Assessing the Contribution of Hearing Loss In Prediction Models for Dementia Developed and Validated Using Data from the Canadian Longitudinal Study on Aging

Therese Chan

Thesis submitted to the Faculty of Graduate and Postdoctoral Studies in partial fulfillment of the requirements for the MSc degree in Epidemiology

School of Epidemiology and Public Health
Faculty of Medicine
University of Ottawa

Preface

Ethics approval for the study was initially obtained from the Research Ethics Board of Bruyère Continuing Care in March of 2021 and has been renewed annually. Data for secondary data analysis was obtained in March of 2021 from the Canadian Longitudinal Study on Aging after submitting a data access request in 2020.

TC was responsible for data acquisition, performing the analysis, interpreting of the results, and drafting and revising the thesis monograph. AH and DG co-supervised TC by helping with conceptualizing the project, providing statistical support, assisting with the interpretation of results, and providing valuable feedback for revising this monograph.

Abstract

Introduction: Hearing impairment is an emerging modifiable risk factor for dementia, but the relative predictive abilities of subjective and objective measures of hearing in dementia risk prediction algorithms are unclear. The objective was to develop and validate prediction models for 3-year incidence of dementia in older Canadians, and to evaluate the independent contribution of self-rated hearing impairment and audiometry-based moderate hearing loss.

Methods: Baseline (2011 to 2015) and 3-year follow-up data from the Comprehensive cohort of the Canadian Longitudinal Study of Aging were used to build logistic regression models for 3-year incidence of dementia. Individuals who were under 55 years of age, reported physician-diagnosed dementia at baseline, and/or did not have data on dementia status at follow-up were excluded, producing a sample of 19,830 older Canadians. Hearing impairment was defined subjectively as self-reporting fair or poor hearing (versus excellent, very good, or good hearing) and was defined objectively as having a better-ear pure-tone average of the speech-frequencies (500, 1000, 2000, and 4000 Hz) above 40 dB with audiometry.

Results: Both hearing measures were associated with dementia incidence after adjustment with other risk factors (self-rated fair/poor hearing adjusted odds ratio (aOR) 1.76, CI 0.96-3.23, audiometry-derived hearing loss aOR 2.60, CI 1.38-4.87). Audiometrically-derived hearing loss and self-rated hearing had similar population discrimination (c-statistic of model with self-rated hearing = 0.803, CI 0.752-0.859, c-statistic of model with audiometrically confirmed hearing loss = 0.808, CI 0.762-0.870) and similar calibration.

Conclusion: Due to the accessibility of the self-reported hearing measure, the use of self-rated hearing in dementia risk prediction tools may have a larger clinical impact than audiometrically-defined hearing ability. Model performance within subgroups (e.g., older age groups,

hypertension status, etc.) must be evaluated in future work to assess the magnitude of miscalibration, if any, in the use of self-reported hearing ability compared to audiometry.

Acknowledgements

Thank you to Dr. Doug Manuel – your wisdom, support, and guidance has helped me expand my skillset and broaden my understanding of different methodologies for statistical analysis. To Dr. Amy Hsu, who took a chance on me during a transitory time of my life when I was on the brink of making the jump to pivot from basic science to the field of epidemiology. Your mentorship and patience, your words of encouragement during the highs and lows of this Masters, and your strong belief in me and my (supposed) potential were key to helping me through this journey of completing my Masters.

Thank you also to Dr. Steven Hawken and Dr. Michael Schlossmacher for making time in your busy schedules to serve as my thesis evaluators. Many thanks to Dr. Stacey Fisher for your responses to my occasional DemPoRT-related questions and for laying the important groundwork to support this work. Thank you to the members of the Project Big Life lab at large who on multiple occasions have cheered me on and supported me at various stages in my journey. Special thanks to Mary Scott and Dr. Wenshan Li for your conversations and insights when I initially took interest in the field and for your continued support after I joined the lab group. Also, thank you to Yulric Sequeira, Carol Bennett, and Dr. Juan Li for their thoughtful suggestions and insights on coding, troubleshooting, statistical methodology, and literature to consult for additional information on methods.

To Monica, my psychotherapist and mental health counsellor, thank you for being a gentle and warm voice of compassion during two cloudier periods of time for me. Tangentially, thank you to the University of Ottawa for making a few positive changes over the past 6.5 years that I have been at this university, expanding on the mental health resources available and adding therapists to increase capacity at both the main campus and the Faculty of Medicine campus.

Thank you to my family – in particular, my mom and my sister – for their unending love and support during every part of my journey. Thank you to my friends, especially my decade-long friends Ting, Jenny, and Emma, for being thoughtful, empathetic listeners when hearing at length about my exciting progress and daunting challenges and setbacks with this thesis. Finally, to my partner, Phill: thank you for being a solid rock, a patient soul, and a calm voice of reason no matter the season of life we've been in.

List of Tables

List of Figures

List of Appendices

List of Abbreviations

aOR	Adjusted odds ratio
AUC	Area under the ROC curve
BPTA	Better-ear pure-tone average
CCHS	Canadian Community Health Survey
CCHS-HA	Canadian Community Health Survey – Healthy Aging
CHMS	Canadian Health Measures Survey
CI	Confidence interval
CIHR	Canadian Institutes of Health Research
CLSA	Canadian Longitudinal Study on Aging
COPD	Chronic obstructive pulmonary disease
dB	Decibel
DemPoRT	Dementia Population Risk Tool
FI-NTRF	Frailty index of non-traditional risk factors
HL	Hearing loss
HR	Hazard ratio
IQR	Interquartile range
MCI	Mild cognitive impairment
MET	Metabolic equivalent of task
MICE	Multivariate imputation by chained equations
OR	Odds ratio
PAF	Population attributable fraction
PTA	Pure-tone average
ROC	Receiver operating characteristic
RR	Relative risk or risk ratio
SLAS	Singapore Longitudinal Ageing Study
uOR	Unadjusted odds ratio

Table of Contents

CHAPTER 1: INTRODUCTION

1.1 Background and rationale

Dementia is a growing concern for our nationally aging population and for our healthcare system. According to the Alzheimer Society of Canada's Landmark Study, an estimated 597,300 individuals in Canada were living with dementia in 2020 and this number is expected to reach almost 1 million by 2030[1]. Given the current lack of cure for dementia, Canada's national Dementia Strategy has highlighted that there is a great need to focus on developing strong primary prevention strategies for dementia[2]. Additionally, approximately 40% of dementia cases may be attributable to potentially modifiable risk factors, such as education, hypertension, smoking, physical inactivity, and social isolation[3]. Therefore, dementia onset may be delayed and/or prevented by implementing effective interventions targeting modifiable risk factors. In order to help individuals understand their risk and engage in preventative health interventions, the use of risk communication tools may be of value in clinical and community settings.

While many risk prediction models for dementia have been developed[4–9], very few have been implemented in clinical settings or as publicly-available tools that can be easily used in community settings. The Dementia Population Risk Tool (DemPoRT) is a risk-communication tool developed by the Project Big Life Research Team (www.ProjectBigLife.ca) to inform older adults of their five-year risk of developing dementia[10,11]. The tool is based on a prediction model that includes 28 variables pertaining to self-reported sociodemographic characteristics, lifestyle, function, and health condition risk factors as predictors[10]. Despite this being a comprehensive model, researchers have in recent years developed a deeper understanding of the number of incident cases of dementia that may be attributable to modifiable risk factors. While the 2017

Lancet Commission report on dementia suggested that modifiable risk factors account for approximately 35% of new dementia cases, the 2020 updated report – which looked at novel modifiable risk factors – updated the attributable fraction to 40%[3,12]. As we discover additional risk factors associated with dementia, there is an imperative to improve these models through the inclusion of these new risk factors that may predict dementia incidence.

An emerging modifiable risk factor for dementia that is not currently in the algorithm supporting DemPoRT is hearing impairment. A study from the Lancet Commissions has found that, among the currently known modifiable risk factors for dementia, hearing impairment has the largest population attributable fraction[3]. This indicates that there would be the largest percent reduction in new dementia cases in successfully eliminating hearing impairment compared to eliminating any other modifiable risk factor for dementia. Additionally, it has been shown among older adults that hearing aid use after a diagnosis of hearing impairment may alter the trajectory of cognitive decline[13].

Unfortunately, research has shown that there is a high prevalence of undetected hearing loss in Canada, especially in mid-life stages where dementia risk can be reduced[14]. This may be due to the fact that while pure-tone audiometry is a standard method for diagnosing hearing loss, it is not routinely conducted in clinical or research settings. In terms of research examining the relationship between hearing loss and dementia, many epidemiological studies use self-reported hearing impairment. Despite the relatively high concordance of approximately 70% between self-rated hearing ability and audiometry[15,16], there is conflicting literature regarding whether self-rated hearing ability is sufficient to predict the incidence of dementia in older adults[17–19],

with few studies comparing self-rated hearing measures with audiometric data for validity in the context of dementia outcomes.

1.2 Thesis objectives

The overall goal of this project was to develop and validate prediction models for 3-year incidence of dementia in Canadian older adults, focusing on the contribution of self-reported fair/poor hearing ability and audiometrically confirmed moderate or greater bilateral hearing loss.

Using data from the Baseline and Follow-up 1 waves of the Canadian Longitudinal Study on Aging, my specific research objectives were three-fold:

1) Report the baseline prevalence of self-rated hearing impairment and audiometrically-defined hearing loss in older Canadian adults (55+ years of age) with or without dementia by Follow-up 1.
2) Describe the independent contribution of self-reported hearing impairment and audiometrically-confirmed hearing loss in prediction models for dementia, and evaluate whether hearing impairment (regardless of its definition) is predictive of dementia incidence.
3) Assess whether the prediction model relying on audiometrically-confirmed hearing loss outperforms (in terms of discrimination as well as calibration) a prediction model that uses self-reported hearing impairment.

1.3 Hypotheses

Hypothesis 1 (Corresponding with Objective 2): Given the existing body of literature suggesting a strong association between hearing impairment (defined in different ways) and dementia or cognitive decline in many studies[20–23], I hypothesized at the outset that hearing impairment would be predictive of dementia, regardless of the method of ascertainment of hearing impairment.

Hypothesis 2 (Corresponding with Objective 3): I hypothesized at the outset that there would be improved population discrimination and improved population calibration in using the audiometrically-defined measure of hearing loss in the prediction modelling over the self-reported measure of hearing ability. Improved discrimination was hypothesized because ascertainment of hearing loss via audiometric testing would be expected to improve the classification of an individual's true hearing ability (greater sensitivity and specificity) and, thus, should improve the model's ability to classify an individual as higher risk or lower risk for developing dementia. I also anticipated that the observed and predicted probabilities of incident dementia would be more aligned (i.e., better calibrated) when using audiometrically-defined hearing loss in the prediction model.

1.4 Thesis outline

This thesis will be presented as follows: Chapter 2 provides a summary of the literature surrounding dementia, risk prediction models for dementia, and hearing impairment as a risk factor and potential predictor of dementia. Chapter 3 describes the data source and methods used in this thesis. Chapter 4 outlines the results in relation to the research questions mentioned above

in this introductory chapter. Chapter 5 contains a discussion of the results and their implications, where the research questions are revisited and addressed with some additional commentary regarding strengths, limitations, and future directions of this work. The bibliography of references is located in Chapter 6. Chapter 7 contains the appendices, which consist of supplementary material, documentation, or additional work related to the thesis that do not directly relate to answering a specific research question outlined but support the work conducted to complete the thesis.

CHAPTER 2: LITERATURE REVIEW

2.1 Dementia

2.1.1 Dementia incidence and risk factors for dementia

Dementia is a general term used to describe symptoms associated with cognitive decline that impacts an individual's memory, reasoning, and ability to carry out day-to-day tasks[1]. According to the 2022 Landmark Study, in Canada, there was an estimated 597,300 individuals living with dementia in 2020, and this estimate is expected to rise to almost 1 million by 2030[1]. The annual incidence of dementia as of 2020 was 124,000 new cases in Canada, equivalent to 15 new cases every hour. The incidence is projected to increase to 187,000 new dementia cases per year, or 21 new cases per hour[1].

There are several well-studied risk factors for dementia. For example, one genetic risk factor for dementia or Alzheimer's disease may be having apolipoprotein E, and in particular, possessing the E4 allele[24–29]. It is important to note that while this contributes to a genetic predisposition for dementia, it is not deterministic of having the disease; individuals can engage in preventative measures focused on modifiable risk factors to lower their risk for developing dementia. Dementia is more prevalent among women than men, as women tend to live longer and are thus subject to survival bias[30]. Increasing age, lower education level, higher body mass index, cardiovascular diseases (e.g. stroke, heart disease, etc.), physical inactivity, depression, excess alcohol consumption, and smoking are factors that have been commonly suggested to be associated with elevated dementia risk[12,23,31–33].

A risk prediction model, also known as a prognostic model, calculates an individual's risk for an outcome by accounting for a combination of several predictors[34]. After the development and validation of a risk prediction model, if it is a well-performing algorithm, it can be implemented in clinical settings to inform decision making regarding staging targeted interventions.

2.1.2 Existing dementia risk prediction algorithms

A systematic review of existing dementia risk prediction models by Hou et al. identified 61 studies; among these, 39 articles modelled dementia risk in late life and 4 studies modelled mid-life risk of developing dementia[35]. Moreover, 15 studies performed risk prediction of conversion from mild cognitive impairment (MCI) to Alzheimer's disease and 3 focused on dementia risk among individuals with diabetes[35]. The most common variables included in the models evaluated in this review were age, sex, education, cognition variables, body mass index, alcohol intake, and genetic variables[35]. There is a high reliance on cognitive test scores in many existing dementia prediction models. Based on the systematic review, 36 studies (59%) included cognitive test scores or subjective cognitive complaints, with 17 of these studies basing their risk prediction models solely either on a single cognitive test result or on neuropsychological batteries[35]. The most common cognition-related variable was the Mini Mental State Examination (MMSE), but other common cognition variables included in dementia prediction algorithms were the Consortium to Establish a Registry for Alzheimer's Disease neuropsychological assessment battery and the Alzheimer's Disease Assessment Scale-cognitive subscale[35]. The only mention of hearing impairment in this review was in a supplementary file that indicated that hearing trouble and ear trouble were included as predictors in only one of the 61 studies highlighted in this review (described in more detail in Section 2.2.3)[9,35].

2.1.3 The Dementia Population Risk Tool (DemPoRT)

The Dementia Population Risk Tool (DemPoRT) is a risk-communication tool designed primarily for community-dwelling older adults aged 55 and above[10,11]. Using self-reportable risk factors as predictors, it calculates the five-year incidence of dementia at the population level. The algorithms were sex-specific Fine and Gray subdistribution hazard models that account for death as a competing risk. The models were built using cycles 2001, 2003, 2005, and 2007-2008 of the Canadian Community Health Survey (CCHS) (n = 47,739), and temporal validation used cycles 2009-2010 and 2011-2012 (n = 27,721)[10].

A study protocol was published pre-specifying the model specification in addition to the analysis plan[36]. Outlining the variables of interest and study plan prior to model development minimizes the risk of overfitting and increases transparency. The models included sociodemographic factors (e.g. age, ethnicity, education, marital status), general health indicators (e.g. stress, self-rated health), health behaviours (e.g. smoking status, pack years of smoking, number of drinks consumed in a week, former drinker status, leisure physical activity, and consumption of fruit and vegetables, potatoes, and juice), functional measures (e.g. number of activities requiring assistance), and health condition factors (e.g. heart disease, stroke, diabetes, mood disorders, high blood pressure, chronic obstructive pulmonary disease (COPD), epilepsy, body mass index), and a design variable (e.g. survey cycle). In the validation cohort, the DemPoRT models had great discrimination (c-statistic = 0.83, 95% CI = 0.81-0.85 for both men and women) and demonstrated good calibration (calibration slope and intercept were 0.8666 and 0.0128, respectively)[10]. The models were also well calibrated across a range of subgroups for

sociodemographic categories, behavioural risk exposure groups, by diabetes status, and by hypertension status[10].

Reduced models were developed using a step-down procedure that examined the effect of eliminating variables to produce a more parsimonious model[10]. Using the step-down procedure, variables were removed from the model one by one to see which yielded the smallest decrease in R^2. Variables continue to be removed until the Akaike Information Criterion is minimized[37]. Creating a more parsimonious model that still maintains good model performance improves the applicability and interpretability of the algorithm, as the model is simpler. The reduced models performed well in terms of discrimination (males: c-statistic = 0.82, 95% CI = 0.81-0.84; females: c-statistic = 0.83, 95% CI = 0.82-0.83) and calibration (males: calibration slope = 0.8285, intercept = 0.0079; females: calibration slope = 0.8335, intercept = 0.0101)[10].

DemPoRT was the first risk-communication tool for dementia that predicts the incidence of dementia at the population level. Beyond its ability to be used in the context of population health planning, it can also be used in a clinical setting by both clinicians and their patients to assess individual-level dementia risk. This tool is widely accessible due to its use of only self-reportable measures as opposed to having some reliance on cognitive testing or neuropsychological batteries that would require examiners and additional resources to perform. DemPoRT is freely available as a web calculator online at ProjectBigLife.ca along with other risk-communication tools the team has developed[11].

2.2 Hearing impairment – an emerging risk factor for dementia

An emerging modifiable risk factor for dementia that does not exist in the original DemPoRT model or most other dementia risk prediction algorithms is hearing impairment. In the 2017 review by the Lancet Commission on dementia and an update to this review three years later in 2020, hearing impairment was consistently identified as one of the most significant potentially modifiable risk factors associated with dementia risk[3,12]. More specifically, it was the most important midlife modifiable risk factor for dementia, with a relative risk ratio of 1.9 based on the latest study (95% CI 1.4-2.7)[12]. The authors also found that hearing loss had the largest population attributable fraction (PAF) out of all the modifiable risk factors evaluated in this review; therefore, these findings indicate that there would be the greatest percent reduction in new dementia cases if hearing loss were eliminated compared to eliminating any other modifiable risk factor for dementia[12]. The weighted PAF of 8.2% for hearing loss derived from this research suggests that untreated hearing loss may be attributable to approximately 8% of incident dementia cases worldwide[12].

According to the World Report on Hearing published in 2021 by the WHO, there is an estimated 1.5 billion people worldwide who experience some level of hearing loss, with 430 million with moderate-to-severe bilateral hearing loss[38]. Unaddressed hearing loss is associated with an annual burden of $980 billion that comes from productivity losses and societal and healthcare-related costs[38]. Similar to dementia, hearing loss is highly prevalent among older age groups. Based on analyses from the 2012-2013 cycles of the Canadian Health Measures Survey (CHMS), 19.2% of Canadians aged 20 to 79 have mild-or-greater speech-frequency hearing loss (95% CI 16.9-21.7%), but 65.0% of individuals aged 70 to 79 have this level of hearing impairment (95%

CI 56.4-72.7%)[39]. Furthermore, 93.8% of individuals between the ages of 70 and 79 were estimated to have some degree of high-frequency hearing loss (95% CI 88.1-96.8%)[39].

2.2.1 Etiology behind the relation between hearing impairment and dementia

The specific etiology of the relationship between hearing impairment and dementia remains unclear. However, several hypothesized mechanisms behind the causal pathway have been suggested in the literature. One is that hearing loss may increase the cognitive load on the brain; it may divert cognitive resources to auditory processing at the expense of working memory or other cognition-related processes, thereby reducing one's performance on cognitive tests or on cognitively demanding tasks[40]. There is also a growing body of literature suggesting that hearing loss and sensory deprivation can lead to direct changes in brain structure and brain functioning that can contribute to cognitive decline[40]. For instance, associations have been found between hearing impairment and smaller overall brain volume[41,42]. Longitudinal studies have observed decreases in temporal lobe volume among individuals with hearing impairment, and this is significant as the temporal lobes play an integral role in spoken language processing and visual memory[42,43].

Another suggested mechanism is that hearing loss could lead to social isolation and/or depression[40]. Both social isolation and depression have been demonstrated to contribute to and/or manifested in dementia[40,44,45]. Additionally, the causal pathway between hearing impairment and dementia could be mediated by reduced physical activity or cognitively stimulating activities, such as reading or puzzle-building[40]. Because hearing loss could interfere with both physical and

cognitively stimulating activities, an individual with hearing loss may gradually decrease their engagement in these activities, consequently leading to decreased cognitive functioning.

Any one of these pathways, or all of the pathways described above, could be contributing to the causal pathway between hearing impairment and dementia. It has also been hypothesized that sensory impairment and cognitive impairments have more of a correlational relationship and co-occur quite frequently because they have many risk factors in common, such as genetic factors, age, and vascular diseases[40,44].

2.2.2 Existing studies on the association between hearing impairment and dementia

Beyond the Lancet Commission reports[3,12], there is an increasing body of literature supporting the link between hearing impairment and dementia or cognitive decline at large[20–22,46–49]. A meta-analysis of 14 prospective cohort studies found an independent association between hearing loss and dementia (Hazard ratio (HR) = 1.59, 95% CI 1.37-1.86)[50]. They also identified no significant subgroup differences when they stratified the analyses by the method used to ascertain hearing loss (audiometry versus self-report or ICD codes), follow-up duration (less than 10 years versus 10 or more years), data source used to ascertain dementia status (clinical evaluation versus ICD codes), and whether apolipoprotein E status was controlled for in the study[50].

Based on the findings from this meta-analysis, one may then expect the use of hearing aids after a diagnosis of hearing impairment to potentially alter the trajectory of cognitive decline. One longitudinal retrospective study showed that older adults with MCI who used hearing aids were at a significantly lower risk of converting to dementia compared to individuals who did not use

hearing aids (HR=0.73, 95% CI 0.61-0.89)[13]. Another study showed that older adults' scores on the MMSE and the Geriatric Depression Scale significantly improved within three months of getting a hearing aid fit[51]. In a study by Sarant et al., they found clinically and statistically significant improvements in cognition after 18 months of hearing aid use among a cohort of adults aged 62 to 82[52]. Further research is necessary to evaluate the trajectory of cognitive decline with longer follow-up periods for hearing aid use and with larger sample sizes, as the prior two studies mentioned had sample sizes of less than 100 individuals.

2.2.3 Hearing impairment in risk prediction models for dementia

While there appears to be a strong association between hearing impairment and dementia, it is currently unclear how predictive hearing impairment may be of dementia in a risk prediction model, after adjusting for other risk factors. Hearing impairment is not a common predictor included in dementia risk prediction algorithms. As hearing loss is an emerging risk factor that has gained more traction only in more recent years, very few dementia risk prediction models currently exist with hearing impairment as a predictor.

Only one dementia risk prediction model[9] evaluated in the systematic review by Hou et al.[35] included hearing impairment as a predictor. Published in 2011, this study by Song et al. used data from the Canadian Study of Health and Aging (n=7,239 included for analysis) to first evaluate 19 characteristics that were "not known to predict dementia" (i.e., "non-traditional risk factors") and their association with 5-year and 10-year death, Alzheimer's disease, and all-cause dementia compared to cognitively normal individuals[9]. Hearing trouble was significantly associated with all outcomes (e.g., unadjusted odds ratio (uOR) = 4.2 (95% CI 2.1-8.6) and uOR

= 3.8 (95% CI 2.2-6.4) for 5-year and 10-year incident Alzheimer's disease, respectively; uOR = 4.4 (95% CI 2.5-7.9) and uOR = 3.9 (2.4-6.1) for 5-year and 10-year incident all-type dementia, respectively). Reporting ear trouble was also significantly associated with all outcomes (e.g., uOR = 2.0 (95% CI 1.5-2.6) and uOR = 1.8 (95% CI 1.4-2.2) for 5-year and 10-year incident Alzheimer's disease, respectively; uOR = 1.9 (95% CI 1.5-2.4) and uOR = 1.8 (95% CI 1.4-2.2) for 5-year and 10-year incident all-type dementia, respectively)[9]. Then, hearing trouble, ear trouble, and the 17 other factors not known to predict dementia were used to construct a frailty index of non-traditional risk factors (FI-NTRF) that was included in a risk prediction model for 10-year all-cause dementia[9]. Song et al. calculated the FI-NTRF as the proportion of non-traditional risk factors that an individual reports, yielding scores between 0 and 1. When adjusting for age, sex, baseline cognition, and education, the FI-NTRF was predictive of dementia (aOR 1.02, 95% CI 1.01-1.05)[9]. The area under the curve (AUC) for the FI-NTRF in predicting 10-year incident dementia was a moderate 0.66 (± 0.03)[9].

One recently developed risk index for MCI or dementia (that was published after the aforementioned systematic review of dementia prediction models[35]) contained hearing loss as a predictor[4]. Using data from the Singapore Longitudinal Ageing Study (SLAS), the model was developed using the SLAS-1 cohort (n=2804) and validated using the SLAS-2 cohort (n=3246). Both cohorts were comprised of community-dwelling older adults aged 55 and above residing in the South East region of Singapore. Participants of the SLAS-1 cohort were recruited from 2003 to 2004 and were followed up twice in approximately 3-year increments (2005-2007 and 2007-2009), while participants of the SLAS-2 cohort were recruited between 2009 and 2013 and had a follow-up assessment 3 to 5 years (mean 4.5 years) later (2013-2018). Stepwise selection was

performed to create a parsimonious model comprised of 7 variables chosen from 20 risk factors spanning the health, lifestyle, and psychosocial categories. Hearing loss was among the 7 final variables included in the risk index. The other 6 variables selected for inclusion were age, sex, years of schooling, life satisfaction, depression, and the number of cardio-metabolic risk factors (identified as pre-diabetes or diabetes, hypertension, wide waist circumference, and dyslipidemia). In this study, an individual was considered to have hearing loss if they self-reported a "problem hearing well" or failed a whisper test. A whisper test, sometimes called a whispered voice test, is a simple test wherein the examiner stands at arm's length behind a patient and instructs the patient to obstruct the auditory canal of one ear by rubbing their tragus – that way, one ear is tested at a time[53]. The examiner whispers a number-letter-number combination and the patient is asked to repeat what they hear. A failure (i.e., hearing impairment) is defined as getting only 2 out of 6 total numbers or letters correct during two total trials[53]. Sensitivity of this test in adults across four studies ranged from 90-100%, while specificity was 70-87%[53].

