. 119). UCP, Chicago.

Torre, P., Cruickshanks, K. J., Nondahl, D. M., & Wiley, T. L. (2003). Distortion product otoacoustic emission response characteristics in older adults. Ear and Hear, 24(1), 20-29.

Tremblay KL, Piskosz M, Souza P. (2003, Jul). Effects of age and age-related hearing loss on the neural representation of speech cues. Clin Neurophysiol, 114(7):1332-43.

Tu NC, Friedman RA. (2018, Feb). Age-related hearing loss: Unraveling the pieces. Laryngoscope Investig Otolaryngol. 21;3(2):68-72.

Uchida, Y., Ando, F., Nakata, S., Ueda, H., Nakashima, T., Niino, N., & Shimokata, H. (2006). Distortion product otoacoustic emissions and tympanometric measurements in an adult population-based study. Auris Nasus Larynx, 33(4), 397-401.

Uchida, Y., Sugiura, S., Nishita, Y., Saji, N., Sone, M., & Ueda, H. (2019). Age-related hearing loss and cognitive decline - The potential mechanisms linking the two. Auris Nasus Larynx, 46(1), 1-9.

Valentijn SA, et al. (2005). Change in sensory functioning predicts change in cognitive functioning: results from a 6-year follow-up in the Maastricht ageing study. J Am Geriatr Soc, 53(3):374–380.

Vaughan, N., Storzbach, D., and Furukawa, I. (2008). Investigation of potential cognitive tests for use with older adults in audiology clinics. J. Am. Acad. Audiol. 197, 533–541.

Verhaeghen P, Salthouse TA. (1997, Nov). Meta-analyses of age-cognition relations in adulthood: estimates of linear and nonlinear age effects and structural models. Psychol Bull, Nov;122(3):231-49.

Vinck, B. M., De Vel, E., Xu, Z.-M., & Cauwenberge, P. B. J. (1996). Distortion Product Otoacoustic Emissions: A Normative Study. Audiol, 35(5), 231-245.

von Gablenz, P., Hoffmann, E., & Holube, I. (2020). Gender-specific hearing loss in German adults aged 18 to 84 years compared to US-American and current European studies. PloS one, 15(4), e0231632-e0231632.

van Rooij, J. C., & Plomp, R. (1990). Auditive and cognitive factors in speech perception by elderly listeners. J Acoust Soc Am, 87(S1), S25-S26.

Wang X, Cheng Z. (2020, Jul) Cross-Sectional Studies: Strengths, Weaknesses, and Recommendations. Chest. 158(1S): S65-S71.

Wilson RH, McArdle R. (2005, Jul-Aug) Speech signals used to evaluate functional status of the auditory system. J Rehabil Res Dev, 42(4 Suppl 2):79-94.

Wong PC, Jin JX, Gunasekera GM, Abel R, Lee ER, Dhar S. (2009). Ageing and cortical mechanisms of speech perception in noise. Neuropsychologia 47: 693–703, 2009.

Winblad B, Palmer K, Kivipelto M, Jelic V, Fratiglioni L, Wahlund LO, Nordberg A, Bäckman L, Albert M, Almkvist O, Arai H, Basun H, Blennow K, de Leon M, DeCarli C, Erkinjuntti T, Giacobini E, Graff C, Hardy J, Jack C, Jorm A, Ritchie K, van Duijn C, Visser P, Petersen RC. Mild cognitive impairment--beyond controversies, towards a consensus: report of the International Working Group on Mild Cognitive Impairment. J Intern Med. 2004 Sep;256(3):240-6.

Wallhagen, M. I. (2010). The stigma of hearing loss. The gerontologist, 50(1), 66-75. Van Lier, L. (1967). Presbycusis in a Non Noise-Exposed Population. ORL, 29(5), 301-304.

Walton JP, Frisina RD, O'Neill WE. (1998, Apr) Age-related alteration in processing of temporal sound features in the auditory midbrain of the CBA mouse. J Neurosci 1;18(7):2764-76.

Wattamwar, K., Qian, Z. J., Otter, J., Leskowitz, M. J., Caruana, F. F., Siedlecki, B., Spitzer, J. B., & Lalwani, A. K. (2018). Association of Cardiovascular Comorbidities with Hearing Loss in the Older Old. JAMA Otolaryngol Head Neck Surg, 144(7), 623-629.

