Objective Measures of Health and Wellbeing of Older Adults in Northern Ireland

The NICOLA Study Wave 1

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Northern Ireland Cohort for the Longitudinal Study of Ageing
... Understanding today for a healthier tomorrow

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Foreword

I am delighted to have been asked to write a foreword for the NICOLA Wave 1 Health Assessment report.

As we get older we all want to continue to lead fulfilling lives and be able to stay independent, in good health. However, we also know that as we age we face new challenges and have more concerns over our health. This health assessment report from Wave 1 of the NICOLA study was compiled during 2020/21, at a prescient moment when the current COVID 19 pandemic brought to public consciousness, like never before, the vulnerability of older people and the wide range of issues that can affect their health and wellbeing.

The findings of this report complement those from the previously published Wave 1 "*Early Findings Report*". Importantly, the value of this current report lies in its combination of objective and subjective measures of health and wellbeing and covers the common age-related disorders related to physical, cardiovascular, cognitive and mental health including hearing loss, loss of eyesight and depression. The report also provides in-depth information regarding the dietary patterns and dietary intakes of older adults in NI and provides high quality nationally representative data on the types and quantities of foods consumed by older adults in Northern Ireland. A final element of the report are findings from the laboratory analyses of biological samples which will help scientists gain a better understanding of biological pathways leading to disease and help identify those at greatest risk of developing a specific condition or illness. NICOLA can thus assist policy makers to ensure that resources are targeted more appropriately, thus ensuring maximum impact.

The Commissioner for Older People for Northern Ireland (COPNI) looks forward to using these findings to inform our ongoing and future work with older people. The report will serve as a valuable source of reference for addressing the current and future needs of our ageing population. Additionally, the data presented will provide invaluable evidence for tailoring and targeting policies and interventions to specific groups of our ageing population. As NICOLA continues to expand, we look forward to using this rich data resource in the years ahead and I congratulate all involved with the NICOLA project for their vital work which will help us better support our ageing population.

Eddie Lynch
Commissioner for Older People for Northern Ireland

Acknowledgements

NICOLA would not have been possible without the contributions and support of many groups and individuals.

Firstly, we would like to acknowledge the vision and commitment of our funders: the Atlantic Philanthropies, the Economic and Social Research Council, the UKCRC Centre of Excellence for Public Health Northern Ireland, the Centre for Ageing Research and Development in Ireland, the Office of the First Minister and Deputy First Minister, the Health and Social Care Research and Development Division of the Public Health Agency, the Wellcome Trust/Wolfson Foundation and Queen's University Belfast. We would also like to state that any views expressed in this report are not necessarily those of the funders.

NICOLA's first Principal Investigator was Professor Ian Young. He established a broadly based academic team in QUB to take the study forward through its first wave, and this report is also testament to his leadership and vision.

The authors are extremely grateful for the contributions by members of the NICOLA Scientific Steering Committee, and the valuable advice and insight offered to the study team by the NICOLA Stakeholder Council. We thank the members of the NICOLA team who are involved in the ongoing, day-to-day management and administration of the NICOLA study, and especially staff at the Wellcome Trust-Wolfson Northern Ireland Clinical Research Facility who facilitated the clinical health assessments. A special thanks go to Dr Bernadette McGuinness who was the Clinical Lead of the Health Assessment and invested a significant amount of time and effort into managing the Health Assessment. We are also grateful to the team of Research Nurses and Research Assistants who diligently conducted the NICOLA health assessments.

Finally, and most importantly, we would like to thank our participants among the over 50s of Northern Ireland, who have exceeded our expectations in their enthusiasm and participation in the health assessment. It is a privilege and pleasure to have them involved in NICOLA and we are grateful to those who gave up valuable time to attend the Clinical Research Facility or, where that was not possible, allow the research nurses to visit them in their home. Without their dedication, patience and commitment, neither this report, nor the resource for future research offered by NICOLA would have been possible.

Abbreviations

1KGP3	1000 Genomes Project Phase3 Reference Panel
ALT	Alanine aminotransferase
AMD	Age related macular degeneration
AST	Aspartate aminotransferase
ApoA1	Apolipoprotein A
ApoB	Apolipoprotein B
AP	Alkaline phosphatase
AST	Aspartate aminotransferase
BMI	Body mass index
CAPI	Computer assisted personal interview
CFD	Colour fundus photograph
CKD	Chronic kidney disease
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
CRP	C-reactive protein
DP	Dietary pattern
eGFR	Estimated glomerular filtration ratio
ETDRS	Early Treatment Diabetic Retinopathy Sutdy
ELSA	English Longitudinal Study of Ageing
EPIC	European Prospective Investigation into Cancer and Nutrition
ESRD	End-Stage Renal Disease
FFQ	Food frequency questionnaire
GGT	Gamma glutamyltransferase
HbA1c	Non-fasting glycated haemoglobin
HDL	High-density lipoproteins
HRC	Haplotype Reference Consortium
IALSA	Integrative Analysis of Longitudinal Studies of Ageing

Abbreviations

IBD	Identity by descent
IQR	Inter-quartile range
LDL	Low-density lipoproteins
Lp(a)	Lipoprotein(a)
MCI	Mild cognitive impairment
MMSE	Mini Mental State Examination
MOCA	Montreal Cognitive Assessment
NICOLA	Northern Ireland Cohort for the Longitudinal Study of Ageing
NICRF	Northern Ireland Clinical Research Facility
ORA	Ocular response analyser
PC	Principal components
QC	Quality control
QUB	Queen's University Belfast
SCQ	Self-completion questionnaire
SD-OCT	Spectral domain optical coherence tomography
SHBG	Sex hormone-binding globulin
SNP	Single nucleotide polymorphism
TILDA	The Irish Longitudinal Study of Ageing
VCDR	Vertical cup to disk ratio
WEMWBS	Warwick Edinburgh Mental Wellbeing Score

Contents

1 Introduction

Authors: Frank Kee, Charlotte Neville

In the developed world, as life expectancy increases and birth rate declines, the proportion of older people increases. As the proportion of older people rises, so will the prevalence of chronic disease and the number of people living with health related problems and disability. However, it is important for older people to remain independent for as long as possible and to continue to lead a fulfilling life doing the things that they enjoy.

The Northern Ireland COhort for the Longitudinal study of Ageing (NICOLA) is a representative sample of ~8,500 people from across Northern Ireland. The study, which was set up in 2012, aims to understand what it is like to grow older in Northern Ireland. This NICOLA report was compiled in 2020/21, during the height of the COVID-19 pandemic, when the vulnerability of older adults and the importance of wellbeing and resilience were increasingly at the forefront of people's minds.

This report presents comprehensive findings from the NICOLA Wave 1 Clinical Health Assessment, a fundamental component of the NICOLA research which took place between 2014 and 2018. The measurements which were carried out by trained nurses and research assistants at the Wellcome Trust-Wolfson Clinical Research Facility, based at the Belfast City Hospital, form an integral part of the NICOLA survey and provide a uniquely rich dataset. The findings presented encapsulate the core objective measures of health and wellbeing of older adults who took part in the health assessment and the findings are presented in the context of common age-related issues such as cognitive health, measures of frailty and physical health, hearing and eye health. The report also presents comprehensive findings relating to other modifiable lifestyle behaviours, including dietary intake. The findings complement those reported in the previously published "Early key findings" report. The information obtained from objective measures of health

and function as measured during the health assessment can often by very different to information obtained by subjective self-reported methods. By examining both measures we can identify previously undiagnosed illnesses such as high blood pressure or diabetes and it can also alert us to early signs of decline in health or physical function prior to symptomatic disease. The accumulation of findings generated from the health assessment will ultimately enable us to explore the interactions between genetics, environmental factors and diet on health related outcomes.

We employed a robust and comprehensive battery of standardised assessments of cardiovascular function, respiratory function, physical function including hand grip strength, balance, walk speed, visual health, hearing and cognitive health which are comparable to those used in other longitudinal studies internationally. Other standard clinical measures including blood pressure, height, weight, and waist circumference were also collected. Biological samples including blood and urine were collected for detailed laboratory analysis, including genetic analysis. Dietary intake was assessed using the EPIC food frequency questionnaire. A validation of the food frequency questionnaire against a 4-day food diary (the dietary assessment method currently in use in the National Diet and Nutrition Survey within the UK) (reference method) and a panel of biomarkers of fruit and vegetable intake as objective biological indicators was also performed in a subset of participants. This work will allow us to address the lack of dietary validation studies in older people to date, and will allow us to test numerous hypotheses around diet-disease and diet-function relationships in older people.

The data from the NICOLA Health Assessment will give us a more comprehensive picture and understanding of the health challenges faced by today's older adults and provide a discovery platform for researchers to try to unravel and address these challenges. The findings will also undoubtedly provide a key knowledge base for decision makers developing and prioritising policy initiatives that are core to the health and wellbeing of our older population. For example, by identifying the characteristics of the older most vulnerable population, NICOLA can assist policy makers in ensuring that those at greatest risk receive targeted support. Furthermore, the longitudinal design of NICOLA makes it well placed to continuously monitor changes in the health status of older adults and review the impact of health policies on outcomes in Northern Ireland. As we follow the NICOLA participants into old age, the insights will be further enriched, so the full potential of the data resource has yet to be exploited. More in-depth research on various health domains is ongoing and the identification of biomarkers of ageing continues to be a major avenue of ongoing work as illustrated by growing partnerships and joint funding with partners in the US.[1-2]

[1] US-Ireland Research & Development Partnership Programme Award worth ~£3.6 million [Grant ref numbers: NIH reference R01AG068937, HSC R&D file reference number STL/5569/19, MRC Grant reference number MC_PC_20026], Total award ~£3.6 million.

[2] US-National Institute of Health (NIH) Award [NIA RO1 AG060167-01A1 NIH (USA)], Harmonizing Cognitive Assessments in Irish, English, and American Longitudinal Studies: Supporting Cross-National Research on the Epidemiology of Dementia. Northern Ireland PI, Total award $3,933,815; NI component £1,316,531.

The work presented within this report demonstrates the multi-disciplinary nature of NICOLA. Each chapter provides a synopsis of the methodology used along with the key findings. The chapters are structured across domains that address keys indicators of ageing namely: physical function, eye health and hearing, cognitive function, dietary intake and cardiovascular health. Within each chapter we have provided informative tables and figures to summarise data across the various domains of age, sex, marital status, education level, deprivation level, location (urban/rural) and location of health assessment. Findings are compared, where relevant, against those of other longitudinal studies of ageing, such as The Irish Longitudinal Study of Ageing (TILDA), the English Longitudinal Study of Ageing (ELSA), or government recommendations.

In Chapter 2 we describe key characteristics of participants in terms of physical function and body composition, factors which alone are often very telling of a person's heath status and quality of life. Changes in body composition are a normal part of ageing and often occur simultaneously with declines in physical function. In NICOLA we used objective measures of strength, mobility and balance to capture overall physical function. From these data, we can in turn identify those at future risk of many health conditions including loss of independence.

In Chapter 3 we examine the prevalence and impact of chronic debilitating disorders / decline in sensory function including vision and hearing. With increasing age, the incidence of eye diseases such as cataract, age-related macular degeneration, glaucoma, and diabetic retinopathy increases significantly. Despite most of the cohort wearing either contact lenses or glasses, a relatively large proportion of unreported sight threatening eye disease was discovered on the retinal images suggesting attendance at eye examinations may not be a frequent as recommended. Hearing loss also becomes more prominent particularly in the 70+ age group. Hearing aids can improve several aspects of life that have been compromised by hearing loss. However, despite the availability of hearing aids and major technical progress in the last decade, uptake of hearing aids is poor and only a relatively small proportion of adults with hearing impairment seek help for their hearing problems and use hearing aids.

In Chapter 4 we report on the neuropsychological and cognitive health of older adults. Preventing dementia and cognitive decline is a global health priority. Cognitive function and mental wellbeing outcomes were gauged with a battery of standardised tests. Using the data collected we were able to look at differences in cognition and mental wellbeing according to age, gender and other demographic domains. The diverse range of data collected will allow us to carry out in-depth analyses to ascertain and understand the factors that affect cognitive function and ageing.

In Chapter 5 we explore dietary intake of older adults. A healthy diet is an integral part of healthy ageing and plays a key role in chronic disease prevention and in reducing the risk of cognitive decline. Exploring the effects of diet on the ageing process is a particular focus of NICOLA. Dietary intake was captured using a food frequency questionnaire and from this we have been able to carry out in-depth analysis of food intake and dietary patterns. The richness of data generated from this work will facilitate investigations between nutrition, health and well-being.

In Chapter 6 we provide an overview of cardiovascular health and in particular the prevalence of hypertension and diabetes in older adults. The prevalence of both diabetes and hypertension increases sharply with age but can only be dealt with at a population level if we know how many go undiagnosed with these conditions.

In Chapters 7 and 8 we report on a range of biomarkers (biochemical and molecular, respectively) that have been analysed to date. Participants were asked to provide biological samples, namely blood and urine as part of the health assessment. All laboratory analyses were conducted in accredited laboratories by trained technical staff. Detailed laboratory analysis of these samples including genetic analysis allows us to explore biomarkers of disease. Analysis of a wide spectrum of biomarkers of health including epigenetic markers will help us understand the biological pathways to health outcomes and when we know how to identify those at highest risk of developing a specific illness, this may allow early intervention at a time when it may be most effective for preventing the onset of disease or reducing illness.

In Chapter 9 we provide an overview of the health assessment methodology used within NICOLA. Given that the detailed health assessment was only conducted on a subset of the original sample, the findings were weighted to be closer to the structure of the Northern Ireland population, ensuring that the reported findings were more representative of the older adult population of Northern Ireland.

The assessment of health and wellbeing is, and will continue to be, an important component of the NICOLA study. The overall scope and wealth of information collected during the health assessment allows us to investigate markers of ageing and their social and biological determinants and consequences, underscoring its value for policy makers, the research community and wider economy. The study design is harmonised with similar ageing cohorts in the global Integrative Analysis of Longitudinal Studies of Ageing (IALSA) network, enabling comparative studies and learning from best practice, which is important for identifying local population needs and the modernisation of health and socio-economic policies and public services for older adults. What resonates from this report is the enormous contribution that older adults make and will continue to make to health related research and society. In time, we hope the findings generated will ultimately lead to appropriate, evidence-based, health and wellbeing policies for older people to promote healthy ageing.

2 Physical function and body composition

Authors: Ilona McMullan, Charlotte Neville, Mark Tully (Research Group Lead)

Citation

McMullan I, Neville CE, Tully MA (2021). Chapter 2, Physical function and body composition of older adults. In: NICOLA Health Assessment Report. 2021.

Key Findings

- Declines in grip strength, mobility and balance were observed in adults aged 50 years and over, indicating a steady decline in physical function with increasing age.
- Although body mass index decreased with increasing age, there was an increase in the percentage body fat. Loss of bone density and muscle mass may explain this.
- Inequalities were also observed in some of the measures. Adults aged 50 years and over who had attained a higher education, were married, and those living in rural areas appeared to have better physical function.

2.1 Introduction

Healthy ageing is achieved when life expectancy increases while at the same time the burden of disease is minimised. Physical function is one of the most important indicators of health status in older adults and is closely related to quality of life. At population level, impaired physical function is associated with increased mortality (1) and greater use of health services (2).

Physical function is the ability to perform activities of daily living. It is a vital component of an individual's ability to live independently at home. The ability to carry out activities of daily living like household chores, mobility, personal hygiene and preparing food requires the interplay of a number of the nervous, cardiorespiratory and musculoskeletal systems. Some diseases alter the function of one or more of these systems, which is manifested in altered physical function (3).

Objective tests of strength, mobility and balance are robust early indicators of declines in physical function. These biomarkers can therefore provide an indication of future risk of many health conditions and loss of independence. They are therefore useful indicators of healthy ageing as well as being a sign that early intervention is required. This chapter describes the physical function of older adults aged 50 years and over in Northern Ireland.

2.2 Grip Strength

Gip strength affects every day function, such as the ability to hold heavy objects, and declines with age. Grip strength is often used as an indicator of overall body strength as well as general health. Our recent review of the health outcomes associated with grip strength has demonstrated that having a higher grip strength is associated with a reduced risk of early mortality, cardiovascular disease and disability (4). It is also a good indicator of biological ageing, whereby the bodies systems are ageing faster than average for a person of a similar age (5).

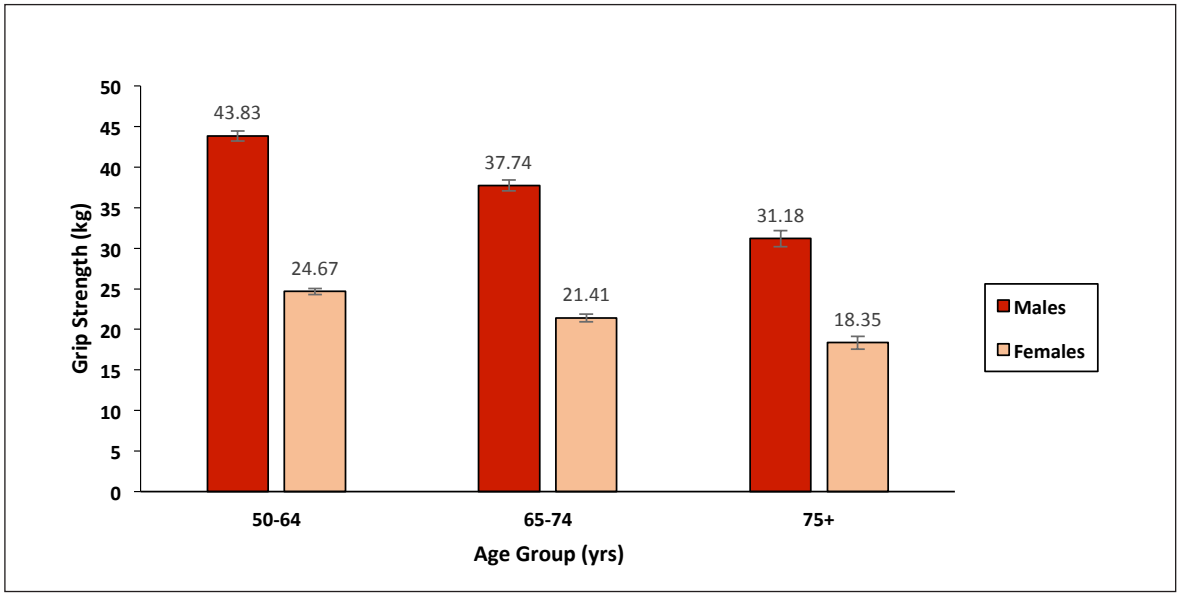
Grip strength was measured using a handheld device called a dynamometer (see Figure 2.1). Participants in the NICOLA study were asked to squeeze the device as hard as possible. The data presented represents the average of two tests using the dominant hand.

Figure 2.1: Grip strength dynamometer

Overall, grip strength was lower in women (23.0 kg) than men (39.8 kg), and this decreased with age (see Table 2.1). Between the ages of 50 - 64 and 65 – 74 years, there was an overall decrease in grip strength of 3.2 kg, which is clinically significant (above what is recognized as the level of decline that would represent a clinically important difference of between 2.4 and 2.7 kg) (6). These signs of functional decline emerging between these ages demonstrates a need for early intervention to maintain function and health. Other notable differences were married individuals or those living with a partner who had a higher grip strength. There was also an apparent difference by deprivation area, with those living in the most deprived areas having the lowest grip strength (see Table 2.1). Perhaps not surprisingly, NICOLA participants from rural areas had the highest grip strength as many were from agricultural backgrounds (see Table 2.1).

Figure 2.2 suggests that age related decline was greater for men than women. These values are within the expected normal ranges for this age group. For example, the normal strength for a 50 to 64 year old is between 42.3 kg and 47.6 kg for men and between 25.3 kg and 28.7 kg for women (7). However, the rate of decline over time appears to be greater in men than women.

Figure 2.2: Grip strength by age group and sex in NICOLA participants



Note: Grip strength measured as the average of two tests using the dominant hand. Error bars represent 95% confidence intervals

2.3 Timed Up and Go Test

The 'timed up and go' test is a test of mobility commonly used in clinical practice to measure mobility and risk of falling (8, 9). Mobility impairments reflect multi-system impairments and often precedes the onset of physical disability, falls and cognitive impairment. Slower test speeds have also been shown to be related to an increased risk of heart conditions and mortality in older adults (10).

Participants in NICOLA were asked to stand up from a chair, walk three meters and return to the chair. The activity was timed from the moment they started to stand up until they were fully seated again. Typical values range from 8 - 11.5 seconds with a faster time indicating better mobility. A time greater than 12 to 15 seconds is often used as an indicator of a high risk of falling (11).

The average time taken to complete the 'timed up and go' test by the NICOLA participants was 10.1 seconds. Younger participants aged 50 - 64 years (9.3 secs) completed the test in the fastest times. On average, participants age 75 years and over took 12.5 seconds to complete the test indicating a high risk of falling. Overall, there were little differences between men and women (10.0 secs versus 10.1 secs). However, on average females aged 75 years and over took 13.1 seconds to complete the test.

The data also suggests that a lower time to complete the test (i.e. better function) was observed in individuals who had attained higher education, were married, or

those who were least deprived. By contrast, people living in rural areas had better function according to this test (see Table 2.1).

These data indicate that older adults aged 50 - 64 years in the NICOLA study took approximately two more seconds to complete the 'timed up and go' test than the same age group in the TILDA cohort in the Republic of Ireland, indicating poorer mobility in the NICOLA participants (12).

2.4 Step Test

The 'step up' test is an assessment of dynamic standing balance, combining a measure of balance and lower-extremity motor control (13). Participants were asked to step one foot fully on and then off a 7.5 cm block step in 15 seconds. Each leg was tested separately and the number of times they stepped up was counted and averaged across the right and left foot. The greater number of steps completed corresponded to better dynamic standing balance. Typically, healthy older adults will complete between 12 and 26 steps in 15 seconds (14).

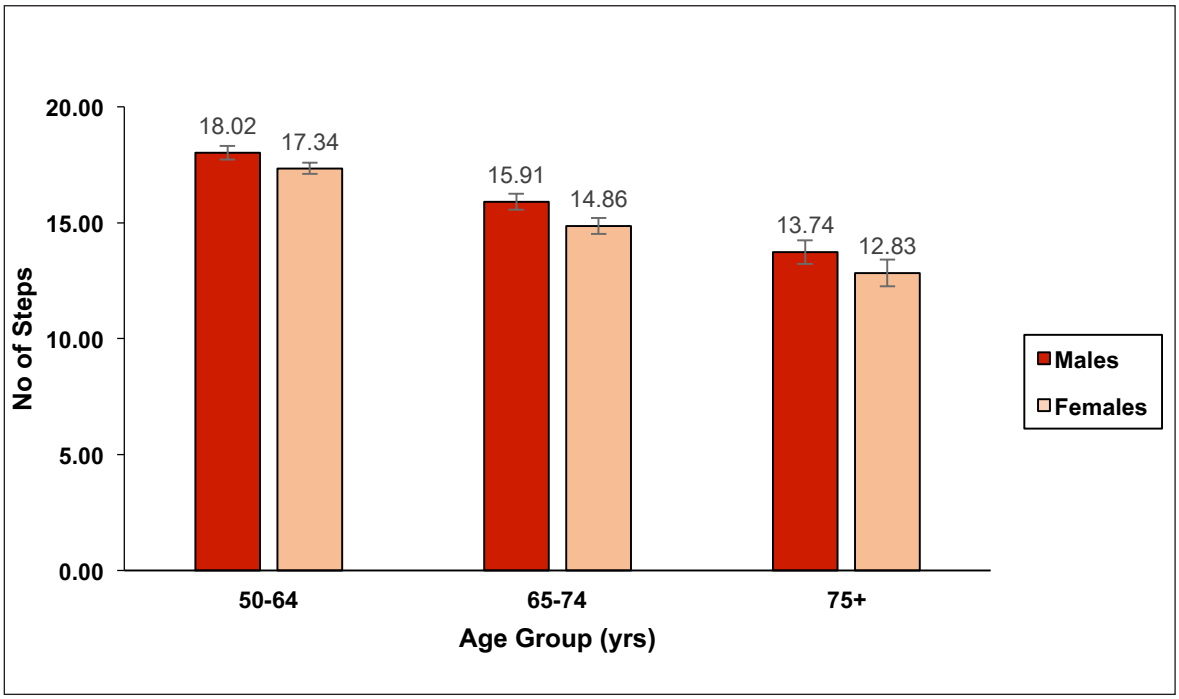
There were little overall differences in the number of steps between men and women. However, small differences were seen between age groups (see Figure 2.3), and there was also a steady decline with age. The oldest age group completed 75% of the steps of the youngest age group (see Table 2.1). Those who were married, had completed a higher level of education and were least deprived were also able to complete more steps. (see Table 2.1).