This risk score for progression to MCI-or-dementia had an AUC of 0.73 (95% CI 0.70-0.75) in the study's derivation cohort (SLAS-1). The risk score was validated using an independent cohort (SLAS-2) to assess the external validity of the model. The AUC was found to be 0.74 (95% CI 0.72-0.77) in this validation cohort. Based on this study's risk prediction model, having a hearing problem was significantly associated with incident MCI-or-dementia (OR = 2.59, 95% CI 1.10-6.13). However, the inclusion of both self-reported hearing impairment and a whisper test as part of their definition of hearing loss prevents us from drawing any conclusions about a singular diagnostic method for hearing loss and its predictive ability of dementia.

2.2.4 Methods of measuring hearing impairment

There currently is no universal definition for hearing impairment and for the more specific, sub-categories of mild, moderate, severe, and profound hearing loss. Moreover, while pure-tone audiometry testing is the gold standard method used for assessing hearing loss in clinical settings, it is not regularly performed among middle-aged or older adults. A potential consequence of this is that there is a high level of unperceived hearing loss. For example, one study found that approximately 77% of middle to older-aged Canadians have undetected high-frequency hearing loss, which equates to 6.3 million individuals[14].

Epidemiological studies often rely on self-reported hearing impairment as audiometry is more resource-intensive and time-consuming. Some work has been done to compare self-reported hearing impairment with audiometric test results; despite the high concordance between these two measures, it remains unclear whether they can be used interchangeably and whether self-reported hearing measures are suitable substitutes to the gold standard. Fausto et al. compared subjective and objective hearing measures and cognitive abilities among individuals with and without MCI using the Cognitive Self-Report Questionnaire, which has a hearing subscale comprised of four questions asking about one's ability to hear in four scenarios: on the phone, in noisy places, when listening to someone who speaks quietly, and when listening to someone who speaks quickly[17]. They found that the hearing subscale explained a significant amount of variance in pure-tone audiometry ($R^2 = 0.39$, $p<0.001$) and concluded that the CSRQ was an appropriate self-report measure for hearing[17]. In contrast, Hoff et al. cautioned the usage of self-reported hearing loss in epidemiological geriatric research. They used subjective and objective

measures of hearing to look at the cross-sectional association of hearing loss with cognitive function. While there was an association between hearing impairment and cognitive decline when hearing ability was ascertained audiometrically, they did not find this association when hearing ability was self-reported[18].

Kim et al. looked at the concordance between self-rated hearing status and audiometrically defined hearing loss within individuals who were cognitively normal, individuals with MCI, and individuals with dementia[19]. The sensitivity and specificity for self-rated hearing ability was 71.2% and 85.9% among individuals with no cognitive deficits[19]. However, the accuracy of the measures wane with increasing cognitive impairment; among individuals with MCI and among individuals with dementia, the sensitivity and specificity were 61.1% and 84.9%, and 52.6% and 81.2%, respectively[19]. With the low sensitivity observed with self-rated hearing, the authors reminded that underreporting of true hearing loss may occur when using a self-reported measure of hearing impairment[19]. However, based on existing literature, it is unclear whether a hearing measure derived from audiometric testing will result in a superior-performing dementia risk prediction algorithm that outweighs the population-level benefits of the reach and accessibility of a model that uses a self-reported hearing measure.

CHAPTER 3: METHODS

This thesis adheres to the Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis (TRIPOD) statement for prediction model development and validation[54,55].

3.1 Data source: The Canadian Longitudinal Study on Aging

3.1.1 Study design

The CLSA is a nation-wide Canadian prospective cohort study comprising 51,338 individuals who were aged 45 to 85 at time of recruitment[56]. The overall CLSA platform seeks to explore the dynamic trajectories of the aging process and study the relationships between a large span of behavioural and health-related variables in mid-life and older aged Canadians. Baseline data collection took place between 2011 and 2015, and follow-up data collections take place in approximately 3-year increments for over 20 years until 2033 or until death of the participant[56]. Only Baseline and Follow-up 1 data were available for secondary data analysis at the time of requesting for data access for this project.

All participants are asked to respond to a core set of questions regarding demographics, health status, health service usage, lifestyle/behaviour, social measures, and psychological measures. The CLSA is comprised of two distinct cohorts: the Comprehensive cohort and the Tracking cohort. The CLSA Comprehensive cohort includes 30,097 Canadian respondents aged 45-85 years who completed both the core questions (via a face-to-face, in-home, computer-assisted personal interview) and on-site clinical assessments, between 2011 and 2015 for Baseline data collection and between 2015 and 2018 for Follow-up 1 data collection[57]. The local data

collection sites (DCS) conduct various evaluations such as the neuropsychological battery, audiometric hearing test, and urine and blood sampling. The CLSA Tracking cohort is comprised of 21,241 individuals who are only asked to complete the core set of questions via computer-assisted telephone interviews[57].

3.1.2 Participants (Sampling, recruitment, eligibility criteria, response rates)

Random sampling stratified by age, sex, province of residence, and education level was conducted within three sampling frames: 1) random digit dialing of landline telephones; 2) the use of healthcare registration databases; and 3) the CCHS – Healthy Aging (CCHS-HA), a cross-sectional, nationally representative survey conducted by Statistics Canada in 2008-2009 that seeks to collect information on various factors that may influence healthy aging[56,58,59]. Recruitment for the CLSA Tracking cohort used all three sampling frames while recruitment for the Comprehensive cohort used only the first two sampling frames[56].

Individuals who were part of the CLSA Comprehensive cohort had to reside within 25 to 50 kilometres of 11 urban data collection sites located in one of the following seven provinces: British Columbia, Alberta, Manitoba, Ontario, Quebec, Nova Scotia, and Newfoundland and Labrador[56]. Full-time members of the Canadian Armed Forces, individuals deemed as having cognitive impairment or could not respond to the interviews in English or French at baseline, and individuals living in a long-term care institution, in one of Canada's territories, or on a Federal First Nations settlement or reserve were excluded from the CLSA[58]. The response rates for the Tracking cohort overall was 9% while the response rate for the Comprehensive cohort was 10%, with a pooled overall response rate of 10%[60].

3.1.3 Inclusion and exclusion criteria for secondary data analysis

A cohort creation flowchart visually outlining the exclusions can be found in **Figure 1**. For this thesis, I primarily focused on the Comprehensive cohort since data on both self-rated hearing ability and audiometric hearing test are available for these participants. Because DemPoRT was developed based on an older adult population of individuals who were 55 and above, individuals in the CLSA who were under 55 years of age at baseline were excluded (n=7,595). I subsequently removed 65 participants with a physician diagnosis of dementia at baseline, 1,857 participants who were lost to follow-up (due to death (n=526), withdrawal from the study (n=786), or being unable to complete Follow-up 1 data collection or unable to be contacted (n=545)), and 750 participants who had missing Follow-up 1 dementia status. The final cohort consisted of 19,830 individuals, of whom 54 (0.3%) had dementia at Follow-up 1.

3.2 Measures

3.2.1 Outcome

The outcome of interest, 3-year incidence of dementia, was defined as a self-reported physician diagnosis of dementia at Follow-up 1. This was determined based on a response of "yes" to the following question at Follow-up 1: "Has a doctor ever told you that you have dementia or Alzheimer's disease?".

3.2.2 Primary exposure – hearing impairment

The main exposures of interest consisted of two measures of hearing ability at baseline: self-reported hearing ability and hearing ability ascertained by audiometry testing. The CLSA data

gives us the rare opportunity to compare self-reported hearing impairment and audiometrically defined hearing impairment in the Comprehensive cohort.

Self-rated hearing at baseline was assessed using a Likert scale, spanning excellent to poor, in response to the question: "Is your hearing [poor, fair, good, very good, excellent], using a hearing aid if you use one…". Due to limited sample sizes in the excellent (n=4 among individuals with incident dementia, n=4019 among individuals without incident dementia) and poor categories (n=1 among individuals with incident dementia, n=332 among individuals without incident dementia), I dichotomized self-rated hearing, yielding categories of "fair or poor" and "good, very good, or excellent". This dichotomous categorization of self-rated hearing ability has been commonly used in other studies[14,61–63].

Hearing ability ascertained by audiometric testing at baseline was derived by calculating the pure-tone average (PTA) of the speech frequencies (500, 1000, 2000, and 4000 Hz) in the better-hearing ear. This PTA was chosen as it is the most commonly used in clinical practice and in epidemiological studies[20,21,64,65]. Furthermore, while measures based on the worse-hearing ear account for asymmetric hearing impairment and have been used in a few studies[14,39], a summary measure using the better-hearing ear was chosen as it is ultimately a more comprehensive measure of one's overall hearing ability, is more commonly used both in studies evaluating prevalence of hearing loss[66–68] and studies evaluating the association between hearing loss and cognition or other factors[18,20,21,64,65], and has been the metric used by the World Health Organization (WHO)[68–70]. Based on work from the WHO, moderate-to-severe hearing loss (also called disabling hearing loss by the WHO) was defined as having a better-ear PTA (BPTA)

greater than 40 dB[68,69]. This is also called moderate bilateral hearing loss, as one's hearing ability in the other (i.e., poorer hearing) ear would, by definition, be worse than the 40 dB threshold.

3.2.3 Additional hearing-related covariates used for imputation

Because one of the primary exposure variables – audiometrically defined bilateral moderate hearing loss – had over 5% missingness (n=1,028, 5.2% missing), and as self-rated hearing ability also had some degree of missingness (n=18, 0.1% missing), the following variables were included when imputing to allow for better imputation of missing data for the hearing variables: hearing difficulty with background noise, self-reported use of hearing aids, and degree of bilateral hearing loss. Hearing difficulty with background noise was determined through the question, "Do you find it difficult to follow a conversation if there is background noise, such as TV, radio or children playing, even if using a hearing aid as usual?". Use of hearing aids was self-reported based on a "yes" response to two questions: "Do you use any aids, specialized equipment, or services for persons who are deaf or hard of hearing, e.g., a volume control telephone or TV decoder?" and "Do you now use hearing aids?". The degree of bilateral hearing loss, derived from audiometric data, was categorized as no hearing loss, mild hearing loss, and moderate or greater hearing loss. The latter two categories were based on the WHO's definitions for mild hearing loss (better-hearing ear PTA greater than 25 dB) and moderate or greater hearing loss (better-hearing ear PTA greater than 40 dB)[68,69]. Detailed descriptions of the approach and steps taken for imputation are provided in Section 3.3.2.

3.2.4 Variable specification of DemPoRT predictors

The variable specification of DemPoRT predictors using CLSA data is summarized in **Appendix 1**. When possible, CLSA variables with the most similar wording of questions and categories to the CCHS were selected. For example, the question in the CCHS used to assess whether a participant required help with finances was "Because of any physical condition or mental condition or health problem, do you need the help of another person: … with looking after your personal finances such as making bank transactions or paying bills?". In the CLSA, the following question was the best match: "Can you handle your own money without help (i.e., you write cheques, pay bills, etc.)?". Transformations to obtain the DemPoRT predictors matched as closely as possible to the original transformations performed when deriving and validating the original DemPoRT model in CCHS data. For example, pack years of smoking in the CLSA was calculated based on the same function used to calculate pack years in the CCHS. Minor modifications were made to transform smoking variables (e.g., count of cigarettes smoked daily) that were categorical in the CLSA (i.e., 1-5, 6-10, 11-15, 16-20, 21-25, 26+ cigarettes) to the equivalent variable in the CCHS that was continuous; in this particular case, the average value was obtained and used for each category.

3.3 Statistical methods and analyses

3.3.1 Statistical software

All analyses were conducted using the R software (version 4.1.0). The 'recodeflow' package in R was used to recode and derive DemPoRT variables within the CLSA.

3.3.2 Missingness and imputation

The proportion of missing values for each variable in the pre-imputed dataset are shown in **Appendix 2**. There were no missing responses for age, sex, and multilingualism. All DemPoRT and hearing variables had less than 1% missing, except leisure physical activity (n=279, 1.4% missing), bilateral moderate hearing loss (n=1,028, 5.2% missing), and degree of hearing loss by BPTA (n=1,028, 5.2% missing).

Most participants (n=18,599, 93.8%) in the CLSA sample had no missing responses to the full suite of DemPoRT variables (**Appendix 3**) and 17,649 (89.0%) of CLSA participants in the sample had non-missing responses to all DemPoRT variables, self-rated hearing, and bilateral hearing loss (**Appendix 4**). There were 1,042 participants (5.3%) within the sample who had 1 hearing variable (self-rated hearing or moderate bilateral hearing loss) missing and there were 2 individuals (0.01%) within the sample with both main hearing impairment variables missing (**Appendix 5**). The majority of individuals (n=949, 91.1%) with a missing response for a hearing variable had no missing responses to any DemPoRT variables. Few participants (n=39, 0.2%) had 5 or more missing responses to key hearing variables and/or DemPoRT variables.

The variables included for imputation were dementia status at Follow-up 1, all DemPoRT covariates (except for survey year, which was the same for everyone in the CLSA cohort), the hearing covariates of interest, and additional hearing-related variables (outlined in section 3.2.3), which were included to allow for more optimal imputation of the two hearing variables of interest. Multiple imputation was conducted using the 'mice' package, which performs multivariate imputation by chained equations (MICE)[71,72]. Regression models created from the

'mice' function utilize data from individuals with non-missing data with characteristics similar to individuals with a given missing value to obtain predicted values for the missing value. With the 'mice' function, different default imputation methods are used depending on the nature of the variable: 1) predictive mean matching for numeric data, 2) logistic regression imputation for categorical variables with 2 categories, 3) polytomous regression imputation for unordered categorical variables, and 4) proportional odds modelling for ordered categorical variables. Five imputed datasets were created, and the baseline DemPoRT characteristics were evaluated across all five datasets and the original, unimputed dataset (**Appendix 6**). After finding no noticeably large differences in counts and proportions for the categorical variables and medians and interquartile ranges (IQR) for the continuous variables, one dataset (the fifth dataset in **Appendix 6**) was used for subsequent modelling and analysis steps. This decision was also informed by prior team experience finding no meaningful differences when pooling results from multiply imputed datasets for a similarly built risk prediction model[73].

3.3.3 Data cleaning and model specification

Using the tableone package in R, counts and frequencies of categorical variables and medians and IQRs of continuous variables were evaluated in the whole sample pre- and post-imputation and stratified by sex and outcome. To assess whether there are significant differences between individuals with and without incident dementia, chi-square tests were used for categorical variables and Kruskal-Wallis tests were used for continuous variables as many continuous variables did not follow a normal distribution.

The overall approach of model specification for the original DemPoRT model in CCHS data followed Harrell general approach as well as guidelines from Steyerberg[74,75]. Just like the original DemPoRT work using CCHS data, weights were not used in the analyses using CLSA data as I am assessing individual dementia risk and am not intending to conduct population-level reporting in these analyses. Drinks last week, fruit and vegetable consumption, potato consumption, juice consumption, physical activity, pack years, and BMI were truncated at the 99.5th percentile to prevent extreme values from skewing risk estimates due to being overly influential to the DemPoRT risk score. Truncations to extreme values also help to lower measurement error risks.

Mimicking the original DemPoRT model development, each DemPoRT variable was centred upon their mean, which allows for missing responses to take on the sample's average response. Centering the model helps make the process of model recalibration in other populations easier and gives flexibility in scenarios where there are missing responses. Restricted cubic splines were then applied to continuous variables, using the same number of knots as what was defined for each variable in the original DemPoRT model[10]. Restricted cubic splines are piecewise cubic polynomial functions that are constrained to be linear before the first knot and after the last knot[74]. They are typically used to model non-linear relationships in a flexible manner. As per Harrell's recommendations, variables with three knots had their knots placed at the 10th, 50th, and 90th centiles of the distribution, while variables prespecified to have 5 knots had the knots placed at the 5th, 27.5th, 50th, 72.5th, and 95th centiles[74].

A sex-specific DemPoRT score was derived for each individual by using the beta coefficients of the predictors from the original CCHS-based reduced DemPoRT model[10]. The formulas of the sex-specific DemPoRT scores can be found in **Appendix 7**.

After calculating the DemPoRT score for each individual in the sample, three logistic regression models were fit with three-year incident dementia as the outcome: 1) DemPoRT score as the base model, 2) DemPoRT score + self-rated hearing (i.e., the model with self-rated hearing), and 3) DemPoRT score + audiometrically defined bilateral moderate hearing loss (i.e., the model with audiometric data). Instead of including each DemPoRT predictor as separate covariates in each model, using the sex-specific DemPoRT score as a singular, continuous variable in each model was chosen due to preserve statistical power due to the low incidence of dementia in the CLSA cohort (n=54). As Steyerberg describes in work regarding updating models in new settings, this method of having the DemPoRT score as a singular linear predictor in the new model allows for the recalibration of the model slope and intercept for the new CLSA-based sample to give the new base model[75]. Models 2 and 3 implement model extension methods described by Steyerberg in addition to the recalibration previously described[75]. Selective extension of an existing model occurs when additional potential predictors available in new datasets are considered, are included in the model, and are evaluated for added predictive ability. The full formulas and beta coefficients of these CLSA-based DemPoRT models can be found in **Appendix 8**. Odds ratios and 95% confidence intervals were obtained from these logistic regression models by exponentiating coefficients (summary in **Table 5** and full list in **Appendix 9**). Because odds ratios are conventionally known as measures of association and are not measures of risk, the odds ratios were converted to relative risks (RR) (via formula found in

Appendix 10) for the two hearing measures to determine their contribution of risk in the prediction models and to evaluate their predictive ability[76].

Furthermore, using the five-year dementia risk formula derived in the original CCHS-based work[10] (formula in **Appendix 11**), the five-year risk of dementia was estimated for each individual in the CLSA sample. This formula utilizes the sex-specific baseline hazards of the original DemPoRT reduced model and each individual's DemPoRT score. The median and IQR of 5-year dementia risk, stratified by sex (**Table 1**) or dementia status (**Table 2**), were descriptively reported for the CLSA sample.

3.3.4 Model performance

Model validation was performed for the three logistic regression models using bootstrap resampling. Bootstrap resampling involves sampling from an original dataset with replacement to create a new dataset of the same size that may have duplicate observations[74]. This process is repeated until the desired number of sample datasets are obtained. Optimism-corrected bootstrap validation was performed using the 'validate()' function in the 'rms' R package, where 500 resamples of size 19,830 were created with replacement. Optimism-corrected bootstrap validation yields nearly unbiased estimates of model performance and tends to have higher precision than cross-validation. Moreover, while derivation and validation of the original DemPoRT model using CCHS data was performed via split sampling, bootstrap validation was the preferred method for this dataset due to the limited number of individuals with the outcome of interest.

Optimism-corrected estimates of model performance were obtained through several steps. First, the apparent model performance was estimated in the original sample (i.e. $Index_{original}$). Second, a bootstrap resample of the same size was created, the model was fit on the bootstrap sample, and model performance assessed (i.e. $Index_{training}$). Third, the model coefficients from the bootstrap resample were applied to the original sample and the performance measures were assessed again (i.e. $Index_{test}$). Fourth, the difference between the measures from the previous two steps was calculated (i.e. $Index_{training} - Index_{test}$). This difference is the estimated bias (i.e., optimism or overfitting). Fifth, steps two to four were repeated several times using often several hundred bootstrap resamples to obtain an averaged optimism estimate. Finally, this averaged optimism value was subtracted from the apparent performance measures obtained in step 1 to produce the optimism-corrected estimates of model performance[74].

Model performance was evaluated using discrimination and calibration. Discrimination assesses a model's ability to differentiate between individuals who are at a higher risk of developing the outcome of interest and individuals who are at a lower risk for the outcome[74,77]. The measure used for measuring discrimination was Harrell's concordance statistic, also known as the c-statistic, c-index, or area under the receiver operating characteristic (ROC) curve (AUC). The c-statistic involves looking at all possible pairs of individuals in the dataset where one subject in the pair has the outcome and the other does not. It calculates the proportion of pairs that appropriately had a higher predicted probability assigned to the individual with the outcome compared to the individual without the outcome. The c-statistic was derived from Somers' D statistic (annotated Dxy in the output from the 'validate' function) using the following formula: (C-statistic) = 0.5 * ((Somers' D statistic) + 1) [78]. While thresholds for sufficient discrimination

are not clearly defined, c-statistics above 0.7, 0.8, and 0.9 are typically associated with acceptable/good, excellent, and outstanding discrimination, respectively[79].

Calibration evaluates how well a model's predicted risk matches the observed risk[74,77]. Calibration slopes and intercepts closer to 1 and 0, respectively, are indicative of a better calibrated model. While there are no clearly defined thresholds for good calibration, a calibration slope above 1 indicates that the predicted probabilities are too conservative (i.e., not extreme enough) while a slope less than 1 suggests that predictions are too extreme (i.e., the estimates for low probabilities are too low and the estimates for high probabilities are too high). An intercept that is below 0 is indicative of a general over-estimation of predicted probabilities; an intercept above 0 means that the predicted probabilities were generally too low[80,81]. Calibration plots were created using the "calibrate" function within the 'rms' R package. This function uses non-parametric locally weighted scatterplot smoothing (LOWESS) to create smooth curves depicting optimism-corrected estimates of the observed versus predicted probabilities of the outcome[78].

The Brier score and the Nagelkerke R^2 are both composite measures of discrimination and calibration that assess the overall performance of a model[77]. The Brier score is a measure of overall performance that evaluates the mean squared error between the observed values and predicted values. It is a score between 0 and 0.25, where a value of 0 indicates a model with perfect accuracy. A value of 0.25 indicates that there is a completely non-informative model, as this would be akin to predicting a 50% probability of the binary outcome to each individual, thus yielding a squared error of 0.5^2. The Nagelkerke R^2 is another measure of overall performance that calculates the fraction of variation in the outcome variable that can be explained by the

algorithm[82]. Values for this measure range from 0 to 1, with a value closer to 1 being preferable as it is indicative of more variation explained.

3.4 Ethics, data access, and funding

In March of 2021, this study obtained research ethics approval from the Bruyère Continuing Care Research Ethics Board (Protocol #M16-21-014). Subsequently, I submitted and was approved for renewal on March 2, 2022 and February 22, 2023 (**Appendix 17**). Approval to access the de-identified CLSA data was received in January 2021 under Application #2006031 and the data access agreement was finalized in March 2021 (**Appendix 18**). The analyses were conducted using the CLSA Baseline Comprehensive Dataset version 5.0 and Follow-up 1 Comprehensive Dataset version 3.0. The funding sources for this thesis were the AMS Healthcare Small Grant in Compassion and Artificial Intelligence, the Canadian Institutes of Health Research (CIHR) Catalyst Grant, and Queen Elizabeth II Graduate Scholarship in Science and Technology. The CLSA is funded by the Canada Foundation for Innovation and by CIHR (through the grant reference: LSA 94473).

CHAPTER 4: RESULTS

After applying exclusion criteria to the CLSA Comprehensive cohort, there were 19,830 individuals remaining in the sample for analysis (**Figure 1**). Of the remaining individuals, 10,041 individuals (50.6%) from the sample are female while 9,789 individuals (49.4%) are male.

4.1 Participants and baseline characteristics

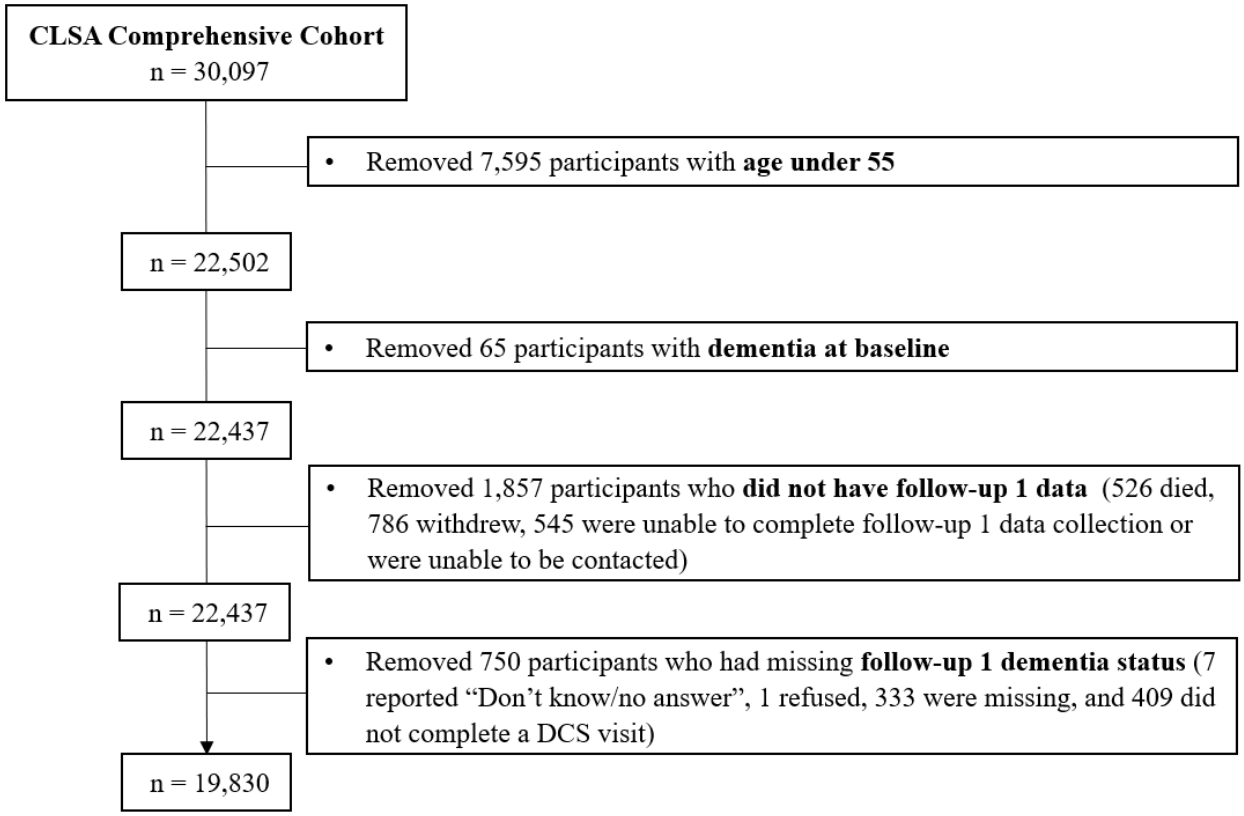

Figure 1. Cohort creation for secondary data analysis.