Wechsler, D. (1991). Manual for the wechsler adult intelligence-scale revised. New York: Psychological Corpration. Wild, C. J., Yusuf, A., Wilson, D. E., Peelle, J. E., Davis, M. H., & Johnsrude, I. S. (2012). Effortful listening: the processing of degraded speech depends critically on attention. J Neurosci, 32(40), 14010- 14021.

Wetterberg H, Najar J, Rydén L, Ribbe M, Rydberg Sterner T, Zettergren A, Guo X, Falk Erhag H, Sacuiu S, Kern S, Skoog I. (2021, May). Dementia remains the major predictor of death among octogenarians. A study of two population cohorts of 85-year-olds examined 22 years apart. Eur J Epidemiol.36(5):507-517.

Wetterberg, H., Rydén, L., Ahlner, F., Falk Erhag, H., Gudmundsson, P., Guo, X., Joas, E., Johansson, L., Kern, S., Mellqvist Fässberg, M., Najar, J., Ribbe, M., Sterner, T. R., Samuelsson, J., Sacuiu, S., Sigström, R., Skoog, J., Waern, M., Zettergren, A., & Skoog, I. (2022). "Representativeness in population-based studies of older adults: five waves of cross-sectional examinations in the Gothenburg H70 Birth Cohort Study". BMJ open, 12(12), e068165.

White JA, Burgess BJ, Hall RD, Nadol JB. (2000, Mar) Pattern of degeneration of the spiral ganglion cell and its processes in the C57BL/6J mouse. Hear Res, 141(1-2):12-8.

Wiley, T. L., Chappell, R., Carmichael, L., Nondahl, D. M., & Cruickshanks, K. J. (2008). Changes in hearing thresholds over 10 years in older adults. J Am Acad Audiol, 19(4), 281-371.

Wingfield A, Grossman M. (2006, Dec). Language and the ageing brain: patterns of neural compensation revealed by functional brain imageing. J Neurophysiol, 96(6):2830-9.

World Health Organization. (2001) The International Classification of Functioning, Disability and Health: ICF; WHO: Geneva, Switzerland, 2001.WHO methods and data sources for country-level causes of death 2000-2019, pp7-15, WHO, Dec 2020

World Health Organization. (2015). World report on ageing and health. World Health Organization. Retrieved 2023 September 05 from https://www.who.int/publications/i/item/9789241565042

World Health Organization, (2019a). Deafness and Hearing. Retrieved 2019 May 20 from https://www.who.int/news-room/fact-sheets/detail/deafness-and-hearing-loss

World Health Organization, (2019b). Prevention of blindness and deafness. Retrieved 2019 May 20 from https://www.who.int/pbd/deafness/hearing_impairment_grades/en/

World Health Organization (2021). World report on hearing.: Geneva; 2021. Available from: https://www.who.int/teams/communicable-diseses/sensory-functions-disability-and-rehabilitation/highlghting-priorities-for-ear-and-heringactivities/highlighting-priorities-for-ear-and-hearing-care [cited 2021 Mar 9].

World Health Organization, (1991) Report of the Informal Working Group On Prevention Of Deafness And Hearing Impairment Programme Planning. Retrieved 2020 January 23 https://apps.who.int/iris/handle/10665/58839

Yellin MW, Jerger J, Fifer RC. (1989). Norms for disproportionate loss in speech intelligibility. Ear Hear, 10: 231–4.

Zeng, F. G., Kong, Y. Y., Michalewski, H. J., & Starr, A. (2005). Perceptual consequences of disrupted auditory nerve activity. J Neurophysiol, 93, 3050–3063

Zhan, W., Cruickshanks, K. J., Klein, B. E., Klein, R., Huang, G. H., Pankow, J. S., Gangnon, R. E., & Tweed, T. S. (2010). Generational differences in the prevalence of hearing impairment in older adults. Am J Epidemiol, 171(2), 260-266.

Öberg M, Marcusson J, Nägga K, Wressle E. (2012, Feb). Hearing difficulties, uptake, and outcomes of hearing aids in people 85 years of age. Int J Audiol, 51(2):108-15.