Table 2.1: Physical function in NICOLA participants

	Grip strength (kg)		Timed up and go test (secs)		Step test (average steps)	
	Mean	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**
Overall	31.2	30.8, 31.5	10.1	10.0, 10.2	16.4	16.3, 16.6
Gender						
Males	39.8	39.3, 40.2	10.0	9.9, 10.1	16.7	16.5, 16.9
Females	23.0	22.7, 23.3	10.1	10.0, 10.2	16.2	16.0, 16.4
Age group (yrs)						
50 - 64	33.3	32.7, 33.8	9.3	9.2, 9.4	17.6	17.4, 17.8
65 - 74	30.0	29.4, 30.7	10.5	10.3, 10.6	15.4	15.2, 15.7
75 +	25.5	24.6, 26.4	12.5	12.1, 12.8	13.4	13.0, 13.7
Marital status						
Married/living with partner	32.4	31.9, 32.9	9.8	9.7, 9.9	16.8	16.6, 17.0
Single	29.2	27.8, 30.7	10.5	10.2, 10.9	15.9	15.3, 16.5
Separated/divorced/widowed	27.5	26.7, 28.3	10.9	10.7, 11.2	15.2	14.9, 15.5
Education						
Primary/none /don't know	30.2	29.2, 31.2	11.1	10.8, 11.4	15.1	14.2, 14.9
Secondary	30.9	30.3, 31.6	10.3	10.1, 10.4	16.1	15.8, 16.3
Tertiary	31.8	31.2, 32.4	9.5	9.3, 9.6	17.5	17.4, 17.5
Deprivation score						
0. 0.11 (least deprived)	31.7	31.0, 32.5	9.9	9.7, 10.1	17.2	16.9, 17.5
0.12 – 0.17	32.0	31.1, 32.8	9.8	9.6, 9.9	16.7	16.4, 17.0
0.18 – 0.23	31.4	30.6, 32.3	10.0	9.8, 10.3	16.2	15.9, 16.5
0.24 – 0.33	30.2	29.3, 31.2	10.1	9.9, 10.4	16.0	15.7, 16.4
> 0.33 (most deprived)	29.8	28.8, 30.9	10.8	10.5, 11.1	15.5	15.1, 16.1
Region						
Belfast	29.3	28.4, 30.2	10.4	10.2, 10.7	16.3	15.9, 16.6
Other city or town	31.2	30.6, 31.7	10.1	10.0, 10.2	16.5	16.3, 16.7
Rural area	32.2	31.5, 32.9	9.8	9.7, 10.0	16.5	16.2, 16.7

Note: Error bars represent 95% confidence intervals

Figure 2.3 Step test by age group and sex in NICOLA participants



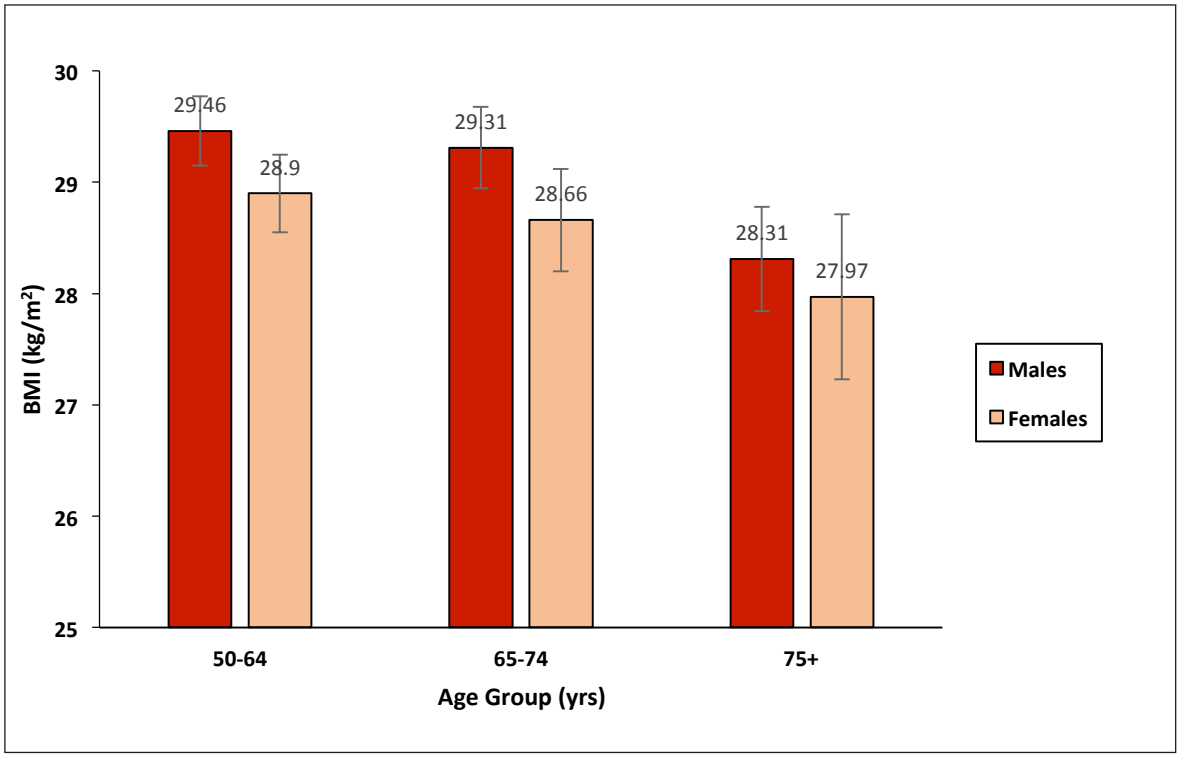
Note: Error bars represent 95% confidence intervals

2.5 Body Composition

The ageing process leads to many changes in body composition, including an increase in body mass, brought about by an increase in the proportion of the body which is fat. We usually measure if an individual is overweight using body mass index (BMI), which is a measure of the weight relative to their height. An individual with a BMI over 25 kg/m^2 is considered overweight and over 30 kg/m^2 is considered obese.

On average, NICOLA participants were overweight with a BMI of 29.0 kg/m^2, with most participants having a BMI between 28.8 and 29.1 kg/m^2 (Table 2.2). BMI decreased with age in both males and females (see Figure 2.4).

Figure 2.4: BMI by age group and sex in NICOLA participants



Note: Error bars represent 95 % confidence intervals

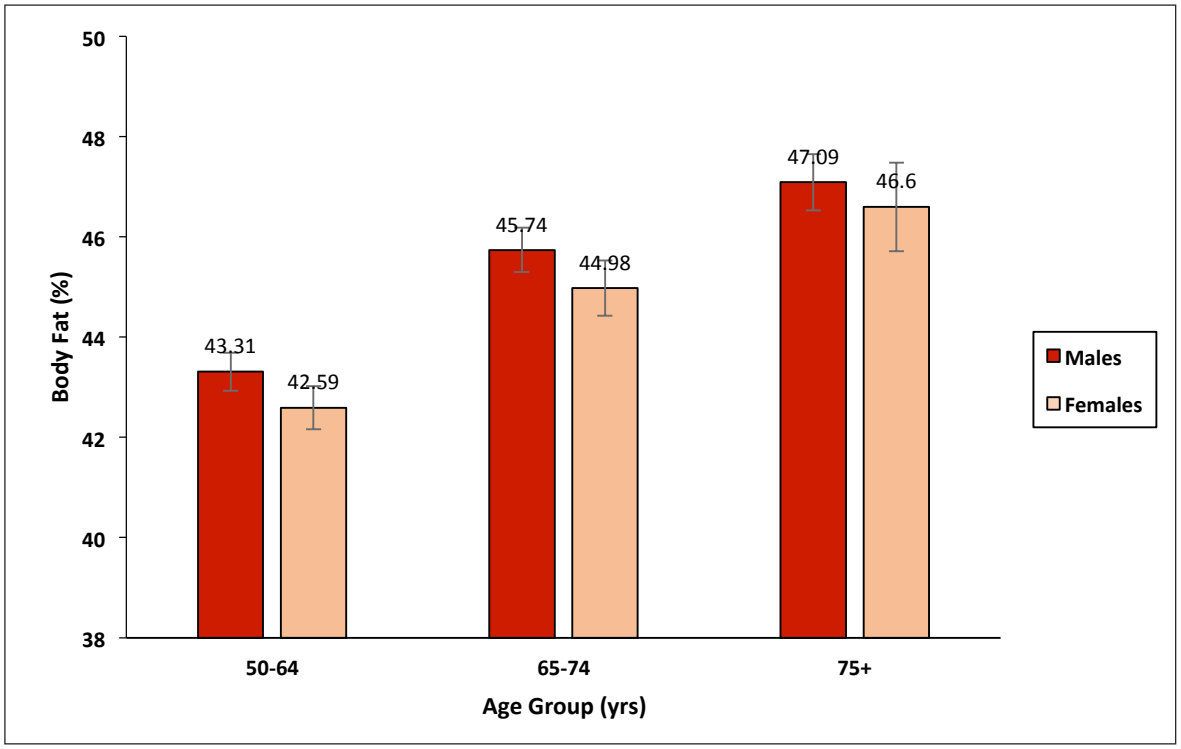
However, bone density and muscle mass also decrease with age and therefore BMI is not always a useful measure in older adults. Reductions in body weight and BMI may be due to these changes and not fat loss. Therefore, we have also included a number of other measures of body composition. Using a special scale that measures body composition based on the rate at which an electrical current travels through the body known as bioelectrical impedance, we measured the percentage of the body that was fat. Body fat accounted for approximately 45% of NICOLA participant's body mass (Table 2.2). Despite BMI declining, percentage body fat increased in both men and women, significantly between the ages of 50 - 64 and 65 – 74 years (see Figure 2.5).

Table 2.2: Body composition in NICOLA participants

	Weight (kg)		BMI (kg/m²)		Waist (cm)		Waist: hip ratio		% Body fat	
	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI
Overall	79.7	79.1, 80.2	29.0	28.8, 29.1	95.8	95.4, 96.3	0.91	0.91, 0.92	44.2	44.0, 44.4
Gender										
Males	87.2	86.5, 87.9	29.2	29.0, 29.4	101.9	101.3, 102.5	0.97	0.97, 0.98	44.7	44.4, 45.0
Females	72.7	72.0, 73.4	28.7	29.0, 28.4	90.2	89.5, 90.8	0.86	0.85, 0.86	43.8	43.5, 44.1
Age group (yrs)										
50 - 64	81.0	80.2, 81.7	29.2	28.9, 29.4	95.1	94.5, 95.7	0.9	0.90, 0.91	42.9	42.6, 43.2
65 - 74	79.2	78.3, 80.2	29.0	28.7, 29.3	96.8	96.0, 97.6	0.92	0.92, 0.93	45.4	45.0, 45.7
75 +	75.6	74.3, 76.9	28.2	27.7, 28.6	96.4	95.2, 97.6	0.93	0.92, 0.93	46.9	46.4, 47.4
Marital status										
Married/ living with partner	80.1	79.5, 80.7	28.8	28.6, 29.0	95.6	95.1, 96.2	0.91	0.91, 0.92	43.8	43.6, 44.1
Single	80.6	78.2, 82.9	29.5	28.8, 30.3	96.9	94.9, 99.0	0.91	0.90, 0.93	44.9	44.0, 45.8
Separated/ divorced/ widowed	78.0	76.8, 79.2	29.3	28.9, 29.7	96.1	95.1, 97.1	0.91	0.91, 0.92	45.39	44.9, 45.9
Education										
Primary/ none /don't know	80.6	79.3, 82.0	29.6	29.2, 30.0	99.4	98.3, 100.6	0.95	0.94, 0.96	46.27	45.8, 46.9
Secondary	80.3	79.4, 81.2	29.3	29.1, 29.6	96.4	95.7, 97.1	0.91	0.91, 0.92	44.57	44.2, 44.9
Tertiary	78.7	77.9, 79.5	28.3	28.1, 28.6	93.8	93.1, 94.5	0.9	0.89, 0.90	43.1	42.8, 43.4
Deprivation score										
0 – 0.11 (least deprived)	78.9	77.9, 79.9	28.3	28.0, 28.6	94.5	93.6, 95.3	0.91	0.90, 0.91	43.6	43.2, 43.9
0.12 – 0.17	79.5	78.4, 80.6	28.8	28.5, 29.2	95.2	94.3, 96.2	0.91	0.90, 0.92	43.9	43.5, 44.4
0.18 – 0.23	80.2	78.9, 81.4	29.0	28.6, 29.4	96.0	95.0, 97.1	0.91	0.91, 0.92	44.3	43.8, 44.8
0.24 – 0.33	80.2	78.9, 81.5	29.5	29.1, 29.9	96.8	95.7, 97.9	0.92	0.91, 0.92	44.9	44.4, 45.5
> 0.33 (most deprived)	80.2	78.7, 81.7	29.6	29.1, 30.1	97.8	96.5, 99.0	0.93	0.92, 0.94	45.0	44.4, 45.6
Region										
Belfast	80.0	78.6, 81.3	29.3	28.9, 29.8	96.1	94.9, 97.3	0.91	0.90, 0.92	44.7	44.2, 45.3
Other city or town	79.2	78.4, 79.9	28.7	28.5, 29.0	95.4	94.8, 96.1	0.91	0.91, 0.92	44.0	43.7, 44.3
Rural area	80.4	79.4, 81.3	29.1	28.8, 29.4	96.3	95.4, 97.1	0.92	0.91, 0.92	44.3	43.9, 44.7

Note: Error bars represent 95% confidence intervals

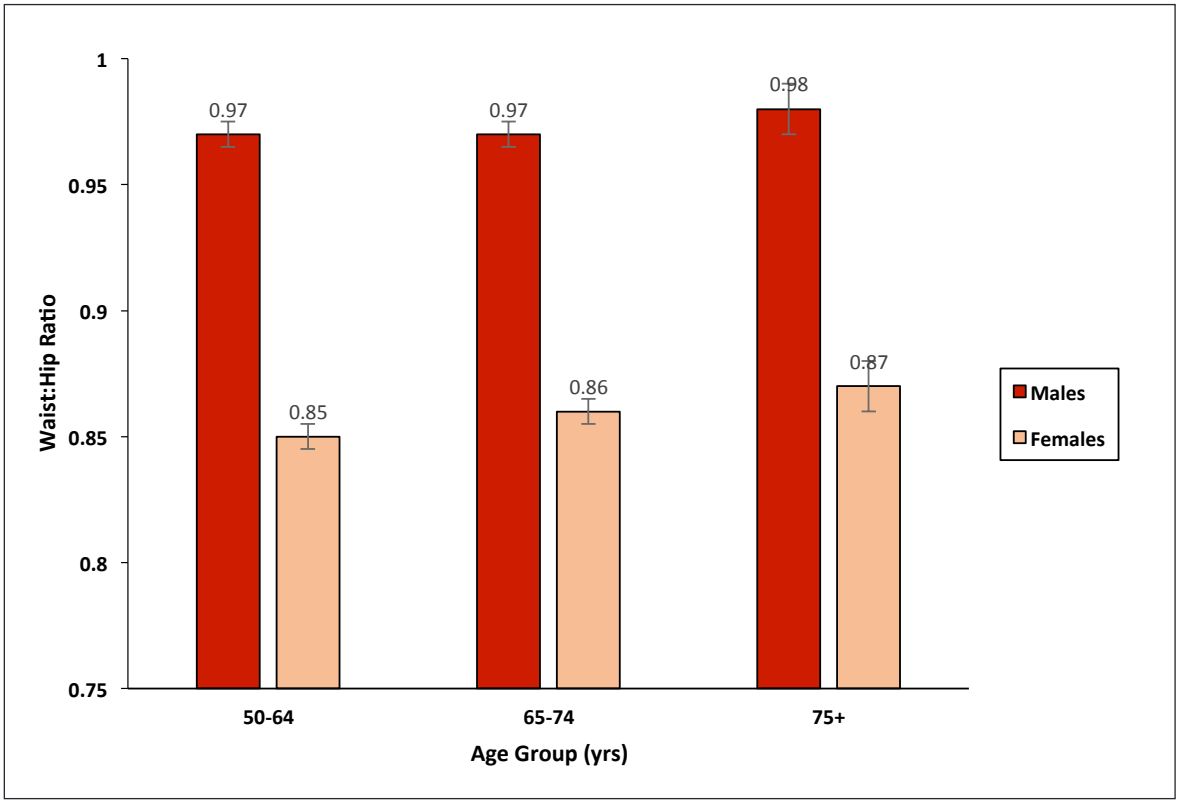
Figure 2.5: Percentage body fat by age group and sex in NICOLA participants



Note: Error bars represent 95% confidence intervals

The amount of fat distributed around the abdomen was measured using a tape measure. Men with a waist circumference of 94 cm or more and women with a waist circumference of 80 cm or more are more likely to develop obesity-related health problems. On average, men in the NICOLA cohort had a waist circumference of 101.9 cm and women had a waist circumference of 90.2 cm. As well as measuring waist, the ratio of waist to hip circumference is also used to indicate health risk. A waist:hip ratio above 0.90 for men and above 0.85 for women indicates increased risk of a number of diseases including heart disease and type 2 diabetes and is a better predictor of early mortality than BMI or waist circumference in older adults (15). The average waist:hip ratio was higher than the recommended level for both men (0.97) and women (0.86), and remained unchanged over time in both groups (see Figure 2.6).

Figure 2.6: Waist:hip ratio by age group and sex in NICOLA participants



Note: Error bars represent 95% confidence intervals

2.6 Conclusion

Ageing is associated with a decline in physical function. In the NICOLA participants, we observed that these changes began between the ages of 50 and 64 years and then continued over time. Early intervention can delay these age related changes, reducing their impact on health and the ability to maintain activities of daily living into later life.

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3 Eye Health and Hearing

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Citation

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Key Findings

- Glaucoma was present in 3.2% of NICOLA participants.
- During the baseline CAPI, only 30% of participants with glaucoma reported having been previously diagnosed with the disease so the majority of cases had been unknown.
- Of those who met our case definition of having diabetes, only 6.7% showed signs of retinopathy while 2.3% had maculopathy which is lower than expected.
- Only 6.5% of those with background retinopathy, 50% of those with pre-proliferative retinopathy and 60% of those with proliferative retinopathy reported a positive history of diabetic retinopathy during the baseline CAPI interview.
- Approximately 75% of participants showed retinal changes consistent with normal ageing, 16% had early age-related macular degeneration (AMD), 7.2% had intermediate AMD and 1.1% had advanced AMD in their worst eye.
- Only 8.1% of participants with intermediate AMD (high risk of progression to advanced AMD and sight loss within 5 years) were aware of the condition.

Key Findings continued

- The majority (n = 2765, 75%) of older adults reported that their hearing was good, very good or excellent while approximately one quarter reported their hearing to be fair or poor.
- Men were more likely to report poor or fair hearing compared to women.
- Not being married and not having higher education was associated with hearing loss.
- Hearing loss was more prominent in the 70+ age group compared to younger age groups.
- Hearing aid use was low in older adults, despite 25% of NICOLA participants reporting hearing loss.

3.1 Introduction

Ageing changes how our senses (hearing, vision, taste, smell and touch) provide information about the world around us. While ageing affects all our senses, hearing and vision suffer the greatest declines. This can result in lifestyle changes due to problems with communication, enjoyment of activities, participating in social interactions and in severe cases can lead to isolation.

Even in the absence of disease, significant losses in visual function are known to occur during normal ageing. Indeed, elderly individuals with good visual acuity often report difficulties with everyday visual tasks, such as driving at night or adjusting to lighting after coming in from outdoors (1).

Vision is known to make a central contribution to most tasks of daily living and a wide variety of cognitive abilities including reasoning and memory (2-4). Consequently, even in the presence relatively good visual acuity, decreases in visual function with age are related to a decreased quality of life, mobility and independence (5). Understanding the extent of this in Northern Ireland is important for resource allocation and policy planning.

Age is also known to substantially increase the incidence of eye diseases such as cataract, age-related macular degeneration (AMD) (6), glaucoma (7), and diabetic retinopathy which are the second, third, fourth and fifth leading causes of moderate to severe vision loss globally (8). The leading cause worldwide is uncorrected refractive error.

Hearing is essential for healthy ageing, enabling good communication with friends and family, participation in society and retention of our independence, wellbeing and quality of life. Hearing loss is highly prevalent in the older population and is the most common sensory impairment in older adults (9). Approximately 40% of UK adults aged over 50 have some form of hearing loss (10) and this figure increases to 90% of in those aged 80 years and over (10). One in six (approx. 300,000) older adults in Northern Ireland suffer from hearing loss (11).

Hearing loss by itself can be difficult to cope with, but if left untreated, hearing loss can have a profound impact on overall quality of life and everyday life through its effect on the ability to communicate and remain independent (12). Untreated hearing loss also has indirect health, psychosocial, and economic effects, thus resulting in increased feelings of loneliness, emotional distress, social isolation and withdrawal from social situations (13-17). Those experiencing hearing loss are also likely to have other age-related conditions and are at greater risk of falls and frailty (18), as well as higher rates of cognitive decline (19-21).

The timely provision of hearing aids can improve several aspects of life that are compromised by hearing loss (22). However, it has been reported that people wait on average 10 years before seeking help for hearing loss and up to 45% of affected people have delayed referral to NHS hearing services (23). The frequency of use of hearing aids by adults with hearing loss is also low.

Hearing loss can be very gradual, therefore, early identification of older adults with hearing problems and auditory assessment is important so that people can benefit from hearing aids as early as possible (24), and to accurately estimate prevalence of hearing loss in older populations (25).

3.2 Measurement of self-reported visual function and age-related eye disease.

Several questions in the baseline CAPI addressed participant's own perception of their visual function, glasses use and also if they had any diagnosed age-related eye disease (age-related macular degeneration, diabetic retinopathy, glaucoma or cataract).

Use of glasses or contact lenses

Most participants wore either glasses or contact lenses (95.3%) (Table 3.1), compared to 69.2% in the EPIC Norfolk Study (26). There was no substantial difference across age, sex, marital status, education, income or region category.

Table 3.1: Distribution of glasses or contact lens use

	Do you wear Glasses or Contact Lenses?	
	Yes	No
	n (weighted %)	n (weighted %)
Overall	3488 (95.3)	152 (4.2)
Gender		
Males	1672 (95)	84 (4.7)
Females	1816 (95.6)	68 (3.7)
Age group (yrs)		
50 - 64	1854 (93.7)	113 (5.8)
65 - 74	1157 (97.6)	27 (2.2)
75 +	477 (96.5)	12 (2.9)
Marital status		
Married/living with partner	2515 (95.1)	119 (4.6)
Single	238 (97.7)	5 (2.1)
Separated/divorced/widowed	735 (95.3)	28 (4)
Education		
Primary/none /don't know	551 (95.6)	23 (3.9)
Secondary	1526 (95.1)	69 (4.4)
Tertiary	1411 (95.6)	60 (4.1)
Deprivation score		
0 – 0.11 (least deprived)	947 (95.7)	38 (3.7)
0.12 – 0.17	716 (93.6)	44 (6)
0.18 – 0.23	701 (95.6)	28 (3.9)
0.24 – 0.33	634 (96)	24 (4)
> 0.33 (most deprived)	490 (95.7)	18 (3.8)
Region		
Belfast	611 (95.8)	22 (3.6)
Other city or town	1775 (95.7)	70 (3.8)
Rural area	1102 (94.5)	60 (5.3)
Location of health assessment		
Clinical facility	3299 (95.2)	149 (4.4)
Home	189 (97.3)	3 (1.9)

Values are n unweighted, % weighted. Total n = 3655, missing = 15

Visits to the Optometrist in the last 12 months

Women were more likely to have attended an optometrist than men and the likelihood increased across the age categories (Table 3.2). There was no obvious trend with marital status or education but those living within a relatively more deprived area were less likely to have attended recently and only half of those who opted for the home health assessment had attended an Optometrist in the last 12 months.

Table 3.2: Distribution of visits to the Optometrist in the last 12 months.

	Visited an Optometrist in the last 12 months	
	Yes	No
	n (weighted %)	n (weighted %)
Overall	2242 (60.7)	1401 (38.9)
Gender		
Males	1026 (58)	732 (41.8)
Females	1216 (63.2)	669 (36.1)
Age group (yrs)		
50 - 64	1103 (54.6)	866 (44.9)
65 - 74	782 (65.5)	403 (34.1)
75 +	357 (71)	132 (28.4)
Marital status		
Married / living with partner	1588 (59.6)	1048 (40.1)
Single	166 (68.6)	77 (30.8)
Separated / divorced / widowed	488 (61.1)	276 (38.3)
Education		
Primary / none / don't know	362 (62.6)	211 (36.5)
Secondary	938 (57.8)	659 (41.8)
Tertiary	942 (63.3)	531 (36.5)
Deprivation score		
0 – 0.11 (least deprived)	660 (66.5)	328 (33.1)
0.12 - 0.17	472 (62.1)	288 (37.6)
0.18 - 0.23	425 (58.1)	305 (41.2)
0.24 - 0.33	412 (63)	245 (36.7)
> 0.33 (most deprived)	273 (52.8)	235 (46.7)
Region		
Belfast	410 (64.5)	226 (35.1)
Other city or town	1138 (60.4)	709 (39.2)
Rural area	694 (58.9)	466 (40.5)
Location of health assessment		
Clinical facility	2135 (61.2)	1316 (38.4)
Home	107 (54.7)	85 (44.5)

Values are n unweighted, % weighted. Total n = 3655, missing = 12

Self-reported prevalence of age-related eye-disease

Participants were asked:
Have you ever suffered from any of the following eye diseases?
(You can select more than one answer)

1. Cataract
2. Macular Degeneration
3. Glaucoma
4. Diabetic related eye disease
5. None of the above
6. Do not know
7. Prefer not to answer

Cataract

Overall, just over a fifth of participants reported having cataracts (23.3%) (Table 3.3) and this proportion showed a very steep age-related increase with 61% of those over 75 years having cataracts compared to 7.5% in the 50 - 64 year old age group. By comparison, approximately 35% of TILDA participants aged over 75 years in Wave 1 reported cataract (27). There was no obvious gradient with marital status, education, or income. Twice as many of those undertaking a home health assessment reported cataracts than those who attended the clinical research facility.

Table 3.3: Distribution of self-reported cataract.

	Self-reported history of cataract	
	Yes	No
	n (weighted %)	n (weighted %)
Overall	775 (23.2)	2865 (76.3)
Gender		
Males	344 (20.9)	1413 (78.9)
Females	431 (25.4)	1452 (73.9)
Age group (yrs)		
50 - 64	146 (7.5)	1824 (92.1)
65 - 74	337 (30)	849 (69.9)
75 +	292 (61.1)	192 (37.5)
Marital status		
Married/living with partner	475 (18.9)	2160 (80.8)
Single	56 (26.2)	187 (73.1)
Separated/divorced/widowed	244 (33.3)	518 (65.8)
Education		
Primary / none / don't know	195 (36.5)	380 (63.1)
Secondary	307 (19.6)	1286 (79.8)
Tertiary	273 (17.7)	1199 (82)
Deprivation score		
0 – 0.11 (least deprived)	240 (25.7)	746 (73.8)
0.12 - 0.17	153 (22.2)	607 (77.3)
0.18 - 0.23	139 (22)	590 (77.4)
0.24 - 0.33	146 (24)	512 (76)
> 0.33 (most deprived)	97 (21.7)	410 (77.5)
Region		
Belfast	154 (27)	481 (72.6)
Other city or town	414 (24.4)	1431 (75.1)
Rural area	207 (19.3)	953 (80.2)
Location of health assessment		
Clinical facility	691 (21.4)	2758 (78.2)
Home	84 (46.1)	107 (52.4)

Values are n unweighted, % weighted. Total n = 3655, missing = 12

Approximately 8% of participants reported having previous cataract surgery (Table 3.4), this also was strongly age related. Twice as many of those with only primary education reported having had cataract surgery compared to those with more education. More of those who lived in urban areas reported having had surgery than those from rural locations.