Table 1 shows baseline characteristics of the final CLSA sample, stratified by sex, following imputation and variable specification of DemPoRT predictors. Females were slightly younger (median 65 years, IQR 60–73 years) than males (median 66 years, IQR 61–73 years) (median age of 65 vs 66 among males). The proportion of individuals who were divorced, widowed, or

single were higher among females than males by 9.3%, 10.8%, and 1.9%, respectively. Females had fewer pack years of smoking (median 0 pack years, IQR 0.0-21.4 pack years) than males (median 6.6 pack years, IQR 0.0-30.6 pack years), had fewer drinks in a given week (females: median 2 drinks, IQR 0-6 drinks; males: median 4 drinks, IQR 0-10 drinks), and ate more fruits and vegetables daily (females: median 3.4, IQR 2.5-4.7; males: median 2.7, IQR 1.9-3.7). Females were more likely to require help with one or more activities of daily living, as 22.6% of females required help with one or more activities while 9.7% of males required help with one or more activities. The proportion of participants with heart disease, stroke, diabetes, and high blood pressure were higher among males than females by 7.9%, 0.6%, 5.1%, and 3.5%, respectively. Meanwhile, mood disorders and COPD were more prevalent in females than males, with a difference in prevalence of 8.4% and 1.6%, respectively.

The table also presents sex-specific dementia status at Follow-up 1 (females: n=26, 0.3%; males: n=28, 0.3%) and 5-year dementia risk score based on applying the CCHS-derived DemPoRT algorithm to this sample. Females had a higher 5-year predicted risk of incidence of dementia (using the baseline hazards from the original DemPoRT model) than males (5% vs. 3%), and had a wider range of risk of dementia (IQR 2-10%) compared to males (IQR 1-7%).

Table 1. Baseline characteristics, dementia status at Follow-up 1, and 5-year dementia risk, stratified by sex.

Variable	Level	Male	Female	Overall
n		9789	10041	19830
Age (median [IQR])		66.0 [61.0, 73.0]	65.0 [60.0, 73.0]	66.0 [60.0, 73.0]
Ethnicity (%)	White	9300 (95.0)	9641 (96.0)	18941 (95.5)
	South East Asian/Chinese/ Japanese/Korean/Filipino	114 (1.2)	92 (0.9)	206 (1.0)
	South Asian/Arab/West Asian	130 (1.3)	59 (0.6)	189 (1.0)
	Other/Multiple Origin/Unknown	245 (2.5)	249 (2.5)	494 (2.5)
Education (%)	Less than high school	493 (5.0)	677 (6.7)	1170 (5.9)
	High school graduate	826 (8.4)	1125 (11.2)	1951 (9.8)
	Some post-secondary education	747 (7.6)	821 (8.2)	1568 (7.9)
	Post-secondary graduate	7723 (78.9)	7418 (73.9)	15141 (76.4)
Marital status (%)	Now married/common-law	7693 (78.6)	5680 (56.6)	13373 (67.4)
	Divorced	873 (8.9)	1829 (18.2)	2702 (13.6)
	Widowed	572 (5.8)	1668 (16.6)	2240 (11.3)
	Single	651 (6.7)	864 (8.6)	1515 (7.6)
Multilingualism (%)	Yes	3540 (36.2)	3195 (31.8)	6735 (34.0)
	No	6249 (63.8)	6846 (68.2)	13095 (66.0)
Stress (%)	Not at all stressful	3188 (32.6)	2721 (27.1)	5909 (29.8)
	Not very stressful	3972 (40.6)	4330 (43.1)	8302 (41.9)
	A bit stressful	2203 (22.5)	2482 (24.7)	4685 (23.6)
	Quite a bit stressful	377 (3.9)	456 (4.5)	833 (4.2)
	Extremely stressful	49 (0.5)	52 (0.5)	101 (0.5)
Self-rated health (%)	Excellent	2022 (20.7)	2096 (20.9)	4118 (20.8)
	Very good	4006 (40.9)	4292 (42.7)	8298 (41.8)
	Good	2936 (30.0)	2820 (28.1)	5756 (29.0)
	Fair	697 (7.1)	708 (7.1)	1405 (7.1)
	Poor	128 (1.3)	125 (1.2)	253 (1.3)
Pack years of smoking (median [IQR])		6.6 [0.0, 30.6]	0.0 [0.0, 21.4]	0.0 [0.0, 26.0]
Smoking status (%)	Non-smoker	2508 (25.6)	3513 (35.0)	6021 (30.4)
	Former smoker quit 5+ years	4313 (44.1)	3552 (35.4)	7865 (39.7)
	Pack years (median [IQR])	29.7 [20.0, 40.5]	22.8 [12.8, 31.5]	26.0 [16.0, 36.0]
	Former smoker quit 0 to 5 years	2271 (23.2)	2301 (22.9)	4572 (23.1)
	Pack years (median [IQR])	0.01 [0.01, 0.01]	0.01 [0.01, 0.01]	0.01 [0.01, 0.01]
	Current smoker	697 (7.1)	675 (6.7)	1372 (6.9)
	Pack years (median [IQR])	28.6 [18.4, 37.8]	25.4 [15.3, 33.8]	26.7 [16.4, 36.4]
Former drinker (%)	Yes	996 (10.2)	1240 (12.3)	2236 (11.3)
	No	8793 (89.8)	8801 (87.7)	17594 (88.7)
Number of drinks last week (median [IQR])		4.0 [0.0, 10.0]	2.0 [0.0, 6.0]	3.0 [0.0, 7.0]
Fruit and vegetable consumption (median [IQR])		2.7 [1.9, 3.7]	3.4 [2.5, 4.7]	3.0 [2.1, 4.1]

Juice consumption (median [IQR])		0.3 [0.0, 1.0]	0.1 [0.0, 0.7]	0.1 [0.0, 1.0]
Potato consumption (median [IQR])		0.3 [0.1, 0.4]	0.3 [0.1, 0.4]	0.3 [0.1, 0.4]
Leisure physical activity (average kcal/kg/day) (median [IQR])		3.9 [1.2, 7.3]	2.6 [1.0, 5.5]	3.1 [1.1, 6.4]
Number of activities needing help (%)	None	8837 (90.3)	7772 (77.4)	16609 (83.8)
	1	882 (9.0)	2096 (20.9)	2978 (15.0)
	2	43 (0.4)	135 (1.3)	178 (0.9)
	3	19 (0.2)	27 (0.3)	46 (0.2)
	4	7 (0.1)	8 (0.1)	15 (0.1)
	5	1 (0.0)	3 (0.0)	4 (0.0)
Heart disease (%)	Yes	1733 (17.7)	986 (9.8)	2719 (13.7)
	No	8056 (82.3)	9055 (90.2)	17111 (86.3)
Stroke (%)	Yes	218 (2.2)	160 (1.6)	378 (1.9)
	No	9571 (97.8)	9881 (98.4)	19452 (98.1)
Diabetes (%)	Yes	2134 (21.8)	1679 (16.7)	3813 (19.2)
	No	7655 (78.2)	8362 (83.3)	16017 (80.8)
Mood disorder (%)	Yes	1188 (12.1)	2057 (20.5)	3245 (16.4)
	No	8601 (87.9)	7984 (79.5)	16585 (83.6)
High blood pressure (%)	Yes	4299 (43.9)	4056 (40.4)	8355 (42.1)
	No	5490 (56.1)	5985 (59.6)	11475 (57.9)
COPD (%)	Yes	519 (5.3)	697 (6.9)	1216 (6.1)
	No	9270 (94.7)	9344 (93.1)	18614 (93.9)
Epilepsy (%)	Yes	87 (0.9)	98 (1.0)	185 (0.9)
	No	9702 (99.1)	9943 (99.0)	19645 (99.1)
Body mass index (median [IQR])		27.6 [25.1, 30.6]	27.0 [23.8, 31.1]	27.3 [24.5, 30.8]
Survey year (%)	CCHS 11-12	9789 (100.0)	10041 (100.0)	19830 (100.0)
Dementia at follow-up 1 (%)	Dementia	28 (0.3)	26 (0.3)	54 (0.3)
	No dementia	9761 (99.7)	10015 (99.7)	19776 (99.7)
DemPoRT Score (median [IQR])		0.0 [-0.9, 0.8]	-0.6 [-1.6, 0.1]	-0.3 [-1.2, 0.4]
5-year dementia risk (median [IQR])		0.03 [0.01, 0.07]	0.05 [0.02, 0.10]	0.04 [0.01, 0.08]

4.2 Baseline characteristics of the cohort stratified by dementia status

Table 2. Baseline characteristics stratified by dementia status.

Variable	Level	Dementia	No dementia	p-value	Overall
n		54	19776		19830
Age (median [IQR])		76.5 [72.0, 80.0]	66.0 [60.0, 73.0]	<0.001	66.0 [60.0, 73.0]
Sex (%)	Female	26 (48.1)	10015 (50.6)	0.818	10041 (50.6)
	Male	28 (51.9)	9761 (49.4)		9789 (49.4)
Ethnicity (%)	White	54 (100.0)	18887 (95.5)	0.468	18941 (95.5)
	South East Asian/Chinese/ Japanese/Korean/Filipino	0 (0.0)	206 (1.0)		206 (1.0)
	South Asian/Arab/West Asian	0 (0.0)	189 (1.0)		189 (1.0)
	Other/Multiple Origin/Unknown	0 (0.0)	494 (2.5)		494 (2.5)
Education (%)	Less than high school	4 (7.4)	1166 (5.9)	0.122	1170 (5.9)
	High school graduate	9 (16.7)	1942 (9.8)		1951 (9.8)
	Some post-secondary education	7 (13.0)	1561 (7.9)		1568 (7.9)
	Post-secondary graduate	34 (63.0)	15107 (76.4)		15141 (76.4)
Marital status (%)	Now married/common-law	31 (57.4)	13342 (67.5)	0.143	13373 (67.4)
	Divorced	9 (16.7)	2693 (13.6)		2702 (13.6)
	Widowed	11 (20.4)	2229 (11.3)		2240 (11.3)
	Single	3 (5.6)	1512 (7.6)		1515 (7.6)
Multilingualism (%)	Yes	14 (25.9)	6721 (34.0)	0.269	6735 (34.0)
	No	40 (74.1)	13055 (66.0)		13095 (66.0)
Stress (%)	Not at all stressful	13 (24.1)	5896 (29.8)	0.001	5909 (29.8)
	Not very stressful	15 (27.8)	8287 (41.9)		8302 (41.9)
	A bit stressful	20 (37.0)	4665 (23.6)		4685 (23.6)
	Quite a bit stressful	4 (7.4)	829 (4.2)		833 (4.2)
	Extremely stressful	2 (3.7)	99 (0.5)		101 (0.5)
Self-rated health (%)	Excellent	11 (20.4)	4107 (20.8)	<0.001	4118 (20.8)
	Very good	14 (25.9)	8284 (41.9)		8298 (41.8)
	Good	21 (38.9)	5735 (29.0)		5756 (29.0)
	Fair	4 (7.4)	1401 (7.1)		1405 (7.1)
	Poor	4 (7.4)	249 (1.3)		253 (1.3)
Pack years of smoking (median [IQR])		7.0 [0.0, 34.4]	0.0 [0.0, 26.0]	0.181	0.0 [0.0, 26.0]
Smoking status (%)	Non-smoker	15 (27.8)	6006 (30.4)	0.641	6021 (30.4)
	Former smoker quit 5+ years	22 (40.7)	7843 (39.7)		7865 (39.7)
	Former smoker quit 0 to 5 years	11 (20.4)	4561 (23.1)		4572 (23.1)
	Current smoker	6 (11.1)	1366 (6.9)		1372 (6.9)
Former drinker (%)	Yes	9 (16.7)	2227 (11.3)	0.299	2236 (11.3)
	No	45 (83.3)	17549 (88.7)		17594 (88.7)
Number of drinks last week (median [IQR])		2.0 [0.0, 7.0]	3.0 [0.0, 7.0]	0.235	3.0 [0.0, 7.0]

Fruit and vegetable consumption (median [IQR])		2.6 [1.7, 3.4]	3.0 [2.1, 4.1]	0.006	3.0 [2.1, 4.1]
Juice consumption (median [IQR])		0.6 [0.1, 1.0]	0.1 [0.0, 1.0]	0.012	0.1 [0.0, 1.0]
Potato consumption (median [IQR])		0.3 [0.1, 0.6]	0.3 [0.1, 0.4]	0.229	0.3 [0.1, 0.4]
Leisure physical activity (average kcal/kg/day) (median [IQR])		1.9 [0.4, 4.8]	3.1 [1.1, 6.4]	0.016	3.1 [1.1, 6.4]
Number of activities needing help (%)	None	35 (64.8)	16574 (83.8)	<0.001	16609 (83.8)
	1	16 (29.6)	2962 (15.0)		2978 (15.0)
	2	3 (5.6)	175 (0.9)		178 (0.9)
	3	0 (0.0)	46 (0.2)		46 (0.2)
	4	0 (0.0)	15 (0.1)		15 (0.1)
	5	0 (0.0)	4 (0.0)		4 (0.0)
Heart disease (%)	Yes	16 (29.6)	2703 (13.7)	0.001	2719 (13.7)
	No	38 (70.4)	17073 (86.3)		17111 (86.3)
Stroke (%)	Yes	5 (9.3)	373 (1.9)	0.001	378 (1.9)
	No	49 (90.7)	19403 (98.1)		19452 (98.1)
Diabetes (%)	Yes	13 (24.1)	3800 (19.2)	0.464	3813 (19.2)
	No	41 (75.9)	15976 (80.8)		16017 (80.8)
Mood disorder (%)	Yes	7 (13.0)	3238 (16.4)	0.622	3245 (16.4)
	No	47 (87.0)	16538 (83.6)		16585 (83.6)
High blood pressure (%)	Yes	26 (48.1)	8329 (42.1)	0.448	8355 (42.1)
	No	28 (51.9)	11447 (57.9)		11475 (57.9)
COPD (%)	Yes	5 (9.3)	1211 (6.1)	0.5	1216 (6.1)
	No	49 (90.7)	18565 (93.9)		18614 (93.9)
Epilepsy (%)	Yes	1 (1.9)	184 (0.9)	1	185 (0.9)
	No	53 (98.1)	19592 (99.1)		19645 (99.1)
Body mass index (median [IQR])		26.7 [23.4, 28.0]	27.3 [24.5, 30.8]	0.022	27.3 [24.5, 30.8]
Survey year (%)	CCHS 11-12	54 (100.0)	19776 (100.0)	NA	19830 (100.0)
Self-rated hearing (%)	Good-Excellent	39 (72.2)	17341 (87.7)	0.001	17380 (87.6)
	Fair-Poor	15 (27.8)	2435 (12.3)		2450 (12.4)
Bilateral moderate hearing loss (%)	Yes	14 (25.9)	1096 (5.5)	<0.001	1110 (5.6)
	No	40 (74.1)	18680 (94.5)		18720 (94.4)
DemPoRT Score (median [IQR])		0.8 [0.2, 1.2]	-0.3 [-1.2, 0.4]	<0.001	-0.3 [-1.2, 0.4]
5-year dementia risk (median [IQR])		0.10 [0.08, 0.14]	0.04 [0.01, 0.08]	<0.001	0.04 [0.01, 0.08]

Table 2 shows descriptive statistics of DemPoRT variables at baseline stratified by dementia status at Follow-up 1. Only 54 individuals (0.3%) had incident dementia at Follow-up 1. Individuals with incident dementia were on average 10.5 years older compared to individuals without incident dementia ($p<0.001$). Compared to individuals without the outcome, individuals

with incident dementia also had higher self-rated stress levels ($p=0.001$); they had a higher baseline prevalence of reporting a bit of stress, quite a bit of stress, or extreme stress (by 13.4%, 3.2%, and 3.2%, respectively) and a lower prevalence of reporting quite a bit of stress and extreme stress (by 5.7% and 14.1%, respectively). There were lower proportions of self-reported excellent or very good health (by 0.4% and 16.0%, respectively) and higher proportions of good, fair, or poor health (by 9.9%, 0.3%, and 6.1%) among individuals with dementia than individuals without dementia ($p<0.001$). Moreover, individuals with dementia consumed fruits and vegetables 0.4 fewer times per day ($p=0.006$), drank juice 0.5 more times per day ($p=0.012$), and had lower levels of daily leisure physical activity (by 1.2 kcal/kg/day, i.e., metabolomic equivalent of task units (MET), $p=0.016$). There were significant differences ($p<0.001$) in the number of activities of daily living where the participants required assistance with between the two groups. For example, 29.6% and 5.6% of individuals with incident dementia required help with 1 or 2 tasks, respectively, at baseline. However, 15.0% and 0.9% of individuals without incident dementia required help with 1 or 2 tasks, respectively. The prevalence of heart disease and stroke were higher among individuals with incident dementia, by 15.9% ($p=0.001$) and 7.4% ($p=0.001$), respectively.

Individuals with the outcome of interest were less educated, had a lower baseline prevalence of multilingualism (by 8.1%), and had a higher baseline prevalence of being former drinkers (by 5.4%), having diabetes (by 4.9%), high blood pressure (by 6.0%), COPD (by 3.2%), and epilepsy (by 1.0%) than individuals who did not develop dementia at follow-up 1, but these differences were found to be statistically insignificant (i.e., $p>0.05$).

At baseline, 27.8% of individuals with incident dementia reported fair or poor hearing (**Table 2**), while 12.3% of individuals without incident dementia reported fair or poor hearing (p=0.001). Bilateral moderate hearing loss was present in 25.9% of participants who developed dementia at follow-up 1 but was only present in 5.5% of participants who did not develop dementia at follow-up 1 (p<0.001). Based on the original DemPoRT algorithm, the median 5-year risk of developing dementia was 10% among individuals who developed dementia by follow-up 1, but was 4% among individuals who did not develop dementia by follow-up 1 (p<0.001).

Additionally, the prevalence of hearing impairment differs by age and sex. **Table 3** displays the baseline prevalence of hearing impairment across age groups. With increasing age, there was a significant increase in the proportion of participants reporting fair or poor hearing (p<0.001). A similar trend was observed with bilateral moderate hearing loss and increasing age; only 1.4% of individuals aged 55 to 64 have bilateral moderate hearing loss, while 4.6% of participants aged 65 to 74 and 16.0% of individuals aged 75 and above have hearing loss ascertained by audiometry, respectively (p<0.001). **Table 4** outlines the baseline prevalence of hearing impairment stratified by sex. There was a higher proportion of fair-poor self-rated hearing and bilateral moderate hearing loss among males than females (15.8% vs. 9.0%, p<0.001, and 7.3% vs. 3.9%, p<0.001, respectively).

Table 3. Baseline hearing impairment characteristics, stratified by age group at baseline.

Variable n	Level	55-64 9006	65-74 6525	75+ 4299	p-value	Overall 19830
Self-rated hearing (%)	Good-Excellent	8140 (90.4)	5691 (87.2)	3549 (82.6)	<0.001	17380 (87.6)
	Fair-Poor	866 (9.6)	834 (12.8)	750 (17.4)		2450 (12.4)
Bilateral moderate hearing loss (%)	Yes	125 (1.4)	299 (4.6)	686 (16.0)	<0.001	1110 (5.6)
	No	8881 (98.6)	6226 (95.4)	3613 (84.0)		18720 (94.4)

Table 4. Baseline hearing impairment characteristics, stratified by sex.

Variable n	Level	Male 9789	Female 10041	p-value	Overall 19830
Self-rated hearing (%)	Good-Excellent	8242 (84.2)	9138 (91.0)	<0.001	17380 (87.6)
	Fair-Poor	1547 (15.8)	903 (9.0)		2450 (12.4)
Bilateral moderate hearing loss (%)	Yes	714 (7.3)	396 (3.9)	<0.001	1110 (5.6)
	No	9075 (92.7)	9645 (96.1)		18720 (94.4)

4.3 Unadjusted and adjusted odds for 3-year incidence of dementia

Table 5 shows the unadjusted and adjusted odds of having a physician diagnosis of dementia in three years. Prior to adjusting for the DemPoRT score, the unadjusted models showed almost 3 times the odds of 3-year incidence of dementia among individuals who had fair to poor hearing compared to those with good to excellent hearing (uOR = 2.74, 95% CI 1.51-4.98), and there was almost 6 times the odds of the outcome among individuals who had bilateral hearing loss compared to those without (uOR = 5.97, 95% CI 3.24-11.00). The models indicate that after adjusting for sex-specific DemPoRT score, individuals reporting fair or poor self-rated hearing ability continued to show increased odds of 3-year incidence of dementia (aOR = 1.76, 95% CI

0.96-3.23), although this was found to be only approaching statistical significance (p=0.0672). Bilateral moderate hearing loss at 40 dB, after adjusting for sex-specific DemPoRT score, was significantly associated with the odds of 3-year incident dementia (aOR = 2.60, 95% CI 1.38-4.87, p-value = 0.0033).

Table 5. Unadjusted odds ratios (uOR) and adjusted odds ratios (aOR) and 95% confidence intervals for odds of 3-year incident dementia.

Model & Variable name	**Category**	**Unadjusted Model**				**Adjusted Model***			
		uOR	**95% CI**		**p-value**	**aOR***	**95% CI**		**p-value**
Model with self-rated hearing ability									
Self-rated hearing ability	Fair-poor vs. Excellent-good	2.74	1.51	4.98	0.0009	1.76	0.96	3.23	0.0672
Model with bilateral moderate hearing loss									
Bilateral moderate HL	Bilateral HL vs. No HL	5.97	3.24	11.00	1.06E-08	2.60	1.38	4.87	0.0030

*aOR = Adjusted odds ratio. Adjusted for sex-specific DemPoRT score.

The formulas of the three models, showing intercepts and beta coefficients of the model covariates, can be found in **Appendix 8**, and a full list of the odds ratios of all covariates is shown in **Appendix 9**. For the base model, the model with self-rated hearing ability, and the model with audiometric data, a 1-unit increase in sex-specific DemPoRT score was highly associated with the odds of 3-year incidence of dementia (aOR = 3.53, 95% CI 2.48-5.01; aOR = 3.38 95% CI 2.38-4.80; and aOR = 3.17, 95% CI 1.38-4.87, for the respective models).

Appendix 10 shows the conversion of each aOR corresponding to hearing impairment into a relative risk (RR) as a measure of the contribution of hearing impairment to risk prediction of dementia. Due to the low incidence of dementia in this sample, the OR approximated the RR[76]. After adjusting for the sex-specific DemPoRT score, the risk of 3-year incidence of dementia was 76% higher among individuals self-reporting fair or poor hearing compared to individuals self-reporting excellent, very good, or good hearing (RR = 1.76, 95% CI 0.96-3.22). Meanwhile, the risk of incident dementia was over 2 times higher among individuals with bilateral moderate hearing loss (RR = 2.59, 95% CI 1.38-4.84).

4.4 Model performance

Table 6. Model performance with bootstrap validation (500 resamples) and optimism correction.

Model	**Base model**	**Model with self-rated hearing ability**	**Model with audiometric data**
Model composition	***DemPoRT Score alone***	***DemPoRT Score + Self-rated hearing ability***	***DemPoRT Score + bilateral moderate HL***
Discrimination			
C-statistic (95% CI)	0.8020 (0.7519, 0.8629)	0.8025 (0.7518, 0.8587)	0.8080 (0.7617, 0.8703)
Calibration			
Calibration slope	1.0208	1.0001	1.0005
Calibration intercept	0.1261	0.0151	0.0166
Overall performance			
Brier Score	0.0027	0.0027	0.0027
Nagelkerke R^2	0.0920	0.0935	0.0993

Detailed output of performance metrics using 500 bootstrap resamples and showing indices before and after optimism correction can be found in **Appendix 12, Appendix 13, and Appendix 14**, which showed that there was minimal optimism correction for each of the models.

The measures assessing model performance for the three models using 500 bootstrap resamples and optimism correction are summarized in **Table 6**.

4.4.1 Overall performance

For overall performance, all three models had the same Brier score of 0.0027. Thus, based on the Brier score alone, there were no differences in general model performance between the three models. The Nagelkerke R^2 of the three models increased from 0.0920 for the base DemPoRT score model to 0.0935 and 0.0993 for the model with self-rated hearing ability model and the model with audiometric data, respectively. A Nagelkerke R^2 closer to 1 is preferable as it suggests that more variation in the outcome that is explained by the model. The base model has the least variation explained among the three models evaluated and is therefore the poorest performing model overall using this metric. Conversely, the model with audiometric data has the most variation in the outcome explained by its algorithm, and therefore has the best overall performance based on the Nagelkerke R^2.

4.4.2 Discrimination

In terms of discrimination, there were no major differences in c-statistic between the various models. The c-statistic only increased marginally from 0.8020 (95% CI 0.7519-0.8629) for the base model of sex-specific DemPoRT score to 0.8025 (95% CI 0.7518-0.8587) and 0.8080 (95% CI 0.7617-0.8703) for the model with self-rated hearing ability model and the model with audiometric data, respectively. A c-statistic above 0.8 is generally known to be indicative of excellent discrimination[79]; therefore, all three models have excellent performance in terms of discrimination. The model utilizing audiometric data has the best discriminatory ability, but all

three models have comparable levels of discrimination as there is less than a 0.01-0.05 unit variation between the c-statistic values of the three models.

4.4.3 Calibration

The calibration slopes were 1.0208, 1.0001, and 1.0005 for the base DemPoRT score model the model with self-rated hearing ability model, and the model with audiometric data, respectively. As all three slopes are above 1, this suggests that the predicted probabilities from all three models may not be extreme enough. However, the slopes are all close to 1, indicating good calibration overall for all three models. The calibration intercept was 0.1261 for the base model and decreased to 0.0151 and 0.0166 for the model with self-rated hearing ability model and the model with audiometric data, respectively. As the three intercepts are values above 0, there appears to be slight under-estimation of predicted probabilities overall for all three models, but these are otherwise well-calibrated models. Because the slopes and intercepts of the two models with hearing impairment are marginally closer to 1 and 0, respectively, than the base model, this suggests that they are slightly better calibrated than the base model.

4.4.4 Calibration plots

The calibration plots using 500 bootstrap resamples are depicted in **Figure 2**, **Figure 3**, and **Figure 4**. Each plot has a histogram at the top indicating the distribution of predicted probability, an "ideal" line indicating perfect calibration, an apparent curve for the calibration using bootstrap validation but without bias correction, and a bias-corrected curve. When predicting low probabilities, all three models are well calibrated as the bias-corrected curve overlaps the ideal line. The calibration plot of the base DemPoRT score model (**Figure 2**) shows the largest

deviations from the ideal line for predicted probabilities greater than approximately 0.01. **Figure 3**, depicting the calibration plot for the model with self-rated hearing ability, has the smallest deviations from the "ideal" line denoting perfect calibration. The calibration plot for the model containing audiometrically-ascertained hearing impairment (**Figure 4)** appears to have some deviations; in particular, this model appears to underpredict when predicting probabilities greater than approximately 0.025. However, the span of predicted probabilities is the largest in the plot for the model using audiometric data; the predicted probabilities span 0.00 to approximately 0.06 in this model while the predicted probabilities span 0.00 to approximately 0.05 in the other two models.

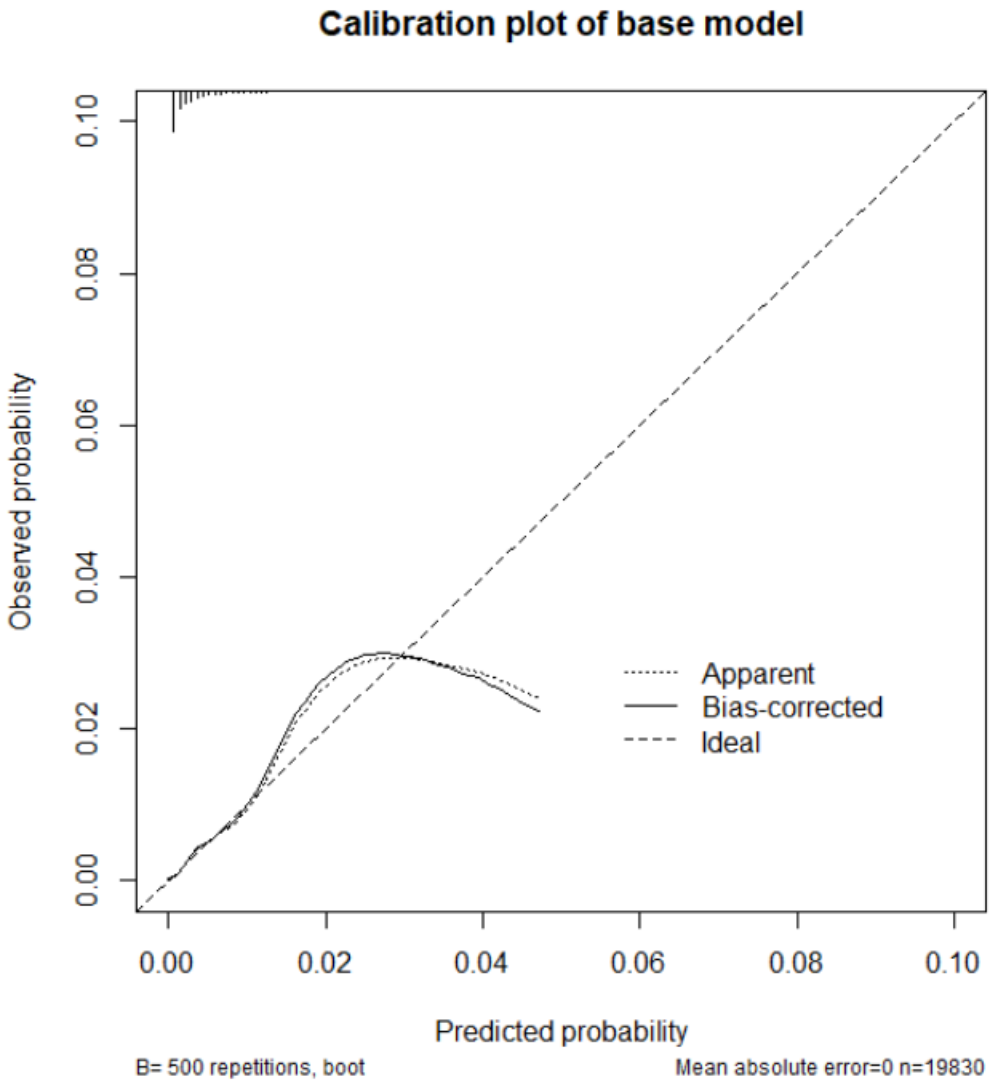

Figure 2. Calibration plot of the base model (DemPoRT score).

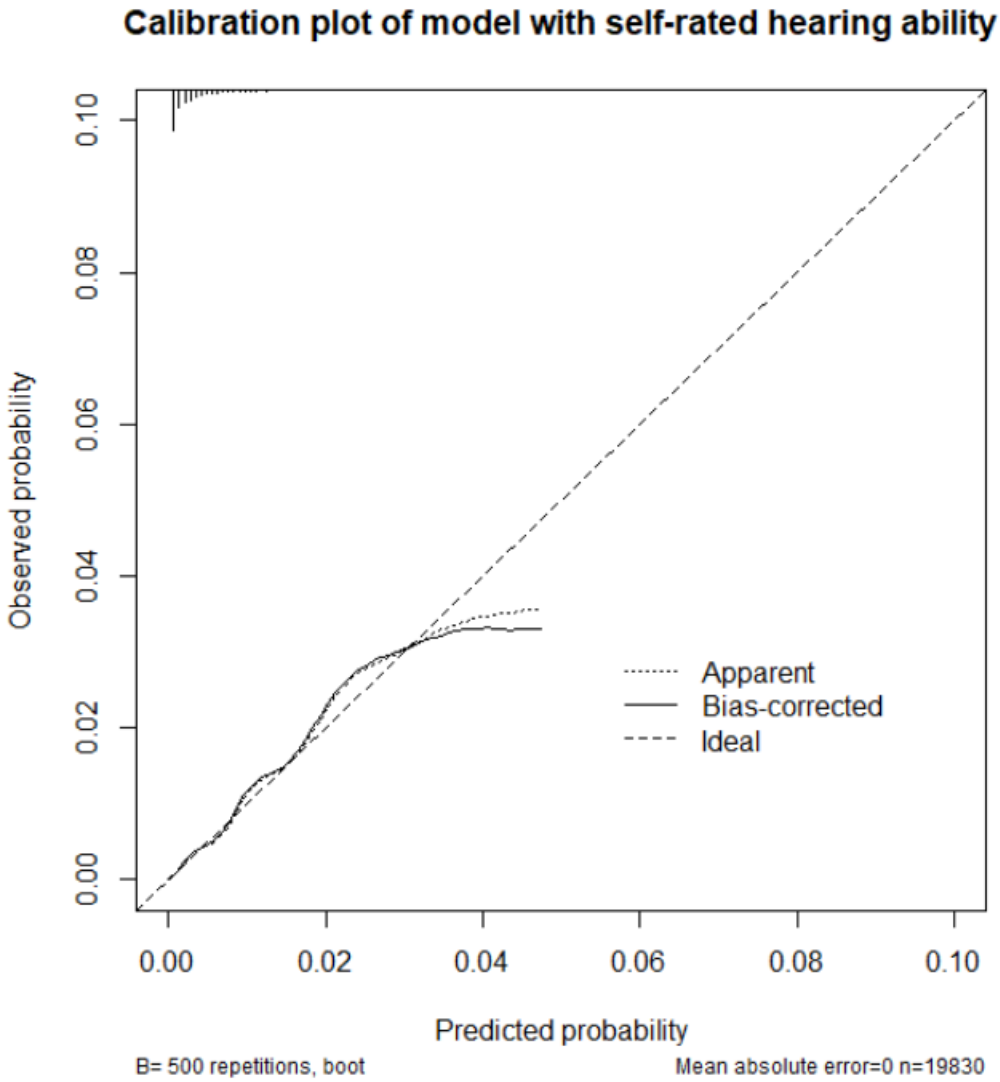

Figure 3. Calibration plot of the model with self-rated hearing ability.

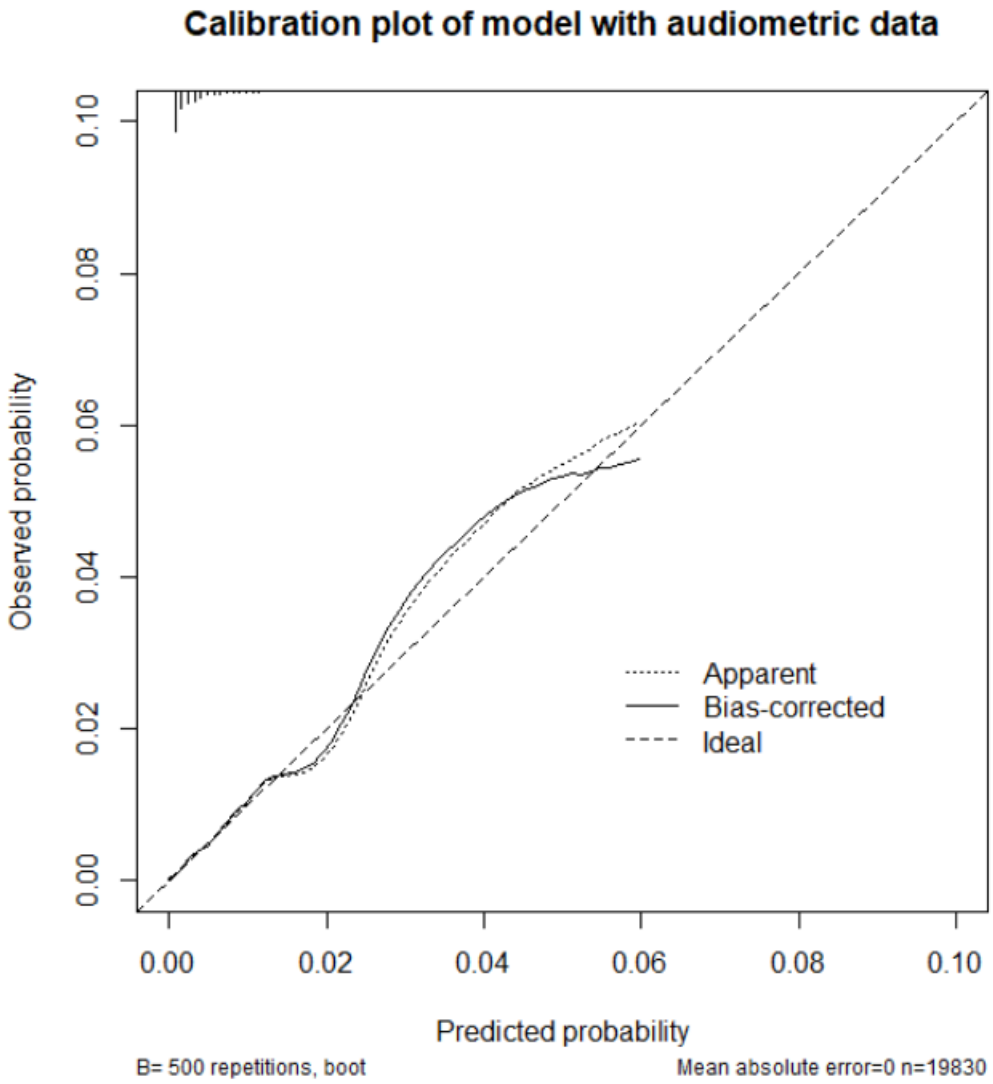

Figure 4. Calibration plot of the model with audiometric data.

4.5 Additional metrics for assessing added value of a predictor

Appendix 15 shows additional performance metrics conducted on the original sample of 19,830 and that are used in the context of assessing the added value of a predicter compared to a base model[83], especially when traditionally used measures of performance (e.g., Brier score, c-statistic, etc.) may not be very informative[83,84]. The likelihood ratio test comparing the base model and the model with self-rated hearing ability had a p-value of 0.0795, and the likelihood ratio test comparing the base model and the model with bilateral moderate hearing loss had a p-value of 0.0062. Using the likelihood ratio chi-squares, the fraction of total predictive information gained by adding self-rated hearing and bilateral moderate hearing loss is 0.0435 and 0.0997, respectively.

CHAPTER 5: DISCUSSION

5.1 Summary of findings for the research aims and interpretation

The main research objective was to develop, validate, and compare prediction models for 3-year incidence of dementia in Canadian older adults, with a specific interest in evaluating the contribution of self-reported fair or poor hearing ability and audiometrically confirmed bilateral moderate hearing loss to predicting future dementia incidence.

5.1.1 First research aim

The first research aim was to report the baseline prevalence of hearing impairment in older Canadian adults (i.e., 55 years of age and older) with or without dementia by Follow-up 1. Based on data from the CLSA, 27.8% of older adults with incident dementia self-reported fair or poor hearing at baseline. Comparatively, 12.3% of individuals without incident dementia had fair or poor hearing ability ($p=0.001$). Moreover, the baseline prevalence of bilateral moderate hearing loss was 25.9% among individuals with dementia by Follow-up 1 and was 5.5% among individuals without dementia by Follow-up 1 ($p<0.001$).

5.1.2 Second research aim

The second aim sought to describe the independent contribution of hearing impairment in prediction models for dementia and to assess whether hearing impairment (be it self-reported or confirmed via audiometric testing) is predictive of dementia incidence. To address this research objective, logistic regression models were built consisting of an individual's sex-specific DemPoRT score and either self-reported hearing ability or audiometrically defined bilateral moderate hearing loss. After adjusting for DemPoRT score, a self-reported fair or poor hearing

ability was highly associated with the odds of 3-year incidence of dementia, with an adjusted OR of 1.76 (95% CI 0.96-3.23). This finding was approaching significance and is likely due to having a small sample size of (54) individuals with the primary outcome. Furthermore, bilateral moderate hearing loss was also highly associated with incident dementia, with an adjusted OR of 2.60 (95% CI 1.38-4.87). The ORs were converted to RRs, which allow for the evaluation of the contribution of hearing impairment on risk prediction of dementia. Because the outcome was extremely rare in this sample, the ORs approximated the RRs (RR = 1.76, 95% CI 0.96-3.22 for self-rated fair/poor hearing ability, RR = 2.59, 95% CI 1.38-4.84 for bilateral hearing loss). These RRs suggest that, after adjusting for sex-specific DemPoRT score, both measures of hearing impairment are highly predictive of dementia risk.

The predefined hypothesis regarding this research question was that hearing impairment is likely predictive of dementia based on prior literature finding strong associations between hearing loss and dementia[3,16,22,85]. The findings from this thesis reject the null hypothesis of having no association between hearing impairment and dementia, and the relative risks from the prediction models suggest hearing impairment is highly predictive of future dementia incidence, regardless of whether it is defined via self-report or through audiometric testing.

5.1.3 Third research aim

The third research objective was to evaluate whether a prediction algorithm using audiometrically defined hearing loss outperforms (in terms of discrimination and/or calibration) a prediction model that relies on self-reported hearing ability. Discrimination (which evaluates a model's ability to separate individuals at higher risk from individuals who are at lower risk of the

outcome[74,77]) was assessed using the c-statistic and calibration (which calculates the accuracy of the model's predicted risk compared to the observed risk[74,77]) was evaluated using the calibration slope and intercept in addition to calibration plots.

The c-statistic of the base model that included just the DemPoRT score was 0.8020 (95% CI = 0.7519-0.8629). The model including self-rated hearing impairment had a c-statistic of 0.8025 (95% CI = 0.7518-0.8587) and the model using hearing loss ascertained with audiometry had a c-statistic of 0.8080 (95% CI = 0.7617-0.8703). A c-statistic above 0.8 has been generally known in literature to be indicative of an excellent performing model in terms of discrimination[79], and all three models fit this criterion. Because the c-statistic of the model using self-rated hearing ability was 0.8025, while the c-statistic of the model ascertaining hearing impairment with audiometry was 0.8080, these findings suggest that a prediction model using audiometrically-confirmed hearing loss may slightly outperform a model using self-reported hearing ability in terms of discrimination. However, as the confidence intervals overlap across the three models and the difference in c-statistic is less than 0.01, there appears to be no major difference in discrimination between the three models.

For the base model, the model including self-rated hearing ability, and the model using audiometrically ascertained hearing loss, the calibration slopes were 1.0208, 1.0001, and 1.0005, respectively. The calibration intercepts were 0.1261, 0.0151 and 0.0166 for the three models, respectively. A calibration slope above 1 suggests that the predicted probabilities generated from the model are too conservative, and a slope below 1 suggests that the predicted probabilities are too extreme. Meanwhile, a calibration intercept below 0 suggests that the model generally over-

estimated predicted probabilities and an intercept above 0 indicates that the model's predicted probabilities were under-estimated. Therefore, a slope of 1 and an intercept of 0 are desired and are characteristics of a perfectly calibrated model. While the calibration slopes and intercepts decrease between the base model and the two models with hearing impairment, the model using self-rated hearing ability has the calibration slope that is closest to 1 and the calibration intercept that is closest to 0. Therefore, using these measures of calibration alone suggest that this model is the best calibrated overall among the three models evaluated by a small margin. When comparing the calibration plots of the different models, while all three models appear to be well-calibrated when predicting low probabilities, the calibration plot for the base model appears to have the most deviations from the diagonal line depicting perfect calibration when predicting probabilities beyond 0.01. Meanwhile, the calibration plot for the model with self-rated hearing ability had the least deviations, and the calibration plot for the model including audiometrically-confirmed hearing impairment had moderate deviations, underpredicting when predicting probabilities greater than approximately 0.025. However, the span of predicted probabilities was the largest (0 to ~0.06) in the plot for the model using audiometric data compared to the other two models (0 to ~0.05). The ability of this model to predict a larger range of probabilities suggests that the model using audiometric data may have slightly better calibration than the other two models. Therefore, taking into account all measures of calibration, there is no consensus of a model that has superior calibration between the two models with hearing impairment. Because none of the calibration measures show uncertainty (as the R packages used for evaluating calibration do not currently include the option to calculate 95% CIs), no firm conclusions can be made with high confidence, but these findings overall suggest that there are no major differences in calibration between the two models with hearing impairment.

The hypothesis regarding this research question was that a prediction model using hearing loss ascertained by audiometry would likely outperform the prediction model using self-reported hearing ability in terms of both discrimination and calibration. The reasoning underlying improved discrimination with the audiometric data was that audiometric testing would allow for improved sorting of individual's hearing abilities due to improved sensitivity and specificity, especially among individuals with fair to good hearing. As discrimination is based on classification ability, using a variable that can more accurately identify an individual's true hearing ability should in turn lead to improved discrimination. Similarly, calibration was expected to be better in the model using audiometrically defined hearing impairment because of the better classification from using a more accurate measure of hearing via audiometry. At the outset, I suspected that some individuals in this sample would likely misclassify their hearing ability (especially under-reporting hearing impairment) when self-reporting, which would likely lead to lower concordance between the observed and predicted probabilities of the outcome (i.e., underestimating their own risk for dementia) when using the model with self-reported hearing ability. **Appendix 16** shows the distribution of baseline self-rated hearing ability stratified by baseline bilateral moderate hearing loss, the overall percent agreement between the two measures, and the sensitivity and specificity of the self-rated hearing measure. There was high concordance between the two measures, with an 87.1% overall agreement between self-rated hearing ability and bilateral hearing loss ascertained with audiometry. The specificity of self-rated hearing status was 89.6%. However, the sensitivity of self-rated hearing ability was only 45.0%; this means that 55% of individuals who had audiometrically confirmed hearing loss had self-reported good, very good, or excellent hearing.

The results indicate that there are no notably meaningful differences between the three models in terms of discrimination, though the model using audiometrically-confirmed hearing impairment had the best c-statistic by a small margin. Despite the high overall concordance between the methods of ascertainment, in reality, a fair amount of misclassification will occur in using the self-rated hearing ability measure, and this could explain the minor (albeit insignificant) improvement in discrimination from using the audiometrically-defined hearing measure. The misclassification resulting from the use of the self-rated hearing variable has been observed in other studies that examined the accuracy of a self-rated hearing measure compared to audiometry-derived measures of hearing. For example, Ramage-Morin et al. used data from the CHMS to show that individuals with hearing loss ascertained by audiometry often do not self-report having hearing impairment; in fact, they estimated that approximately 6.3 million (77%) of the 8.2 million older adult Canadians with audiometrically-defined high-frequency hearing loss have unperceived hearing loss[14]. Another study has found differing concordance levels between self-rated hearing and audiometry-derived measures depending on the individual's cognition status[19]. They found a sensitivity and specificity for self-rated hearing status of 71.2% and 85.9% within older adults with no cognitive impairment, 61.1% and 84.9% within individuals with MCI, and 52.6% and 81.2% among individuals with dementia, respectively[19].

The findings pertaining to calibration were mixed, but overall, there were no significant differences in calibration between the two models that include hearing impairment. Hamalainen et al. previously used CLSA data to generate violin plots of the BPTA of the mid-frequencies (i.e., 1000, 2000, 3000, 4000 Hz) of participants across the five different categories of self-

reported hearing ability, stratified by age group[61]. They visually observed that among individuals aged 75 and above, the majority of individuals with excellent hearing did not have moderate audiometrically-defined hearing impairment and most of the individuals reporting poor hearing indeed had moderate hearing impairment. However, the concordance between the two measures was weakest among the middle three categories of very good, good, and fair hearing[61]. With the large discrepancy between the two measures, especially within these middle categories of self-reported hearing ability, I had expected that the effect of the self-rated hearing measure would be attenuated due to the misclassification, which would in turn make the audiometric-based model perform better in both discrimination and calibration than the self-reported hearing ability-based model. However, the overall agreement between the two measures could be driven by individuals who have either excellent or poor hearing as opposed to the middle categories. It is possible that while there are no clear differences in overall calibration between the models with hearing impairment, there may be certain subgroups of the population for which the model with audiometric data would be better calibrated. For instance, calibration may be superior in the model using audiometrically defined hearing loss for individuals who report within the middle range of very good, good, or fair hearing ability.

As no model with hearing impairment is distinctively superior in terms of population-level discrimination or calibration, the ideal algorithm to use and implement will likely depend on the context and the target population. There is a trade-off between the significantly larger reach and accessibility of the self-rated hearing measure and the slight additional specificity gained from using the audiometrically-derived hearing measure. As these models perform quite similarly, for uses by the general public through a web-based platform such as ProjectBigLife.ca, the use of

self-assessment of hearing ability is likely sufficient. When audiometric testing has been performed and that data is available to older adults who are referred from audiology clinics, there is no harm in leveraging that data to obtain an evaluation of dementia risk.

5.2 Comparison with other findings

While there exist very few dementia risk prediction models that include hearing impairment as a predictor, the SLAS risk index for MCI and dementia published in 2021 by Ng et al. did include hearing loss as one of their predictors[4]. In their risk index, the authors defined hearing loss via either self-report or through a whisper test. The model is more parsimonious than the DemPoRT model, containing 7 variables in total. The findings for the independent contribution of hearing impairment to incident MCI-or-dementia were similar to my results. Ng et al. found that hearing impairment was significantly predictive of conversion to MCI or dementia (OR = 2.59, 95% CI 1.10-6.13)[4]. I also found that hearing impairment was predictive of 3-year incidence of dementia, regardless of whether it was defined objectively or subjectively (aOR = 1.76 (95% CI 0.96-3.23) for model with self-rated hearing, aOR = 2.60 (95% CI 1.38-4.87). The risk score generated from SLAS data had an AUC of 0.73 in the development cohort and an AUC of 0.74 in the validation cohort. Comparatively, all three of the models that I developed using CLSA data were better performing (c-statistic of 0.802 for the base model, c-statistic of 0.803 for the model with self-rated hearing, and c-statistic of 0.808 for the model with audiometric data). The follow-up time is similar to this work (derivation cohort had an average of 3 years of follow-up while the validation cohort had an average of 4 years of follow-up). The samples of the SLAS-1 derivation cohort and the SLAS-2 validation cohort were smaller overall (n = 1,601 and 3,051, respectively) compared to that of the CLSA (n=19,830), but both SLAS cohorts have a larger number of

individuals with the outcome, as they include both MCI and dementia in their outcome definition.

The other prediction model with hearing impairment as a predictor was by Song et al. using data from the Canadian Study of Health and Aging[9]. However, the model composition was different; hearing trouble and ear trouble were two of 19 non-traditional risk factors evaluated, and the proportion of these non-traditional risk factors was used as the covariate in the model. As the contribution of each non-traditional risk factor to MCI-or-dementia prediction is likely different, one cannot determine from this study the predictive value of hearing trouble or ear trouble on MCI or dementia prediction through this model. Additionally, the model's AUC was 0.66 (0.03), which suggests that the model has moderate discrimination. The models developed in this thesis had superior discrimination, with c-statistics above 0.8 for all three models.

5.3 Strengths

One major strength of this work is that it is one of the few existing risk prediction models for dementia that includes hearing impairment, regardless of the method of ascertainment of hearing ability (i.e., self-reported or assessed objectively via audiometry). Additionally, this research used the same data to build in parallel two risk prediction models for dementia that included hearing impairment defined in different ways. The models were directly compared to each other in order to investigate which method of ascertainment of hearing impairment contributed to the best performing model in terms of discrimination and calibration. To my knowledge, no prior work has previously investigated different means of defining hearing impairment in the context of dementia risk prediction to this extent of detail.

This research utilizes data from a new, ongoing national-level Canadian longitudinal study; very few research teams have thus far utilized data from the CLSA for prediction modelling purposes, irrespective of whether the outcome is related to cognitive decline or not[86,87]. Another strength of this thesis work is that it leverages the already well-performing DemPoRT model to control for other dementia risk factors.