Table 3.4: Distribution of history of cataract surgery

	Self-reported history of cataract surgery		
	Right Eye	Left Eye	Both Eyes
	n (weighted %)	n (weighted %)	n (weighted %)
Overall	43 (1.4)	42 (1.1)	192 (5.9)
Gender			
Males	22 (1.4)	25 (1.3)	86 (5.2)
Females	21 (1.4)	17 (1)	106 (6.5)
Age group (yrs)			
50 - 64	13 (0.7)	13 (0.6)	25 (1.1)
65 - 74	16 (1.6)	15 (1.2)	60 (5.8)
75 +	14 (3)	14 (2.6)	107 (21.3)
Marital status			
Married/living with partner	25 (1.1)	30 (1.1)	105 (4.3)
Single	5 (1.9)	1 (0.4)	13 (6.1)
Separated/divorced/widowed	13 (1.9)	11 (1.4)	74 (9.9)
Education			
Primary/none/don't know	15 (2.8)	9 (1.5)	48 (9.0)
Secondary	11 (0.7)	12 (0.8)	74 (4.9)
Tertiary	17 (1.2)	21 (1.3)	70 (4.7)
Deprivation score			
0 – 0.11 (least deprived)	9 (1)	15 (1.4)	63 (7)
0.12 - 0.17	12 (1.9)	9 (1.3)	40 (6.5)
0.18 - 0.23	11 (1.9)	6 (0.7)	32 (5)
0.24 - 0.33	8 (1.3)	4 (0.6)	35 (6.1)
> 0.33 (most deprived)	3 (0.7)	8 (1.6)	22 (4.6)
Region			
Belfast	7 (1.1)	7 (1.3)	43 (7.1)
Other city or town	22 (1.3)	24 (1.3)	112 (7)
Rural area	14 (1.5)	11 (0.7)	37 (3.4)
Location of health assessment			
Clinical facility	38 (1.2)	38 (1.1)	158 (4.9)
Home	5 (2.8)	4 (1.5)	34 (17.7)

Values are n unweighted, % weighted. Total n = 3655, missing = 3378

Glaucoma

Just under 3% of participants reported a previous diagnosis of glaucoma, with this proportion showing a strong age-related gradient. A diagnosis of glaucoma was twice as common in those who were separated, divorced or widowed compared to the other marital status categories. It was also more common in those with just primary education and those living in urban locations compared to those from rural areas (Table 3.5). Trends for age and sex were broadly like those reported in the TILDA Wave 1 health assessment report (27).

Table 3.5: Distribution of positive history of glaucoma.

	Self-reported Glaucoma		
	Yes	No	Don't know
	n (weighted %)	n (weighted %)	n (weighted %)
Overall	92 (2.9)	3545 (96.4)	5 (0.2)
Gender			
Males	45 (2.6)	1708 (96.7)	3 (0.2)
Females	47 (3.1)	1837 (96.2)	2 (0.2)
Age group (yrs)			
50 - 64	29 (1.6)	1936 (97.6)	1 (0.1)
65 - 74	29 (2.5)	1157 (97.4)	1 (0.1)
75 +	34 (7.6)	452 (91)	3 (1)
Marital status			
Married/living with partner	52 (2)	2580 (97.5)	3 (0.2)
Single	6 (2)	237 (96.9)	NA
Separated/divorced/widowed	34 (5.2)	728 (93.7)	2 (0.5)
Education			
Primary/none/don't know	23 (4.8)	547 (93.6)	4 (0.9)
Secondary	36 (2.2)	1561 (97.4)	NA
Tertiary	33 (2.2)	1437 (97.4)	1 (0.1)
Deprivation score			
0 – 0.11 (least deprived)	24 (2.7)	960 (96.6)	2 (0.3)
0.12 - 0.17	13 (1.8)	749 (98.1)	NA
0.18 - 0.23	19 (3.1)	710 (96.2)	NA
0.24 - 0.33	25 (4.7)	631 (94.7)	2 (0.6)
> 0.33 (most deprived)	11 (2.1)	495 (96.6)	1 (0.3)
Region			
Belfast	21 (4)	614 (95.6)	NA
Other city or town	48 (3)	1793 (96.1)	4 (0.3)
Rural area	23 (2.1)	1138 (97.4)	1 (0.2)
Location of health assessment			
Clinical facility	79 (2.5)	3367 (96.9)	4 (0.2)
Home	13 (7.1)	178 (91.2)	1 (0.9)

Values are n unweighted, % weighted. Total n = 3655, missing = 13

Age-related macular degeneration (AMD)

A positive history of AMD was reported by 2.5% of participants overall (Table 3.6), including just over 8% of those aged over 75 years reflecting the strong association of the disease with age. There was no obvious difference in self-reported prevalence based on sex, education, deprivation, marital status or location.

Table 3.6: Distribution of positive history of age-related macular degeneration

	Self-reported age-related macular degeneration		
	Yes	No	Don't know
	n (weighted %)	n (weighted %)	n (weighted %)
Overall	90 (2.5)	3545 (96.9)	9 (0.3)
Gender			
Males	51 (2.8)	1705 (96.9)	2 (0.2)
Females	39 (2.2)	1840 (96.9)	7 (0.4)
Age group (yrs)			
50 - 64	16 (0.7)	1951 (98.7)	4 (0.2)
65 - 74	32 (2.5)	1150 (97)	3 (0.4)
75 +	42 (8.1)	444 (90.7)	2 (0.5)
Marital status			
Married/living with partner	59 (2.1)	2572 (97.3)	7 (0.3)
Single	6 (2.4)	237 (97.2)	1 (0.4)
Separated/divorced/widowed	25 (3.3)	736 (95.6)	1 (0.2)
Education			
Primary/none/don't know	14 (2.8)	558 (96.2)	3 (0.6)
Secondary	36 (2.2)	1558 (97.3)	3 (0.2)
Tertiary	40 (2.6)	1429 (96.8)	3 (0.3)
Deprivation score			
0 – 0.11 (least deprived)	26 (2.5)	959 (96.9)	3 (0.3)
0.12 - 0.17	23 (3)	739 (96.9)	NA
0.18 - 0.23	14 (2.4)	713 (96.6)	2 (0.4)
0.24 - 0.33	18 (2.6)	637 (96.9)	2 (0.3)
> 0.33 (most deprived)	9 (1.9)	497 (97.1)	2 (0.5)
Region			
Belfast	17 (2.2)	615 (96.8)	4 (0.8)
Other city or town	49 (2.9)	1792 (96.3)	4 (0.3)
Rural area	24 (2)	1138 (97.8)	1 (0.1)
Location of health assessment			
Clinical facility	81 (2.3)	3362 (97)	9 (0.3)
Home	9 (4.2)	183 (95)	NA

Values are n unweighted, % weighted. Total n = 3655, missing = 11

Diabetic Retinopathy

Only 29 participants reported having diabetic retinopathy with no obvious trends across categories (Table 3.7).

Table 3.7: Distribution of positive history of diabetic retinopathy

	Self-reported Diabetic Retinopathy		
	Yes	No	Don't Know
	n (weighted %)	n (weighted %)	n (weighted %)
Overall	29 (0.8)	3609 (98.5)	8 (0.4)
Gender			
Males	21 (1.1)	1734 (98.5)	4 (0.3)
Females	8 (0.5)	1875 (98.6)	4 (0.4)
Age group (yrs)			
50 - 64	10 (0.5)	1959 (99)	2 (0.1)
65 - 74	15 (1.3)	1170 (98.3)	2 (0.4)
75 +	4 (0.6)	480 (97.7)	4 (1)
Marital status			
Married/living with partner	22 (0.9)	2613 (98.7)	4 (0.3)
Single	2 (1.1)	241 (98.6)	1 (0.3)
Separated/divorced/widowed	5 (0.6)	755 (98.1)	3 (0.6)
Education			
Primary/none/don't know	4 (0.8)	567 (98)	4 (0.8)
Secondary	13 (0.8)	1583 (98.7)	2 (0.2)
Tertiary	12 (0.9)	1459 (98.8)	2 (0.1)
Deprivation score			
0 – 0.11 (least deprived)	11 (1.1)	977 (98.6)	1 (0.1)
0.12 - 0.17	4 (0.5)	758 (99.4)	NA
0.18 - 0.23	8 (1.4)	718 (97.3)	4 (0.9)
0.24 - 0.33	5 (0.7)	651 (98.8)	1 (0.2)
> 0.33 (most deprived)	1 (0.1)	505 (98.7)	2 (0.6)
Region			
Belfast	6 (0.9)	628 (98.1)	3 (0.9)
Other city or town	18 (1)	1823 (98.2)	5 (0.4)
Rural area	5 (0.5)	1158 (99.4)	NA
Location of health assessment			
Clinical facility	28 (0.8)	3420 (98.6)	6 (0.3)
Home	1 (0.3)	189 (97.6)	2 (1.3)

Values are n unweighted, % weighted. Total n = 3655, missing = 9

3.3 Health assessment measurement of eye health

Visual acuity

Habitual visual acuity was measured using an ETDRS chart in full illumination at 4 metres with the participant's own glasses or contact lenses in place, and also with a pinhole. The pinhole acuity provides an estimate of the potential visual acuity if a full refraction was undertaken and is what we have presented here. Distance visual acuity is the standard metric for quantifying visual function and is known to be associated with quality of life as well as providing a gross indication of ocular health.

Mean visual function was good in this population (0.06LogMAR~6/7 Snellen) with sex, marital status, education and economic status showing little variation across categories (Table 3.8). The most significant deficit was seen in those aged over 75 years whose mean acuity was nearly a line worse than the previous category. Those who undertook a home assessment had much lower mean acuity than those who attended the clinical research facility (0.06 versus 0.36 LogMAR, 6/7 versus 6/14 Snellen).

Table 3.8: Distribution of pin hole distance visual acuity (Better eye)

	Distance Visual Acuity (Pin hole) Better Eye
	ETDRS (Number of letters)
	Mean (Standard deviation)
Overall	0.06 (0.12)
Gender	
Males	0.04 (0.1)
Females	0.06 (0.1)
Age group (yrs)	
50 - 64	0.02 (0.08)
65 - 74	0.06 (0.12)
75 +	0.12 (0.12)
Marital status	
Married/living with partner	0.04 (0.1)
Single	0.06 (0.1)
Separated/divorced/widowed	0.06 (0.12)
Education	
Primary/none/don't know	0.10 (0.12)
Secondary	0.04 (0.1)
Tertiary	0.02 (0.1)
Deprivation score	
0 – 0.11 (least deprived)	0.04 (0.1)
0.12 - 0.17	0.04 (0.1)
0.18 - 0.23	0.04 (0.12)
0.24 - 0.33	0.06 (0.14)
> 0.33 (most deprived)	0.06 (0.1)
Region	
Belfast	0.04 (0.1)
Other city or town	0.04 (0.12)
Rural area	0.04 (0.1)
Location of health assessment	
Clinical facility	0.06 (0.12)
Home	0.36 (0.2)

Values are n unweighted, % weighted. Total n = 3655, missing = 9

Refractive error

Auto refraction (Shin Nippon Auto Refractor RK900) was measured in both eyes prior to pupil dilation. To summarise, we used the most severe eye to examine the distribution of refractive error in the NICOLA population. The mean refractive error was 0.83 with the population becoming more hypermetropic (long sighted) with age (Table 3.9) which is consistent with other longitudinal ageing studies (28). The magnitude of hypermetropia increased across deprivation score categories and was higher in those reporting only a primary education.

Table 3.9: Distribution of Refractive error (most severe eye)

	Spherical equivalent from auto refractor Dioptres
	Most severe eye
	Mean (Standard deviation)
Overall	0.83 (2.9)
Gender	
Males	0.93 (2.69)
Females	0.74 (3.09)
Age group (yrs)	
50 - 64	0.47 (3)
65 - 74	1.24 (2.76)
75 +	1.44 (2.53)
Marital status	
Married/living with partner	0.77 (2.92)
Single	0.77 (2.92)
Separated/divorced/widowed	1.13 (2.81)
Education	
Primary/none/don't know	1.55 (2.73)
Secondary	0.97 (2.92)
Tertiary	0.45 (2.89)
Deprivation score	
0 – 0.11 (least deprived)	0.61 (2.83)
0.12 - 0.17	0.69 (2.72)
0.18 - 0.23	0.78 (2.77)
0.24 - 0.33	1.12 (3.16)
> 0.33 (most deprived)	1.26 (3.13)
Region	
Belfast	1.05 (2.49)
Other city or town	0.73 (3.15)
Rural area	0.9 (2.66)

Values are n unweighted, % weighted. Total n = 3655, missing = 9

Retinal imaging

The ophthalmic tests included multi-modal retinal imaging using a standard retinal fundus camera (Canon CX-1 Fundus Camera (Canon U.S.A., Inc.), wide-field retinal imaging (Optos plc, Dunfermline, UK) and spectral domain optical coherence tomography (SD-OCT) imaging (Heidelberg Engineering, Heidelberg, Germany). Participants were given the option of having the pupils of neither, one eye or both eyes dilated (Tropicamide 1%). Colour fundus photography (CFP), wide-field retinal imaging and SD-OCT images were captured irrespective of pupillary dilation.

Age-related Macular Degeneration

Standardised multi-modal retinal grading identified drusen size, presence of hyper pigmentation, presence of focal or geographic atrophy or signs of retinal neovascularisation. Participants were then classified according to the Beckman Clinical Classification system (29).

Approximately 75% of participants showed retinal changes consistent with normal ageing (Class 0 or 1), 16% had early AMD, 7.2% had intermediate AMD and 1.1% had advanced AMD in their worst eye (Table 3.10). This is higher than in the TILDA study which reported an estimated overall prevalence of 7.2%, with early / intermediate accounting for 6.6% and 0.6% with late AMD (30).

Of participants with advanced AMD on retinal imaging, approximately 40% did not report a positive history in the health assessment. Only 8.1% of participants with intermediate AMD (high risk of progression to advanced AMD and sight loss within 5 years) were aware of the condition.

Table 3.10: Distribution of age-related macular degeneration based on multi-modal imaging and standardised retinal grading

	Age-related macular degeneration Beckman Clinical Classification (based on worst eye)				
	No AMD No drusen or pigment	Normal Ageing <63 µm drusen, no pigment	Early AMD >63 µm drusen < 125 µm drusen, no pigment	Intermediate AMD >125 µm drusen and / or pigment	Advanced AMD Neovascular AMD or geographic atrophy
	n (weighted %)	n (weighted %)	n (weighted %)	n (weighted %)	n (weighted %)
Overall	1637 (48.8)	761 (23.1)	525 (16)	235 (7.2)	26 (1.1)
Gender					
Males	789 (48.5)	374 (23.7)	232 (14.9)	129 (7.7)	15 (1.4)
Females	848 (49.1)	387 (22.5)	293 (17)	106 (6.6)	11 (0.8)
Age group (yrs)					
50 - 64	962 (51.5)	481 (26.7)	271 (14.8)	87 (4.9)	1 (0.1)
65 - 74	506 (46.5)	229 (21.1)	189 (17.5)	98 (9)	11 (1.5)
75 +	169 (43.1)	51 (13)	65 (17.2)	50 (12.3)	14 (4.3)
Marital status					
Married/living with partner	1249 (50.4)	568 (23.7)	368 (14.9)	165 (6.8)	14 (0.7)
Single	99 (45.2)	51 (23.6)	44 (20.2)	14 (7)	1 (0.7)
Separated/divorced/ widowed	289 (45.3)	142 (21)	113 (17.8)	56 (8.3)	11 (2.2)
Education					
Primary/none/ don't know	225 (46.2)	105 (21.9)	80 (15.8)	40 (7.6)	12 (3)
Secondary	706 (48.6)	338 (23.5)	237 (16.7)	104 (7.2)	7 (0.5)
Tertiary	706 (50.9)	318 (23.3)	208 (15.1)	91 (6.8)	7 (0.5)
Deprivation score					
0 – 0.11 (least deprived)	466 (50)	215 (23.4)	141 (15.5)	60 (6.7)	4 (0.7)
0.12 - 0.17	336 (47)	150 (20.8)	129 (19.2)	58 (8.5)	2 (0.4)
0.18 - 0.23	342 (50.3)	147 (22.2)	110 (16.2)	40 (5.5)	9 (1.9)
0.24 - 0.33	275 (46.8)	148 (26.4)	77 (13.7)	44 (8.2)	6 (1)
> 0.33 (most deprived)	218 (49.3)	101 (22.9)	68 (15.3)	33 (7.3)	5 (1.4)
Region					
Belfast	282 (49.3)	139 (22.6)	88 (16)	35 (6)	6 (1)
Other city or town	819 (47.8)	377 (22.8)	284 (16.9)	127 (7.6)	14 (1.2)
Rural area	536 (50.2)	245 (23.9)	153 (14.4)	73 (7.1)	6 (0.8)

Values are n unweighted, % weighted. Total n = 3655, missing = 471

Glaucoma

The NICOLA health assessment included stereo colour optic disc photography and intra-ocular pressure measurement using an Ocular response analyser (ORA). As it did not include an assessment of visual fields a definitive diagnosis of glaucoma could not be made. Therefore other clinically important measurements were made in NICOLA participants aged 50 years or older who attended the health assessment including: a vertical cup to disk ratio (VCDR) ≥ 0.7 and/or VCDR asymmetry ≥ 0.2 and/or vertical neuroretinal rim ratio (NRRR) ≤ 0.1 on optic disc stereo photography and/or IOP ≥ 25 mmHg on ORA tonometry (Goldmann correlated IOP (IOPg)), these measurements being made after an invitation for an additional examination by a glaucoma expert (AAB) and visual field testing. Additional tests performed at this visit included: (i) visual field testing using Humphrey's Matrix frequency doubling technology (FDT) perimetry (Carl Zeiss Meditec Inc., Dublin, CA, USA) in low illumination. (ii) Gonioscopy: performed at the slit lamp by the glaucoma expert. (iii) Pupil dilation (except in patients with narrow anterior chamber angle) and biomicroscopy including optic disc examination.

We found that glaucoma was prevalent in 3.2% of NICOLA participants (Table 3.11). Our results are comparable to pooled estimations of glaucoma prevalence in European populations in the age range 40 – 80 years (2.93%, 95%CI 1.85%, 4.40%) (31). Only 30% of participants with glaucoma reported a positive history during the CAPI interview.

Table 3.11: Distribution of Glaucoma using ISGEO Classification.

	Glaucoma The International Society of Geographical and Epidemiological Ophthalmology (ISGEO) Classification	
	Absent (both eyes)	Present (either eye)
	n (weighted %)	n (weighted %)
Overall	3202 (96.8)	103 (3.2)
Gender		
Males	1549 (96.7)	52 (3.3)
Females	1653 (96.9)	51 (3.1)
Age group (yrs)		
50 - 64	1804 (97.8)	39 (2.2)
65 - 74	1039 (96.5)	37 (3.5)
75 +	359 (93.5)	27 (6.5)
Marital status		
Married / living with partner	2374 (97.2)	70 (2.8)
Single	209 (96.1)	8 (3.9)
Separated / divorced / widowed	619 (95.9)	25 (4.1)
Education		
Primary / none / don't know	475 (97)	14 (3)
Secondary	1396 (96.6)	47 (3.4)
Tertiary	1331 (96.9)	42 (3.1)
Deprivation score		
0 – 0.11 (least deprived)	895 (97.6)	24 (2.4)
0.12 - 0.17	679 (96.6)	22 (3.4)
0.18 - 0.23	650 (96.9)	22 (3.1)
0.24 - 0.33	553 (96.5)	18 (3.5)
> 0.33 (most deprived)	425 (96.3)	17 (3.7)
Region		
Belfast	560 (96.1)	20 (3.9)
Other city or town	1629 (96.9)	50 (3.1)
Rural area	1013 (97)	33 (3)

Values are n unweighted, % weighted. Total n = 3655, missing = 350

Diabetic retinopathy and maculopathy

Features consistent with diabetic retinopathy were assessed on all imaging modalities including the wide-field retinal imaging. The English Classification system was used to assign participants to categories based on their most severe eye. Of those who met our diabetes case definition, only 6.7% of participants showed signs of retinopathy (Table 3.12) and 2.3% maculopathy (Table 3.13) which is lower than expected. A recent systematic review and meta-analysis of diabetic eye disease in European populations reported a prevalence of any diabetic retinopathy and diabetic macular oedema of 25.7% and 3.7% respectively among individuals with diabetes (6).

Only 6.5% of those with background retinopathy, 50% of those with pre-proliferative retinopathy and 60% of those with proliferative retinopathy reported a positive history of DR during the CAPI interview.

Table 3.12: Distribution of diabetic maculopathy on the basis of multi-modal imaging and standardised retinal grading

	Diabetic Retinopathy The English Grading Scheme			
	R0 No retinopathy	R1 Background retinopathy	R2 Pre-proliferative retinopathy	R3 Proliferative retinopathy
	n (weighted %)	n (weighted %)	n (weighted %)	n (weighted %)
Overall	285 (93.3)	18 (4.5)	1 (0.2)	9 (1.8)
Gender				
Males	208 (91.4)	12 (6.1)	1 (0.8)	5 (1.7)
Females	177 (95.6)	6 (2.5)	NA	4 (1.9)
Age group (yrs)				
50 - 64	158 (91.9)	8 (5)	1 (1.1)	3 (2)
65 - 74	157 (92.7)	8 (4.9)	NA	6 (2.4)
75 +	70 (97.6)	2 (2.4)	NA	NA
Marital status				
Married/living with partner	262 (92.5)	14 (5.7)	6 (1.9)	NA
Single	33 (93)	NA	1 (2.6)	1 (4.4)
Separated/divorced/widowed	90 (95.4)	4 (3.4)	2 (1.2)	NA
Education				
Primary/none/ don't know	86 (93.2)	3 (3.8)	1 (1.3)	2 (1.7)
Secondary	181 (94.2)	9 (4.8)	0	2 (1)
Tertiary	118 (91.7)	6 (4.8)	0	5 (3.5)
Deprivation score				
0 – 0.11 (least deprived)	85 (96.4)	1 (1.5)	2 (2.1)	0
0.12 - 0.17	76 (91.6)	7 (7.6)	1 (0.8)	0
0.18 - 0.23	82 (88.1)	6 (7)	4 (3.1)	1 (1.9)
0.24 - 0.33	75 (95.6)	2 (1.7)	2 (2.7)	0
> 0.33 (most deprived)	67 (96.1)	2 (3.9)	0	0
Region				
Belfast	64 (95.9)	4 (4.1)	0	0
Other city or town	201 (92.3)	11 (6)	5 (1.7)	0
Rural area	120 (93.4)	3 (2.1)	4 (3)	1 (1.5)

Values are n unweighted, % weighted. Total n = 432, missing = 19 (only Diabetes cases)

Table 3.13: Distribution of diabetic maculopathy according to multi-modal imaging and standardised retinal grading.

	Diabetic Maculopathy The English Grading Scheme	
	Absent (both eyes)	Present (either eye)
	n (weighted %)	n (weighted %)
Overall	415 (97.7)	11 (2.3)
Gender		
Males	228 (97.3)	7 (2.7)
Females	187 (98.3)	4 (1.7)
Age group (yrs)		
50 - 64	168 (96.9)	4 (3.1)
65 - 74	172 (97.9)	6 (2.1)
75 +	75 (99.2)	1 (0.8)
Marital status		
Married / living with partner	283 (98)	7 (2)
Single	32 (92.7)	2 (7.3)
Separated / divorced / widowed	100 (99)	2 (1)
Education		
Primary / none / don't know	94 (97.8)	2 (2.2)
Secondary	195 (99)	2 (1)
Tertiary	126 (95.2)	7 (4.8)
Deprivation score		
0 – 0.11 (least deprived)	91 (100)	0
0.12 - 0.17	83 (97.7)	3 (2.3)
0.18 - 0.23	91 (95.2)	5 (4.8)
0.24 - 0.33	80 (96.6)	3 (3.4)
> 0.33 (most deprived)	70 (100)	0
Region		
Belfast	71 (99.1)	1 (0.9)
Other city or town	217 (98.5)	5 (1.5)
Rural area	127 (95.7)	5 (4.3)

Values are n unweighted, % weighted. Total n = 432, missing = 6 (only diabetes cases)

3.4 Health assessment measurement of hearing

In NICOLA, a variety of questions were used to assess hearing ability and coping with hearing problems. Participants were asked:

1) Do you use any of the following aids or appliances to help you with your hearing?

   Hearing-aid (all of the time), Hearing-aid (some of the time), Amplifier, None of the above

2) Is your hearing (with or without a hearing-aid)….

   Excellent, Very good, Good, Fair, Poor

In accordance with a previous validation study of self-reported hearing loss in TILDA (32), a response of 'excellent', 'very good' or 'good' was classified as normal hearing, while a response of 'fair' or 'poor' indicated hearing loss.

The potential negative consequences of poor hearing were also examined in NICOLA. Participants were asked:

1) Can you follow a conversation with one person (with or without a hearing-aid)?

   With no difficulty, with some difficulty, with much difficulty, no I cannot

2) Can you follow a conversation with four people (with or without a hearing-aid)?

   With no difficulty, with some difficulty, with much difficulty, no I cannot

3) Can you use a normal telephone (not adapted for hearing impairment)?

   With no difficulty, with some difficulty, with much difficulty, no I cannot

4) Do you experience ringing or buzzing noises in your head or in one or both ears that lasts for more than five minutes at a time?

5) Have you ever been worried, annoyed or upset when these noises are their worst?

6) Have you ever worked in a noisy place where you had to shout to be heard?