Additionally, the use of self-reportable, modifiable risk factors increases the model's ability to be implemented in clinical and community settings. Developing both a model that uses self-reported hearing impairment and a model that utilizes audiometric testing gives flexibility for individuals or clinicians to pick the model that most appropriately fits the level of resources and information they have at their disposal (i.e., whether they have access to audiometric testing).

5.4 Limitations

This work has several limitations to consider. For instance, there were very few incident dementia cases due to several factors: only Follow-up 1 data was available at the time of conducting the analyses, the follow-up period is a short timeframe of three years, and the CLSA is still a relatively young cohort of older adults. Because there were few new self-reported physician diagnoses of dementia at Follow-up 1 that were not present at baseline, there was limited power to perform subgroup analyses to evaluate model performance among subgroups.

Another sample size-related limitation is that self-rated hearing was dichotomized into fair or poor hearing vs excellent, very good, or good hearing. This recategorization was done because

there were small cell sizes in some of the individual hearing groups, particularly among individuals with dementia. While this is a common recategorization of self-rated hearing performed in numerous studies that use this same five-point scale of self-rating hearing ability[14,61–63], it does lead to imprecision.

Moreover, the audiometrically-defined bilateral hearing loss variable was a dichotomized variable derived from a continuous variable that represented the PTA of the better-hearing ear. While the cut-off point of 40 dB for the BPTA has been used in numerous epidemiological studies[20,21,64,65], is clinically meaningful for diagnosing hearing impairment in audiology clinics, and has been deemed by the WHO as the threshold for disabling hearing loss in its work using this threshold[68], some biostatisticians such as Harrell caution against the dichotomization of continuous variables. Some of the negative effects associated with dichotomizing continuous variables are a loss of useful information from binning, reduced precision of estimated values, and reduced power in associated tests[74]. Of note, while linearity assumptions aren't often met when using continuous variables because the relationships between these variables and the outcome are seldom linear, Harrell argues that categorizing or dichotomizing a variable subconsciously creates a more problematic assumption that there is a flat relationship between the categorized variable and the outcome within a given category[74]. Additionally, using hearing as a continuous measure would be able to add to the evidence that there is a dose-response relationship between severity of hearing loss and cognitive decline[20,65,88,89].

Another limitation is that the outcome, the variables used to make the DemPoRT score, and the hearing covariates (other than the audiometry-derived hearing loss variable) were all self-

reported measures. Therefore, these measures are subject to reporting bias and misclassification that can impact study results. For example, having the outcome be a self-report of a physician diagnosis of dementia instead of a physician diagnosis of dementia may alter study findings, be it through an under-report of incident dementia cases (e.g., individuals may not be actively receiving treatment for dementia and/or do not believe they have dementia) or an over-report (e.g., individuals may be aware that dementia is part of their family history and/or could have been told by a physician that they are at high risk of dementia, and thus believe they have dementia).

Another limitation is that the CLSA sample is not representative of certain populations, such as older adults who cannot answer in English or French and individuals who are not community-dwelling at baseline (e.g., those who live in a long-term care residence). Additionally, as many individuals from the Comprehensive cohort were recruited via random digit dialling, this excludes deaf individuals from that sampling frame. Exclusion of individuals who are not community dwelling or who are deaf are may attenuate estimates, as the CLSA sample is healthier without these subgroups. Regarding the exclusion of deaf individuals, a recent article commented on the need to make cognitive aging studies more inclusive of individuals with sensory deficits, especially individuals with uncorrected significant or severe sensory deficits[44]. They are a high-risk subgroup and their lack of inclusion in studies limits the generalization of study results to a narrower group of older adults with no to limited or moderate vision or hearing impairments[44].

Data regarding the date of death of participants who were lost to follow-up because of death was not available at the time of analysis. Moreover, individuals with an unknown dementia status at follow-up were excluded from the analyses. Therefore, death as a competing risk unfortunately could not be accounted for in this thesis work, unlike the original DemPoRT model that was developed using CCHS data.

5.5 Future directions

5.5.1 Subgroup analyses

There are several components to this project that should and will be explored in the future, beyond this thesis. For instance, it is currently unclear whether there are specific subgroups for which these new models predict dementia risk poorly. Therefore, as a more immediate next step, subgroup analyses will be performed to better establish the predictive accuracy of the different models within subsets of the sample. There will be specific emphasis on evaluating model performance within higher-risk subgroups, as individuals with these risk factors would likely benefit from obtaining a more accurate estimate of dementia risk from a given model. Performing subgroup analyses will help us gain a better understanding of whether there are specific higher risk subgroups for which it would be fruitful for a clinician to refer a patient to an audiologist for an audiometric hearing test in order to obtain a more accurate estimate of the patient's risk of dementia. Because the current sample size is too small to perform subgroup analyses, they were not presented as part of this thesis, but can be explored as new CLSA follow-up data is made available.

5.5.2 New data available

Additionally, because Follow-up 2 data has recently been released, there is interest in applying similar modelling to create dementia risk algorithms for 6-year incidence of dementia. The longer follow-up period in this aging longitudinal cohort would be expected to increase the number of individuals with the outcome of interest. Consequently, this would increase the statistical power toward model building and circumvent sample size issues that one might come across when performing certain analyses such as the aforementioned subgroup analyses.

5.5.3 Implementation of hearing loss and other novel risk factors into the DemPoRT algorithm

While much more work is required for this to take place, there is interest in eventually potentially adding hearing impairment and other new risk factors to the DemPoRT model that is implemented as a web-based calculator hosted on ProjectBigLife.ca, the research lab's knowledge translation platform[11]. In fact, the Public Health Agency of Canada is interested in funding a new project with our team to support the incorporation of additional risk factors into the DemPoRT algorithm for population planning. They have also expressed intent on utilizing this work to help them specifically estimate at the national level the burden of hearing loss on dementia.

5.6 Significance and implications

DemPoRT has already been implemented online as a freely available web calculator tool on ProjectBigLife.ca[11]. Therefore, the original DemPoRT model can be used by both clinicians and patients to assess dementia risk on an individual basis. As shown in this research, the inclusion of

additional risk factors, such as hearing impairment, can improve discrimination and precision of dementia risk estimation. For the inclusion of hearing impairment to the current web calculator, the vision would be that, by default, individuals would use the DemPoRT model with self-reported hearing ability. Alternatively, if a patient has results and/data from audiometric testing, these could be input into the web calculator and the model including audiometrically derived hearing impairment would be used to estimate their dementia risk. This would be practical in a clinical setting such as at the Elizabeth Bruyère Hospital, wherein there is an audiology clinic onsite. Additionally, the inclusion of hearing impairment to the DemPoRT algorithm would complement the usage and novel auditory assessment tools in geriatric settings. For instance, there is a new initiative called the SHOEBOX Quicktest that has recently been implemented and is being tested in Bruyère's Memory Program and Geriatric Rehabilitation Program. The SHOEBOX Quicktest is an innovative iPad-based auditory screening tool that facilitates quick and easy hearing tests to patients in less than two minutes[90]. While more research is required to assess the implementation of such a hearing screening tool within a memory clinic, the SHOEBOX Quicktest has so far been shown to be effective at identifying undiagnosed hearing impairment in older adults with mild cognitive impairment[90].

Moreover, DemPoRT is the first multivariate dementia risk prediction algorithm to be designed with population use in mind, allowing for policy makers to project dementia burden to inform future decision-making. Statistics Canada and the Public Health Agency of Canada have committed to utilize the DemPoRT algorithm for the national microsimulation model for dementia.

5.7 Conclusion

Hearing impairment is an emerging risk factor for dementia that has yet to be incorporated into in many dementia risk prediction models. Little work has been done to assess hearing impairment's predictive ability of dementia risk and to evaluate what definition of hearing impairment (i.e., self-reported or audiometrically defined) would yield a better performing model in terms of discrimination and/or calibration. Through this thesis work, using data from the CLSA, I found that the prevalence of self-rated fair or poor hearing ability was 15.5% greater among individuals with 3-year incidence of dementia compared to individuals without incident dementia, and the prevalence of audiometrically defined bilateral moderate hearing loss was 20.4% greater among participants with dementia compared to those without the outcome of interest. Both measures of hearing impairment were found to be highly predictive of future dementia incidence. Furthermore, there were no noticeably large differences in performance (i.e., discrimination and calibration) between the model with audiometrically defined hearing loss and the model with self-rated hearing ability. Due to the accessibility of the self-rated hearing measure compared to the audiometry-derived measure, the model using self-rated hearing is expected to have a greater impact in its ability to reach and affect more individuals. Further research is required to evaluate the performance of the prediction models within various subgroups and to determine whether certain higher-risk subgroups for dementia may benefit from getting referrals to audiology clinics to get a more accurate estimate of their risk of developing dementia.

CHAPTER 6: REFERENCES

1 Armstrong JJ. Navigating the path forward for dementia in Canada; The Landmark Study. 2022 https://alzheimer.ca/sites/default/files/documents/Landmark-Study-Report-1-Path_Alzheimer-Society-Canada.pdf (accessed Jan 11, 2023).

2 Public Health Agency of Canada. A Dementia Strategy for Canada: Together We Aspire. 2019 https://www.canada.ca/content/dam/phac-aspc/images/services/publications/diseases-conditions/dementia-strategy/National Dementia Strategy_ENG.pdf (accessed Jan 11, 2023).

3 Livingston G, Sommerlad A, Orgeta V, *et al.* Dementia prevention, intervention, and care. *Lancet* 2017; **390**: 2673–734.

4 Ng TP, Lee TS, Lim WS, *et al.* Development, Validation and Field Evaluation of the Singapore Longitudinal Ageing Study (SLAS) Risk Index for Prediction of Mild Cognitive Impairment and Dementia. *J Prev Alzheimer's Dis* 2021. DOI:10.14283/jpad.2021.19.

5 Kivipelto M, Ngandu T, Laatikainen T, Winblad B, Soininen H, Tuomilehto J. Risk score for the prediction of dementia risk in 20 years among middle aged people: a longitudinal, population-based study. *Lancet Neurol* 2006; **5**: 735–41.

6 Exalto LG, Quesenberry CP, Barnes D, Kivipelto M, Biessels GJ, Whitmer RA. Midlife risk score for the prediction of dementia four decades later. *Alzheimer's Dement* 2014; **10**: 562–70.

7 Walters K, Hardoon S, Petersen I, *et al.* Predicting dementia risk in primary care: Development and validation of the Dementia Risk Score using routinely collected data. *BMC Med* 2016; **14**. DOI:10.1186/s12916-016-0549-y.

8 Anstey KJ, Cherbuin N, Herath PM. Development of a New Method for Assessing Global Risk of Alzheimer's Disease for Use in Population Health Approaches to Prevention. *Prev Sci* 2013; **14**: 411–21.

9 Song X, Mitnitski A, Rockwood K. Nontraditional risk factors combine to predict Alzheimer disease and dementia. *Neurology* 2011; **77**: 227–34.

10 Fisher S, Manuel DG, Hsu AT, *et al.* Development and validation of a predictive algorithm for risk of dementia in the community setting. *J Epidemiol Community Health* 2021; : jech-2020-214797.

11 Project Big Life. https://www.projectbiglife.ca/ (accessed March 10, 2023).

12 Livingston G, Huntley J, Sommerlad A, *et al.* The Lancet Commissions Dementia prevention, intervention, and care: 2020 report of the Lancet Commission The Lancet Commissions. *Lancet* 2020; **396**: 413–46.

13 Bucholc M, McClean PL, Bauermeister S, *et al.* Association of the use of hearing aids with the conversion from mild cognitive impairment to dementia and progression of dementia: A longitudinal retrospective study. *Alzheimer's Dement Transl Res Clin Interv* 2021; **7**. DOI:10.1002/trc2.12122.

14 Ramage-Morin PL, Banks R, Pineault D, Atrach M. Unperceived hearing loss among Canadians aged 40 to 79. *Heal Reports* 2019; **30**: 11–20.

15 Nondahl DM, Cruickshanks KJ, Wiley TL, Tweed TS, Klein R, Klein BEK. Accuracy of self-reported hearing loss. *Audiology* 1998; **37**: 295–301.

16 Amieva H, Ouvrard C, Giulioli C, Meillon C, Rullier L, Dartigues JF. Self-reported hearing loss, hearing aids, and cognitive decline in elderly adults: A 25-year study. *J Am*

Geriatr Soc 2015; **63**: 2099–104.
17 Fausto BA, Badana ANS, Arnold ML, Lister JJ, Edwards JD. Comparison of Subjective and Objective Measures of Hearing, Auditory Processing, and Cognition Among Older Adults With and Without Mild Cognitive Impairment. *J Speech, Lang Hear Res* 2018; **61**: 945–56.
18 Hoff M, Skoog J, Bodin TH, *et al.* Hearing loss and cognitive function in early old age: comparing subjective and objective hearing measures. *Gerontology* 2022; published online Dec 14. DOI:10.1159/000527930.
19 Kim AS, Betz JF, Albert M, *et al.* Accuracy of self- and proxy-rated hearing among older adults with and without cognitive impairment. *J Am Geriatr Soc* 2022; **70**: 490–500.
20 Lin FR, Metter EJ, O'Brien RJ, Resnick SM, Zonderman AB, Ferrucci L. Hearing loss and incident dementia. *Arch Neurol* 2011; **68**: 214–20.
21 Lin FR, Yaffe K, Xia J, *et al.* Hearing Loss and Cognitive Decline in Older Adults. *JAMA Intern Med* 2013; **173**: 293–9.
22 Gurgel RK, Ward PD, Schwartz S, Norton MC, Foster NL, Tschanz JT. Relationship of hearing loss and dementia: A prospective, population-based study. *Otol Neurotol* 2014; **35**: 775–81.
23 Brewster KK, Hu MC, Zilcha-Mano S, *et al.* Age-Related Hearing Loss, Late-Life Depression, and Risk for Incident Dementia in Older Adults. *Journals Gerontol - Ser A Biol Sci Med Sci* 2021; **76**: 827–34.
24 Corder EH, Saunders AM, Strittmatter WJ, *et al.* Gene dose of apolipoprotein E type 4 allele and the risk of Alzheimer's disease in late onset families. *Science* 1993; **261**: 921–3.
25 Strittmatter WJ, Saunders AM, Schmechel D, *et al.* Apolipoprotein E: High-avidity binding to β-amyloid and increased frequency of type 4 allele in late-onset familial Alzheimer disease. *Proc Natl Acad Sci U S A* 1993; **90**: 1977–81.
26 Saunders AM, Strittmatter WJ, Schmechel D, *et al.* Association of apolipoprotein E allele ϵ4 with late-onset familial and sporadic alzheimer's disease. *Neurology* 1993; **43**: 1467–72.
27 Teter B, Raber J, Nathan B, Crutcher KA. The presence of apoE4, not the absence of apoE3, contributes to AD pathology. *J Alzheimer's Dis* 2002; **4**: 155–63.
28 Pankratz N, Byder L, Halter C, *et al.* Presence of an APOE4 allele results in significantly earlier onset of Parkinson's disease and a higher risk with dementia. *Mov Disord* 2006; **21**: 45–9.
29 Uddin MS, Kabir MT, Al Mamun A, Abdel-Daim MM, Barreto GE, Ashraf GM. APOE and Alzheimer's Disease: Evidence Mounts that Targeting APOE4 may Combat Alzheimer's Pathogenesis. *Mol Neurobiol* 2019; **56**: 2450–65.
30 Shaw C, Hayes-Larson E, Glymour MM, *et al.* Evaluation of Selective Survival and Sex/Gender Differences in Dementia Incidence Using a Simulation Model. *JAMA Netw Open* 2021; **4**: e211001–e211001.
31 Sofi F, Valecchi D, Bacci D, *et al.* Physical activity and risk of cognitive decline: A meta-analysis of prospective studies. *J Intern Med* 2011; **269**: 107–17.
32 Öhlin J, Gustafson Y, Littbrand H, Olofsson B, Toots A. Low or declining gait speed is associated with risk of developing dementia over 5 years among people aged 85 years and over. *J Aging Phys Act* 2021; **29**: 678–85.
33 Nianogo RA, Rosenwohl-Mack A, Yaffe K, *et al.* Risk Factors Associated With

Alzheimer Disease and Related Dementias by Sex and Race and Ethnicity in the US. *JAMA Neurol* 2022; published online May 9. DOI:10.1001/JAMANEUROL.2022.0976.
34 Steyerberg EW, Moons KGM, van der Windt DA, *et al.* Prognosis Research Strategy (PROGRESS) 3: Prognostic Model Research. *PLoS Med* 2013; **10**. DOI:10.1371/journal.pmed.1001381.
35 Hou XH, Feng L, Zhang C, Cao XP, Tan L, Yu JT. Models for predicting risk of dementia: a systematic review. *J Neurol Neurosurg Psychiatry* 2019; **90**: 373–9.
36 Fisher S, Hsu A, Mojaverian N, *et al.* Dementia Population Risk Tool (DemPoRT): Study protocol for a predictive algorithm assessing dementia risk in the community. *BMJ Open* 2017; **7**. DOI:10.1136/bmjopen-2017-018018.
37 Ambler G, Brady AR, Royston P. Simplifying a prognostic model: A simulation study based on clinical data. *Stat Med* 2002; **21**: 3803–22.
38 World Health Orgazination. World Report on Hearing. 2021.
39 Feder K, Michaud D, Ramage-Morin P, McNamee J, Beauregard Y. Prevalence of hearing loss among Canadians aged 20 to 79: Audiometric results from the 2012/2013 Canadian health measures survey. *Heal Reports* 2015; **26**: 18–25.
40 Whitson HE, Cronin-Golomb A, Cruickshanks KJ, *et al.* American Geriatrics Society and National Institute on Aging Bench-to-Bedside Conference: Sensory Impairment and Cognitive Decline in Older Adults. *J Am Geriatr Soc* 2018; **66**: 2052–8.
41 Rigters SC, Bos D, Metselaar M, *et al.* Hearing impairment is associated with smaller brain volume in aging. *Front Aging Neurosci* 2017; **9**: 2.
42 Lin FR, Ferrucci L, An Y, *et al.* Association of Hearing Impairment with Brain Volume Changes in Older Adults. *Neuroimage* 2014; **90**: 84.
43 Armstrong NM, An Y, Doshi J, *et al.* Association of Midlife Hearing Impairment With Late-Life Temporal Lobe Volume Loss. *JAMA Otolaryngol Neck Surg* 2019; **145**: 794–802.
44 Powell DS, Oh ES, Reed NS, Lin FR, Deal JA. Hearing Loss and Cognition: What We Know and Where We Need to Go. *Front Aging Neurosci* 2022; **13**: 821.
45 Abraham AG, Hong C, Deal JA, *et al.* Are cognitive researchers ignoring their senses? The problem of sensory deficit in cognitive aging research. *J Am Geriatr Soc* 2023; published online Jan 20. DOI:10.1111/jgs.18229.
46 Liu CM, Lee CTC. Association of Hearing Loss With Dementia. *JAMA Netw open* 2019; **2**: e198112.
47 Croll PH, Vinke EJ, Armstrong NM, *et al.* Hearing loss and cognitive decline in the general population: a prospective cohort study. *J Neurol* 2020. DOI:10.1007/s00415-020-10208-8.
48 Heywood R, Gao Q, Nyunt MSZ, *et al.* Hearing Loss and Risk of Mild Cognitive Impairment and Dementia: Findings from the Singapore Longitudinal Ageing Study. *Dement Geriatr Cogn Disord* 2017; **43**: 259–68.
49 Wang J, Wang F, Han P, *et al.* Gender-specific associations of speech-frequency hearing loss, high-frequency hearing loss, and cognitive impairment among older community dwellers in China. *Aging Clin Exp Res* 2021. DOI:10.1007/s40520-021-01990-0.
50 Liang Z, Li A, Xu Y, Qian X, Gao X. Hearing Loss and Dementia: A Meta-Analysis of Prospective Cohort Studies. *Front Aging Neurosci* 2021; **13**. DOI:10.3389/fnagi.2021.695117.

51 Kumar KJA, Vidyalakshmi M. Effects of hearing aid on improving cognition and depressive symptoms in elderly. *Int J Otorhinolaryngol Head Neck Surg* 2021; **7**: 639–42.
52 Sarant J, Harris D, Busby P, *et al.* The Effect of Hearing Aid Use on Cognition in Older Adults: Can We Delay Decline or Even Improve Cognitive Function? *J Clin Med* 2020; **9**. DOI:10.3390/JCM9010254.
53 Pirozzo S, Papinczak T, Glasziou P. Whispered voice test for screening for hearing impairment in adults and children: systematic review. *BMJ Br Med J* 2003; **327**: 967.
54 Collins GS, Reitsma JB, Altman DG, Moons KGM. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): The TRIPOD Statement. *Eur Urol* 2015; **67**: 1142–51.
55 Moons KGM, Altman DG, Reitsma JB, *et al.* Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): Explanation and elaboration. *Ann Intern Med* 2015; **162**: W1–73.
56 Raina PS, Wolfson C, Kirkland SA. CANADIAN LONGITUDINAL STUDY ON AGING (CLSA) PROTOCOL: Canadian Longitudinal Study on Aging Protocol. *Can Longitud Study Aging Protoc* 2009; **28**: 221.
57 Raina P, Wolfson C, Kirkland S, Griffith L. The Canadian Longitudinal Study on Aging (CLSA) Report on Health and Aging in Canada - Findings from Baseline Data Collection. 2018. https://www.clsa-elcv.ca/doc/2639 (accessed June 29, 2020).
58 Raina P, Wolfson C, Kirkland S, *et al.* Cohort Profile: The Canadian Longitudinal Study on Aging (CLSA). Int. J. Epidemiol. 2019; **48**: 1752-1753J.
59 Statistics Canada. Canadian Community Health Survey (CCHS) - Healthy Aging. 2010 http://www.statcan.gc.ca/eng/statistical-programs/document/5146_D1_T1_V1-eng.pdf.
60 Canadian Longitudinal Study on Aging (CLSA). Sampling and computation of response rates and sample weights for the Tracking (telephone interview) participants and Comprehensive participants - technical document #3965. 2020 https://www.clsa-elcv.ca/doc/3965 (accessed April 26, 2022).
61 Hämäläinen A, Pichora-Fuller MK, Wittich W, Phillips NA, Mick P. Self-report Measures of Hearing and Vision in Older Adults Participating in the Canadian Longitudinal Study of Aging are Explained by Behavioral Sensory Measures, Demographic, and Social Factors. *Ear Hear* 2021; : 1–18.
62 Viljanen A, Törmäkangas T, Vestergaard S, Andersen-Ranberg K. Dual sensory loss and social participation in older Europeans. *Eur J Ageing* 2014; **11**: 155–67.
63 Malani P, Kullgren J, Solway E, *et al.* Hearing Loss Among Older Adults: Screening and Testing. 2021 www.healthyagingpoll.org (accessed Dec 22, 2022).
64 Mick P, Kawachi I, Lin FR. The association between hearing loss and social isolation in older adults. *Otolaryngol - Head Neck Surg (United States)* 2014; **150**: 378–84.
65 Golub JS, Sharma RK, Rippon BQ, Brickman AM, Luchsinger JA. The Association Between Early Age-Related Hearing Loss and Brain β-Amyloid. *Laryngoscope* 2021; **131**: 633–8.
66 Goman AM, Lin FR. Prevalence of hearing loss by severity in the United States. *Am J Public Health* 2016; **106**: 1820–2.
67 Sharma RK, Lalwani AK, Golub JS. Prevalence and Severity of Hearing Loss in the Older Old Population. JAMA Otolaryngol. - Head Neck Surg. 2020; **146**: 762–3.
68 World Health Organization. Addressing the rising prevalence of hearing loss. 2018.

https://apps.who.int/iris/handle/10665/260336 (accessed April 27, 2022).
69 World Health Orgazination. Report of the Informal Working Group on Prevention of Deafness and Hearing Impairment Programme Planning. 1991; : 1–24.
70 Mathers C, Smith A, Concha M. Global burden of hearing loss in the year 2000. *World Heal Organ* 2000; : 1–30.
71 van Buuren S, Groothuis-Oudshoorn K. mice: Multivariate imputation by chained equations in R. *J Stat Softw* 2011; **45**: 1–67.
72 van Buuren S. Flexible Imputation of Missing Data, Second Edition. Boca Raton, Florida: Chapman and Hall/CRC, 2018 DOI:10.1201/9780429492259.
73 Manuel DG, Tuna M, Bennett C, *et al.* Development and validation of a cardiovascular disease risk-prediction model using population health surveys: The Cardiovascular Disease Population Risk Tool (CVDPoRT). *CMAJ* 2018; **190**: E871–82.
74 Harrell FEJ. Regression Modeling Strategies: With Applications to Linear Models, Logistic and Ordinal Regression, and Survival Analysis, Second Ed. Springer, 2001.
75 Steyerberg EW. Clinical Prediction Models, 2nd Ed. Springer International Publishing, 2009 DOI:10.1007/978-3-030-16399-0.
76 Hunter E, Kelleher JD. A review of risk concepts and models for predicting the risk of primary stroke. *Front Neuroinform* 2022; **16**. DOI:10.3389/fninf.2022.883762.
77 Steyerberg EW, Vickers AJ, Cook NR, *et al.* Assessing the performance of prediction models: A framework for traditional and novel measures. Epidemiology. 2010; **21**: 128–38.
78 Harrell FEJ. Package 'rms' Title Regression Modeling Strategies. *CRAN R-project* 2022. https://github.com/harrelfe/rms%0Ahttp://biostat.mc.vanderbilt.edu/rms (accessed Dec 18, 2022).
79 Hosmer DW, Lemeshow S, Sturdivant RX. Applied Logistic Regression: Third Edition. Wiley, 2013 DOI:10.1002/9781118548387.
80 Van Calster B, McLernon DJ, Van Smeden M, *et al.* Calibration: The Achilles heel of predictive analytics. *BMC Med* 2019; **17**: 1–7.
81 Vergouwe Y, Steyerberg EW, Eijkemans MJC, Habbema JDF. Validity of prognostic models: When is a model clinically useful? *Semin Urol Oncol* 2002; **20**: 19–37.
82 Nagelkerke NJD. A Note on a General Definition of the Coefficient of Determination. *Biometrika* 1991; **78**: 691–2.
83 Harrell Jr FE. Statistically Efficient Ways to Quantify Added Predictive Value of New Measurements. Stat. Think. 2020. https://www.fharrell.com/post/addvalue/#introduction (accessed June 4, 2021).
84 Hastie T et. all. Springer Series in Statistics The Elements of Statistical Learning. 2009 http://www.springerlink.com/index/D7X7KX6772HQ2135.pdf (accessed Dec 18, 2022).
85 Thomson RS, Auduong P, Miller AT, Gurgel RK. Hearing loss as a risk factor for dementia: A systematic review. *Laryngoscope Investig Otolaryngol* 2017; **2**: 69–79.
86 Wang Z, Boulanger L, Berger D, *et al.* Development and internal validation of a multimorbidity index that predicts healthcare utilisation using the Canadian Longitudinal Study on Aging. *BMJ Open* 2020; **10**: 1–9.
87 Corbin D, Lesage F. Assessment of the predictive potential of cognitive scores from retinal images and retinal fundus metadata via deep learning using the CLSA database. *Sci Rep* 2022; **12**: 5767.