7) Have you ever listened to music for more than 3 hours per week at a volume where you need to shout to be heard or if wearing earphones, someone else has had to shout for you to hear them?

Self-rated hearing

Hearing characteristics of the NICOLA participants are presented in Table 3.14. Approximately one in four (25%) older adults reported hearing loss i.e. hearing rated as "*poor*" or "*fair*". Consistent with the results from TILDA, more men reported hearing loss compared to women (31% versus 20%, respectively) (17). Similar to TILDA, the percentage reporting hearing loss increased with advancing age from 22% at age 50 - 64 years to 33% in those aged 75 years and over. Results also showed that not being married and not having a higher education was associated with hearing loss. Other studies have reported similar findings (33-35).

Figure 3.1: Self-rated hearing by age group in men

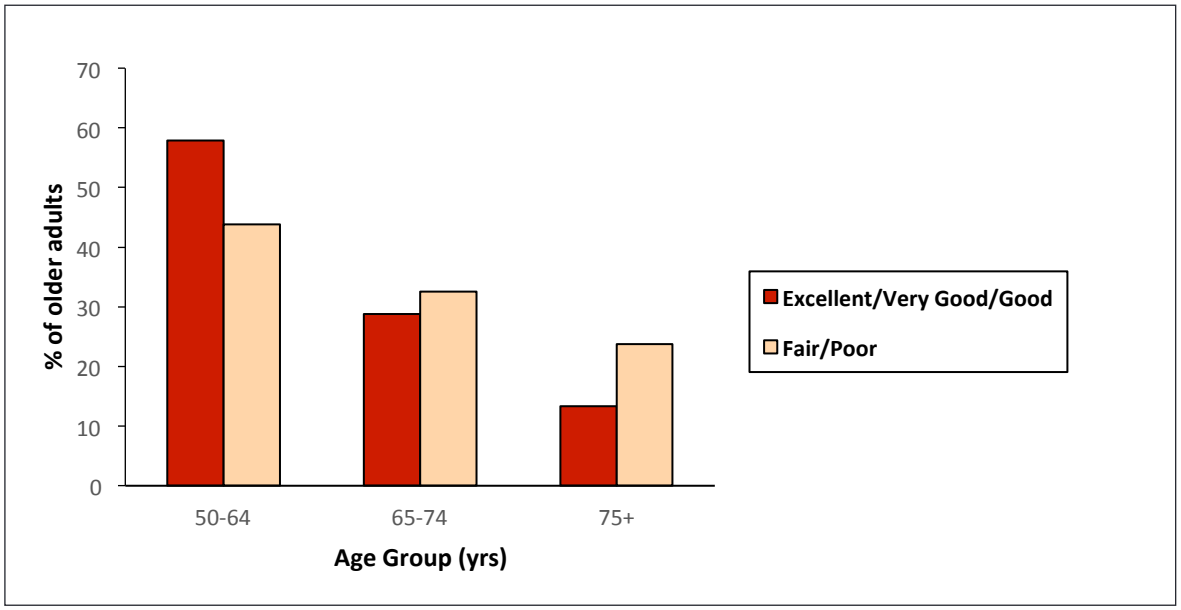

Figure 3.2: Self-rated hearing by age group in women

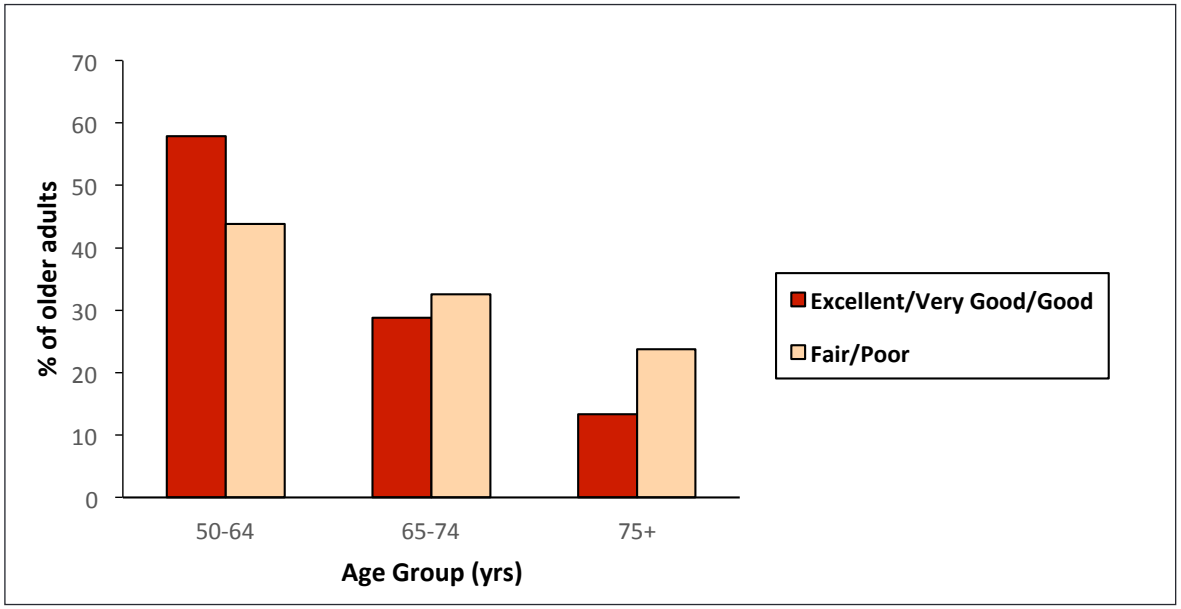

Table 3.14: Use of hearing aids or appliances in older adults (n = 3655)

	Use of hearing aid		Use of amplifier	Quality of hearing	
	All of the time	Some of the time		Excellent / very good / good	Fair / poor
	n (weighted %)	n (weighted %)	n (weighted %)	n (weighted %)	n (weighted %)
Overall	176 (5.4)	171 (5.0)	10 (0.3)	2765 (75)	875 (25)
Gender					
Males	91 (5.7)	104 (6.1)	4 (0.2)	1222 (69)	530 (31)
Females	85 (5.1)	67 (4.0)	6 (0.5)	1543 (80)	345 (20)
Age group (yrs)					
50 - 64	39 (2.0)	26 (1.2)	5 (0.3)	1557 (78)	410 (22)
65 - 74	71 (6.7)	61 (4.7)	2 (0.1)	875 (73)	309 (27)
75 +	66 (13.9)	84 (17.5)	3 (0.8)	333 (67)	156 (33)
Marital status					
Married/living with partner	116 (4.8)	112 (4.5)	6 (0.2)	2030 (76)	603 (24)
Single	14 (5.2)	8 (2.9)	0 (0.0)	192 (79)	51 (21)
Separated/divorced/ widowed	46 (6.9)	51 (6.9)	4 (0.7)	543 (70)	221 (30)
Education					
Primary/none/ don't know	51 (9.0)	46 (7.6)	1 (0.3)	388 (68)	187 (32)
Secondary	72 (4.6)	67 (4.3)	5 (0.4)	1212 (75)	387 (25)
Tertiary	53 (3.6)	58 (3.8)	4 (0.3)	1165 (79)	301 (21)
Deprivation score					
0 – 0.11 (least deprived)	53 (5.9)	54 (6.0)	1 (0.1)	742 (74)	244 (26)
0.12 - 0.17	37 (5.3)	37 (5.6)	0 (0.0)	587 (76)	173 (24)
0.18 - 0.23	30 (4.6)	39 (5.6)	5 (0.6)	552 (74)	180 (26)
0.24 - 0.33	32 (5.8)	26 (4.3)	1 (0.2)	498 (74)	157 (26)
> 0.33 (most deprived)	24 (5.2)	15 (3.1)	3 (0.9)	386 (76)	121 (24)
Region					
Belfast	37 (6.3)	26 (4.2)	1 (0.1)	476 (74)	157 (26)
Other city or town	104 (5.4)	102 (5.4)	3 (0.1)	1574 (76)	463 (24)
Rural area	35 (4.7)	43 (4.8)	6 (0.9)	708 (72)	254 (28)
Location of health assessment					
Clinical facility	154 (4.8)	153 (4.6)	10 (0.4)	2631 (75)	817 (25)
Home	22 (12.4)	18 (10.0)	0 (0.0)	134 (69)	58 (31)

Values are n unweighted, % weighted. Total n = 3655, missing = 10

Use of hearing aids

Although there was a high prevalence of hearing loss reported, the use of hearing aids was low. Only 19% of older adults who reported hearing loss reported using a hearing aid (all or some of the time). Similar findings were reported in older adults in the TILDA study (17). Of those who used a hearing aid or amplifier, just over one third (35%) were aged over 75 years compared to 20% of 65 - 74 year olds and 6% of 50 - 64 year olds. Table 3.15 shows the cross tabulation of hearing loss and hearing aid use.

Table 3.15: Cross tabulation of hearing loss and hearing aid use (n = 3655)

	Do you use any of the following aids or appliances to help you with you hearing?		
		Hearing aid / amplifier (all or some of the time)	No hearing aid
		n (weighted %)	n (weighted %)
Is your hearing (with/ without a hearing aid)....	Excellent	15 (4)	450 (96)
	Very good / Good	175 (8)	2122 (92)
	Fair / Poor	166 (19)	708 (81)

Values are n unweighted, % weighted. Total n = 3655, missing = 19

Impact of hearing loss

Difficulty following a conversation

NICOLA participants were asked if they had any difficulty following a conversation either with one person or with four people. Consistent with the results of TILDA (17), one in 20 (5%) older adults reported difficulty following a conversation with one person and this increased with age, affecting 8% of those aged 75 years and over. Men were more likely to experience difficulty compared to women (6% versus 4%) (Table 3.16).

More individuals experienced some or a lot of difficulty following a conversation with four people (27%). Again, men were more likely to experience difficulty compared to women (32% versus 23%), and difficulty was highest among adults aged 75 years and over compared to those aged 65 - 74 years and 50 - 64 years (39%, 30% and 23%, respectively).

Difficulty using a telephone

Overall, 7% reported difficulty using a telephone. One percent of older adults reported that they were unable to use a normal telephone. Approximately 1 in 10 older adults aged 75+ reported that they had difficulty using a telephone or were unable to use a telephone (10%). This compared to 8% of 65 - 74 year olds and 7% of 50 - 64 year olds. Men were more likely to have difficulty using a telephone compared to women (9% versus 7%).

Presence of noises in head or ears

Over one quarter (29%) of older adults reported that they had been exposed to loud noise over their lifetime. More than three quarters (79%) of those aged 50 - 64 years had experienced this noise sensation, either currently or in the past compared to just over half (54%) of 65 - 74 year olds and one third (33%) of those aged 75 years and over.

Hearing loss and feeling of loneliness or depression

Unlike the findings of TILDA (17), there was no difference in reported feelings of depression or loneliness in those with excellent / very good hearing compared to those with fair / poor hearing (see Tables 3.17 and 3.18).

Table 3.16: Self-reported quality of hearing (n = 3655)

	Ability to follow conversation					
	With 1 person			With 4 people		
	No difficulty	Some difficulty	Much difficulty or can't	No difficulty	Some difficulty	Much difficulty or can't
	n (weighted %)	n (weighted %)	n (weighted %)	n (weighted %)	n (weighted %)	n (weighted %)
Overall	3480 (95)	161 (5)	7 (0.3)	2702 (72)	785 (23)	145 (5)
Gender						
Males	1659 (94)	93 (6)	4 (0.3)	1212 (68)	444 (26)	91 (6)
Females	1821 (96)	68 (4)	3 (0.2)	1490 (77)	341 (20)	48 (3)
Age group (yrs)						
50 - 64	1888 (96)	74 (4)	1 (0)	1547 (77)	375 (20)	47 (3.1)
65 - 74	1129 (94)	54 (5)	3 (0.4)	858 (70)	274 (24)	48 (6)
75 +	453 (92)	33 (7)	3 (1.0)	297 (61)	136 (28)	50 (11)
Marital status						
Married/living with partner	2526 (95)	109 (5)	4 (0.2)	1996 (74)	543 (22)	91 (4)
Single	233 (95)	10 (4)	1 (0.6)	174 (70)	55 (24)	13 (6)
Separated/divorced/ widowed	721 (93)	42 (6)	2 (0.3)	532 (68)	187 (25)	41 (7)
Education						
Primary/none / don't know	534 (93)	36 (6)	5 (0.9)	365 (64)	155 (27)	51 (9)
Secondary	1521 (95)	79 (5)	1 (0.1)	1174 (72)	355 (23)	64 (5)
Tertiary	1425 (96)	46 (4)	1 (0.1)	1163 (79)	275 (19)	30 (2)
Deprivation score						
0 - 0.11 (least deprived)	950 (95)	35 (4)	3 (0.5)	759 (75)	197 (21)	30 (4)
0.12 – 0.17	729 (95)	33 (5)	0 (0)	563 (72)	166 (23)	29 (5)
0.18 – 0.23	693 (94)	38 (5)	2 (0.4)	532 (70)	162 (23)	36 (7)
0.24 – 0.33	633 (97)	22 (3)	0 (0)	486 (72)	143 (24)	24 (4)
> 0.33 (most deprived)	475 (92)	33 (7)	2 (0.5)	362 (71)	117 (23)	26 (6)
Region						
Belfast	598 (94)	34 (6)	1 (0.1)	461 (71)	145 (24)	26 (5)
Other city or town	1953 (95)	88 (5)	3 (0.2)	1521 (73)	432 (22)	71 (5)
Rural area	921 (95)	39 (4)	3 (0.5)	714 (71)	206 (23)	38 (6)
Location of health assessment						
Clinical facility	3306 (95)	144 (5)	5 (0.2)	131 (65)	41 (24)	19 (11)
Home	174 (89)	17 (10)	2 (1.2)	2571 (73)	744 (23)	126 (4)

Values are n unweighted, % weighted. Total n = 3655, missing = 7 for following conversation with one person, missing = 23 for four persons

Table 3.17: Cross tabulation of hearing loss and feelings of depression

		I felt depressed. Would you say this statement describes the way you felt during the past week?			
		Rarely or none of the time (less than 1 day)	Some or a little of the time (1 - 2 days)	Occasionally or a moderate amount of time (3 - 4 days)	All of the time
		n (weighted %)	n (weighted %)	n (weighted %)	n (weighted %)
Is your hearing (with/without a hearing aid)....	Excellent	351 (13)	67 (14)	19 (11)	6 (5)
	Very good	779 (28)	130 (23)	51 (22)	23 (23)
	Good	925 (35)	176 (34)	74 (38)	38 (40)
	Fair	502 (20)	118 (24)	45 (22)	28 (25)
	Poor	96 (4)	25 (5)	10 (7)	6 (7)

Values are n unweighted, % weighted. Total n = 3655, missing n=186

Table 3.18: Cross tabulation of hearing loss and feelings of loneliness

		I felt lonely. Would you say this statement describes the way you felt during the past week?			
		Rarely or none of the time (less than 1 day)	Some or a little of the time (1 - 2 days)	Occasionally or a moderate amount of time (3 - 4 days)	All of the time
		n (weighted %)	n (weighted %)	n (weighted %)	n (weighted %)
Is your hearing (with/without a hearing aid)....	Excellent	374 (13)	40 (10)	16 (9)	11 (12)
	Very good	815 (28)	95 (22)	48 (28)	24 (18)
	Good	973 (35)	148 (39)	54 (36)	37 (36)
	Fair	535 (20)	99 (25)	29 (20)	27 (24)
	Poor	102 (4)	15 (4)	9 (7)	10 (10)

Values are n unweighted, % weighted. Total n = 3655, missing n=194

3.5 Conclusion

Prevalence of eye disease increases substantially with age. Relatively high levels of undiagnosed sight-threatening eye disease were evident when the information from retinal examination was compared with participant self-report. This highlights the importance of regular eye tests according to recommended time intervals for this age group. Hearing loss is highly prevalent among older adults in Northern Ireland, particularly in men. Older men in particular experienced difficulty following a conversation due to hearing loss, and were greatly limited in their ability to follow conversations with several people. Poorer self-rated hearing also had a negative impact on everyday life. Although hearing aids are known to improve several aspects of life that have been compromised by hearing loss, the findings of NICOLA indicate that the use of hearing aids remains low in the general population of older adults. More research is needed to explore the reasons for this low uptake. The findings highlight the importance of early detection of hearing problems for older people. Screening for hearing loss at an earlier stage, and promoting the use of hearing aids, has the potential to improve everyday quality of life and social participation for many older adults and thus promote healthy ageing.

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4 Neuropsychological and Cognitive Health

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Key Findings

- The majority of older adults performed well on cognitive tests.
- Increasing age was associated with poorer cognitive performance.
- Cognitive performance depended on level of education, marital status and level of deprivation. Those with third level education, married and from less deprived areas tended to perform better in cognitive tests compared to the comparison groups.
- Overall mental wellbeing was high in older adults although this varied according to age group, marital status, education, level of deprivation and region.
- 18% of older adults showed signs of depression, with females reporting higher rates of depressive symptoms compared to males.

4.1 Introduction

Cognitive functioning refers to mental abilities, such as the ability to think, plan and recall information. A decline in cognitive function is common with ageing due to changes and atrophy in brain regions that occur across the life-span (1). An indicative example of a cognitive skill that is adversely affected with ageing is working memory: this concerns the temporal storage and elaboration of information in the mind (2). Decline in cognitive function has a profound impact on the health and quality of life of older people and their caregivers. Changes in cognitive ability can impact on a persons' ability to perform everyday tasks and retain their autonomy and independence. Mild cognitive impairment (MCI) is a clinical entity that may predict progression to dementia and is thought of as a transitional stage between normal ageing and dementia. MCI is characterised by minor impairment in cognitive skills, such as memory and thinking but the ability to look after oneself is maintained, while dementia is associated with greater impairment in cognitive skills and function.

In Northern Ireland, approximately 20,000 people were estimated to have dementia in 2015 with only 65% having a formal dementia diagnosis (3). The increasing prevalence of cognitive decline and dementia, and the increasing economic and social burden of caring for those with dementia is a major concern. In 2013 - 2014, the cost for acute care of people with dementia in Northern Ireland exceeded £900,000 (3). Therefore, it is essential to explore demographic characteristics that may be associated with increased likelihood of developing dementia in later life. For example, increasing age and lower levels of education have been found to be associated with greater cognitive decline (4).

4.2 Cognitive Function

In NICOLA, cognitive function was determined using a cognitive battery comprising four standardized measures that assessed memory, planning, attention and reasoning. Cognitive tests took no longer than 30 minutes to complete. Older adults with dementia and severe cognitive impairment were excluded from the NICOLA cohort, therefore, the results presented relate to those who had normal cognitive capacity or those who had MCI. Results are based on 3591 participants who completed the MMSE, 3543 who completed the MoCA, 3546 who completed animal recall and 3354 who completed the Colour Trails 2 assessment. Findings are presented according to age, gender, marital status, level of education, level of deprivation and region.

Mini Mental State Examination (MMSE)

The MMSE (5) was used to assess global cognition. It consists of 30 brief questions that are designed to measure a range of cognitive domains including attention and concentration, memory, language, visuo-constructional skills, calculations and orientation. The MMSE took approximately 5 - 10 minutes to administer. A score (out of 30) based on performance across the 11 components of the test (orientation to time, orientation to place, registration, attention and calculation, recall, naming, repetition, comprehension, reading, writing and drawing) was calculated for each participant. The scores ranged between 0 and 30, with the lowest scores indicating more severe cognitive impairment and scores of 25 or over indicating no cognitive impairment.

Table 4.1 presents the MMSE scores by age, gender, marital status, level of education, area deprivation and region. The mean MMSE score was 28.4 (95% CI 28.38, 28.50). Although the majority of participants showed normal cognition (MMSE score 25 - 30), demographic and lifestyle differences were evident between participants who had mild or moderate cognitive impairment (MMSE score 15 - 24) compared to those who displayed normal levels of cognition. Similar to the findings from the Irish Longitudinal Study on Ageing (TILDA) (6), increasing age was associated with greater cognitive decline. People in the oldest age group (75+ years) were more likely to perform worse on this test compared to the other age groups. As with TILDA, gender did not appear to affect performance in this test. Education level was associated with cognitive impairment with a greater proportion of older adults with no education or only primary education performing worse on this test compared to those with secondary or tertiary education. These findings are in line with the results from TILDA, in which those with lower levels of education were more likely to have cognitive impairment. Married people were less likely to have cognitive impairment compared to single or divorced, separated or widowed people. Level of deprivation also impacted on cognitive ability, with a greater proportion of those from more deprived areas showing mild or moderate impairment compared to those from less deprived areas.

Table 4.1: Overall cognitive performance in NICOLA based on the MMSE test

	Normal cognitive performance (MMSE score 25 - 30)	Mild or moderate impairment (MMSE score 15 - 24)
	n (weighted %)	n (weighted %)
Overall	3449 (94.4)	142 (5.6)
Gender		
Males	1650 (93.9)	77 (6.1)
Females	1799 (94.9)	65 (5.1)
Age group (yrs)		
50 - 64	1913 (97.6)	34 (2.4)
65 - 74	1107 (92.6)	61 (7.4)
75 +	429 (87.2)	47 (12.8)
Marital status		
Married/living with partner	2515 (95.9)	82 (4.1)
Single	230 (92.8)	10 (7.2)
Separated/divorced/widowed	704 (91.1)	50 (8.9)
Education		
Primary/none/don't know	478 (85.5)	76 (14.5)
Secondary	1521 (96.2)	52 (3.8)
Tertiary	1450 (98.9)	14 (1.1)
Deprivation score		
0 – 0.11 (least deprived)	951 (96.5)	24 (3.5)
0.12 - 0.17	728 (95.9)	25 (4.1)
0.18 - 0.23	689 (94.0)	31 (6.0)
0.24 - 0.33	617 (92.8)	33 (7.2)
> 0.33 (most deprived)	464 (92.4)	29 (7.6)
Region		
Belfast	600 (93.9)	27 (6.1)
Other city or town	1934 (94.8)	75 (5.2)
Rural area	907 (93.8)	40 (6.2)

Values are n unweighted, % weighted. Missing = 64

Montreal Cognitive Assessment (MoCA)

The MoCA (7) is another useful instrument to assess overall cognitive performance. It assesses various cognitive domains including memory, visuospatial functioning and language. It is more sensitive than the MMSE to mild cognitive impairment (8). The MOCA assessment takes approximately 5-10 minutes to complete. A score (out of 30 points) based on performance was calculated for each participant with lower scores indicating greater cognitive impairment and scores of 26 or over indicating normal cognitive functioning.

Table 4.2 illustrates the MoCA results from NICOLA based on age, gender, marital status, educational level, deprivation and location. The mean MoCA score was 25.33 (95% CI 25.2, 25.4). Similar to results from the MMSE, the oldest age group (75+ years) was more likely to have cognitive impairment compared to the younger age groups. 54% of males and 46% of females scored below 26 in the MoCA. Those who were married were less likely to have cognitive impairment compared to those who were single or who were separated, divorced or widowed. Those with a higher level of education were also less likely to have cognitive impairment. Just over a quarter (28%) of older adults with tertiary education scored below 26 (i.e mild or moderate impairment) in the MoCA, compared to 78% with primary or no education (78%) and 50% with secondary education. Cognitive impairment was also associated with higher levels of deprivation.

Table 4.2: Overall cognitive performance in NICOLA based on the MoCA test

	Normal cognitive performance MoCA score 26 - 30	Mild or moderate impairment MoCA score 9 - 25
	n (weighted %)	n (weighted %)
Overall	1963 (50.1)	1580 (49.9)
Gender		
Males	862 (45.7)	844 (54.3)
Females	1101 (54.2)	736 (45.8)
Age group (yrs)		
50 - 64	1263 (62.4)	664 (37.6)
65 - 74	566 (43.1)	585 (56.9)
75 +	134 (23.0)	331 (77.0)
Marital status		
Married/living with partner	1464 (52.9)	1109 (47.1)
Single	135 (49.3)	101 (50.7)
Separated/divorced/widowed	364 (43.1)	370 (56.9)
Education		
Primary / none / don't know	125 (21.9)	412 (78.1)
Secondary	789 (49.9)	766 (50.1)
Tertiary	1049 (72.3)	402 (27.7)
Deprivation score		
0 – 0.11 (least deprived)	603 (59.2)	363 (40.8)
0.12 - 0.17	439 (54.9)	303 (45.1)
0.18 - 0.23	379 (48.0)	337 (52.0)
0.24 - 0.33	314 (44.5)	322 (55.5)
> 0.33 (most deprived)	228 (42.1)	255 (57.9)
Region		
Belfast	361 (52.0)	256 (48.0)
Other city or town	1109 (50.7)	874 (49.3)
Rural area	488 (47.6)	447 (52.4)

Values are n unweighted, % weighted. Missing = 112

Verbal fluency – Animal recall

Animal recall is commonly used as a measure of executive function and of verbal semantic fluency. This test required the participant to name as many animals as possible within one minute (4). One point was allocated for each animal named by the participant with the total number reflecting verbal fluency score. Typically, individuals with mild cognitive impairment or dementia have been found to recall less than 17 animals in this test (9). The majority of participants showed normal cognitive performance in this test with similar performance in both males and females. The mean number of animals recalled was 19 (Table 4.3). The 50 - 64 year old age group performed better and recalled more animals compared to those aged 65 - 74 years, however the oldest age group showed better performance in this test compared to the 65 – 74 year old age group. Those who were married also performed better compared to those who were single, or those who were divorced, separated or widowed. A higher level of education was associated with higher animal recall: those with tertiary education recalled more animals compared to those with primary or secondary education. Similarly, the results from TILDA showed that higher levels of education were associated with more animal recalls. Finally, similar to the findings from the MMSE and the MoCA, a higher level of deprivation was associated with increased cognitive impairment (animal recall score of 3 - 16).

Table 4.3: Performance of NICOLA participants in the animal recall test

	Normal cognitive performance (17 - 41 recalls)	Mild or moderate impairment (3 - 16 recalls)
	n (weighted %)	n (weighted %)
Overall	2323 (61.1)	1223 (38.9)
Gender		
Males	1134 (62.2)	575 (37.8)
Females	1189 (60.1)	648 (39.9)
Age group (yrs)		
50 - 64	1453 (73.4)	475 (26.6)
65 - 74	689 (54.1)	468 (45.9)
75 +	181 (66.5)	280 (33.5)
Marital status		
Married/living with partner	1735 (64.5)	833 (35.5)
Single	147 (58.4)	90 (41.6)
Separated/divorced/widowed	441 (53.3)	300 (46.7)
Education		
Primary/none/don't know	214 (38.3)	332 (61.7)
Secondary	966 (61.3)	587 (38.7)
Tertiary	1143 (79.0)	304 (21.0)
Deprivation score		
0 – 0.11 (least deprived)	712 (71.7)	248 (28.3)
0.12 - 0.17	494 (63.1)	247 (36.9)
0.18 - 0.23	443 (57.8)	269 (42.2)
0.24 - 0.33	385 (55.4)	259 (44.6)
> 0.33 (most deprived)	289 (55.8)	200 (44.2)
Region		
Belfast	434 (65.7)	185 (34.3)
Other city or town	1307 (61.9)	676 (38.1)
Rural area	579 (56.7)	357 (43.3)

Values are n unweighted, % weighted. Missing = 109

Colour Trails 2

The Colour Trails 2 test was used to measure executive function and visual scanning. Participants were instructed to draw a line as fast as possible between consecutively numbered circles, alternating between pink and yellow colours (9). For example, the participant would draw a line from the pink 1 to the yellow 2 (avoiding the pink 2) and then to the pink 3 (avoiding the yellow 3) and so on. "Near-misses" referred to a near-miss response defined as the initiation of a line toward an incorrect circle, but without intervention from the research nurse. Up to 10 seconds were allowed for the participant to make a connection between one circle and the next. After 10 seconds had lapsed since the correct response, the research nurse would prompt the participant towards the location of the next correct circle by pointing to it. The length of time taken to complete the test trial was recorded and included the number of near misses, prompts, colour sequence errors and number sequence errors made by the participant.

As presented in Table 4.4, the average time taken to complete the colour trails test was 118 seconds (124 and 113 seconds in males and females, respectively). Furthermore, a higher proportion of females required no prompts and had fewer near misses in comparison to males. Given that the colour trails test has been shown to be a predictor of executive function, these results suggest that females have a higher level of executive function compared to males. Results also varied with age, with those in the 75+ age group taking longer to complete the test than the 50 - 64 year olds and 65 – 74 year olds. The oldest age group also required more prompts and had more errors and misses compared to the younger age groups. Those who were married also tended to perform better compared to those who were single or separated/divorced/widowed. A greater proportion of those with higher levels of education performed better compared to those with primary or secondary education. As with the previous tests, those who were least deprived performed better on the colour trails test compared to those who were most deprived.

Table 4.4: Average time taken to complete the colour trails 2 test and frequency of prompts, near misses, colour errors or number errors

	Average time taken (secs)	Prompts		Near misses		Colour errors		Number errors	
		0	1 or more	0	1 or more	0	1 or more	0	1 or more
Overall	118	1630 (45.9)	1723 (54.1)	2656 (78.7)	697 (21.3)	2280 (66.4)	1073 (33.6)	3092 (91.7)	261 (8.3)
Gender									
Males	124	743 (43.3)	861 (56.7)	1262 (77.9)	342 (22.1)	1079 (65.9)	525 (34.1)	1474 (91.2)	130 (8.8)
Females	113	887 (48.1)	862 (51.9)	1394 (79.3)	355 (20.7)	1201 (66.9)	548 (33.1)	1618 (92.1)	131 (7.9)
Age group (yrs)									
50 - 64	104	1081 (56.2)	787 (43.8)	1532 (82.2)	336 (17.8)	1328 (70.5)	540 (29.5)	1755 (93.8)	113 (6.2)
65 - 74	130	460 (38.8)	628 (61.2)	841 (75.6)	247 (24.4)	708 (62.4)	380 (37.6)	975 (88.5)	113 (11.5)
75 +	158	89 (20.8)	308 (79.2)	283 (71.5)	114 (28.5)	244 (59.1)	153 (40.9)	362 (90.5)	35 (9.5)
Marital status									
Married/ living with partner	115	1241 (48.3)	1214 (51.7)	1957 (78.7)	498 (21.3)	1708 (68.3)	747 (31.7)	2279 (92.6)	176 (7.4)
Single	123	99 (44.4)	119 (55.6)	172 (79.4)	46 (20.6)	146 (66.4)	72 (33.6)	202 (92.7)	16 (7.3)
Separated/ divorced/ widowed	128	290 (39.5)	390 (60.5)	527 (78.4)	153 (21.6)	426 (61.5)	254 (38.5)	611 (88.9)	69 (11.1)
Education									
Primary/ none/don't know	148	140 (29.7)	329 (70.3)	347 (74.8)	122 (25.2)	270 (57.4)	199 (42.6)	416 (89.0)	53 (11.0)
Secondary	119	691 (45.4)	788 (54.6)	1167 (78.8)	312 (21.2)	988 (66.6)	491 (33.4)	1364 (91.8)	115 (8.2)
Tertiary	108	799 (57.6)	606 (42.4)	1142 (81.1)	263 (18.9)	1022 (72.4)	383 (27.6)	1312 (93.4)	93 (6.6)
Region									
Belfast	118	276 (43.4)	303 (56.6)	458 (78.1)	121 (21.9)	385 (65.4)	194 (34.6)	540 (92.4)	39 (7.6)
Other city or town	117	926 (47.2)	949 (52.8)	1490 (79.2)	385 (20.8)	1298 (67.5)	577 (32.5)	1723 (91.6)	152 (8.4)
Rural area	121	424 (44.6)	468 (55.4)	703 (78.0)	189 (22.0)	591 (65.0)	301 (35.0)	823 (91.6)	69 (8.4)
Deprivation score									
0 – 0.11 (least deprived)	113	480 (50.1)	448 (49.9)	759 (81.2)	169 (18.8)	667 (70.6)	261 (29.4)	865 (92.6)	63 (7.4)
0.12 – 0.17	115	355 (48.3)	350 (51.7)	567 (80.7)	138 (19.3)	476 (67.2)	229 (32.8)	658 (93.2)	47 (6.8)
0.18 – 0.23	120	331 (45.9)	344 (54.1)	511 (74.4)	164 (25.6)	470 (68.2)	205 (31.8)	626 (92.5)	49 (7.5)
0.24 – 0.33	123	281 (43.9)	325 (56.1)	486 (80.6)	120 (19.4)	398 (65.0)	208 (35.0)	550 (90.8)	56 (9.2)
> 0.33 (most deprived)	125	183 (39.7)	256 (60.3)	333 (76.0)	106 (24.0)	269 (59.6)	170 (40.4)	393 (89.0)	46 (11.0)

Values are n unweighted, % weighted. Missing n = 301.

4.3 Depression and Mental Wellbeing

Depression is a common but serious mental illness typically characterized by sad, hopeless, or anxious feelings. Later life depression increases the likelihood of morbidity, suicide and self-neglect while also resulting in a decrease in physical, cognitive and social functioning. These factors may contribute to increased risk of mortality (9), as well as loss of independence and diminished quality of life. In older age, depressive syndromes often affect people with chronic medical illnesses, cognitive impairment or disability (10). However, while depression in later life is a recognised condition, diagnosing depression in older adults can be difficult as symptoms can often be masked by their physical conditions or mistaken for symptoms of another illness. Based on the profound impact on health and quality of life, it is therefore important to examine the prevalence of depression within our current ageing population.

Centre for Epidemiological Studies Depression Scale (CES-D)

In NICOLA, depression was measured using the 20-item Centre for Epidemiological Studies-Depression (CES-D) scale (11). The CES-D was originally developed in 1977 and is a commonly used self-report measure to assess degrees of depressive symptoms and detect at-risk individuals for depression in the general population (12). The CES-D consists of 20 items phrased as statements, each one assessing symptoms associated with depression. For each statement, respondents were asked to rate on a scale of 0 to 3 how often they had experienced that symptom over the previous 7 day period ranging from 0 (“rarely or none of the time”) to 3 (“most or all of the time”). Four of the items are positive statements which are inversely scored. Responses to each item were then summed to generate a total score ranging from 0 to 60 with a higher score indicating a higher degree of depressive symptoms. In general, a score of ≥16 is indicative of a person having moderate or potentially clinically relevant depressive symptoms while a score of 8-15 indicates mild or sub-threshold depressive symptoms (11). The CES-D scale has been shown to be reliable at measuring the number, types and duration of depressive symptoms.

The level of depressive symptoms as assessed by the CES-D scale in NICOLA is presented in Table 4.5. The mean CES-D score in the NICOLA cohort was 7.83. Approximately 18% of older adults showed signs of having depression (i.e. CES-D score ≥ 16). There were clear sex and age differences in the rates of people suffering from depression as assessed by the CES-D. In all age groups, women were more likely than men to suffer from depressive symptoms. As presented in Figure 4.1, higher CES-D scores were evident in females across each of the age groups, compared to males. Overall, 20.6% of females had high CES-D scores (score ≥ 16) compared to 15.5% of males. This finding is consistent with those reported by the English Longitudinal Study of Ageing (ELSA) where females (28%) were more likely to report depressive symptoms than males (20%) (13) and with those reported in TILDA where 13% of females scored 16 or above in comparison to 7% of men (14). However, unlike TILDA and ELSA (13,14), mean CES-D score in NICOLA was higher

in the 50 - 64 year old age group compared to the other age groups; 21.6% of 50 - 64 year olds had a CES-D score of ≥16 compared to 14% and 14.2% in the 65 - 74 and 75+ age group, respectively.

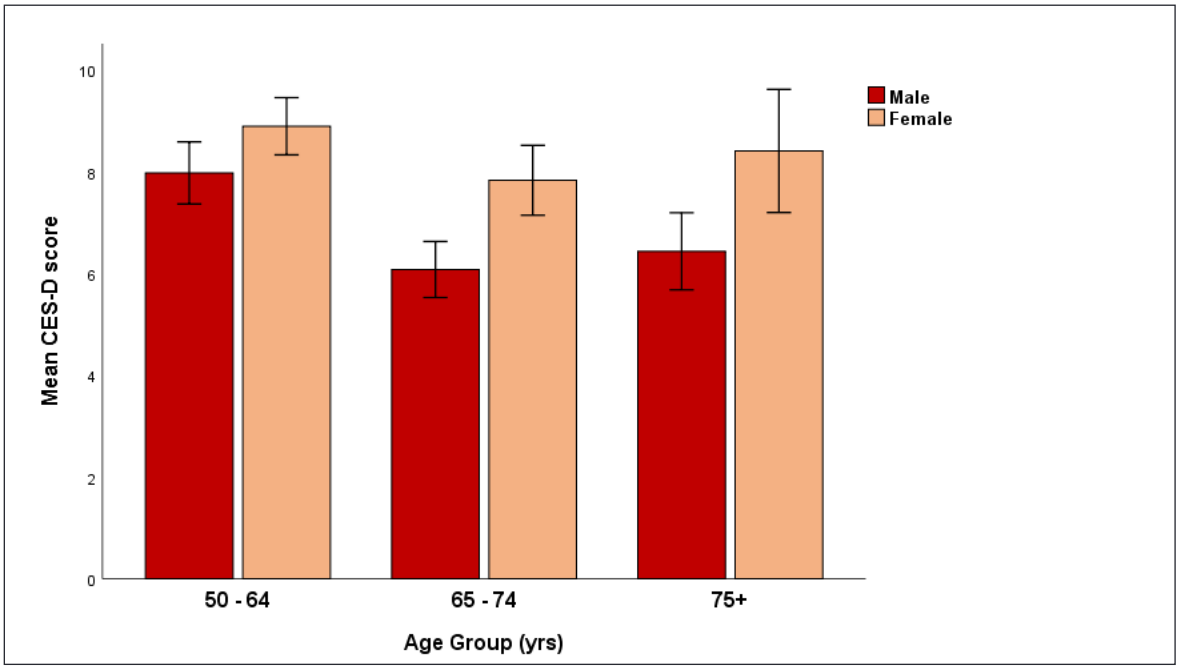
Marital status also affected levels of depression, with a higher proportion of single or divorced / separated / widowed people having high CES-D scores (26.3% and 28.2%, respectively) compared to those who were married (13.4%). There were also clear educational and deprivation differences in the rates of older adults showing symptoms of depression. A greater proportion of those from more deprived areas (29.2%) showed signs of depression compared to less deprived areas (12.9%). Those with lower levels of education also tended to show higher levels of depressive symptoms. Region also impacted somewhat on mood with those living in Belfast showing a higher level of depressive symptoms compared to other areas of Northern Ireland.

Table 4.5: CES-D scores in NICOLA participants

	CES-D score		CES-D score category		
			0 - 7	8 - 15	≥ 16
	Mean	95% CI	n (weighted %)	n (weighted %)	n (weighted %)
Overall	7.83	7.55, 8.12	2202 (59.9)	761 (22.0)	510 (18.1)
Gender					
Males	7.10	6.72, 7.48	1139 (64.3)	341 (20.2)	207 (15.5)
Females	8.53	8.11, 8.94	1063 (55.7)	420 (23.8)	303 (20.6)
Age group (yrs)					
50 - 64	8.49	8.07, 8.90	1164 (57.3)	402 (21.0)	330 (21.6)
65 - 74	6.92	6.48, 7.36	747 (63.0)	251 (23.0)	125 (14.0)
75 +	7.35	6.66, 8.04	291 (62.2)	108 (23.6)	55 (14.2)
Marital status					
Married/living with partner	7.01	6.71, 7.32	1707 (65.1)	537 (21.5)	286 (13.4)
Single	8.91	7.72, 10.11	130 (51.5)	50 (22.3)	50 (26.3)
Separated/divorced/ widowed	10.39	9.65, 11.14	365 (48.3)	174 (23.4)	174 (28.2)
Education					
Primary/none/ don't know	8.40	7.62, 9.19	323 (57.7)	117 (22.0)	87 (20.3)
Secondary	8.42	7.96, 8.88	936 (57.7)	327 (21.4)	259 (20.9)
Tertiary	6.99	6.61, 7.37	943 (64.6)	317 (23.0)	164 (12.5)
Region					
Belfast	9.52	8.73, 10.32	335 (50.6)	148 (25.0)	116 (24.5)
Other city or town	7.59	7.23, 7.96	1256 (61.0)	409 (21.4)	278 (17.6)
Rural area	7.25	6.74, 7.75	606 (63.3)	203 (21.5)	115 (15.2)
Deprivation score					
0 – 0.11 (least deprived)	6.74	6.26, 7.22	654 (67.4)	182 (19.7)	107 (12.9)
0.12 - 0.17	7.31	6.26, 7.22	475 (62.8)	159 (22.3)	90 (14.9)
0.18 - 0.23	7.99	7.36, 8.63	433 (58.2)	169 (23.9)	104 (17.9)
0.24 - 0.33	7.87	7.20, 8.53	382 (59.3)	151 (23.7)	92 (17.0)
> 0.33 (most deprived)	10.52	9.57, 11.47	258 (50.0)	100 (20.8)	117 (29.2)
Location of health assessment					
Clinical facility	7.66	7.37, 7.94	79 (43.5)	42 (23.6)	47 (32.8)
Home	11.25	9.69, 12.81	2123 (61.1)	719 (21.9)	463 (17.0)

Values are mean (95% CI), n unweighted, % weighted. Total n = 3473, missing = 182

Figure 4.1: Mean CES-D score (95% confidence interval) by age group and sex



The Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS)

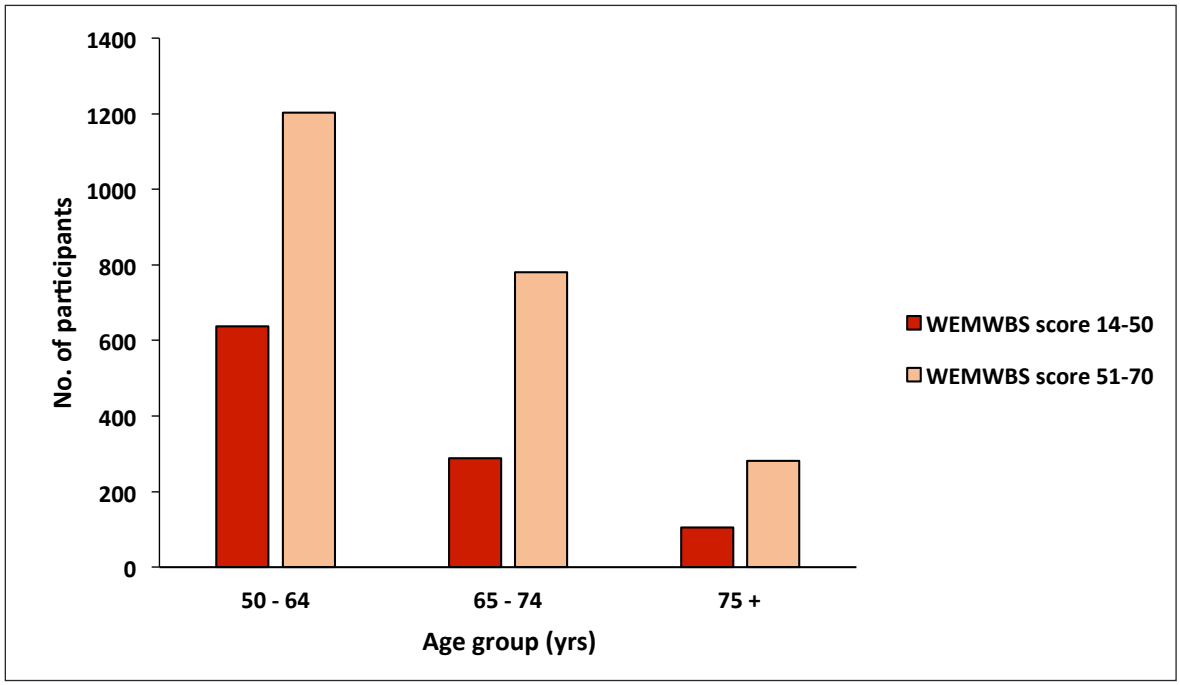
The Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS) is a scale of 14 positively worded items such as "I've been feeling interested in other people" and "I've been feeling good about myself" and is used to assess the mental health of the general population. For each statement, participants were asked to rate on a Likert scale of 1 to 5 how often they had felt like that, with one being "none of the time" and five being "all of the time". Scores on the WEMWBS ranged from 14 to 70, with higher scores indicating higher levels of wellbeing. The WEMWBS has been validated for use in the UK in those aged 16 years and above (15) and specifically for the general population in Northern Ireland (16).

The majority of older adults showed high levels of mental wellbeing with a mean score of 54 in both males and females. This score was slightly higher than that reported for males (WEMWBS score = 50.1) and females (WEMWBS score = 49.6) in the Health Survey for England 2016 (17) and higher than the overall average reported in the Scottish Health Survey 2018 (WEMWBS score = 49.4) (18). Table 4.6 provides an overview of participants in different WEMWBS categories, categorised by their demographic characteristics. Due to the relatively low number of participants who scored between 14 and 30 in the WEMWBS, scores were categorised into those who scored between 14 - 50 and 51 - 70. When split by age, the oldest age group showed higher levels of mental wellbeing than the younger age groups. A higher proportion of married individuals showed higher levels of wellbeing compared to those who were single or those who were divorced, separated or widowed. Levels of wellbeing also appeared to be higher in those with higher levels of education and in those from less deprived areas. Levels of wellbeing were also higher in those living outside the Belfast area.

Table 4.6: WEMWBS scores in NICOLA participants.

	WEMWBS Score 14 - 50	WEMWBS Score 51 - 70
	n (weighted %)	n (weighted %)
Overall	1032 (35.0)	2265 (65.0)
Gender		
Males	480 (33.8)	1125 (66.2)
Females	552 (36.1)	1140 (63.9)
Age group (yrs)		
50 - 64	638 (39.1)	1203 (60.9)
65 - 74	289 (30.5)	781 (69.5)
75 +	105 (28.5)	281 (71.5)
Marital status		
Married/living with partner	681 (31.0)	1746 (69.0)
Single	83 (44.0)	131 (56.0)
Separated/divorced/widowed	268 (43.3)	388 (56.7)
Education level		
Primary / none / don't know	164 (38.0)	307 (62.0)
Secondary	496 (37.8)	955 (62.2)
Tertiary	372 (28.9)	1003 (71.1)
Region		
Belfast	207 (41.9)	348 (58.1)
Other city or town	545 (33.0)	1313 (67.0)
Rural area	277 (34.7)	601 (65.3)
Deprivation score		
0 – 0.11 (least deprived)	244 (28.6)	656 (71.4)
0.12 - 0.17	203 (32.8)	496 (67.2)
0.18 - 0.23	221 (37.3)	444 (62.7)
0.24 - 0.33	177 (32.0)	412 (68.0)
> 0.33 (most deprived)	187 (45.7)	257 (54.3)

Figure 4.2: Frequency of older adults who scored 14-50 and 51-70 on the Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS), according to age group.



With higher than average WEMWBS scores than both those reported in England and Scotland, the data captured in NICOLA suggest that among those aged over 50 years in Northern Ireland and if we extrapolate, among the general population in Northern Ireland, report a good level of mental health and wellbeing. However, in times of economic difficulties and in any public health crisis like that experienced in 2020/21, it will be essential to follow up participants across the different waves of NICOLA to continually assess mental wellbeing.

4.6 Conclusions

This chapter explored cognitive function and mental wellbeing of older adults in Northern Ireland. Levels of cognitive functioning and mental wellbeing were generally high in this cohort of older adults although this depended on age group, marital status, education, deprivation level and region. The findings provide clear evidence that cognitive impairment may disproportionately affect specific groups of older adults, for example those who are from more socially deprived areas and those with poor levels of education. With increasing rates of depression and dementia, the current results highlight the importance of continually monitoring and reviewing the mental wellbeing and cognitive health of older adults, taking into consideration demographic and social circumstances. Recognising the risk factors associated with cognitive decline are immensely important. Ongoing analysis of the cognitive and mental health data collected in NICOLA will enable us to fully explore these associations. Future waves of cognitive data will also allow us to investigate changes in cognitive health over time.

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5 Dietary intake patterns

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Citation

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Key Findings

- Dietary patterns of older adults in Northern Ireland fell into three distinct groups: a healthy pattern, an unhealthy pattern and a diet characterised by a high consumption of alcohol and coffee.
- While many older adults adhere to government recommendations, findings highlight a need for older adults to increase their consumption of low fat dairy foods and reduce overall intakes of high fat, high sugary foods.
- Consumption of energy dense foods was high. Many older adults still opt for refined foods rather than wholegrain versions of foods such as bread, rice and pasta.
- Many older adults consumed adequate amounts of fruit and vegetables. Patterns of fruit and vegetable consumption did not vary across the age group categories. Women consumed more fruit and vegetables per day than men.

Key Findings continued

- Greater fruit and vegetable consumption was evident in those with higher levels of education and socio-economic status.
- Consumption of oily fish was low. Older adults need to be encouraged to eat more fish, especially oily fish. Only 27% of older adults met the recommended intake of 1 portion of oily fish per week.
- Mean consumption of red and processed meat was 1 portion per day (equivalent to 70 g per day), thus meeting the government recommendations.
- 35% of men and 45% of women aged over 50 years reported taking at least one dietary supplement, either regularly or sometimes.

5.1 Introduction: Nutrition and ageing

Nutrition is a critical determinant of health and plays a key role in healthy ageing and chronic disease prevention. Eating a healthy, balanced diet is important as a person gets older because it protects against illness, helps to speed recovery from illness, and importantly, maximises the chances of living longer and independently in good health (1,2). While total energy requirements decrease with advancing age, the dietary requirements for protein, vitamins and minerals remain largely unchanged and for some micronutrients such as calcium and vitamin D, requirements can be higher in later life (2). Therefore, a nutrient dense (rather than calorie dense) diet is critically important for older adults in order to help prevent malnutrition and reduce the risk of chronic disease and frailty.

The ageing process, however, results in many physiological, social and psychological changes that can affect nutritional intake and status, thus increasing the risk of malnutrition. Sensory impairment (e.g. impaired vision and taste), poor oral health, loss of mobility, cognitive decline and psychosocial changes can severely impact dietary intake and diet quality (3,4), while changes in digestion and gastrointestinal function can impair nutrient absorption and reduce gastrointestinal motility. Older adults tend to report a decrease in appetite, food intake and food choice which has wider implications for health and well-being (4, 5) and may increase the risk of coronary heart disease and diabetes in older adults.