88 Irace AL, Armstrong NM, Deal JA, *et al.* Longitudinal Associations of Subclinical Hearing Loss With Cognitive Decline. *Journals Gerontol Ser A* 2022; **77**: 623–31.
89 Deal JA, Betz J, Yaffe K, *et al.* Hearing Impairment and Incident Dementia and Cognitive Decline in Older Adults: The Health ABC Study. *Journals Gerontol Ser A* 2017; **72**: 703–9.
90 Frank A, Goldlist S, Mark Fraser AE, Bromwich M. Validation of SHOEBOX QuickTest Hearing Loss Screening Tool in Individuals With Cognitive Impairment. *Front Digit Heal* 2021; **3**: 1–6.
91 Canadian Longitudinal Study on Aging (CLSA). Data collection site questionnaires (comprehensive). 2015.
92 Canadian Longitudinal Study on Aging. In-Home Questionnaire. 2018.
93 Manuel D, Yusuf W, Vyuha R, Chen K, Bennett C. Simple smoking status — smoke_simple_fun in cchsflow. https://big-life-lab.github.io/cchsflow/reference/smoke_simple_fun.html (accessed March 31, 2023).
94 Big Life Lab. cchsflow/smoking.R. https://github.com/Big-Life-Lab/cchsflow/blob/master/R/smoking.R (accessed March 31, 2023).
95 Manuel D, Yusuf W, Vyuha R, Chen K, Bennett C. Time since quit smoking — time_quit_smoking_fun in cchsflow. https://big-life-lab.github.io/cchsflow/reference/time_quit_smoking_fun.html (accessed March 31, 2023).
96 Manuel D, Yusuf W, Vyuha R, Chen K, Bennett C. Smoking pack-years — pack_years_fun in cchsflow. https://big-life-lab.github.io/cchsflow/reference/pack_years_fun.html (accessed March 31, 2023).
97 Shatenstein B, Payette H. Evaluation of the Relative Validity of the Short Diet Questionnaire for Assessing Usual Consumption Frequencies of Selected Nutrients and Foods. *Nutrients* 2015; **7**: 6362.
98 Statistics Canada. Canadian Community Health Survey (CCHS) Annual Component - Public Use Microdata File, 2009- 2010 Derived Variable (DV) Specifications. 2010; : 1–175.

CHAPTER 7: APPENDICES

Appendix 1. DemPoRT Variable Specification in the CLSA.

Variable	DemPoRT specification	CLSA variable(s) used[91,92]	Transformations (prior to truncating at the 99.5th percentile for continuous variables, centering and splining)
Age	5 knot spline: Valid range: 55-102 (male), 55-101 (female)	AGE_NMBR_COM *Calculated: Date of interview less reported Date of Birth*	None
Sex	Male, Female	SEX_ASK_COM *Are you male or female? (2 categories)*	None
Ethnicity	4 categories: White; South Asian/Arab/ West Asian; South East Asian/ Chinese/Japanese/ Korean/Filipino; Other/Multiple origin/Unknown	SDC_DCGT_COM *Cultural / Racial Background (13 categories)* • *White only* • *Black only* • *Korean only* • *Filipino only* • *Japanese only* • *Chinese only* • *South Asian only* • *Southeast Asian only* • *Arab only* • *West Asian only* • *Latin American only* • *Other racial or cultural origin (only)* • *Multiple racial or cultural origins*	Grouped the 13 categories from the CLSA to match the 4 categories specified by DemPoRT
Education	4 categories: Less than secondary school; Secondary school graduation; Some postsecondary; Postsecondary graduation	ED_UDR04_COM *Highest Level of Education. Derived variable with 4 levels matching those in DemPoRT*	None
Marital status	4 categories: Now married/Common-law; Separated/Divorced; Widowed; Single	SDC_MRTL_COM *What is your current marital/partner status? (5 categories)* • *Single, never married or never lived with a partner* • *Married/Living with a partner in a common-law relationship* • *Widowed* • *Divorced* • *Separated*	Combined "Separated" and "Divorced" categories into 1 category to give a total of 4 categories
Multi-lingualism	Multilingual; Not multilingual	The 29 variables from the Comprehensive cohort with the SDC_LANG_ prefix were used. They were all in response to the question, *"In what languages can you conduct a conversation?"*.	First recoded the 4 open text variables which represented "other" languages that were not accounted for when the CLSA initially coded up the languages

			spoken. Then performed a count of how many languages in which a participant could conduct a conversation. If the count was greater than 1, then they were multilingual. Otherwise, they were not multilingual.
Stress	5 categories: Not at all stressful; Not very stressful; A bit stressful; Quite a bit stressful; Extremely stressful	No self-rated stress variable in the CLSA, but there is a self-rated mental health variable: GEN_MNTL_COM *In general, would you say your mental health is excellent, very good, good, fair, or poor?* • *Excellent* • *Very good* • *Good* • *Fair* • *Poor*	Mapped the CLSA category to the most appropriate category of stress level: • Excellent → Not at all stressful • Very good → Not very stressful • Good → A bit stressful • Fair → Quite a bit stressful • Poor → Extremely stressful
Self-rated health	5 categories: Poor; Fair; Good; Very Good; Excellent	GEN_HLTH_COM *In general, would you say your health is excellent, very good, good, fair, or poor?* • *Excellent* • *Very good* • *Good* • *Fair* • *Poor*	None
Smoking status	4 categories: Non-smoker; Current smoker; Former smoker quit ≥5 years ago; Former daily smoker quit <5 years ago or former occasional smoker	SMK_DSTY_COM *Type of Smoker* • *Daily smoker* • *Occasional smoker (former daily smoker)* • *Occasional smoker (never a daily smoker or has smoked less than 100 cigarettes lifetime)* • *Former daily smoker (non-smoker now)* • *Former occasional smoker (at least 1 whole cigarette, non-smoker now)* • *Never smoked (a whole cigarette)* SMK_STOP_COM *When did you stop smoking cigarettes daily?* • *Less than 1 year ago* • *1-2 years ago* • *3-5 years ago* • *More than 5 years ago*	Used the smoke_simple_fun function[93,94] and modified the time_quit_smoking function[94,95] from the cchsflow R package which creates a derived smoking variable with the 4 categories used in the original DemPoRT model. The CLSA variable SMK_DSTY_COM matches the SMKDSTY_cat5 variable used in the smoke_simple_fun. The SMK_STOP_COM variable was the closest CLSA equivalent to the SMK_09A_B and SMKG09C CCHS variables used in the time_quit_smoking variable, but as the categories were different, I modified the function to accommodate the different categories in SMK_STOP_COM.
Pack years of smoking	3 knot spline: Valid range: 0-112 (male), 0-78 (female)	SMK_100CG_COM *Have you smoked at least 100 cigarettes in your life? (about 4 - 5 packs)*	Used and modified the pack_years_fun function[94,96] from the cchsflow R package.

		• *Equivalent to SMK_01A in cchsflow* SMK_FRSTCG_AG_COM *At what age did you smoke your first whole cigarette?* • *Equivalent to SMKG01C_cont* SMK_CGDL_AG_COM *At what age did you begin smoking cigarettes daily?* • *Equivalent to SMKG203_cont* SMK_NBCG_COM *How many cigarettes do you smoke each day now?* • *Almost equivalent to SMK_204* SMK_NBCG_NB_COM *How many cigarettes do you smoke each day now? If 26 +, how many?* • *No CCHS equivalent, but is used to get a more accurate estimation of number of cigarettes.* SMK_LST30_COM *On how many of the last 30 days did you smoke at least one cigarette?* • *Equivalent to SMK_05C* SMK_NB30_COM *On the days that you smoked, how many cigarettes did you usually smoke?* • *Almost equivalent to SMK_05B* SMK_NB30_NB_COM *On the days that you smoked, how many cigarettes did you usually smoke? If 26+, how many?* • *No CCHS equivalent, but is used to get a more accurate estimation of number of cigarettes.* SMK_SMKDL_AG_COM *At what age did you begin to smoke daily?* • *Equivalent to SMKG207_cont* SMK_NBDL_COM *When you smoked daily, how many cigarettes did you usually smoke each day?* • *Almost equivalent to SMK_208* SMK_NBDL_NB_COM *When you smoked daily, how many cigarettes did you usually smoke each day? If 26+, how many?* • *No CCHS equivalent, but is used to get a more accurate estimation of number of cigarettes.* SMK_STOP_COM *When did you stop smoking cigarettes daily?* • *Equivalent to SMK_09A_B* SMK_DSTY_COM *Type of Smoker*	The CLSA variables were mapped to their cchsflow variable equivalent. For the variables that required reporting a count of the number of cigarettes, as the CLSA made the variable categorical in nature (e.g., 1-5, 6-10, 11-15, 16-20, 21-25, 26+ cigarettes) as opposed to the CCHS-equivalent variable that was continuous, the average number of cigarettes in a given category was calculated. Custom functions were created using the following pairs of variables to create CLSA-based derived variables that were closer matches to the SMK_204, SMK_05B, and SMK_208 variables: SMK_NBCG_COM & SMK_NBCG_NB_COM; SMK_NB30_COM & SMK_NB30_NB_COM; SMK_NBDL_COM & SMK_NBDL_NB.

		• *Equivalent to SMKDSTY_A*	
Number of drinks last week	3 knot spline: Valid range: 0-50 (male), 0-24 (female)	ALC_EVER_COM *Have you ever drunk alcohol?* ALC_FREQ_COM *About how often during the past 12 months did you drink alcohol?* *1-7, 96, 98, 99, 77 (i.e. 4 extra): Almost every day (incl. 6 times a week); 4-5 times a week; 2-3 times a week; Once a week; 2-3 times a month; About once a month; Less than once a month; Never; Don't know/No answer; Refused; Missing* *The following questions were responses to the prompt "In a typical week during the past 12 months, how many drinks of each of the following do you drink on weekdays?" for the following drinks:* ALC_RDWD_NB_COM *Red wine* ALC_WHWD_NB_COM *White wine* ALC_BRWD_NB_COM *Beer* ALC_LQWD_NB_COM *Liquors* ALC_OTWD_NB_COM *Another kind of alcohol* *The following questions were responses to the prompt "In a typical week during the past 12 months, how many drinks of each of the following do you drink on the weekend?" for the following drinks:* ALC_RDWE_NB_COM *Red wine* ALC_WHWE_NB_COM *White wine* ALC_BRWE_NB_COM *Beer* ALC_LQWE_NB_COM *Liquors* ALC_OTWE_NB_COM *Another kind of alcohol*	To replicate the CCHS derived variable ALWDWKY, I created a variable summing all of the alcoholic drinks consumed in a typical week. If they never drank (i.e., ALC_EVER = No), or if they did not drink in the past 12 months (i.e., ALC_FREQ = Never), the number of drinks last week = 0.
Former drinker	Yes; No	ALC_EVER_COM *Have you ever drunk alcohol?* ALC_FREQ_COM *About how often during the past 12 months did you drink alcohol?* *Almost every day (incl. 6 times a week); 4-5 times a week; 2-3 times a week; Once a week; 2-3 times a month; About once a month; Less than once a month; Never; Don't know/No answer; Refused; Missing*	If an individual ever drank alcohol (i.e., ALC_EVER = 1) and they did not drink in the last 12 months (i.e., ALC_FREQ = Never), then former drinker = 1.
Fruit & vegetable consumption	3 knot spline: Valid range: 0-50 (male), 0-24 (female)	NUT_FRUT_NB_COM *How often do you usually eat fruit (fresh, frozen, canned)?* NUT_GREEN_NB_COM	Calculated the sum of the four variables to obtain the number of times per day an individual consumed fruits and vegetables.

		How often do you usually eat green salad (lettuce, with or without other ingredients)? NUT_CRRT_NB_COM *How often do you usually eat carrots (fresh, frozen, canned, eaten on their own or with other food, cooked or raw)?* NUT_VGOT_NB_COM *How often do you usually eat other vegetables (except carrots, potatoes or salad)?* These are derived variables. Each reflect the frequency of food item consumption based on the number of reported times per DAY. Conversions of (times/ 365), (times/ 7) & (times/ 30) were used for participants who reported frequencies in years, weeks and months.[97]	
Potato consumption	3 knot spline: Valid range: 0-2	NUT_PTTO_NB_COM *How often do you usually eat potatoes (boiled, mashed or baked)?* This is a derived variable. It reflects the frequency of food item consumption based on the number of reported times per DAY. Conversions of (times/ 365), (times/ 7) & (times/ 30) were used for participants who reported frequencies in years, weeks and months.[97]	None
Juice consumption	3 knot spline: Valid range: 0-6 (male), 0-5 (female)	NUT_PURE_NB_COM *How often do you usually drink 100% pure fruit juices (orange, grapefruit or tomato,...)?* This is a derived variable. It reflects the frequency of food item consumption based on the number of reported times per DAY. Conversions of (times/ 365), (times/ 7) & (times/ 30) were used for participants who reported frequencies in years, weeks and months.[97]	None
Leisure physical activity (average kcal/kg/day)	3 knot spline: Valid range: 0-16 (male), 0-12 (female)	PA2_WALK_MCQ *Over the past 7 days, how often did you take a walk outside your home or yard for any reason? For example, for pleasure or exercise, walking to work, walking the dog, etc.* PA2_WALKHR_MCQ *On average, how many hours per day did you spend walking?* PA2_EXER_MCQ	Replicated creating the PACDEE CCHS derived variable[98] that calculates an individual's daily energy expenditure using METs. For each pair of questions, if an individual's response to the first question was not 0 or not applicable, then the number of times an individual engaged in an activity in a week was

		Over the past 7 days, how often did you do any exercises specifically to increase muscle strength and endurance, such as lifting weights or push-ups, etc.? PA2_EXERHR_MCQ *On average, how many hours per day did you engage in exercises to increase muscle strength and endurance?* PA2_LSPRT_MCQ *Over the past 7 days, how often did you engage in light sports or recreational activities such as bowling, golf with a cart, shuffleboard, badminton, fishing or other similar activities?* PA2_LSPRTHR_MCQ *On average, how many hours per day did you engage in these light sports or recreational activities?* PA2_MSPRT_MCQ *Over the past 7 days, how often did you engage in moderate sports or recreational activities such as ballroom dancing, hunting, skating, golf without a cart, softball or other similar activities?* PA2_MSPRTHR_MCQ *On average, how many hours per day did you engage in these moderate sports or recreational activities?* PA2_SSPRT_MCQ *Over the past 7 days, how often did you engage in strenuous sports or recreational activities such as jogging, swimming, snowshoeing, cycling, aerobics, skiing, or other similar activities?* PA2_SSPRTHR_MCQ *On average, how many hours per day did you engage in these strenuous sports or recreational activities?*	multiplied by the average duration, in hours, of that activity. This value was then divided by 7 (to get the daily frequency) and was multiplied by the corresponding MET value associated with the activity. Based on the Statistic's Canada documentation for the PACDEE variable, walking = 3 METs, strength training = 3 METs, light activity = 3 METs, moderate activity = 5 METs, vigorous activity = 8 METs. Then, the energy expenditure for each activity is added together to generate an amount for the total daily energy expenditure. Notes: Individuals with a non-response (e.g., don't know, refused, etc.) are assigned a score of 0 METs for that activity to match what Statistics Canada does for their PACDEE computation.
Number of activities needing help	7 categories: None; 1; 2; 3; 4; 5; 6 (sum of functional measures below requiring assistance) 1) Personal hygiene and care 2) Locomotion in the home 3) Meal preparation	See variables listed below for each individual category of functional measures	Summed up the number of activities below (Hygiene_cat, Locomotion_cat, MealPrep_cat, Errands_cat, OHousework_cat, Finances_cat) needing help (range of 0 to 6).

	4) Running errands 5) Ordinary housework 6) Finances		
	Personal hygiene and care Yes; No	ADL_ABLDR_COM *Can you dress and undress yourself without help (including picking out clothes and putting on socks & shoes)?* IAL_ABLMED_COM *Can you take your own medicine without help (in the right doses at the right time)?* ADL_ABLFD_COM *Can you eat without help (i.e., you are able to feed yourself completely)?* ADL_ABLBT_COM *Can you take a bath or shower without help?* ADL_BATH_COM *Do you ever have trouble getting to the bathroom in time?* ADL_ABLAP_COM *Can you take care of your own appearance without help, for example, combing your hair, shaving (if male)?*	Created a dichotomous variable Hygiene_cat. If a participant cannot do at least one of the personal hygiene and care tasks without help (i.e. can't dress/undress without help, can't take medicine without help, can't eat without help, can't take a bath/shower without help, has trouble getting to the bathroom in time (coded as 1), or can't take care of own appearance without help (coded as 2)), then Hygiene_cat=1
	Locomotion in the home Yes; No	ADL_ABLWK_COM *Can you walk without help?* • *If respondent reports "no", a subsequent question is asked (below). If respondent says "yes", the question below is skipped.* ADL_HPWK_COM *Can you walk with some help from a person, or with the use of a walker or crutches, etc.?*	Created a dichotomous variable Locomotion_cat. If the response is "no" to the 2nd question in the locomotion series of questions, then locomotion = 1. I decided not to base it solely on the first question (ADL_ABLWK) because this question is phrased "Can you walk without help?" and some people may answer "no" because they need a walker but can otherwise move around their house without assistance of another individual. Instead, I am interested in knowing whether respondents cannot walk even with a walker or crutch.
	Meal preparation Yes; No	IAL_ABLML_COM *Can you prepare your own meals without help (i.e., you plan and cook full meals yourself)?* • *If respondent reports "no", a subsequent question is asked (below). If respondent says "yes", the question below is skipped.* IAL_HPML_COM	Created a dichotomous variable MealPrep_cat. If response is "no" to the 2nd question in the meal prep series of questions, then MealPrep_cat = 1. I am not basing this solely on the 1st question (IAL_ABLML) because we want to allow for some flexibility as some people may

		Can you prepare your own meals with some help (i.e., you can prepare some things but are unable to cook full meals yourself)?	physically be able to operate pots/pans but occupationally don't know how to cook). Thus, I am trying to include some people who have the functional capacity to cook but don't because they don't know how to cook.
	Running errands Yes; No	IAL_ABLGRO_COM *Can you go shopping for groceries or clothes without help (taking care of all shopping needs yourself)?* IAL_ABLTRV_COM *Can you get to places out of walking distance without help (i.e., you drive your own car, or travel alone on buses, or taxis)?*	Created a dichotomous variable Errands_cat. If the response is "no" to either question (each of which are the 1st question of each series of 3 questions for a given task), then errands =1. I am trying to determine if they can live on their own, as a lack of ability to do so is a sign of a cognitive deficit.
	Ordinary housework Yes; No	IAL_ABLWRK_COM *Can you do your housework without help (i.e., you can clean floors, etc.)?* • *If respondent reports "no", a subsequent question is asked (below). If respondent says "yes", the question below is skipped.* IAL_HPWRK_COM *Can you do your housework with some help (i.e., you can do light housework but need help with heavy work)?*	Created a dichotomous variable OHousework_cat. If the response was "no" to the 2nd question in the series, then OHousework_cat = 1. I am not basing this solely on the 1st question (IAL_ABLWRK) because different people have different definitions of ordinary housework and, therefore, I opted for some flexibility.
	Finances Yes; No	"IAL_ABLMO_COM *Can you handle your own money without help (i.e., you write cheques, pay bills, etc.)?*	None (renamed to Finances_cat).
Heart disease	Yes; No	CCC_HEART_COM *Has a doctor ever told you that you have heart disease (including congestive heart failure, or CHF)?*	None
Stroke	Yes; No	CCC_CVA_COM *Has a doctor ever told you that you have experienced a Stroke or CVA? (cerebrovascular accident)?*	None
Diabetes	Yes; No	DIA_DIAB_COM *Has a doctor ever told you that you have diabetes, borderline diabetes or that your blood sugar is high?*	None
Mood disorders	Yes; No	CCC_MOOD_COM *Has a doctor ever told you that you have a mood disorder such as depression (including manic depression), bipolar disorder, mania, or dysthymia?*	None
High blood pressure	Yes; No	CCC_HBP_COM *Has a doctor ever told you that you have high blood pressure or hypertension?*	None

COPD	Yes; No	CCC_COPD_COM *Has a doctor told you that you have/had any of the following: emphysema, chronic bronchitis, chronic obstructive pulmonary disease (COPD), or chronic changes in lungs due to smoking?*	None
Epilepsy	Yes; No	CCC_EPIL_COM *Has a doctor ever told you that you have epilepsy?*	None
Body mass index	3 knot spline: Valid range: 10-44 (male), 10-47 (female)	HWT_DBMI_COM *Body Mass Index. This is a CLSA derived variable that was created from a Comprehensive cohort participant's measured height and weight.*	None
Survey year	6 categories: 2001; 2003; 2005; 2007/2008; 2009/2010; 2011/2012	N/A	Because of the design of the CLSA, all CLSA participants would be in the same survey year. As the CLSA is a newer, ongoing study, All participants were mapped to the 2011/2012 survey year (i.e., the most recent cycle used in the original CCHS-based DemPoRT model).

Appendix 2. Baseline characteristics pre-imputation and proportions of missing values for each variable.

Variable	Level	Overall
n		19830
Age (median [IQR])		66.0 [60.0, 73.0]
Sex (%)	Female	10041 (50.6)
	Male	9789 (49.4)
Ethnicity (%)	White	18925 (95.4)
	South East Asian/Chinese/ Japanese/Korean/Filipino	205 (1.0)
	South Asian/Arab/West Asian	189 (1.0)
	Other/Multiple Origin/Unknown	493 (2.5)
	Missing	18 (0.1)
Education (%)	Less than high school	1167 (5.9)
	High school graduate	1949 (9.8)
	Some post-secondary education	1567 (7.9)
	Post-secondary graduate	15109 (76.2)
	Missing	38 (0.2)
Marital status (%)	Now married/common-law	13370 (67.4)
	Divorced	2701 (13.6)
	Widowed	2240 (11.3)
	Single	1514 (7.6)
	Missing	5 (0.0)
Multilingualism (%)	Yes	6735 (34.0)
	No	13095 (66.0)
Stress (%)	Not at all stressful	5906 (29.8)
	Not very stressful	8299 (41.9)
	A bit stressful	4680 (23.6)
	Quite a bit stressful	832 (4.2)
	Extremely stressful	100 (0.5)
	Missing	13 (0.1)
Self-rated health (%)	Excellent	4115 (20.8)
	Very good	8291 (41.8)
	Good	5754 (29.0)
	Fair	1403 (7.1)
	Poor	252 (1.3)
	Missing	15 (0.1)
Pack years of smoking (median [IQR])		0.0 [0.0, 26.0]
	Missing	180 (0.9)
Smoking status (%)	Non-smoker	5983 (30.2)
	Former smoker quit 5+ years	7806 (39.4)
	Former smoker quit 0 to 5 years	4546 (22.9)
	Current smoker	1364 (6.9)
	Missing	131 (0.7)

Former drinker (%)	Yes	2235 (11.3)
	No	17587 (88.7)
	Missing	8 (0.0)
Number of drinks last week (median [IQR])		3.0 [0.0, 7.0]
	Missing	135 (0.7)
Fruit and vegetable consumption (median [IQR])		3.0 [2.1, 4.1]
	Missing	39 (0.2)
Juice consumption (median [IQR])		0.1 [0.0, 1.0]
	Missing	46 (0.2)
Potato consumption (median [IQR])		0.3 [0.1, 0.4]
	Missing	7 (0.0)
Leisure physical activity (average kcal/kg/day) (median [IQR])		3.1 [1.1, 6.4]
	Missing	279 (1.4)
Number of activities needing help (%)	None	16572 (83.6)
	1	2963 (14.9)
	2	176 (0.9)
	3	45 (0.2)
	4	15 (0.1)
	5	4 (0.0)
	Missing	55 (0.3)
Heart disease (%)	Yes	2698 (13.6)
	No	17011 (85.8)
	Missing	121 (0.6)
Stroke (%)	Yes	371 (1.9)
	No	19379 (97.7)
	Missing	80 (0.4)
Diabetes (%)	Yes	3795 (19.1)
	No	15960 (80.5)
	Missing	75 (0.4)
Mood disorder (%)	Yes	3230 (16.3)
	No	16529 (83.4)
	Missing	71 (0.4)
High blood pressure (%)	Yes	8303 (41.9)
	No	11416 (57.6)
	Missing	111 (0.6)
COPD (%)	Yes	1200 (6.1)
	No	18515 (93.4)
	Missing	115 (0.6)
Epilepsy (%)	Yes	184 (0.9)
	No	19591 (98.8)
	Missing	55 (0.3)
Body mass index (median [IQR])		27.3 [24.5, 30.8]
	Missing	85 (0.4)

Survey year (%)	CCHS 11-12	19830 (100.0)
Dementia at follow-up 1 (%)	Dementia	54 (0.3)
	No dementia	19776 (99.7)
Self-rated hearing (%)	Good-Excellent	17366 (87.6)
	Fair-Poor	2446 (12.3)
	Missing	18 (0.1)
Bilateral moderate hearing loss (%)	Yes	1007 (5.1)
	No	17795 (89.7)
	Missing	1028 (5.2)
Hearing difficulty with background noise (%)	Yes	7736 (39.0)
	No	12038 (60.7)
	Missing	56 (0.3)
Self-reported use of hearing aids (%)	Yes	1284 (6.5)
	No	18545 (93.5)
	Missing	1 (0.0)
Degree of bilateral hearing loss (%)	No hearing loss	14016 (70.7)
	Mild hearing loss	3779 (19.1)
	Moderate or greater hearing loss	1007 (5.1)
	Missing	1028 (5.2)

Appendix 3. Distribution of participants with 0 to 9 DemPoRT variables missing.