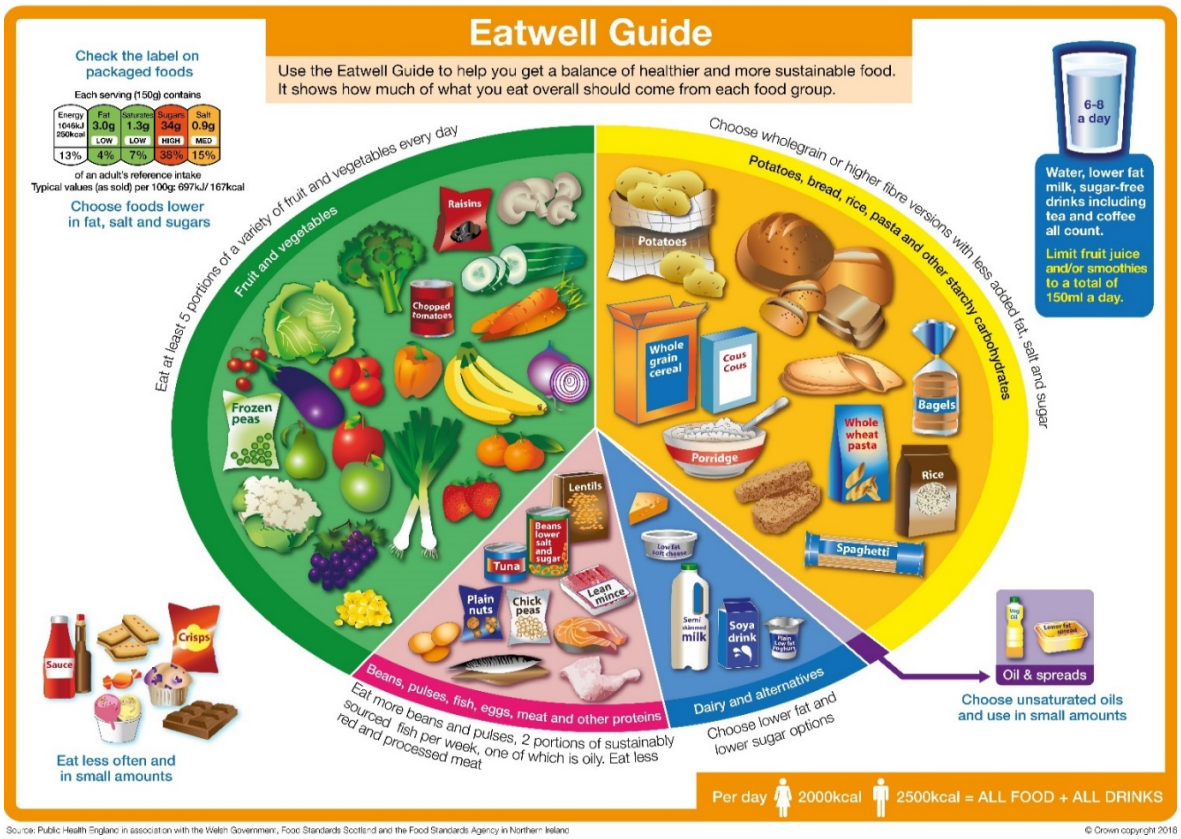
Healthy eating guidelines for older adults in Northern Ireland are based on The Eatwell Guide (https://www.nhs.uk/live-well/eat-well/the-eatwell-guide/), a

health education tool designed to provide a visual representation of the types and proportions of foods that should be consumed from each of the five food groups in order to achieve a healthy, balanced diet (Figure 5.1) (6).

Based on the Eatwell Guide, the key messages for older adults are to:

- Eat at least 5 portions of a variety of fruit and vegetables every day;
- Base meals on potatoes, bread, rice, pasta or other starchy carbohydrates; choosing wholegrain versions where possible;
- Have some dairy or dairy alternatives (such as soya drinks); choosing lower fat and lower sugar options;
- Eat some beans, pulses, fish, eggs, meat and other proteins (including 2 portions of fish every week, one of which should be oily);
- Choose unsaturated oils and spreads and eat in small amounts;
- Drink 6 - 8 cups/glasses of fluid a day;
- If consuming foods and drinks high in fat, salt or sugar have these less often and in small amounts.

Figure 5.1: The Eatwell Guide (Food Standards Agency) (6)



Despite the long-established recommendations and public health messages, the Northern Ireland population as a whole is still failing to achieve a healthy balanced diet. The most recent evidence relating to the dietary intake of older adults in Northern Ireland comes from the National Diet and Nutrition Survey (combined results of Years 5 to 9; 2012/13-2016/17) which is a national cross-sectional survey designed to assess the dietary habits, nutrient intake and nutritional status of a representative sample of the general population living in private households in the UK. Unlike the NICOLA study, dietary intakes were assessed using self-completed four day food diaries. The key findings of the report (6) showed that:

- Consumption of '5-A-Day' fruit and vegetable portions was below the recommendation in all age/sex groups. Adults aged 65 years and over consumed on average 3.3 portions per day with approximately 80% not meeting the 5-A-Day recommendation.
- Average consumption of oily fish was equivalent to 30 - 60 g per week in adults, well below the recommended 1 portion (140 g) per week.
- Mean intakes of non-starch polysaccharide were found to be significantly lower than the dietary reference values (DRV).
- Similarly, vitamin D intake in older adults was reported to be below recommended dietary guidelines.
- In contrast, mean intakes of total fat and saturated fat were reported to be above recommended government guidelines.

The Eatwell Guide does not include reference to the frequency of serving or recommended portion sizes for foods with the exception of the following:

Fruit and vegetables: at least 5 portions of a variety of fruit and vegetables per day.

Red[a] and processed meat: limit to 70 g per day if you usually consume more than 90 g every day.

Fish: eat 2 portions per week, at least 1 portion per week should be oily fish[b] (140 g).

This chapter describes the habitual dietary intake of NICOLA participants and compares it with recommended intakes based on the Eatwell Guide. It also examines dietary habits and factors which can affect food intake such as food

[a] Red meat includes beef, lamb, pork, sausages, burgers and kebabs, offal, processed red meat and other red meat.

[b] Oily fish includes anchovies, carp, trout, mackerel, herring, jack fish, pilchards, salmon (incl canned), sardines, sprats, swordfish, tuna (fresh only) and whitebait.

preparation, food eaten outside the home, shopping and the prevalence of special diets. All proportions presented have been weighted to ensure that results are representative of the Northern Ireland population of adults aged 50 years and over.

5.2 Methodology

NICOLA is unique in that it is one of the few longitudinal studies of ageing which includes a detailed dietary assessment (7,8). Dietary intake of NICOLA participants was assessed using the validated 130-item food frequency questionnaire (FFQ), previously used by the European Prospective Investigation of Cancer (EPIC) study. Although FFQs are prone to measurement error and recall bias, particularly over-estimation of 'healthy' foods, and under-estimation of less 'healthy' foods (9,10) and lack the detail that can be acquired using a food diary or multiple 24-hour recalls (11), for a large population based study such as NICOLA they have the advantage in that they can be easily administered, are less burdensome for participants, they can be self-completed and are useful for ranking participants in relation to their food intake. The FFQ consisted of two parts which were designed to assess habitual food intake over the previous 12 month period:

- ***Part 1*** contained a list of 130 foods within the following food groups: meat and fish, bread and savoury snacks, cereals, potatoes, rice and pasta, dairy products and fats, sweets or snacks, soups, sauces and spreads, drinks and fruit and vegetables. For each food item, participants were asked to indicate the frequency of consumption (in the past 12 months) ranging from never or less than once per month, 1 - 3 times per month, once a week, 2 - 4 per week, 5 - 6 per week, once a day, 2 - 3 per day, 4 - 5 per day and 6 + times per day (refer to Figure 5.2). The servings for each food item were specified in terms of units or common portions (e.g. one apple, one slice of bread) or household measures (e.g. glass, cup, spoon). An average portion size was assigned to each food item.
- ***Part 2*** included additional questions on type and brand of breakfast cereal; type of fat used in frying, roasting, grilling or baking; the amount of visible fat on meat, and the type and quantity of milk. Participants were also asked about supplement use, specific diets and shopping and cooking responsibilities.

Figure 5.2: Example of a food item from the FFQ used in NICOLA

FOODS AND AMOUNTS	AVERAGE USE LAST YEAR								
MEAT AND FISH (medium serving)	Never or less than once/month	1-3 per month	Once a week	2-4 per week	5-6 per week	Once a day	2-3 per day	4-5 per day	6+ per day
Beef: roast, steak, mince, stew or casserole									
Beefburgers									

5.3 Dietary intake in NICOLA participants

This section describes the mean daily consumption of key food groups and how this compares with government recommendations.

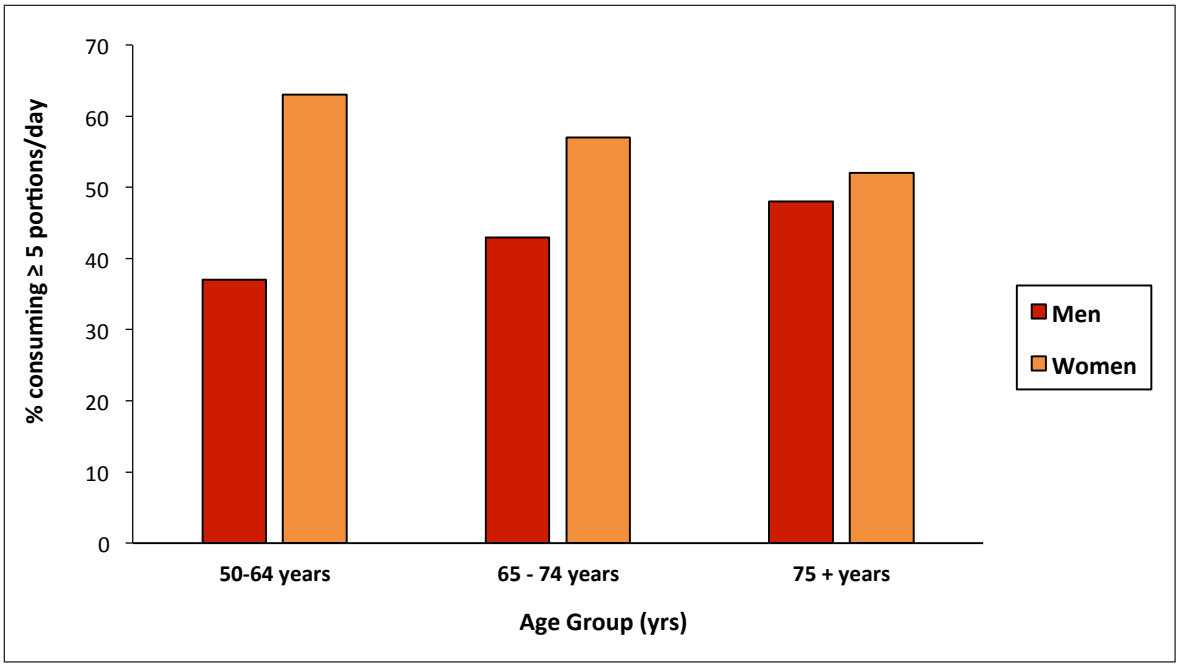
Fruit and vegetable intake

- Regardless of age group, the majority of older adults reported high consumption of fruit and vegetables (see Tables 5.1 and 5.2). On average, almost two thirds (64%) of older adults met the '5-a-day' fruit and vegetable recommendation. Almost one quarter (23%) reported consuming 3 - 4 portions per day, 12% consumed 1 - 2 portions per day while 2% reported consuming less than 1 portion per day. In all age categories, more women met the '5-a-day' fruit and vegetable recommendation than men (72% versus 52%). Marital status played a role in fruit and vegetable intake with higher intakes observed in those who were married compared to those who were single or separated, divorced, widowed. Greater fruit and vegetable consumption was also evident in those with higher levels of education and in those with higher socio-economic status.

Table 5.1: Fruit and vegetable intakes in NI older adults (n = 2844, missing 811)

	Categories of fruit and vegetable intake			
	< 1 portion/d	1-2 portions/d	3-4 portions/d	≥ 5 portions/d
	n (weighted %)	n (weighted %)	n (weighted %)	n (weighted %)
Overall	35 (2)	291 (12)	619 (23)	1899 (64)
Gender				
Males	21 (2)	187 (15)	368 (28)	778 (55)
Females	14 (1)	104 (9)	251 (18)	1121 (72)
Age group (yrs)				
50 - 64	24 (2)	162 (12)	332 (23)	985 (63)
65 - 74	8 (1)	91 (11)	192 (20)	656 (68)
75 +	3 (1)	38 (12)	95 (25)	258 (62)
Marital status				
Married/living with partner	16 (1)	199 (10)	431 (21)	1438 (67)
Single	9 (6)	19 (15)	46 (24)	114 (56)
Separated/divorced/widowed	10 (2)	73 (14)	142 (25)	347 (59)
Education				
Primary/none/ don't know	7 (2)	60 (16)	110 (26)	236 (55)
Secondary	20 (2)	146 (12)	299 (24)	776 (62)
Tertiary	8 (1)	85 (7)	210 (18)	887 (74)
Deprivation score				
0 – 0.11 (least deprived)	5 (1)	63 (8)	167 (21)	581 (70)
0.12 - 0.17	5 (1)	51 (9)	127 (22)	407 (67)
0.18 - 0.23	8 (2)	66 (12)	131 (22)	383 (64)
0.24 - 0.33	9 (2)	60 (13)	108 (24)	316 (61)
> 0.33 (most deprived)	8 (3)	51 (16)	86 (24)	212 (57)
Region				
Belfast	8 (2)	58 (15)	104 (23)	301 (61)
Other city or town	16 (1)	163 (11)	357 (23)	1095 (65)
Rural area	11 (2)	69 (11)	158 (22)	502 (65)
Location of health assessment				
Clinical facility	29 (1)	268 (11)	594 (23)	1831 (65)
Home	6 (6)	23 (20)	25 (21)	68 (52)

Figure 5.3: Percentage of older adults consuming 5 or more portions of fruit and vegetables per day by age and gender



Red and processed meat

- Red and processed meat was consumed by the majority of older adults. Older adults reported consuming on average 1 portion (average serving) of red and processed meat (see Table 5.2) which is in line with the current recommendation that adult intakes should not exceed 70 g per day. Men consumed more red and processed meat than women. The majority of older adults tended to consume meat with very little visible fat on meat, with 70% reporting that they ate as little visible fat as possible, while 15% ate some of the visible fat. The majority of older adults reported a preference for eating meat well done (47%) or medium (43%).

Table 5.2: Mean intake of fruit, vegetables and red and processed meat in NI older adults

	Fruit (portions/d)	Vegetables (portions/d)	Fruit and vegetables (portions/d)	Red and processed meat (portions/d)
	Weighted mean (SD)	Weighted mean (SD)	Weighted mean (SD)	Weighted mean (SD)
Overall	3.0 (2.7)	4.1 (2.9)	7.1 (4.7)	1.1 (0.7)
Gender				
Males	2.6 (2.3)	3.6 (2.4)	6.1 (3.8)	1.2 (0.7)
Females	3.4 (2.9)	4.5 (3.2)	7.9 (5.1)	1.0 (0.7)
Age group (yrs)				
50 - 64	2.9 (2.9)	4.1 (2.7)	7.1 (4.8)	1.1 (0.8)
65 - 74	3.2 (2.6)	4.2 (3.3)	7.3 (4.9)	1.1 (0.7)
75 +	3.0 (2.2)	3.7 (2.4)	6.7 (3.7)	1.1 (0.6)
Marital status				
Married/living with partner	3.0 (2.4)	4.2 (2.9)	7.2 (4.4)	1.1 (0.7)
Single	3.2 (3.3)	3.7 (2.7)	6.9 (4.9)	0.9 (0.7)
Separated/divorced/widowed	3.1 (3.2)	3.8 (2.9)	6.9 (5.2)	1.1 (0.8)
Education				
Primary/none/ don't know	2.9 (2.9)	3.6 (3.2)	6.4 (4.9)	1.2 (0.7)
Secondary	2.9 (2.5)	4.0 (2.7)	6.9 (4.3)	1.2 (0.8)
Tertiary	3.3 (2.8)	4.5 (2.8)	7.8 (4.8)	1.0 (0.6)
Deprivation score				
0 – 0.11 (least deprived)	3.1 (2.5)	4.3 (2.7)	7.4 (4.3)	1.0 (0.6)
0.12 - 0.17	3.1 (2.3)	4.0 (2.5)	7.1 (3.9)	1.1 (0.7)
0.18 - 0.23	3.0 (2.6)	4.2 (3.0)	7.1 (4.8)	1.2 (0.8)
0.24 - 0.33	3.0 (2.6)	4.0 (3.5)	6.9 (4.9)	1.1 (0.7)
> 0.33 (most deprived)	3.0 (3.4)	3.8 (2.7)	6.8 (5.2)	1.2 (0.8)
Region				
Belfast	3.0 (3.2)	3.8 (2.6)	6.7 (5.1)	1.1 (0.8)
Other city or town	3.1 (2.7)	4.1 (3.0)	7.1 (4.6)	1.1 (0.7)
Rural area	3.0 (2.4)	4.2 (2.9)	7.1 (4.4)	1.2 (0.7)
Location of health assessment				
Clinical facility	3.1 (2.7)	4.1 (2.9)	7.1 (4.7)	1.1 (0.7)
Home	2.4 (2.0)	3.8 (2.8)	6.2 (4.2)	1.2 (0.9)

Fish

- Consumption of oily fish was low (mean 0.1 portions/day) (see Table 5.3). Only 27% of older adults met the government recommendation for oily fish with 20% reporting that they consumed oily fish once a week and 7% 2-4 times per week. Just under a quarter (22%) reported never (or less than once a month) consuming oily fish while 24% consumed it 1-3 times per month. Consumption of white fish (fresh or frozen) was also low, with only one third of older adults consuming white fish once a week. In comparison, battered fish was consumed by many older adults. More than a third (39%) reported consuming battered fish 1 - 3 times per month while 19% consumed it at least once a week. A further 42% reported consuming battered fish less than once a month or never.

Table 5.3: Mean intakes of fruit and vegetables, red and processed meat and oily fish in older adults

	Weighted mean (SD) (portions/d)	Weighted median (IQR) (portions/d)	Range (portions/d
Fruit	3.0 (2.7)	2.5 (1.3, 4.0)	0 – 35.5
Vegetables	4.1 (2.9)	3.5 (2.3, 5.2)	0 – 50.5
Fruit and vegetables	7.1 (4.7)	6.3 (4.1, 8.9)	0 – 58.5
Red and processed meat	1.1 (0.9)	1.0 (0.6,1.4)	0 - 13
Oily fish	0.1 (0.13)	0.07 (0.0,0.14)	0 - 1

(missing = 811)

Dairy foods

- In terms of milk consumption, the majority of older adults reported using reduced fat milk. Just over three quarters (76%) reported using semi-skimmed milk, while 11% used skimmed milk. Other milks consumed included 1% fat milk (0.6%), almond milk (0.2%), oat milk (0.1%), goat's milk (0.2%) and other non-specific milks (0.6%). Only 12% reported using whole / full cream milk. Two thirds of older adults reported consuming a quarter (34%) to half a pint (34%) of milk each day including milk with tea, coffee, cereals etc. Approximately one quarter (27%) reported consuming more than half a pint of milk each day while 5% reported that they do not take any milk.
- Yoghurt consumption was low, with 36% and 70% reporting that they never consumed (or consumed less than once a month) low fat yoghurt or full fat yoghurt, respectively. Low fat yoghurts were consumed more often than full fat yoghurts.
- Full fat cheddar, brie and edam cheese was consumed more frequently than low fat soft cheese or cottage cheese, with 5% reporting that they consumed it once a day or 5 - 6 times a week (compared to 1% for low fat soft cheese). Just over a third of older adults reported consuming cheese 2 - 4 times per week, 23% once a week and 17% 1 - 3 times per month (versus 5%, 9% and 16% for low fat

soft cheeses, respectively). 15% never consumed (or consumed less than once a month) full fat cheese compared to 70% for low fat cheese.

- Egg consumption was high, with more than third (37%) reporting that they consumed eggs 2 - 4 times per week while just over a quarter (29%) consuming eggs once a week.
- Butter was commonly used as a spread, with over a third (37%) reporting that they used it daily (16% once a day, 17% 2 - 3 times per day, 4% more than 4 times per day). Use of other fat spreads was lower, with just over a quarter (27%) reporting that they consumed polyunsaturated margarine daily and only 6% reporting daily use of low fat and very low fat spreads.

Fats and Oils

- Commonly reported cooking oils for frying were sunflower oil (36%), olive oil (20%), rapeseed oil (18%), extra virgin olive oil (4%), corn oil (2%) and one calorie spray oil (2%). A small minority (8%) reported not using any fat for cooking, while 3% reported using butter for cooking.

Bread, pasta, rice and cereals

- Breakfast cereals (excluding porridge and Ready brek) were consumed by more than half of older adults (54%). The most commonly purchased cereals (excluding porridge) included Cornflakes (22%), Weetabix (17%), Muesli (11%), Branflakes (8%), Special K (7%), Shredded Wheat (6%) and Crunchy Nut Cornflakes (4%).
- Porridge consumption was high, with just over a quarter consuming it once a day or more (26%), 7% consuming it 5 - 6 times per week, 15% 2 - 4 times per week, 7% once a week, 11% 1-3 times per month and 35% never or less than once a month.
- Bread consumption was high, however, there were no differences in the overall frequency of consumption of white bread versus wholemeal bread. However, those with higher levels of education tended to consume wholemeal bread more frequently than those with lower levels of education. Those who were least deprived also reported greater consumption of wholemeal bread compared to those who were most deprived.
- White rice and white pasta was consumed more often than the wholemeal versions.

High fat and sugary foods

- The majority of older adults reported eating chips at least once a week. Approximately 1% reported consuming chips once a day or 5 - 6 times per week, 14% 2 - 4 times per week, 37% once a week and 29% 1 - 3 times per month. Men reported more frequent consumption of chips compared to women (54% of men reported consuming chips once a week or more versus 48% in women).

- Just over a quarter of older adults (28%) reported consuming sweet chocolate biscuits at least once a day. Consumption of plain sweet biscuits was similar. In comparison, confectionery and sweet consumption was low, with over half consuming chocolate bars / sweets / toffees less than 3 times per month. Just over one third reported consuming chocolate at least once a week. There was no difference in frequency of consumption of chocolate bars between men and women.
- Approximately one third (33%) of older adults reported consuming milk pudding 1 - 3 times per month while almost one quarter (22%) consumed it more than once a month. Consumption of ice cream was slightly higher with 37% consuming ice cream 1 - 3 times per month.
- Addition of sugar to tea, coffee or cereal was low, with only 20% adding it to tea, coffee or cereal.
- Consumption of crisps and peanuts (or other nuts) was low, with 41% and 47% never consuming (or consuming less than once a month) crisps or nuts, respectively.
- The majority of older adults (47%) reported eating food that was fried at home less than once a week, with just over a third (35%) reporting 1 - 3 times per week. The frequency of eating fried food away from home was low, with the majority of older adults reporting that they only had it less than once a week (59%) or not at all (30%).

Salt

- Approximately 1 in 4 (24%) older adults reported that they did not add salt to their food during cooking, 20% rarely added salt, 19% sometimes, 19% usually and 17% always added salt during cooking.

Hot and cold beverages

- Tea was the most commonly consumed hot beverage, with more than one third (38%) reporting that they had a cup 2 - 3 times per day, and almost one third (32%) having a cup more than 4 - 5 times per day. Eleven percent reported that they never drank tea (or drank it less than once a month).
- Coffee consumption was also high, with 40% drinking a cup of instant or ground coffee at least once a day. Almost a third (30%) reported that they never drank coffee (or drank it less than once a month). Only 20% reported drinking decaffeinated coffee.
- Approximately 13% reported consuming cocoa or hot chocolate as a hot drink while 5% reported consuming malted hot drinks such as Horlicks and Ovaltine, mainly 1 - 3 times per month (2%).

- In terms of cold drinks, over one third (37%) reported consuming low calorie or diet fizzy soft drinks while 30% consumed non low calorie soft drinks. Consumption of pure fruit juice was high with almost two thirds (62%) reporting that they drank pure fruit juice. Forty one percent reported consuming fruit squash or cordials.

5.4 Dietary patterns in older adults

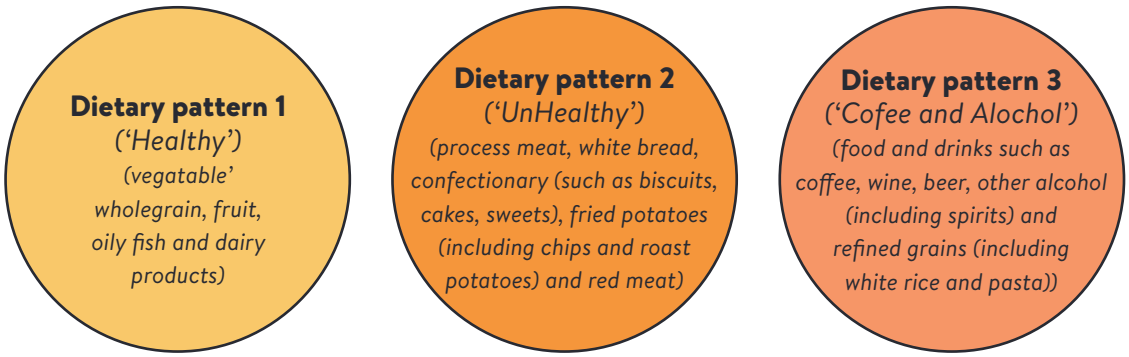
An alternative to assessing intakes of single nutrients or foods is to determine different types of dietary patterns. Analysing dietary patterns (DPs) has many advantages over the more traditional approach of examining individual nutrients to assess disease risk (12,13). DPs summarize the overall diet and help examine the combined effects of food and nutrients. Since nutrients are not consumed in isolation, the strength of associations between DPs and morbidity risk may be greater than between individual nutrients or foods and morbidity risk (12-15). In order to examine dietary patterns in older adults, all of the food and drink items in the FFQ were condensed into 36 food groups. Food items/groups were then aggregated together in the analysis according to how well they correlated with one another. Three distinct dietary patterns were determined:

Dietary pattern 1 ('Healthy') characterised by a high consumption of foods such as vegetables, wholegrains, fruit, oily fish and dairy products.

Dietary pattern 2 ('Unhealthy') characterised by a high consumption of foods such as processed meat, white bread, confectionary (such as biscuits, cakes, sweets), fried potatoes (including chips and roast potatoes) and red meat.

Dietary pattern 3 ('Coffee and Alcohol') characterised by a high consumption of food and drinks such as coffee, wine, beer, other alcohol (including spirits) and refined grains (including white rice and pasta) and low consumption of tea, potatoes, cereals and high fibre breads.

Figure 5.4: Dietary patterns in NICOLA



Together, these three dietary patterns accounted for approximately 22.3% of the total variance in this population with dietary pattern 1 explaining 9.5% of the variance, dietary pattern 2 explaining 6.8% and dietary pattern 3 explaining 5.9% of the variance.

The dietary patterns generated will be used in future analysis to examine relationships between dietary patterns and health outcomes.

5.5 Alcohol intake

Findings regarding levels of alcohol consumption in NICOLA have previously been reported (16). Regarding the type of alcohol consumed, participants were asked to report their frequency of consumption of wine, beer/lager/cider, port/sherry/liqueur and spirits. Wine was the most commonly consumed alcohol with 39% reporting that they consumed it once a week or more. More women reported consuming wine compared to males (54% versus 46%). Consumption of beer and spirits was less, with 20% reporting that they consumed it once a week or more. The majority of beer and spirit drinkers were men (80% and 52%, respectively). Port, sherry and liqueur consumption was low, with 3% reporting consumption once a week or more. Significant proportions also reported never consuming alcohol or only occasional consumption (49% for wine, 70% for beer, 66% for spirits and 92% for port/sherry/liqueur).

5.6 Supplement use

Almost one third of older adults reported taking a dietary supplement and this did not differ across the age categories (30% of 50 - 64 year olds, 34% of 65 - 74 year olds and 35% of 75+ year olds report regular supplement use, while 9%, 7% and 5% report taking supplements sometimes, respectively). More women reported supplement use compared to men (45% and 35%, respectively). Supplement use was higher in those with third level education (48%) compared to those with secondary (36%) or primary or no education (35%) but did not differ across regions or socio-economic categories as defined by the deprivation score. The most commonly reported supplements were fish oils, omega 3/6/9 supplements, vitamin C, glucosamine and multivitamins.

5.7 Special diets

Approximately 12% of older adults reported following a special diet (4% reported following a diabetic diet, 3% weight reduction diet, 2% low fat diet, 2% cholesterol diet, 1% other medical diet). Half of all special diets were recommended or prescribed by a doctor, nurse, dietician or other medical practitioner. Approximately one third of those on a special diet reported difficulty in following the diet. Some of the reasons for finding it difficult included not being able to eat favourite foods, lack of treats and variety, having a ‘sweet tooth’, liking chocolate too much, living alone, food being within easy reach and lack of willpower. Only 1.6% percent of older adults (1.9% of women, 1.2% of men) reported following a vegetarian diet while 1.3% (0.5% of women, 2.1% of men) reported following a vegan diet.

5.8 Food shopping and cooking

Approximately 1 in 2 (53% of those aged 75+, 49% aged 65 - 74 years and 50% of 50 - 64 year olds) older adults reported doing their own shopping, while less than

a quarter undertook the shopping with a member of their family. Eighteen percent relied solely on a member of their family to do the food shopping for them. Less than 1% of older adults asked a carer or friend to shop for them.

More women than men reported doing their own food shopping (71% and 27%, respectively). Almost half (46%) of older men (versus 7% of women) relied on a member of their family to do their food shopping. Just over a quarter (27%) of older men (versus 21% of women) were accompanied by a member of their family when doing the shopping.

The majority of older adults who were separated, divorced or widowed (85%) or single (78%) reported doing their own food shopping compared to 35% of those who were married or living with a partner. Shopping responsibility did not differ across categories of education or social deprivation.

In terms of cooking, more than one third (35%) of older adults did the main food cooking themselves and this increased with age (54% of 75 + years, 49% of 65 - 74 year olds, 45% of 50 - 64 year olds). This is likely to be because more people aged 75 + live alone and therefore have to cook for themselves. Just over one quarter (28%) of those aged 75 years and over relied on another member of their family to cook their meals compared to 24% of 65 - 74 year olds and 20% of 50 - 64 year olds. The majority of those who were separated, divorced or separated (83%) or single (73%) cooked for themselves, while only 32% who were married or living with a partner did the main cooking. Thirty percent of those married or living with a partner relied on the other member of the family to do the cooking while 38% did the cooking along with the other member of their family. Only a small minority of single, separated, widowed or divorced adults relied on a carer or friend to cook.

There were gender differences in cooking behaviour. Two thirds (66%) of women cooked for themselves compared to just over one quarter (27%) of men. Just over a quarter (26%) of women and one third (33%) of men shared the cooking responsibility with another family member. Forty per cent of men relied on another family member to do the cooking compared to 7% of women. Only 1% of men and women relied on a friend or carer to do the cooking.

There was no difference in cooking responsibility across different education levels or across social deprivation status.

5.9 Dietary Validation Study

Accurately assessing dietary intake in older populations is vital to determine the potential role of diet in healthy ageing. However, accurate estimation of dietary intake is difficult, due to reliance on self-reported measures of food intake which are inherently associated with error. Assessing food choice and/or nutrient intake in older adults can also present particular challenges. In some cases, the respondent

may have little or no involvement in grocery shopping or meal preparation, while in others, impaired memory may affect their ability to recall food intake, or physical limitations may impact of their ability to record intake. While the FFQ is a commonly used dietary assessment tool, there is limited evidence regarding its utility for accurately assessing dietary intake in older adults. It is therefore essential that commonly used dietary assessment methods are validated in older populations. This is vital in view of the ageing of the population and the interest in the role of nutrition in maintaining health and ameliorating age-related decline.

Based on the uncertainty over the utility of a FFQ to accurately assess dietary intake in older adults, a random sub-set of NICOLA participants (n = 95) were invited to take part in a dietary validation study in order to compare the FFQ against a panel of nutritional biomarkers, including vitamin C and carotenoids, a 4-day food diary (reference method) and 24-hour recall. In addition to completing the FFQ and giving a blood sample as part of the standard NICOLA health assessment protocol, participants also provided a saliva sample and completed either i) a 4-day food diary (reference method) or ii) a 4-day food diary and multiple pass 24-hour recall (test method). Dietary assessments (including the blood, urine and saliva sampling) were repeated after a period of 6 months in order to assess seasonal changes in dietary intake. Following the 6 month period, participants were also asked to complete a short lifestyle questionnaire to assess changes in lifestyle and health over the 6 months and a usability-rating questionnaire to assess participant opinions on the different dietary assessment methods used. Self-reported fruit and vegetable intakes were compared across the methods using Spearman's correlation coefficients, examining the percentage of participants classified into the same or adjacent quartile of fruit and vegetable intake, and by deriving weighted kappa statistics and Bland-Altman plots.

Results of the validation study showed that, in comparison to the 4-day food diary (reference method), people completing the FFQ tend to over-report fruit and vegetable intake (mean difference of 5 portions between the FFQ and food diary) and this was noted at the two different time-points (baseline and after 6 months) (17). Positive correlations (all $p < 0.05$) were observed between the FFQ and food diary estimates of fruit and vegetable intake. However, further analysis indicated fair to moderate levels of agreement between methods in being able to rank individuals according to their intakes, for example low, moderate or high intakes. However, over-reporting of fruit and vegetable intake is not uncommon with FFQs (18,19).

Figure 5.5: Difference in fruit and vegetable intake between three dietary assessment methods

Given the common challenges of dietary assessment, especially in relation to quantification of foods consumed, the overall findings from this validation study are consistent with previous cohort studies (9) in that, while over-reporting is evident with the FFQ, the results nonetheless show good comparability in being able to rank individuals according to their intake of food groups, in this case fruit and vegetable intake. On the basis of this, the EPIC FFQ currently being used in NICOLA can be considered acceptable for ranking people according to their fruit and vegetable intake i.e. low, medium, high consumers of fruit and vegetables.

5.10 Future work

Further in-depth dietary analyses are being conducted within NICOLA including energy and nutrient intake analysis which will allow us to explore nutritional adequacy in older adults and provide a more comprehensive and objective assessment of dietary intake. Biochemical markers of nutritional status are also being measured along with more detailed metabolomic analysis. The findings from this work will become available in peer reviewed outputs in due course.

5.11 Conclusions

The results presented here provide a snapshot of the dietary intake and dietary patterns of older adults in Northern Ireland. Although many older adults are following dietary recommendations, there are still areas of dietary intake that require attention in this age group.

Our findings suggest that older adults are still not consuming enough oily fish or high fibre foods such as wholemeal bread or wholemeal pasta. Results also suggest a need for older adults to increase their consumption of low fat dairy foods and reduce overall intakes of high fat, high sugary foods. While self-reported fruit and vegetable intakes appear adequate, there were disparities in intakes depending on gender, marital status, education level and socio-economic status, and over-reporting may have contributed to this finding. Addressing the dietary needs of older people is crucial for the maintenance of health, functional independence and quality of life.

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6 Cardiovascular health and diabetes

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Citation

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Key Findings

- Mean systolic (SBP) and diastolic blood pressure (DBP) of NICOLA participants was 132mmHg and 81 mmHg, respectively.
- In NICOLA, mean blood pressure tended to be higher in men than women.
- 39% of adults aged 50 years and over had hypertension and this increased with age.
- Based on HbA1c levels, 13% of older adults in Northern Ireland had diabetes, 15% were pre-diabetic and 72% were non-diabetic.
- Diabetes is more prevalent in men than women and increases with age.

BLOOD PRESSURE

6.1 Introduction

Blood pressure is a good indicator of cardiovascular health and hypertension (high blood pressure) represents a modifiable risk factor for adverse cardiovascular events such as coronary heart disease and stroke (1). An individual with hypertension is three times more likely to develop heart disease and a stroke and twice as likely to die from these, compared to a person with regular blood pressure (1).

Evidence suggests that many older adults are unaware that they have hypertension In the UK, 1 in 3 adults (around 16 million) have hypertension (a reading of 140/90 mmHg or higher); (2) rising to at least 1 in 2 in those aged 65 years and over (1). In addition, as a person ages, the tendency for postural hypotension (blood pressure drop on standing) increases. This can result in dizziness, light headedness and increases the risk of falls.

6.2 Measurement of blood pressure

In NICOLA, blood pressure was measured using an OMRON™ digital oscillometric blood pressure monitor (Model M10-IT) and inflatable cuff around the upper arm. Mean blood pressure was calculated from three separate blood pressure and heart rate readings, obtained 1 minute apart, using either the left or the right arm, with the participant in a relaxed, seated position. Two measurements were taken while the participant was relaxed and seated, and the third measurement was taken immediately on standing in order to capture the postural drop in blood pressure. Ambient room temperature was recorded prior to the blood pressure measurement. The acceptable temperature range for the blood pressure measurement was 15 - 25°C.

6.3 Results

The mean systolic and diastolic blood pressure of NICOLA participants was 132 and 81 mmHg, respectively. Mean blood pressure was higher in men than in women.

Table 6.1 shows the proportion of adults with systolic blood pressure <140 mmHg and diastolic blood pressure <90 mmHg. The proportion of older adults with evidence of hypertension was high (39%), with the proportion increasing with age. Almost half (47%) of adults aged >75 years had hypertension, compared to 43% of 65 - 74 year olds and just over a third (35%) of 50 - 64 year olds. These findings are similar to those reported in TILDA (3).

More men had hypertension compared to women (46% versus 33%) although a higher percentage of women age >75 years had hypertension compared to men (50% versus 45%). Approximately, half (51%) of those who had hypertension (as measured in the health assessment) were already aware that they had hypertension (based on the self-reported measure in the CAPI) while 49% who had hypertension (based on the health assessment measure) had not previously reported having hypertension. This varied by age, with a higher proportion (57%) in the 75+ age group being aware that they had hypertension compared to the 65 - 74 year old (55%) and 50 - 64 year old (45%) age group. A greater proportion (63%) of single people were also aware that they were hypertensive compared to those who were married (48%) or separated/divorced/widowed (54%). However, the health assessment showed that 33% of single, 40% of married and 42% of separated/divorced/widowed people had hypertension. There was also variation by level of education and deprivation with a higher proportion of those with lower levels of education (58%) previously reporting that they had hypertension compared to those with secondary (50%) or tertiary (44%) education. By comparison, blood pressure measurements performed in the health assessment showed that 44% of those with lower levels of education had hypertension compared to 40% and 36% with secondary and tertiary education, respectively. A higher proportion of those from the most deprived areas (53%) had previously reported that they had hypertension compared to those in the less deprived areas (48%). These findings were confirmed in the health assessment with a higher proportion of those from the most deprived areas (44%) showing hypertension compared to those from less deprived areas (39%).

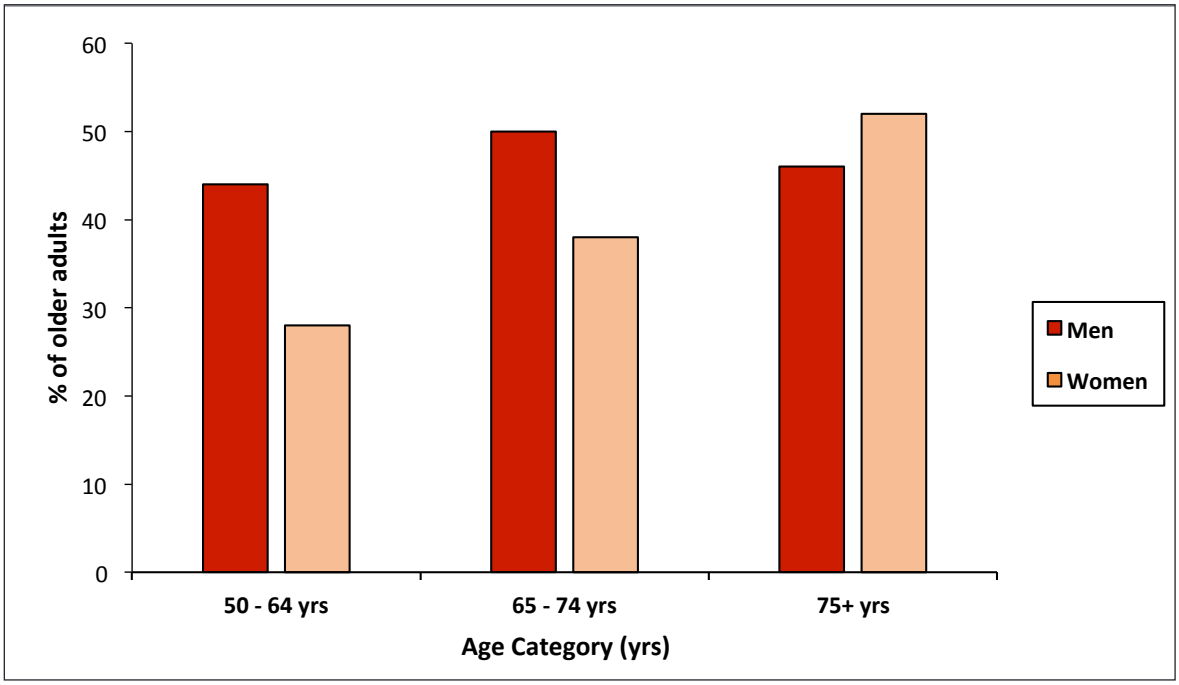
Table 6.1: Mean blood pressure in NICOLA participants and proportions with SBP<140 mmHg and DBP<90 mmHg, respectively

	Systolic Blood Pressure (mmHg)	Diastolic Blood Pressure (mmHg)	Systolic Blood Pressure (<140 mmHg)		Diastolic Blood Pressure (<90 mmHg)	
			Yes	No	Yes	No
	Mean (SD)	Mean (SD)	n (weighted %)	n (weighted %)	n (weighted %)	n (weighted %)
Overall	132 (19)	81 (11)	2378 (65)	1277 (35)	2834 (78)	821 (22)
Gender						
Males	137 (18)	82 (11)	1019 (59)	742 (41)	1313 (76)	448 (25)
Females	129 (19)	80 (11)	1359 (70)	535 (30)	1521 (80)	373 (20)
Age group (yrs)						
50 - 64	130 (18)	82 (11)	1422 (72)	555 (28)	1490 (75)	487 (25)
65 - 74	136 (18)	81 (11)	687 (58)	500 (42)	944 (80)	243 (20)
75 +	138 (20)	78 (11)	269 (54)	222 (47)	400 (81)	91 (19)
Marital status						
Married/living with partner	133 (19)	82 (11)	1715 (35)	928 (65)	2032 (77)	611 (23)
Single	132 (19)	81 (10)	174 (28)	70 (72)	199 (82)	45 (18)
Separated/divorced/ widowed	133 (19)	81 (11)	489 (38)	279 (62)	603 (78)	165 (22)
Education						
Primary/none/ don't know	136 (18)	80 (11)	336 (59)	241 (41)	453 (79)	124 (21)
Secondary	133 (19)	82 (11)	1034 (65)	568 (35)	1219 (76)	383 (24)
Tertiary	131 (19)	81 (11)	1008 (69)	468 (31)	1162 (79)	314 (21)
Deprivation score						
0 – 0.11 (least deprived)	133 (18)	81 (11)	646 (66)	345 (34)	772 (78)	219 (22)
0.12 - 0.17	132 (18)	81 (11)	514 (68)	249 (32)	579 (77)	184 (23)
0.18 - 0.23	133 (19)	81 (11)	473 (65)	260 (35)	580 (79)	153 (21)
0.24 - 0.33	132 (20)	81 (11)	434 (65)	224 (35)	515 (78)	143 (22)
> 0.33 (most deprived)	134 (18)	82 (11)	311 (60)	199 (40)	388 (76)	122 (24)
Region						
Belfast	132 (19)	81 (11)	419 (65)	216 (35)	492 (77)	143 (23)
Other city or town	133 (19)	81 (11)	1327 (64)	721 (36)	1582 (77)	466 (23)
Rural area	133 (19)	81 (11)	626 (65)	338 (35)	754 (79)	210 (21)
Location of health assessment						
Clinical facility	133 (19)	81 (11)	2268 (65)	1194 (35)	2677 (78)	785 (22)
Home	137 (21)	78 (12)	110 (55)	83 (45)	157 (78)	36 (22)

Mean (SD) are unweighted values (SBP n = 3619, DBP n = 3616)

Proportions are based on n = 3655

Figure 6.1: Percentage of NI older adults affected by hypertension (% based on weighted values of NICOLA)



DIABETES

6.4 Introduction

Globally, the prevalence of type 2 diabetes and pre-diabetes has increased rapidly in recent decades and this trend will continue as the population ages. Pre-diabetes, also commonly referred to as borderline diabetes, is characterised by blood glucose levels that are higher than normal but not high enough to be classed as diabetes. It means the person is at greater risk of developing type 2 diabetes (1). Type 1 diabetes is a lifelong condition which occurs when the pancreas produces little or no insulin. Type 2 diabetes is caused by blood glucose levels becoming too high because the insulin produced by the pancreas isn't working as it should or the pancreas can't make enough insulin (1).

In the UK, the number of people diagnosed with diabetes has more than doubled in the last 20 years and the number of people experiencing complications or dying as a results of diabetes is also increasing. It is estimated that more than 5 million people will have diabetes by 2025. Around 1 in 7 older adults have diabetes (1). In Northern Ireland, approximately 100,000 people have been diagnosed with diabetes.

Both Type 1 and Type 2 diabetes are serious conditions that can lead to life changing complications such as amputation and loss of sight. Diabetes is also associated with increased risk of heart attacks, heart disease, kidney disease, stroke and falls (4). People with diabetes are almost 2.5 times more likely to have a heart attack or experience heart failure and twice as likely to have a stroke compared to those without diabetes (4). Although Type 1 diabetes is not currently preventable, more than half of all cases of Type 2 diabetes can be prevented or delayed. Early diagnosis is important as complications can arise five to six years before some people become aware that they have Type 2 diabetes.

As part of the NICOLA health assessment, participants were asked whether or not they had diabetes. Non-fasting glycated haemoglobin (HbA1c) was analysed in blood samples thus providing an overall picture of what average blood glucose levels had been over a period of 8-12 weeks. Non-fasting blood glucose levels were also measured.

6.5 Findings

In NICOLA, more men than women self-reported diabetes. The mean HbA1c level in NICOLA participants was 40 mmol/l which is within the normal range. In relation to HbA1c categories as defined by the European Society of Cardiology (5), estimates from the study suggest that 13% of older adults in Northern Ireland have diabetes, 15% are pre-diabetic and 72% are non-diabetic. Prevalence of diabetes and pre-diabetes increased with age, with 19% of the 75+ age group being diabetic, compared to 8% of 50 - 64 year olds. Results also pointed to a gradient in diabetes prevalence across educational classes, with lower prevalence of diabetes evident in those with secondary or tertiary education.

In NICOLA, 28 participants who self-reported diabetes had normal HbA1c levels (<42 mmol/l). Of the 2647 who reported not having diabetes, 2132 had normal HbA1c levels (i.e. < 42 mmol/l), 382 had prediabetes HbA1c levels (i.e. 42 - 47 mmol/l) and 133 participants had HbA1c levels ≥ 48 mmol/l (cut-off for diabetes).

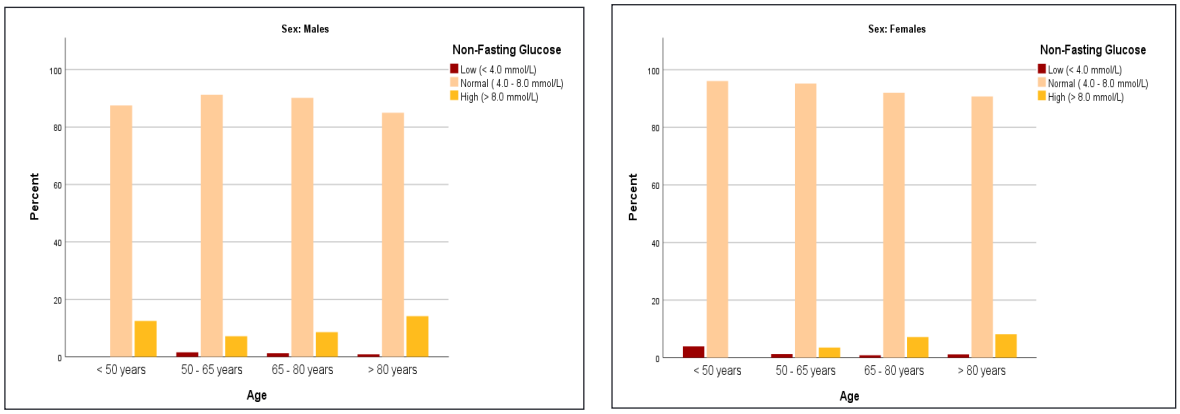
Table 6.2: Self-reported diabetes, HbA1c levels and categories in NICOLA

	Self-reported diabetes		HbA1c	HbA1c Category		
	n (weighted %)	n (weighted %)	(mmol/l)	n (weighted %)	n (weighted %)	n (weighted %)
	Yes	No	Mean (SD)	Normal (< 42 mmol/L)	Prediabetes (42 - 47 mmol/L)	Diabetes (≥ 48 mmol/L)
Overall	339 (11)	3316 (89)	40 (10)	2160 (72)	420 (15)	322 (13)
Gender						
Males	210 (13)	1551 (87)	40 (11)	1034 (71)	202 (16)	168 (13)
Females	129 (8)	1765 (92)	40 (9)	1126 (73)	218 (15)	154 (12)
Age group (yrs)						
50 - 64	142 (8)	1835 (92)	39 (9)	1236 (79)	186 (13)	121 (8)
65 - 74	134 (14)	1053 (86)	41 (10)	691 (70)	135 (15)	132 (15)
75 +	63 (14)	428 (86)	43 (11)	233 (56)	99 (25)	69 (19)
Marital status						
Married/living with partner	225 (10)	2418 (90)	40 (9)	1609 (74)	294 (14)	210 (11)
Single	28 (15)	216 (85)	40 (10)	133 (68)	31 (19)	24 (13)
Separated/divorced/ widowed	86 (12)	682 (88)	41 (11)	418 (67)	95 (17)	88 (16)
Education						
Primary/none/ don't know	81 (15)	496 (85)	42 (10)	294 (62)	89 (20)	77 (18)
Secondary	158 (11)	1444 (89)	40 (10)	921 (73)	184 (15)	146 (12)
Tertiary	100 (7)	1376 (93)	39 (9)	945 (79)	147 (12)	99 (9)
Deprivation score						
0 – 0.11 (least deprived)	70 (8)	921 (92)	39 (9)	618 (76)	124 (16)	58 (8)
0.12 - 0.17	68 (10)	695 (90)	40 (10)	484 (76)	70 (12)	68 (12)
0.18 - 0.23	75 (13)	658 (87)	41 (11)	418 (68)	79 (14)	85 (18)
0.24 - 0.33	71 (12)	587 (88)	40 (9)	362 (69)	86 (18)	61 (13)
> 0.33 (most deprived)	55 (13)	455 (87)	40 (8)	278 (70)	61 (18)	50 (12)
Region						
Belfast	68 (14)	567 (86)	39 (9)	407 (79)	59 (12)	41 (9)
Other city or town	184 (10)	1864 (90)	40 (10)	1181 (70)	253 (16)	202 (14)
Rural area	86 (10)	878 (90)	40 (10)	570 (72)	106 (15)	79 (12)
Location of health assessment						
Clinical facility	300 (10)	3162 (90)	40 (10)	2073 (73)	392 (15)	297 (12)
Home	39 (21)	154 (79)	44 (12)	87 (61)	28 (21)	25 (18)

HbA1c n = 2902, missing n = 753

Non-fasting glucose levels were normal in the majority of the NICOLA participants, with median levels of 5.6 [5.1 – 6.3] mmol/L (Figure 6.2).

Figure 6.2: Percentage of NICOLA participants with low, normal and high serum levels of non-fasting glucose (mmol/L), by age group and sex.



6.6 Conclusions

Timely diagnosis and treatment of both hypertension and diabetes are vital to reducing the burden on healthcare systems. The data presented above provide a valuable reference for the prevalence of hypertension and diabetes in community-dwelling older adults in Northern Ireland and can offer a platform for planning early interventions to improve public health. The findings also suggest that there may be a significant proportion of adults with diabetes who remain undiagnosed. More targeted screening and early intervention may be warranted to help identify those at increased risk of developing diabetes or hypertension.

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7 Biochemical Biomarkers

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Citation

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Key Findings

- Data is available for 28 biochemical biomarkers for 3,082 individuals within the NICOLA Cohort. All individuals participating in the health assessment were also offered rapid testing and feedback for blood glucose and lipid levels.
- Approximately 54% of males and females in the NICOLA cohort had low vitamin D levels. The majority who were deficient in vitamin D were aged over 80 years.
- The majority of the 3082 participants showed results within normal ranges for all other serum-based biochemical biomarkers.
- NICOLA welcomes expressions of interest to collaborate and make maximal use of the data generated. Please contact our NICOLA team for further information: nicola-research@qub.ac.uk

7.1 Introduction

Analysing biological samples allows us to objectively evaluate biomarkers that help provide information about a person's health. For example, testing biomarkers such as blood glucose (blood sugar) levels can identify people with undiagnosed diabetes, while analysing blood lipid levels can provide important information about a person's risk of cardiovascular disease. Often biomarkers can provide an early indication of disease before symptoms develop, provide us with information on how a disease is progressing and / or suggest therapies.