Number of DemPoRT variables missing	Sum of participants with a given number of DemPoRT variables as NA
0	18599
1	994
2	184
3	13
4	1
5	1
6	1
7	31
8	5
9	1

Appendix 4. Distribution of participants with 0 to 10 hearing variables and/or DemPoRT variables missing.

Number of total DemPoRT and/or key hearing variables* missing	Sum of participants with a given number of variables as NA
0	17649
1	1868
2	249
3	21
4	4
5	1
6	1
7	26
8	10
9	0
10	1

*Key hearing variables of interest are self-rated hearing ability and moderate bilateral hearing loss.

Appendix 5. Distribution of participants with hearing variables and DemPoRT variables missing.

Number of DemPoRT variables missing	No key hearing variables* missing (Total = 18786)	One hearing variable missing (Total = 1042)	Two hearing variables missing (Total = 2)
0	17649	949	1
1	919	74	1
2	174	10	0
3	10	3	0
4	1	0	0
5	1	0	0
6	1	0	0
7	26	5	0
8	5	0	0
9	0	1	0

*Covariate hearing variables of interest are self-rated hearing ability and moderate bilateral hearing loss.

Appendix 6. Baseline characteristics of the cohort pre-imputation and post-imputation.

	Level	Un-imputed	Imputed				
Dataset		**-**	**1**	**2**	**3**	**4**	**5**
n		**19830**	**19830**	**19830**	**19830**	**19830**	**19830**
Age (median [IQR])		66.0 [60.0, 73.0]	66.0 [60.0, 73.0]	66.0 [60.0, 73.0]	66.0 [60.0, 73.0]	66.0 [60.0, 73.0]	66.0 [60.0, 73.0]
Sex (%)	Female	10041 (50.6)	10041 (50.6)	10041 (50.6)	10041 (50.6)	10041 (50.6)	10041 (50.6)
	Male	9789 (49.4)	9789 (49.4)	9789 (49.4)	9789 (49.4)	9789 (49.4)	9789 (49.4)
Ethnicity (%)	White	18925 (95.5)	18943 (95.5)	18942 (95.5)	18941 (95.5)	18942 (95.5)	18941 (95.5)
	South East Asian/Chinese/ Japanese/Korean/Filipino	205 (1.0)	205 (1.0)	206 (1.0)	206 (1.0)	206 (1.0)	206 (1.0)
	South Asian/Arab/West Asian	189 (1.0)	189 (1.0)	189 (1.0)	190 (1.0)	189 (1.0)	189 (1.0)
	Other/Multiple Origin/Unknown	493 (2.5)	493 (2.5)	493 (2.5)	493 (2.5)	493 (2.5)	494 (2.5)
Education (%)	Less than high school	1167 (5.9)	1172 (5.9)	1168 (5.9)	1171 (5.9)	1169 (5.9)	1170 (5.9)
	High school graduate	1949 (9.8)	1951 (9.8)	1958 (9.9)	1958 (9.9)	1953 (9.8)	1951 (9.8)
	Some post-secondary education	1567 (7.9)	1569 (7.9)	1570 (7.9)	1568 (7.9)	1569 (7.9)	1568 (7.9)
	Post-secondary graduate	15109 (76.3)	15138 (76.3)	15134 (76.3)	15133 (76.3)	15139 (76.3)	15141 (76.4)
Marital status (%)	Now married/common-law	13370 (67.4)	13372 (67.4)	13374 (67.4)	13373 (67.4)	13372 (67.4)	13373 (67.4)
	Divorced	2701 (13.6)	2701 (13.6)	2701 (13.6)	2701 (13.6)	2702 (13.6)	2702 (13.6)
	Widowed	2240 (11.3)	2241 (11.3)	2241 (11.3)	2240 (11.3)	2242 (11.3)	2240 (11.3)
	Single	1514 (7.6)	1516 (7.6)	1514 (7.6)	1516 (7.6)	1514 (7.6)	1515 (7.6)
Multilingualism (%)	Yes	6735 (34.0)	6735 (34.0)	6735 (34.0)	6735 (34.0)	6735 (34.0)	6735 (34.0)
	No	13095 (66.0)	13095 (66.0)	13095 (66.0)	13095 (66.0)	13095 (66.0)	13095 (66.0)
Stress (%)	Not at all stressful	5906 (29.8)	5907 (29.8)	5908 (29.8)	5908 (29.8)	5909 (29.8)	5909 (29.8)
	Not very stressful	8299 (41.9)	8307 (41.9)	8305 (41.9)	8304 (41.9)	8303 (41.9)	8302 (41.9)
	A bit stressful	4680 (23.6)	4682 (23.6)	4684 (23.6)	4686 (23.6)	4685 (23.6)	4685 (23.6)
	Quite a bit stressful	832 (4.2)	834 (4.2)	833 (4.2)	832 (4.2)	833 (4.2)	833 (4.2)
	Extremely stressful	100 (0.5)	100 (0.5)	100 (0.5)	100 (0.5)	100 (0.5)	101 (0.5)
Self-rated health (%)	Excellent	4115 (20.8)	4116 (20.8)	4117 (20.8)	4118 (20.8)	4117 (20.8)	4118 (20.8)
	Very good	8291 (41.8)	8297 (41.8)	8297 (41.8)	8293 (41.8)	8296 (41.8)	8298 (41.8)
	Good	5754 (29.0)	5757 (29.0)	5760 (29.0)	5759 (29.0)	5760 (29.0)	5756 (29.0)
	Fair	1403 (7.1)	1408 (7.1)	1404 (7.1)	1407 (7.1)	1404 (7.1)	1405 (7.1)
	Poor	252 (1.3)	252 (1.3)	252 (1.3)	253 (1.3)	253 (1.3)	253 (1.3)
Pack years of smoking (median [IQR])		0.0 [0.0, 26.0]	0.0 [0.0, 26.0]	0.0 [0.0, 26.0]	0.0 [0.0, 26.0]	0.0 [0.0, 26.0]	0.0 [0.0, 26.0]
Smoking status (%)	Non-smoker	5983 (30.4)	6023 (30.4)	6030 (30.4)	6025 (30.4)	6020 (30.4)	6021 (30.4)
	Former smoker quit 5+ years	7806 (39.6)	7860 (39.6)	7852 (39.6)	7851 (39.6)	7865 (39.7)	7865 (39.7)
	Former smoker quit 0 to 5 years	4546 (23.1)	4579 (23.1)	4577 (23.1)	4586 (23.1)	4573 (23.1)	4572 (23.1)
	Current smoker	1364 (6.9)	1368 (6.9)	1371 (6.9)	1368 (6.9)	1372 (6.9)	1372 (6.9)
Former drinker (%)	Yes	2235 (11.3)	2236 (11.3)	2236 (11.3)	2235 (11.3)	2236 (11.3)	2236 (11.3)
	No	17587 (88.7)	17594 (88.7)	17594 (88.7)	17595 (88.7)	17594 (88.7)	17594 (88.7)
Number of drinks last week (median [IQR])		3.0 [0.0, 7.0]	3.0 [0.0, 7.0]	3.0 [0.0, 7.0]	3.0 [0.0, 7.0]	3.0 [0.0, 7.0]	3.0 [0.0, 7.0]
Fruit and vegetable consumption (median [IQR])		3.0 [2.1, 4.1]	3.0 [2.1, 4.1]	3.0 [2.1, 4.1]	3.0 [2.1, 4.1]	3.0 [2.1, 4.1]	3.0 [2.1, 4.1]
Juice consumption (median [IQR])		0.1 [0.0, 1.0]	0.1 [0.0, 1.0]	0.1 [0.0, 1.0]	0.1 [0.0, 1.0]	0.1 [0.0, 1.0]	0.1 [0.0, 1.0]

Potato consumption (median [IQR])		0.3 [0.1, 0.4]	0.3 [0.1, 0.4]	0.3 [0.1, 0.4]	0.3 [0.1, 0.4]	0.3 [0.1, 0.4]	0.3 [0.1, 0.4]
Leisure physical activity (averge kcal/kg/day) (median [IQR])		3.1 [1.1, 6.4]	3.1 [1.1, 6.4]	3.1 [1.1, 6.4]	3.1 [1.1, 6.4]	3.1 [1.1, 6.4]	3.1 [1.1, 6.4]
Number of activities needing help (%)	None	16572 (83.8)	16613 (83.8)	16610 (83.8)	16612 (83.8)	16609 (83.8)	16609 (83.8)
	1	2963 (15.0)	2976 (15.0)	2977 (15.0)	2972 (15.0)	2978 (15.0)	2978 (15.0)
	2	176 (0.9)	177 (0.9)	177 (0.9)	180 (0.9)	179 (0.9)	178 (0.9)
	3	45 (0.2)	45 (0.2)	45 (0.2)	46 (0.2)	45 (0.2)	46 (0.2)
	4	15 (0.1)	15 (0.1)	17 (0.1)	16 (0.1)	15 (0.1)	15 (0.1)
	5	4 (0.0)	4 (0.0)	4 (0.0)	4 (0.0)	4 (0.0)	4 (0.0)
Heart disease (%)	Yes	2698 (13.7)	2719 (13.7)	2717 (13.7)	2720 (13.7)	2721 (13.7)	2719 (13.7)
	No	17011 (86.3)	17111 (86.3)	17113 (86.3)	17110 (86.3)	17109 (86.3)	17111 (86.3)
Stroke (%)	Yes	371 (1.9)	377 (1.9)	374 (1.9)	379 (1.9)	376 (1.9)	378 (1.9)
	No	19379 (98.1)	19453 (98.1)	19456 (98.1)	19451 (98.1)	19454 (98.1)	19452 (98.1)
Diabetes (%)	Yes	3795 (19.2)	3814 (19.2)	3813 (19.2)	3812 (19.2)	3816 (19.2)	3813 (19.2)
	No	15960 (80.8)	16016 (80.8)	16017 (80.8)	16018 (80.8)	16014 (80.8)	16017 (80.8)
Mood disorder (%)	Yes	3230 (16.3)	3246 (16.4)	3245 (16.4)	3246 (16.4)	3248 (16.4)	3245 (16.4)
	No	16529 (83.7)	16584 (83.6)	16585 (83.6)	16584 (83.6)	16582 (83.6)	16585 (83.6)
High blood pressure (%)	Yes	8303 (42.1)	8372 (42.2)	8363 (42.2)	8357 (42.1)	8352 (42.1)	8355 (42.1)
	No	11416 (57.9)	11458 (57.8)	11467 (57.8)	11473 (57.9)	11478 (57.9)	11475 (57.9)
COPD (%)	Yes	1200 (6.1)	1208 (6.1)	1209 (6.1)	1215 (6.1)	1215 (6.1)	1216 (6.1)
	No	18515 (93.9)	18622 (93.9)	18621 (93.9)	18615 (93.9)	18615 (93.9)	18614 (93.9)
Epilepsy (%)	Yes	184 (0.9)	187 (0.9)	185 (0.9)	186 (0.9)	185 (0.9)	185 (0.9)
	No	19591 (99.1)	19643 (99.1)	19645 (99.1)	19644 (99.1)	19645 (99.1)	19645 (99.1)
Body mass index (median [IQR])		27.3 [24.5, 30.8]	27.3 [24.5, 30.8]	27.3 [24.5, 30.8]	27.3 [24.5, 30.8]	27.3 [24.5, 30.8]	27.3 [24.5, 30.8]
Survey year (%)	CCHS 11-12	19830 (100.0)	19830 (100.0)	19830 (100.0)	19830 (100.0)	19830 (100.0)	19830 (100.0)
Dementia at follow-up 1 (%)	Dementia	54 (0.3)	54 (0.3)	54 (0.3)	54 (0.3)	54 (0.3)	54 (0.3)
	No dementia	19776 (99.7)	19776 (99.7)	19776 (99.7)	19776 (99.7)	19776 (99.7)	19776 (99.7)
Self-rated hearing (%)	Good-Excellent	17366 (87.7)	17381 (87.7)	17382 (87.7)	17380 (87.6)	17381 (87.7)	17380 (87.6)
	Fair-Poor	2446 (12.3)	2449 (12.3)	2448 (12.3)	2450 (12.4)	2449 (12.3)	2450 (12.4)
Bilateral moderate hearing loss (%)	Yes	1007 (5.4)	1103 (5.6)	1101 (5.6)	1096 (5.5)	1104 (5.6)	1110 (5.6)
	No	17795 (94.6)	18727 (94.4)	18729 (94.4)	18734 (94.5)	18726 (94.4)	18720 (94.4)
Hearing difficulty with background noise (%)	Yes	7736 (39.1)	7761 (39.1)	7757 (39.1)	7758 (39.1)	7757 (39.1)	7761 (39.1)
	No	12038 (60.9)	12069 (60.9)	12073 (60.9)	12072 (60.9)	12073 (60.9)	12069 (60.9)
Self-reported use of hearing aids (%)	Yes	1284 (6.5)	1284 (6.5)	1284 (6.5)	1284 (6.5)	1284 (6.5)	1284 (6.5)
	No	18545 (93.5)	18546 (93.5)	18546 (93.5)	18546 (93.5)	18546 (93.5)	18546 (93.5)

Degree of bilateral hearing loss (%)	No hearing loss	14016 (74.5)	14659 (73.9)	14691 (74.1)	14673 (74.0)	14672 (74.0)	14663 (73.9)
	Mild hearing loss	3779 (20.1)	4068 (20.5)	4038 (20.4)	4061 (20.5)	4054 (20.4)	4057 (20.5)
	Moderate or greater hearing loss	1007 (5.4)	1103 (5.6)	1101 (5.6)	1096 (5.5)	1104 (5.6)	1110 (5.6)

Proportions shown for the un-imputed data column were calculated without accounting for missings.

Appendix 7. Sex-specific DemPoRT score calculation.

Male DemPoRT score (from CCHS DemPoRT reduced model)[10]:

$DemPoRTScore_{male}$ =

(β_{AgeC_rcs1} * AgeC_rcs1) + (β_{AgeC_rcs2} * AgeC_rcs2) + (β_{AgeC_rcs3}*AgeC_rcs3) + (β_{AgeC_rcs4} * AgeC_rcs4) + ($\beta_{EthnSEAsian4C\_cat}$ * EthnSEAsian4C_cat) + ($\beta_{EthnOther4C\_cat}$ * EthnOther4C_cat) + ($\beta_{EthnSWAsian4C\_cat}$ * EthnSWAsian4C_cat) + ($\beta_{MultilingualC\_cat}$ * MultilingualC_cat) + ($\beta_{StressNotVeryC\_cat}$ * StressNotVeryC_cat) + ($\beta_{StressABitC\_cat}$ * StressABitC_cat) + ($\beta_{StressQuiteC\_cat}$ * StressQuiteC_cat) + ($\beta_{StressExtremelyC\_cat}$ * StressExtremelyC_cat) + ($\beta_{SRHealthPoorC\_cat}$ * SRHealthPoorC_cat) + ($\beta_{SRHealthFairC\_cat}$ * SRHealthFairC_cat) + ($\beta_{SRHealthGoodC\_cat}$ * SRHealthGoodC_cat) + ($\beta_{SRHealthVGoodC\_cat}$ * SRHealthVGoodC_cat) + ($\beta_{PackYearsC\_rcs1}$ * PackYearsC_rcs1) + ($\beta_{PackYearsC\_rcs2}$ * PackYearsC_rcs2) + ($\beta_{SmokeFormer5PlusC\_cat}$ * SmokeFormer5PlusC_cat) + ($\beta_{SmokeFormer0to5C\_cat}$ * SmokeFormer0to5C_cat) + ($\beta_{SmokeCurrentC\_cat}$ * SmokeCurrentC_cat) + ($\beta_{DrinksLastWeekC\_rcs1}$ * DrinksLastWeekC_rcs1) + ($\beta_{DrinksLastWeekC\_rcs2}$ * DrinksLastWeekC_rcs2) + ($\beta_{FormerDrinkerC\_cat}$ * FormerDrinkerC_cat) + ($\beta_{FruitVegC\_rcs1}$ * FruitVegC_rcs1) + ($\beta_{FruitVegC\_rcs2}$ * FruitVegC_rcs2) + ($\beta_{PotatoC\_rcs1}$ * PotatoC_rcs1) + ($\beta_{PotatoC\_rcs2}$ * PotatoC_rcs2) + (β_{JuiceC_rcs1} * JuiceC_rcs1) + (β_{JuiceC_rcs2} * JuiceC_rcs2) + ($\beta_{PhysicalActivityC\_rcs1}$ * PhysicalActivityC_rcs1) + ($\beta_{PhysicalActivityC\_rcs2}$ * PhysicalActivityC_rcs2) + ($\beta_{HeartDisC\_cat}$ * HeartDisC_cat) + ($\beta_{StrokeC\_cat}$ * StrokeC_cat) + ($\beta_{DiabetesC\_cat}$ * DiabetesC_cat) + (β_{MoodC_cat} * MoodC_cat) + ($\beta_{HypertensionC\_cat}$* HypertensionC_cat) + ($\beta_{COPDC\_cat}$* COPDC_cat) + ($\beta_{BMIC\_rcs1}$* BMIC_rcs1) + ($\beta_{BMIC\_rcs2}$ * BMIC_rcs2) + ($\beta_{NeedHelp1C\_cat}$ * NeedHelp1C_cat) + ($\beta_{NeedHelp2C\_cat}$ * NeedHelp2C_cat) + ($\beta_{NeedHelp3C\_cat}$ * NeedHelp3C_cat) + ($\beta_{NeedHelp4C\_cat}$ * NeedHelp4C_cat) + ($\beta_{NeedHelp5C\_cat}$ * NeedHelp5C_cat) + ($\beta_{NeedHelp6C\_cat}$ * NeedHelp6C_cat) + ($\beta_{SurveyCycle2C\_cat}$* SurveyCycle2C_cat) + ($\beta_{SurveyCycle3C\_cat}$ * SurveyCycle3C_cat) + ($\beta_{SurveyCycle4C\_cat}$ * SurveyCycle4C_cat) + ($\beta_{SurveyCycle5C\_cat}$ * SurveyCycle5C_cat) + ($\beta_{SurveyCycle6C\_cat}$ * SurveyCycle6C_cat) + ($\beta_{AgeCXPackYearsC\_int}$ * AgeCXPackYearsC_int) + ($\beta_{AgeCXSmokeFormer5PlusC\_int}$ * AgeCXSmokeFormer5PlusC_int) + ($\beta_{AgeCXSmokeFormer0to5C\_int}$ * AgeCXSmokeFormer0to5C_int) + ($\beta_{AgeCXSmokeCurrentC\_int}$ * AgeCXSmokeCurrentC_int) + ($\beta_{AgeCXDrinksLastWeekC\_int}$ * AgeCXDrinksLastWeekC_int) + ($\beta_{AgeCXFormerDrinkerC\_int}$ * AgeCXFormerDrinkerC_int) + ($\beta_{AgeCXFruitVegC\_int}$* AgeCXFruitVegC_int) + ($\beta_{AgeCXPotatoC\_int}$ * AgeCXPotatoC_int) + ($\beta_{AgeCXJuiceC\_int}$ * AgeCXJuiceC_int) + ($\beta_{AgeCXPhysicalActivityC\_int}$ * AgeCXPhysicalActivityC_int) + ($\beta_{AgeCXHeartDisC\_int}$ * AgeCXHeartDisC_int) + ($\beta_{AgeCXStrokeC\_int}$ * AgeCXStrokeC_int) + ($\beta_{AgeCXDiabetesC\_int}$ * AgeCXDiabetesC_int) + ($\beta_{AgeCXMoodC\_int}$ * AgeCXMoodC_int) + ($\beta_{AgeCXHypertensionC\_int}$ * AgeCXHypertensionC_int) + ($\beta_{AgeCXCOPDC\_int}$ * AgeCXCOPDC_int) + ($\beta_{AgeCXBMIC\_int}$ * AgeCXBMIC_int) + ($\beta_{AgeCXNeedHelp1C\_int}$ * AgeCXNeedHelp1C_int) + ($\beta_{AgeCXNeedHelp2C\_int}$ * AgeCXNeedHelp2C_int) + ($\beta_{AgeCXNeedHelp3C\_int}$ * AgeCXNeedHelp3C_int) + ($\beta_{AgeCXNeedHelp4C\_int}$ * AgeCXNeedHelp4C_int) + ($\beta_{AgeCXNeedHelp5C\_int}$ * AgeCXNeedHelp5C_int) + ($\beta_{AgeCXNeedHelp6C\_int}$ * AgeCXNeedHelp6C_int)

Female DemPoRT score (from CCHS DemPoRT reduced model)[10]:

$DemPoRTScore_{female}$ =

(β_{AgeC_rcs1} * AgeC_rcs1) + (β_{AgeC_rcs2} * AgeC_rcs2) + (β_{AgeC_rcs3}*AgeC_rcs3) + (β_{AgeC_rcs4} * AgeC_rcs4) + ($\beta_{EduHSGrad2C\_cat}$ * EduHSGrad2C_cat) + ($\beta_{EduSomePS2C\_cat}$ * EduSomePS2C_cat) + ($\beta_{EduPSGrad2C\_cat}$ * EduPSGrad2C_cat) + ($\beta_{MSDivorcedC\_cat}$ * MSDivorcedC_cat) + ($\beta_{MSWidowedC\_cat}$ * MSWidowedC_cat) + ($\beta_{MSSingleC\_cat}$ * MSSingleC_cat) + ($\beta_{StressNotVeryC\_cat}$ * StressNotVeryC_cat)

+ ($\beta_{StressABitC\_cat}$ * StressABitC_cat) + ($\beta_{StressQuiteC\_cat}$ * StressQuiteC_cat) + ($\beta_{StressExtremelyC\_cat}$ * StressExtremelyC_cat) + ($\beta_{PackYearsC\_rcs1}$ * PackYearsC_rcs1) + ($\beta_{PackYearsC\_rcs2}$ * PackYearsC_rcs2) + ($\beta_{SmokeFormer5PlusC\_cat}$ * SmokeFormer5PlusC_cat) + ($\beta_{SmokeFormer0to5C\_cat}$ * SmokeFormer0to5C_cat) + ($\beta_{SmokeCurrentC\_cat}$ * SmokeCurrentC_cat) + ($\beta_{DrinksLastWeekC\_rcs1}$ * DrinksLastWeekC_rcs1) + ($\beta_{DrinksLastWeekC\_rcs2}$ * DrinksLastWeekC_rcs2) + ($\beta_{FormerDrinkerC\_cat}$ * FormerDrinkerC_cat) + ($\beta_{FruitVegC\_rcs1}$ * FruitVegC_rcs1) + ($\beta_{FruitVegC\_rcs2}$ * FruitVegC_rcs2) + ($\beta_{PotatoC\_rcs1}$ * PotatoC_rcs1) + ($\beta_{PotatoC\_rcs2}$ * PotatoC_rcs2) + (β_{JuiceC_rcs1} * JuiceC_rcs1) + (β_{JuiceC_rcs2} * JuiceC_rcs2) + ($\beta_{PhysicalActivityC\_rcs1}$ * PhysicalActivityC_rcs1) + ($\beta_{PhysicalActivityC\_rcs2}$ * PhysicalActivityC_rcs2) + ($\beta_{HeartDisC\_cat}$ * HeartDisC_cat) + ($\beta_{StrokeC\_cat}$ * StrokeC_cat) + ($\beta_{DiabetesC\_cat}$ * DiabetesC_cat) + (β_{MoodC_cat} * MoodC_cat) + ($\beta_{HypertensionC\_cat}$* HypertensionC_cat) + ($\beta_{COPDC\_cat}$* COPDC_cat) + ($\beta_{EpilepsyC\_cat}$* EpilepsyC_cat) + ($\beta_{BMIC\_rcs1}$* BMIC_rcs1) + ($\beta_{BMIC\_rcs2}$ * BMIC_rcs2) + ($\beta_{NeedHelp1C\_cat}$ * NeedHelp1C_cat) + ($\beta_{NeedHelp2C\_cat}$ * NeedHelp2C_cat) + ($\beta_{NeedHelp3C\_cat}$ * NeedHelp3C_cat) + ($\beta_{NeedHelp4C\_cat}$ * NeedHelp4C_cat) + ($\beta_{NeedHelp5C\_cat}$ * NeedHelp5C_cat) + ($\beta_{NeedHelp6C\_cat}$ * NeedHelp6C_cat) + ($\beta_{SurveyCycle2C\_cat}$* SurveyCycle2C_cat) + ($\beta_{SurveyCycle3C\_cat}$ * SurveyCycle3C_cat) + ($\beta_{SurveyCycle4C\_cat}$ * SurveyCycle4C_cat) + ($\beta_{SurveyCycle5C\_cat}$ * SurveyCycle5C_cat) + ($\beta_{SurveyCycle6C\_cat}$ * SurveyCycle6C_cat) + ($\beta_{AgeCXPackYearsC\_int}$ * AgeCXPackYearsC_int) + ($\beta_{AgeCXSmokeFormer5PlusC\_int}$ * AgeCXSmokeFormer5PlusC_int) + ($\beta_{AgeCXSmokeFormer0to5C\_int}$ * AgeCXSmokeFormer0to5C_int) + ($\beta_{AgeCXSmokeCurrentC\_int}$ * AgeCXSmokeCurrentC_int) + ($\beta_{AgeCXDrinksLastWeekC\_int}$ * AgeCXDrinksLastWeekC_int) + ($\beta_{AgeCXFormerDrinkerC\_int}$ * AgeCXFormerDrinkerC_int) + ($\beta_{AgeCXFruitVegC\_int}$* AgeCXFruitVegC_int) + ($\beta_{AgeCXPotatoC\_int}$ * AgeCXPotatoC_int) + ($\beta_{AgeCXJuiceC\_int}$ * AgeCXJuiceC_int) + ($\beta_{AgeCXPhysicalActivityC\_int}$ * AgeCXPhysicalActivityC_int) + ($\beta_{AgeCXHeartDisC\_int}$ * AgeCXHeartDisC_int) + ($\beta_{AgeCXStrokeC\_int}$ * AgeCXStrokeC_int) + ($\beta_{AgeCXDiabetesC\_int}$ * AgeCXDiabetesC_int) + ($\beta_{AgeCXMoodC\_int}$ * AgeCXMoodC_int) + ($\beta_{AgeCXHypertensionC\_int}$ * AgeCXHypertensionC_int) + ($\beta_{AgeCXCOPDC\_int}$ * AgeCXCOPDC_int) + ($\beta_{AgeCXEpilepsyC\_int}$ * AgeCXEpilepsyC_int) + ($\beta_{AgeCXBMIC\_int}$ * AgeCXBMIC_int) + ($\beta_{AgeCXNeedHelp1C\_int}$ * AgeCXNeedHelp1C_int) + ($\beta_{AgeCXNeedHelp2C\_int}$ * AgeCXNeedHelp2C_int) + ($\beta_{AgeCXNeedHelp3C\_int}$ * AgeCXNeedHelp3C_int) + ($\beta_{AgeCXNeedHelp4C\_int}$ * AgeCXNeedHelp4C_int) + ($\beta_{AgeCXNeedHelp5C\_int}$ * AgeCXNeedHelp5C_int) + ($\beta_{AgeCXNeedHelp6C\_int}$ * AgeCXNeedHelp6C_int)

Coefficients for the DemPoRT reduced models[10]:

Male reduced model		Female reduced model	
Variable	**Coefficient**	**Variable**	**Coefficient**
AgeC_rcs1	0.187761	AgeC_rcs1	0.245279
AgeC_rcs2	-0.21765	AgeC_rcs2	-0.59957
AgeC_rcs3	0.508559	AgeC_rcs3	1.106106
AgeC_rcs4	-0.62908	AgeC_rcs4	-0.83521
EthnSEAsian4C_cat	-0.61373	MSDivorcedC_cat	0.106533
EthnOther4C_cat	0.02033	MSWidowedC_cat	0.054322
EthnSWAsian4C_cat	-0.41585	MSSingleC_cat	0.088459
MultilingualC_cat	0.066602	EduHSGrad2C_cat	-0.06669
StressNotVeryC_cat	-0.01148	EduSomePS2C_cat	-0.12614
StressABitC_cat	0.122989	EduPSGrad2C_cat	-0.10969
StressQuiteC_cat	0.226566	StressNotVeryC_cat	-0.07043

StressExtremelyC_cat	0.241431	StressABitC_cat	0.021274
SRHealthPoorC_cat	0.032454	StressQuiteC_cat	0.072694
SRHealthFairC_cat	0.173588	StressExtremelyC_cat	0.122294
SRHealthGoodC_cat	0.154653	PackYearsC_rcs1	0.006962
SRHealthVGoodC_cat	0.10364	PackYearsC_rcs2	-0.05288
PackYearsC_rcs1	-0.00754	SmokeFormer5PlusC_cat	0.026322
PackYearsC_rcs2	0.01523	SmokeFormer0to5C_cat	0.123884
SmokeFormer5PlusC_cat	0.042471	SmokeCurrentC_cat	0.039407
SmokeFormer0to5C_cat	-0.04816	DrinksLastWeekC_rcs1	-0.02863
SmokeCurrentC_cat	0.09467	DrinksLastWeekC_rcs2	0.027864
DrinksLastWeekC_rcs1	-0.01568	FormerDrinkerC_cat	0.13137
DrinksLastWeekC_rcs2	0.058555	FruitVegC_rcs1	-0.06485
FormerDrinkerC_cat	0.127401	FruitVegC_rcs2	0.040923
FruitVegC_rcs1	-0.06419	PotatoC_rcs1	0.096159
FruitVegC_rcs2	0.073403	PotatoC_rcs2	0.125712
PotatoC_rcs1	-0.03004	JuiceC_rcs1	0.169634
PotatoC_rcs2	0.279881	JuiceC_rcs2	-0.04086
JuiceC_rcs1	0.020219	PhysicalActivityC_rcs1	-0.04655
JuiceC_rcs2	0.054193	PhysicalActivityC_rcs2	0.065911
PhysicalActivityC_rcs1	-0.05575	COPDC_cat	-0.18354
PhysicalActivityC_rcs2	0.038475	HeartDisC_cat	0.067801
COPDC_cat	-0.0933	StrokeC_cat	0.368505
HeartDisC_cat	-0.13957	DiabetesC_cat	0.409517
StrokeC_cat	0.43779	MoodC_cat	0.304973
DiabetesC_cat	0.145147	HypertensionC_cat	-0.00477
MoodC_cat	0.187227	EpilepsyC_cat	0.357291
HypertensionC_cat	-0.08289	BMIC_rcs1	-0.04179
BMIC_rcs1	-0.01979	BMIC_rcs2	0.018018
BMIC_rcs2	0.009216	NeedHelp1C_cat	0.25941
NeedHelp1C_cat	0.450023	NeedHelp2C_cat	0.393474
NeedHelp2C_cat	0.202616	NeedHelp3C_cat	0.475297
NeedHelp3C_cat	0.333814	NeedHelp4C_cat	0.466321
NeedHelp4C_cat	0.47548	NeedHelp5C_cat	0.331867
NeedHelp5C_cat	0.815998	NeedHelp6C_cat	0.62822
NeedHelp6C_cat	0.238077	SurveyCycle2C_cat	0.017878
SurveyCycle2C_cat	-0.17033	SurveyCycle3C_cat	-0.14244
SurveyCycle3C_cat	-0.12998	SurveyCycle4C_cat	-0.23408
SurveyCycle4C_cat	-0.48323	SurveyCycle5C_cat	-0.36546
SurveyCycle5C_cat	-0.42932	SurveyCycle6C_cat	-0.46645
SurveyCycle6C_cat	-0.53153	AgeCXPackYearsC_int	-0.00016
AgeCXPackYearsC_int	2.9E-05	AgeCXSmokeFormer5PlusC_int	0.002123
AgeCXSmokeFormer5PlusC_int	-0.00702	AgeCXSmokeFormer0to5C_int	-0.00743
AgeCXSmokeFormer0to5C_int	-0.00543	AgeCXSmokeCurrentC_int	-0.01223
AgeCXSmokeCurrentC_int	-0.00843	AgeCXDrinksLastWeekC_int	3.86E-05

AgeCXDrinksLastWeekC_int	0.000613	AgeCXFormerDrinkerC_int	-0.00592
AgeCXFormerDrinkerC_int	6.37E-05	AgeCXFruitVegC_int	0.001669
AgeCXFruitVegC_int	0.001341	AgeCXJuiceC_int	-0.00721
AgeCXJuiceC_int	-0.01045	AgeCXPotatoC_int	-0.00689
AgeCXPotatoC_int	-0.01277	AgeCXPhysicalActivityC_int	-0.00125
AgeCXPhysicalActivityC_int	0.001927	AgeCXCOPDC_int	-0.00672
AgeCXCOPDC_int	-0.01101	AgeCXHeartDisC_int	-0.01808
AgeCXHeartDisC_int	-0.00103	AgeCXStrokeC_int	0.000146
AgeCXStrokeC_int	-0.0059	AgeCXDiabetesC_int	-0.02458
AgeCXDiabetesC_int	-0.00962	AgeCXMoodC_int	-0.00279
AgeCXMoodC_int	-0.01159	AgeCXHypertensionC_int	-0.01393
AgeCXHypertensionC_int	-0.00898	AgeCXEpilepsyC_int	-0.03495
AgeCXBMIC_int	0.000454	AgeCXBMIC_int	0.000672
AgeCXNeedHelp1C_int	-0.02014	AgeCXNeedHelp1C_int	-0.02461
AgeCXNeedHelp2C_int	-0.00813	AgeCXNeedHelp2C_int	-0.01661
AgeCXNeedHelp3C_int	-0.01132	AgeCXNeedHelp3C_int	-0.03696
AgeCXNeedHelp4C_int	-0.03555	AgeCXNeedHelp4C_int	-0.0255
AgeCXNeedHelp5C_int	-0.03699	AgeCXNeedHelp5C_int	-0.02349
AgeCXNeedHelp6C_int	-0.03084	AgeCXNeedHelp6C_int	-0.06038

Appendix 8. Formulas for CLSA-based DemPoRT logistic regression models.

Logistic regression models 1-3:

$$logit(p) = \beta_0 + \beta_1(\text{DemPoRT Score})$$
$$logit(p) = \beta_0 + \beta_1(\text{DemPoRT Score}) + \beta_2(\text{Self-rated hearing})$$
$$logit(p) = \beta_0 + \beta_1(\text{DemPoRT Score}) + \beta_2(\text{Bilateral hearing loss})$$

Coefficients from the logistic regression models:

$$logit(p) = -6.1529 + (1.2611)(\text{DemPoRT Score})$$
$$logit(p) = -6.2508 + (1.2172)(\text{DemPoRT Score}) + (0.5660)(\text{Self-rated hearing})$$
$$logit(p) = -6.2550 + (1.1533)(\text{DemPoRT Score}) + (0.9538)(\text{Bilateral hearing loss})$$

Appendix 9. Odds ratios and 95% confidence intervals of all covariates in CLSA-based DemPoRT models for odds of 3-year incidence of dementia.

Model & variable name	Category (if applicable)	Adjusted OR*	2.50%	97.50%	p-value
MODEL 1					
DemPoRTScore	-	3.53	2.48	5.01	1.92E-12
MODEL 2					
DemPoRTScore	-	3.38	2.38	4.80	1.10E-11
Self-rated hearing	Fair-poor vs. Excellent-good	1.76	0.96	3.23	0.0672
MODEL 3					
DemPoRTScore	-	3.17	2.23	4.51	1.39E-10
Bilateral HL at 40 dB	Bilateral HL vs. No HL	2.60	1.38	4.87	0.0030

Appendix 10. Relative risk calculation for hearing impairment covariates.

The following formula was used to convert an odds ratio (OR) for hearing impairment to a relative risk (RR), taking into account the probability of dementia among individuals without hearing impairment (P_0)[76]. Of note, the OR approximates the RR when the outcome is rare, as observed in this sample[76].

$$RR = \frac{OR}{\left((OR - 1) * P_0\right) + 1}$$

Fair/poor self-rated hearing	Audiometrically-defined bilateral hearing loss
$P_0 = 0.002$	$P_0 = 0.002$
$aOR = 1.76$	$aOR = 2.60$
$RR = \frac{1.76}{\left((1.76) * 0.002\right) + 1}$	$RR = \frac{2.60}{\left((2.60 - 1) * 0.002\right) + 1}$
$RR = 1.76$	$RR = 2.59$

Appendix 11. Formula for 5-year risk of dementia.

The following formula and baseline hazards were obtained from the original DemPoRT algorithm using CCHS data[10].

DemPoRT formula for sex-specific 5-year risk of dementia[10]:

$$5\ year\ dementia\ risk = 1 - \exp(-(h_0(5\ years) * \exp(DemPoRTScore)))$$

5-year baseline hazards from CCHS-based models[10]:

$h_0(5\ years)_{male}$ = 0.03026372
$h_0(5\ years)_{female}$ = 0.08718073

The above formula was used to calculate and descriptively report the 5-year risk of dementia among the CLSA sample, stratified by sex (**Table 1**) or dementia status (**Table 2**).

Appendix 12. Performance indices of the base model using 500 bootstrap resamples, before and after optimism correction.

Model 1: DemPoRT score						
	$Index_{original}$	Training	Test	Optimism	$Index_{corrected}$	n
Dxy	0.6011	0.5981	0.6011	-0.003	0.604	500
R2	0.0922	0.0924	0.0922	0.0002	0.092	500
Intercept	0	0	0.1261	-0.1261	0.1261	500
Slope	1	1	1.0208	-0.0208	1.0208	500
B	0.0027	0.0027	0.0027	0	0.0027	500

Appendix 13. Performance indices of model with self-rated hearing ability using 500 bootstrap resamples, before and after optimism correction.

Model 2: DemPoRT score + self-rated hearing ability

	$Index_{original}$	Training	Test	Optimism	$Index_{corrected}$	n
Dxy	0.6072	0.6071	0.6049	0.0023	0.6049	500
R2	0.0964	0.0979	0.095	0.0029	0.0935	500
Intercept	0	0	0.0151	-0.0151	0.0151	500
Slope	1	1	1.0001	-0.0001	1.0001	500
B	0.0027	0.0027	0.0027	0	0.0027	500

Appendix 14. Performance indices of model with audiometric data using 500 bootstrap resamples, before and after optimism correction.

Model 3: DemPoRT score + bilateral moderate hearing loss

	$Index_{original}$	Training	Test	Optimism	$Index_{corrected}$	n
Dxy	0.6161	0.6144	0.6143	0.0001	0.616	500
R2	0.1024	0.1042	0.101	0.0032	0.0993	500
Intercept	0	0	0.0166	-0.0166	0.0166	500
Slope	1	1	1.0005	-0.0005	1.0005	500
B	0.0027	0.0027	0.0027	0	0.0027	500

Appendix 15. Additional metrics for assessing added value of a predicter in original sample of n=19830.

Model	DemPoRT Score	DemPoRT Score + Self-rated hearing ability	DemPoRT Score + Bilateral moderate HL
Metrics for assessing added value of a predictor			
Likelihood ratio chi-square	67.60577[a]	70.68042[b]	75.09166[b]
Likelihood ratio test		3.07465414	7.485888878
p-value from likelihood ratio test		0.07952151	0.006218436
Adequacy of base model (a/b)		0.9564993[c]	0.90031[c]
Fraction of new information from hearing variable (1-c)		0.0435007	0.09969

Additional metrics derived from Harrell[83] – used in the context of assessing the added value of a predictor compared to a base model – were calculated as supplementary analyses. Likelihood ratio tests were conducted to compare the base model against the model with self-rated hearing ability and the model with audiometric data. The "adequacy" of the base model in comparison to each model with hearing impairment was calculated by dividing the likelihood ratio chi-square of the base model by the likelihood ratio chi-square of the model with hearing impairment. The fraction of total predictive information gained through the addition of the new hearing variable was then determined by subtracting the "adequacy" value from 1.

Appendix 16. Distribution of baseline self-rated hearing ability stratified by baseline bilateral moderate hearing loss status.

	Level	Bilateral moderate hearing loss	No bilateral moderate hearing loss	p-value	Overall
n		**1110**	**18720**		**19830**
Self-rated hearing (%)	Fair-Poor	499 (45.0)	1951 (10.4)	<0.001	2450 (12.4)
	Good-Excellent	611 (55.0)	16769 (89.6)		17380 (87.6)

Based on this data, the overall percent agreement between the two hearing impairment measures is 87.1%. The sensitivity of the self-rated hearing measure is 45.0%. The proportion of false negatives is 55.0%. The proportion of false positives is 10.4%. The specificity of the self-rated hearing measure is 89.6%.

Appendix 17. Research Ethics Board approval and renewals.

www.bruyere.org

SOINS CONTINUS
Bruyère
CONTINUING CARE

Bruyère pour des soins continus.
Bruyère Is Continuing Care.

Hôpital Élisabeth-Bruyère Hospital
43, rue Bruyère St.
Ottawa ON K1N 5C8
Tél./Tel.: 613-562-6262
Téléc./Fax: 613-562-6367

Hôpital Saint-Vincent Hospital
60, rue Cambridge St. N.
Ottawa ON K1R 7A5
Tél./Tel.: 613-562-6262
Téléc./Fax: 613-782-2785

Résidence Élisabeth-Bruyère Residence
75, rue Bruyère St.
Ottawa ON K1N 5C8
Tél./Tel.: 613-562-6262
Téléc./Fax: 613-562-4223

Résidence Saint-Louis Residence
879, ch. Hiawatha Park Rd.
Ottawa ON K1C 2Z6
Tél./Tel.: 613-562-6262
Téléc./Fax: 613-683-5001

Village Bruyère Village
879, ch. Hiawatha Park Rd.
Ottawa ON K1C 2Z6
Tél./Tel.: 613-562-6262
Téléc./Fax: 613-683-5001

Centre de médecine familiale Bruyère
Bruyère Family Medicine Centre
75, rue Bruyère St.
Ottawa ON K1N 5C8
Tél./Tel.: 613-241-3344
Téléc./Fax: 613-241-1971

Centre de médecine familiale Primrose
Primrose Family Medicine Centre
35, rue Primrose St.
Ottawa ON K1R 0A1
Tél./Tel.: 613-230-7788
Téléc./Fax: 613-230-7778

Institut de recherche Bruyère
Bruyère Research Institute
43, rue Bruyère St.
Ottawa ON K1N 5C8
Tél./Tel.: 613-562-6045
Téléc./Fax: 613-562-4266

Fondation Bruyère Foundation
43, rue Bruyère St.
Ottawa ON K1N 5C8
Tél./Tel.: 613-562-6319
Téléc./Fax: 613-562-6023

Affilié à / Affiliated with
uOttawa

Thursday, March 11, 2021

Ms. Therese Chan

Re: "Developing a prediction model for dementia in the Canadian population: The role of hearing loss and sensory impairment" (Bruyère REB Protocol # M16-21-014)

Final Approval

Dear Ms. Chan,

The Bruyère Continuing Care Research Ethics Board (REB) is pleased to give you ethical approval for the above noted study for the period of **March 11th, 2021** to **March 11th, 2022**.

The following documents have been approved:

✓ Bruyère Secondary Use of Data Form

The following documents have been acknowledged:

✓ TCPS 2 Certificates
✓ Confidentiality Pledges

The Bruyère Continuing Care REB complies with the membership requirements and operates in compliance with the Tri-Council Policy Statement 2: Ethics Conduct for Research Involving Humans; the International Conference on Harmonization - Good Clinical Practice: Consolidated Guideline; the provisions of the Personal Health Information Protection Act 2004; and the Food and Drug Act of Health Canada and its applicable Regulations.

Please be advised that any complaints made by participants must be reported to the REB. All changes to the approved protocol must be approved by the REB.

Please complete an Annual Project Update/Notification of Termination form 6 weeks prior to the approval end date as noted above.

We wish you the best of luck with your research endeavors.

Sincerely,

[redacted]
Gordon DuVal, SJD

À Bruyère, nous vous promettons... bonté • sécurité • bienveillance
At Bruyère, we promise you... Kind • Safe • Care

SOINS CONTINUS
Bruyère
CONTINUING CARE

Bruyère pour des soins continus.
Bruyère Is Continuing Care.

Hôpital Élisabeth-Bruyère Hospital
43, rue Bruyère St.
Ottawa ON K1N 5C8
Tél./Tel.: 613-562-6262
Téléc./Fax: 613-562-6367

Hôpital Saint-Vincent Hospital
60, rue Cambridge St. N.
Ottawa ON K1R 7A5
Tél./Tel.: 613-562-6262
Téléc./Fax: 613-782-2785

Résidence Élisabeth-Bruyère Residence
75, rue Bruyère St.
Ottawa ON K1N 5C8
Tél./Tel.: 613-562-6262
Téléc./Fax: 613-562-4223

Résidence Saint-Louis Residence
879, ch. Hiawatha Park Rd.
Ottawa ON K1C 2Z6
Tél./Tel.: 613-562-6262
Téléc./Fax: 613-683-5001

Village Bruyère Village
879, ch. Hiawatha Park Rd.
Ottawa ON K1C 2Z6
Tél./Tel.: 613-562-6262
Téléc./Fax: 613-683-5001

Centre de médecine familiale Bruyère
Bruyère Family Medicine Centre
75, rue Bruyère St.
Ottawa ON K1N 5C8
Tél./Tel.: 613-241-3344
Téléc./Fax: 613-241-1971

Centre de médecine familiale Primrose
Primrose Family Medicine Centre
35, rue Primrose St.
Ottawa ON K1R 0A1
Tél./Tel.: 613-230-7788
Téléc./Fax: 613-230-7778

Institut de recherche Bruyère
Bruyère Research Institute
43, rue Bruyère St.
Ottawa ON K1N 5C8
Tél./Tel.: 613-562-6045
Téléc./Fax: 613-562-4266

Fondation Bruyère Foundation
43, rue Bruyère St.
Ottawa ON K1N 5C8
Tél./Tel.: 613-562-6319
Téléc./Fax: 613-562-6023

Affilié à / Affiliated with

uOttawa

Wednesday, March 2, 2022

Dr. Amy Hsu

Re: "Developing a prediction model for dementia in the Canadian population: The role of hearing loss and sensory impairment" (Bruyère REB Protocol #M16-21-014)

Renewal/Extension Approval

Dear Dr. Hsu,

Thank-you for submitting an annual renewal form for the above-named study. The Bruyère Continuing Care Research Ethics Board is pleased to extend ethical approval for the above-named project from March 11, 2022 to March 11, 2023.

We wish you best of luck as you proceed with this study.

Sincerely,

[redacted]

Gordon DuVal, SJD
Chair, Research Ethics Board
Bruyère Continuing Care
gduval@bruyere.org

BRUYÈRE RESEARCH ETHICS BOARD – STUDY RENEWAL

Date: 22 February 2023

Investigator Name: Dr. Amy Hsu

REB Number: **M16-21-014**

Study Title: ***Developing a Prediction Model for Dementia in the Canadian Population: The Role of Hearing Loss and Sensory Impairment***

Dear Dr. Hsu,

Thank you for submitting the Renewal Form for the above mentioned study. The Bruyère Research Ethics Board is please to extend ethical approval for a period of one year.

Approval of this study expires on March-11-24

In the event that changes to the BREB, Protocol or ICF are required, a completed amendment form and updated documents must be submitted to the REB for review and approval before the changes may be incorporated into the study.

A reminder that all projects reviewed by the Bruyère Research Ethics Board must be renewed every 12 months or as otherwise determined by the Board. According to our policies, if we do not receive the renewal request in a timely manner, the REB approval may be terminated and the file closed. Please submit the Renewal Form 30 days in advance of the last approved renewal end date.

We wish you best of luck as you proceed with this study.

Sincerely on behalf of the board,

[redacted]

Kristi Wilde,
Research Ethics Manager

Signing for:
Gordon DuVal, SJD
Chair, Bruyère Research Ethics Board

The Bruyère Research Ethics Board complies with the membership requirements and operates in compliance with the Tri-Council Policy Statement 2: Ethical Conduct for Research Involving Humans; the International Conference on Harmonization – Good Clinical Practice: Consolidated Guideline; the provisions of the Personal Health Information Protection Act 2004, and the Food and Drug Act of Health Canada and its applicable regulations.

Appendix 18. Excerpt of data access approval.

McMaster University

CLSA Access Agreement

This agreement is entered into this Jan. 22 2021 (the "**Effective Date**"), at Hamilton, Ontario.

McMaster University, a University incorporated by special act of the Province of Ontario, Canada, with a main address at 1280 Main Street West, McMaster Innovation Park, Suite 309A, Hamilton, Ontario, Canada, L8S 4K1 ("**McMaster**") is the host institution of the Canadian Longitudinal Study on Aging ("***CLSA***").

AND

Bruyère Research Institute, with a main address at **43 Bruyère St., Ottawa, Ontario, K1N 5C8 ("Approved User *Institution*")**

WHEREAS:

A. Dr. Parminder Raina (McMaster University) is the Lead Investigator for the CLSA funded by a grant from the Canadian Institutes of Health Research (CIHR) and is responsible for the academic obligations under this Agreement

B. Dr. Amy Hsu (the "Approved User") is an Investigator, at the Institution, where he/she carries or wishes to carry out a project entitled Developing a prediction model for dementia in the Canadian population: The role of hearing loss and sensory impairment, for which access to CLSA samples or data (or both) will be required.

C. The document titled "CLSA Data and Biospecimen Access Policy and Guiding Principles" attached, as Schedule A is an integral part of this agreement. All obligations contained therein are part of this agreement.

The parties hereto agree as follows:

1. Definitions

"Agreement" means this CLSA *Access Agreement.*

"DSAC" means the CLSA's Data and Sample Access Committee.

"**Project**" means the **CLSA Data and/or Biospecimen Request Application** described in Schedule B attached hereto.

"Transferred Materials," means the CLSA data and/or the biospecimens described in Schedule B attached hereto.

2. Sample and Data Security.

2.1 Security measures specified in Schedule C attached hereto will apply to all Transferred Materials. The Approved User and Institution undertakes to respect these security measures during the Project and afterwards, during storage of Transferred Materials where necessary.

2.2 The Approved User and Institution shall agree to the audit of their research facility by McMaster to ensure the security and confidentiality of Transferred Materials. These audits may be conducted with reasonable prior notice. Any discrepancies between the security measures specified in Schedule C and what is found at the Approved User and Institution's research facility will have to be corrected within sixty (60) days of notice by McMaster. McMaster will support the costs associated with these audits.

2.3 Transferred Materials, including any copies thereof, may only be used for the Project described in Schedule B and may not be disclosed, transmitted or shipped to anyone except employees working directly with the Approved User and Institution or co-investigators including co-applicants or other personnel from other institution(s), indicated in the Project who will require direct access to the CLSA Data and who agree to be bound by the terms of this Agreement or to persons expressly designated in writing by McMaster. The Approved User shall retain control of the Transferred Material at all times. It is the responsibility of the Approved User and Institution to inform the staff and co-investigators, including co-applicants and other personnel at other third-party institution(s) entering into contact with the Transferred Materials of the obligations contained in the CLSA Data and Biospecimen