Biological samples (urine and blood for DNA, RNA, plasma and serum) were collected at Wave 1 to provide baseline data for 3514 participants in this long-term prospective cohort study. We plan to collect additional biological samples during subsequent Waves of NICOLA.

Multiple biomarker studies have been performed using this early baseline data with biological material safely stored for future biochemistry-based biomarker studies. A full list of the biochemical biomarkers currently available in the NICOLA cohort are presented in Table 7.1 This chapter presents the findings from the biochemical analysis of the samples.

Table 7.1: Overview of biochemical biomarkers and derived phenotypes currently available in the NICOLA cohort

Biomarker	Derived variables
Apolipoprotein A	
Apolipoprotein B	
Cholesterol	
Direct low-density lipoprotein	
Gamma glutamyltransferase	
High-density lipoprotein-cholesterol	
Lipoprotein (a)	
Triglycerides	
Alkaline phosphatase	
Calcium	
Rheumatoid factor	
Vitamin D	
Oestradiol	
Sex hormone-binding globulin	
Testosterone	
Glucose	

Creatinine	eGFR equation based on serum creatinine eGFR combined equation based on serum creatinine and serum cystatin C Chronic Kidney Disease Chronic Kidney Disease Stage End-Stage Renal Disease
Cystatin C	eGFR equation based on serum cystatin C eGFR combined equation based on serum creatinine and serum cystatin C
Phosphate	
Total protein	
Urate	
Urea	
Alanine aminotransferase	
Albumin	
Aspartate aminotransferase	
Direct Bilirubin	
Gamma Glutamyltransferase	
Total Bilirubin	
Abbreviation: eGFR: estimated glomerular filtration ratio	

7.2 Measurement of biochemistry-based biomarkers

Blood samples for biochemical biomarkers were collected in EDTA / clot activator tubes. Samples for glucose testing were collected in tubes containing potassium oxalate / sodium fluoride as a glycolysis inhibitor. The serum tubes were allowed to clot for at least 3 minutes and centrifuged at 3,000 rpm for 10 minutes at 4°C.

All samples were analysed in Hamburg at our collaborator Prof Tanja Zeller's laboratory. An Abbott ARCHITECT i2000 system was used for Testosterone, sex hormone-binding globulin (SHBG) and vitamin D analyses, while the reminder of the tests were carried out on the Abbott ARCHITECT c8000 system. Serum biomarkers were analysed for 3082 participants in the NICOLA Wave 1 cohort, of whom 52.5% were women (n = 1617). The percentage of missing values was 0.29% for SHBG (n = 9); 0.16% for oestradiol (n = 5); 0.13% for testosterone, vitamin D, rheumatoid factor and total bilirubin (n = 4); 0.10% (n = 1) for Lipoprotein (a) (Lp(a)), and 0.06% (n = 2) for the remaining biomarkers analysed. The data presented for the biomarkers below does not take into account any medication that a participant may have been taking, nor any diseases diagnosed. Values in this chapter are presented as mean ± SD or median (interquartile range).

7.3 Cardiovascular biomarkers

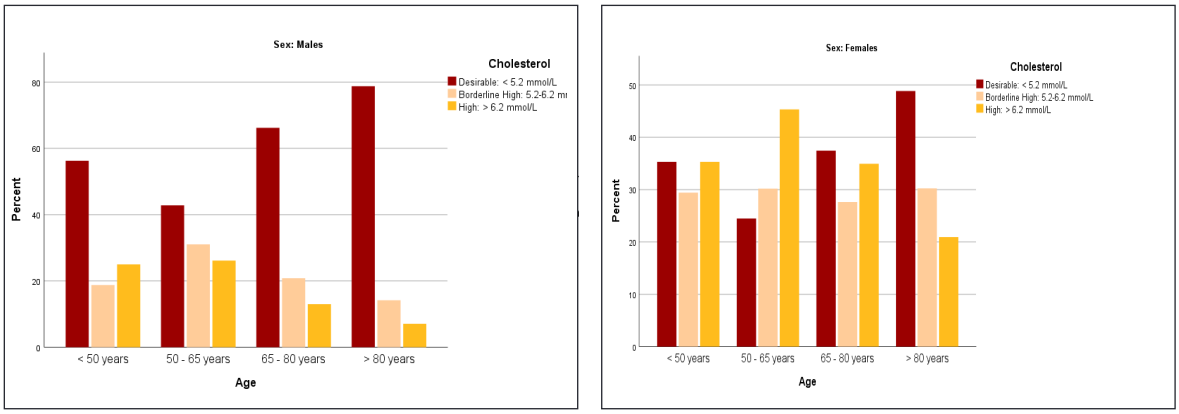
Cardiovascular disease (CVD) has become the leading cause of death globally (1). Approximately 485.6 million people were living with CVD in 2017, 72.7 million new cases were diagnosed and 17.8 million died as a consequence of CVD, which represents 31.8% of all causes of death (1,2). CVD also causes substantial morbidity, estimated to cost €210 billion a year to the EU economy (3).

Dyslipidaemias, characterized by increased plasma levels of low-density lipoprotein cholesterol (LDL), very low-density lipoprotein cholesterol (VLDL), triglyceride (TG), and reduced plasma levels of high-density lipoprotein cholesterol (HDL) are among the modifiable lifestyle risk factors with a high impact on cardiovascular diseases (CVD) (4–8). Their management is therefore crucial in the prevention of CVD. Apolipoproteins are proteins that bind lipids to form lipoproteins (VLDL, LDL and HDL), whose function is to transport lipids in blood, cerebrospinal fluid and lymph. VLDL and LDL both contain one molecule of the major structural glycoprotein apolipoprotein B-100 whereas lipoprotein(a) or Lp(a) contains an additional large glycoprotein, apolipoprotein(a) (9). HDL contains ApoA1 as its major structural protein, being the only non-ApoB-containing lipoprotein in the blood (9).
One of the key components in the development of CVD is the persistent elevation of certain pro-inflammatory biomarkers, like the C-reactive protein (CRP), one of the earliest reversible precursors of atherosclerosis (10–12).

Cholesterol

Cholesterol levels above 5.2 mmol/L are generally considered elevated and related to a higher risk of adverse cardiovascular events. Women in the NICOLA cohort had higher median cholesterol (5.84 mmol/L) levels than men (4.98 mmol/L) (Figure 7.1).

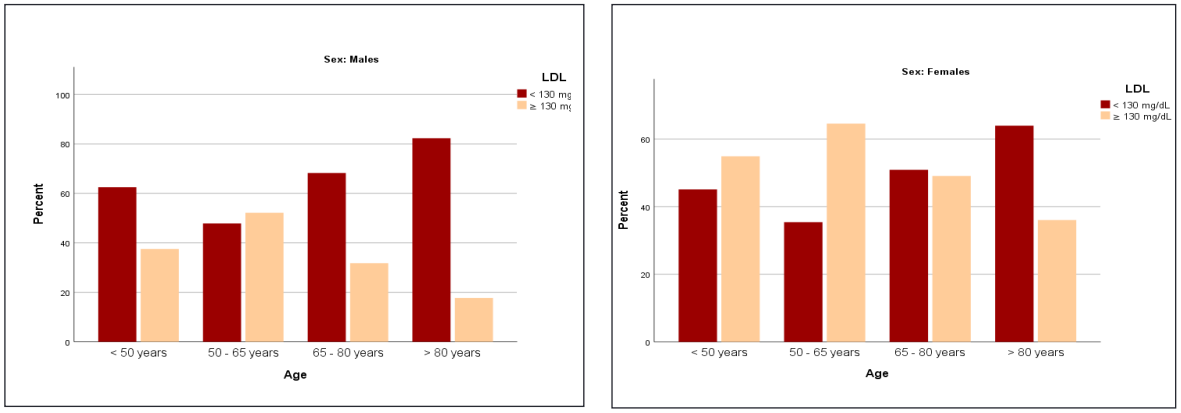
Figure 7.1: Percentage of NICOLA participants with serum levels of cholesterol above / below 5.2 mmol/L, by age group and sex.



Direct Low Density Lipoprotein

Men in the NICOLA cohort had LDL (median) levels of 118 mg/dL versus 136 mg/dL in women. 43.0% of women had normal LDL levels (< 130 mg/dL); 59.6% of men had normal LDL levels (Figure 7.2).

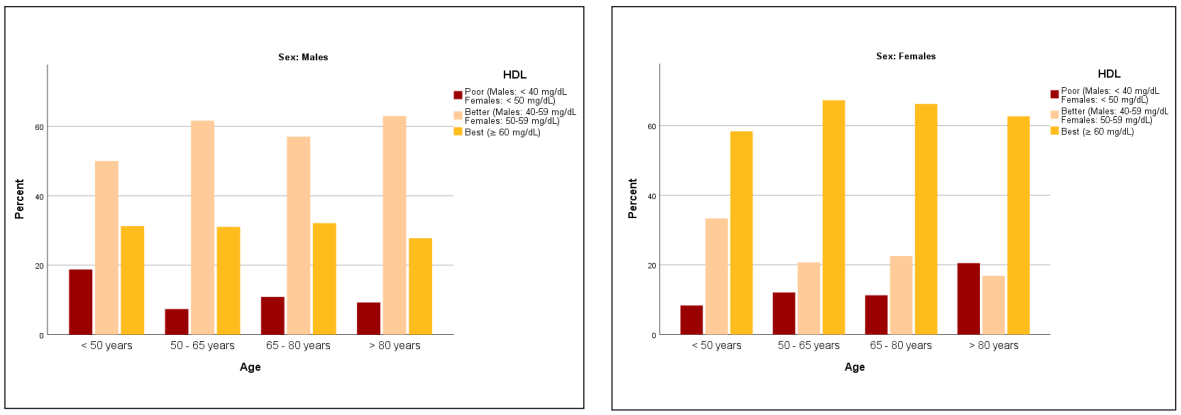
Figure 7.2: Percentage of NICOLA participants with serum levels of low-density lipoproteins above / below 130 mg/dL, by age group and sex.



HDL-Cholesterol

Men in the NICOLA cohort had HDL (median levels) of 54 mg/dL versus 67 mg/dL in women. Women had better/best HDL levels in 88% of cases, versus 91% of men (Figure 7.3).

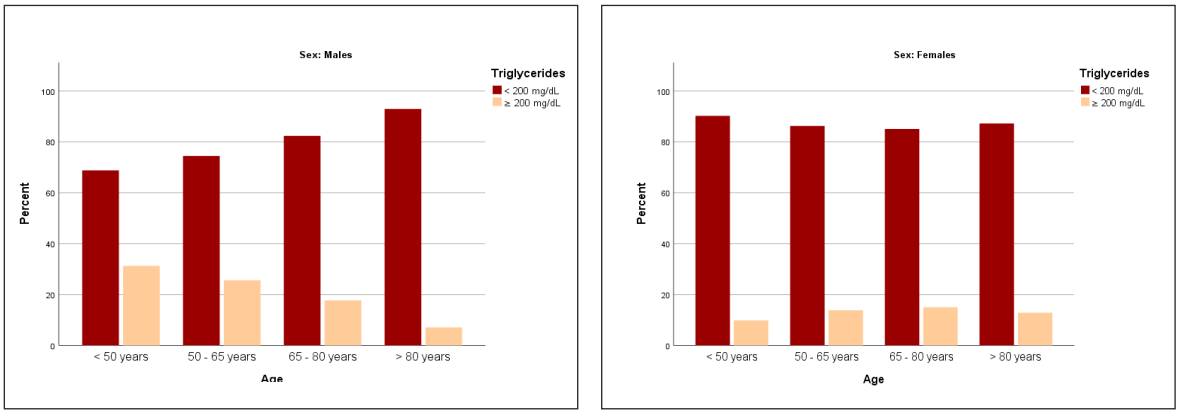
Figure 7.3: Percentage of NICOLA participants with low / normal / high serum levels of high-density lipoproteins, by age group and sex.



Triglycerides

Men in the NICOLA cohort had TG (median levels) of 136 mg/dL versus 121 mg/dL in women. Men had normal TG levels (< 200 mg/dL) in 79% cases, whereas this percentage was 86% in women (Figure 7.4).

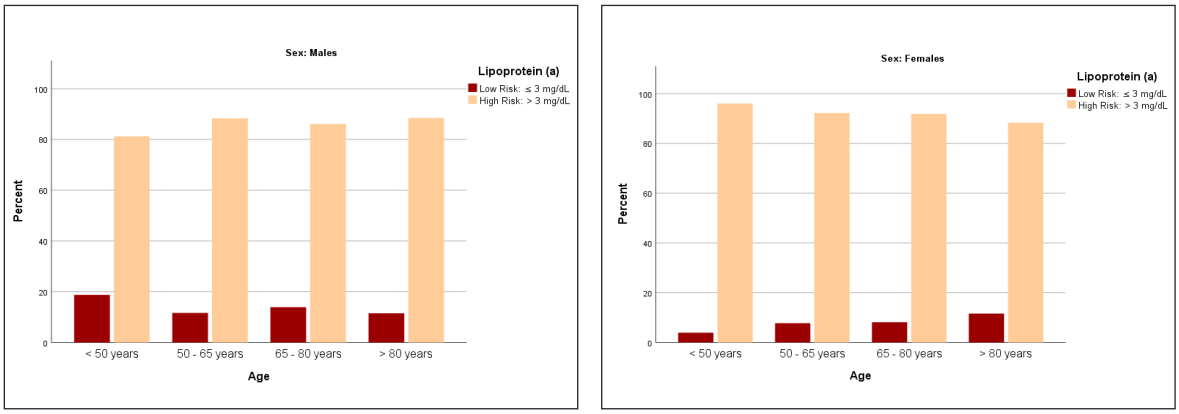
Figure 7.4: Percentage of NICOLA participants with serum levels of triglycerides above / below 200 mg/dL, by age group and sex.



Lipoprotein (a)

Lipoprotein(a), Lp(a), is a modified atherogenic LDL particle that contains apolipoprotein(a), with variable levels in the population. The consensus statement by HEART UK, based on the evidence that Lp(a) is an independent CVD risk factor, recommends its measurement in adults with a personal or family history of premature atherosclerotic CVD, those with first-degree relatives who have Lp(a) levels >200 nmol/l, patients with familial hypercholesterolemia, calcific aortic valve stenosis and those with risk of a cardiovascular event (13). Median levels of Lp(a) in the cohort was 13 mg/dl, and 87% of male and 92% of females had Lp(a) levels above 3 mg/dL, associated with higher CVD risk, regardless of age (Figure 7.5).

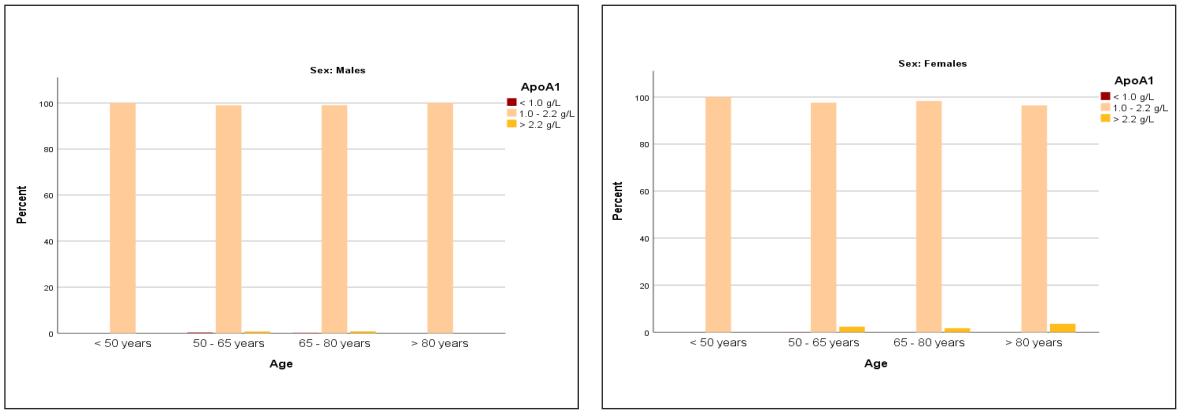
Figure 7.5: Percentage of NICOLA participants with serum levels of Lipoprotein (a), above / below 3 mg/dL, by age group and sex.



Apolipoprotein A1

Almost all NICOLA participants had normal levels of ApoA1 (99% males; 98% females), independent of age (Figure 7.6). Median ApoA1 levels were 1.68 g/dL.

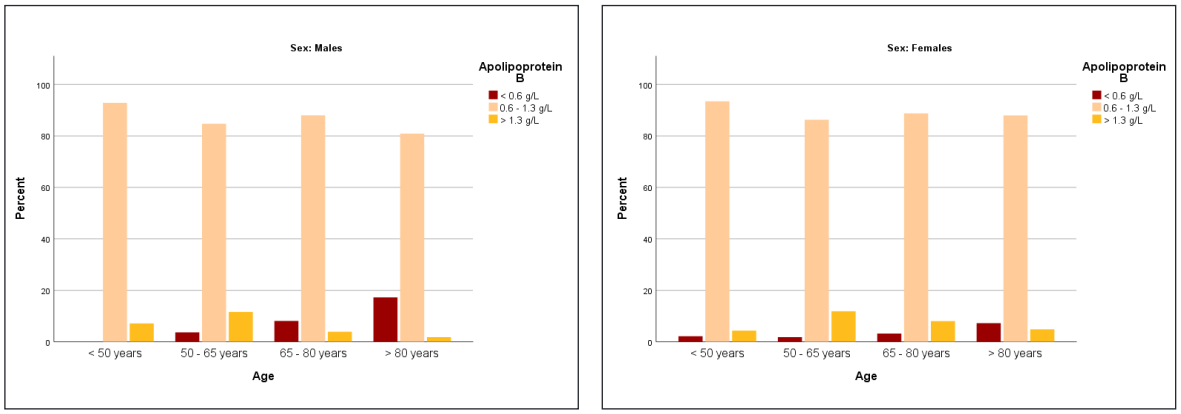
Figure 7.6: Percentage of NICOLA participants with low / normal / high serum levels of apolipoprotein A1 (ApoA1), by age group and sex.



Apolipoprotein B

The majority of NICOLA participants had normal levels of ApoB (86% males; 88% females), regardless of age (Figure 7.7). Median levels of ApoB were 1.04 g/dL in women and 1.0 g/dL in men.

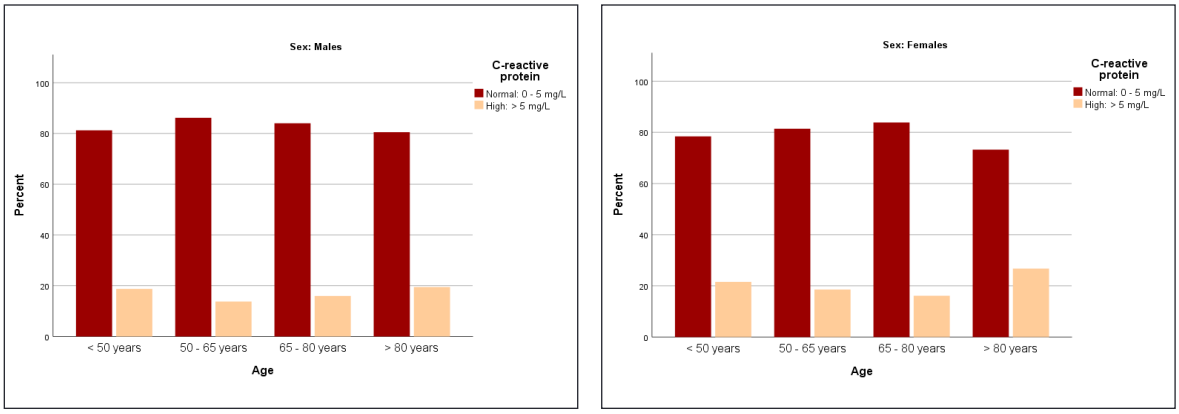
Figure 7.7: Percentage of NICOLA participants with normal / high serum levels of apolipoprotein B, by age group and sex.



C-reactive protein

Approximately 80% of NICOLA participants had CRP levels ≤ 5 mg/L, independent of age and sex (Figure 7.8). Median CRP levels in the cohort were 1.63 mg/L.

Figure 7.8: Percentage of NICOLA participants with serum levels of C-reactive protein, above / below 5 mg/L, by age group and sex.



7.4 Bone and Joint Biomarkers

Musculoskeletal disorders represent ≈17.8% of all causes of the global burden of disease (2), being responsible from 0.22% of all causes of death in 2017, with rheumatoid arthritis (RA) being the single major contributor (1). In fact, RA and osteoarthritis accounted for 20.6 and 303.1 million prevalent cases and 1.2 and 14.9 million incident cases diagnosed globally in 2017 respectively (1,2).

Vitamin D deficiency has classically been associated with musculoskeletal conditions, such as rickets and osteomalacia, although its association with other conditions has also been established (14). Approximately 50% of the UK population have vitamin D insufficiency in spring (15,16), associated with an increased risk of mortality and of several common diseases including CVD, diabetes, cancer and multiple sclerosis (17).

RA is a chronic inflammatory disorder affecting the synovial lining of joints, tendon sheaths, and bursae. Among the many autoantibodies and proteins generated in the course of RA, immunoglobulin M rheumatoid factor (RF) and anti-citrullinated protein antibodies are the two that are most commonly used in clinical practice (18). Both of them are capable of identifying RA in a relatively sensitive and specific way and predict a worse prognosis of the disease (19 – 22).

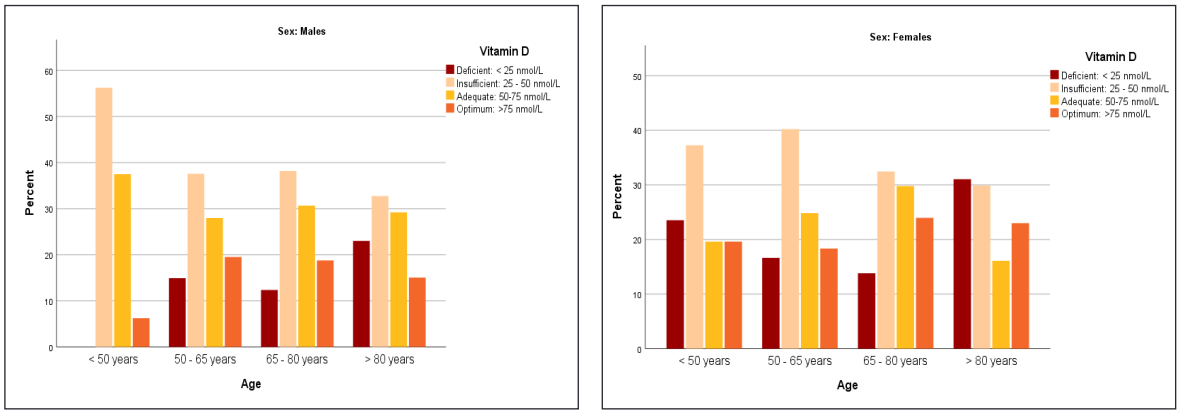
Alkaline phosphatases are widely distributed enzymes (liver, bile ducts, intestine, bone, kidney, placenta, and leukocytes) that catalyse the release of orthophosphate from ester substrates at an alkaline pH. Serum alkaline phosphatase activity may be increased in liver disease (23), bone disorders such as Paget's disease, osteomalacia and bone metastases, but also in normal processes such as during rapid bone growth in children or in the later stages of pregnancy (24).

Calcium is the most prevalent cation in the body, whose serum concentrations are tightly controlled by Parathyroid Hormone and 1, 25-dihydroxyvitamin D. Estimations of serum levels of calcium are used in the diagnosis and treatment of parathyroid disorders, renal disease, a variety of bone disorders, carcinomas, acromegaly and pancreatitis.

Vitamin D

The median value of serum vitamin D among the NICOLA participants was 19.1 ng/mL. In males, 15% of 50 - 65 year olds, 12% of 65 - 80 year olds and 23% of those aged over 80 years were found to be deficient in vitamin D (< 25 nmol/L) (17). In females, 23% of those aged under 50 years, 17% of 50 - 65 year olds, 14% of 65 - 80 year olds and 31% of those aged over 80 years were deficient in vitamin D.

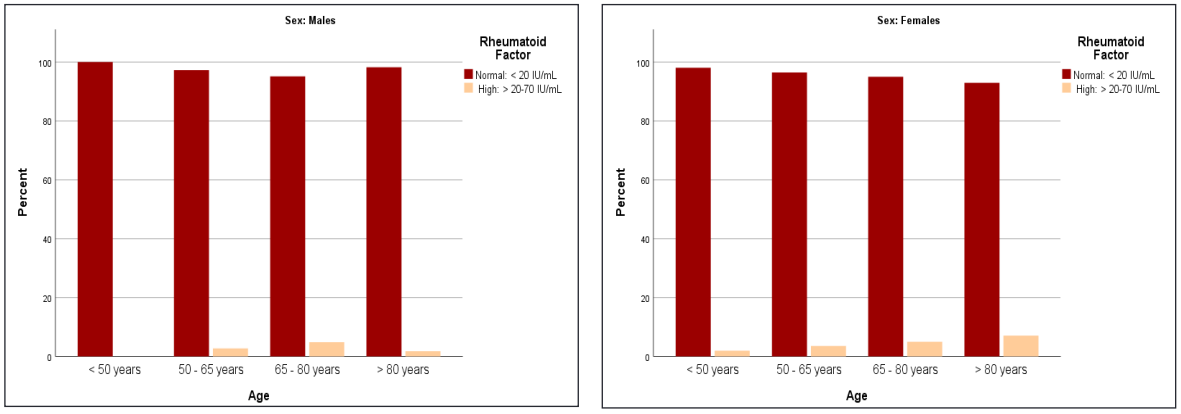
Figure 7.9: Percentage of NICOLA participants with deficient / insufficient / adequate / optimum serum levels of vitamin D, by age group and sex.



Rheumatoid factor

Serum levels of rheumatoid factor were normal in the majority of the NICOLA participants, median 7.1 IU/mL (Figure 7.10).

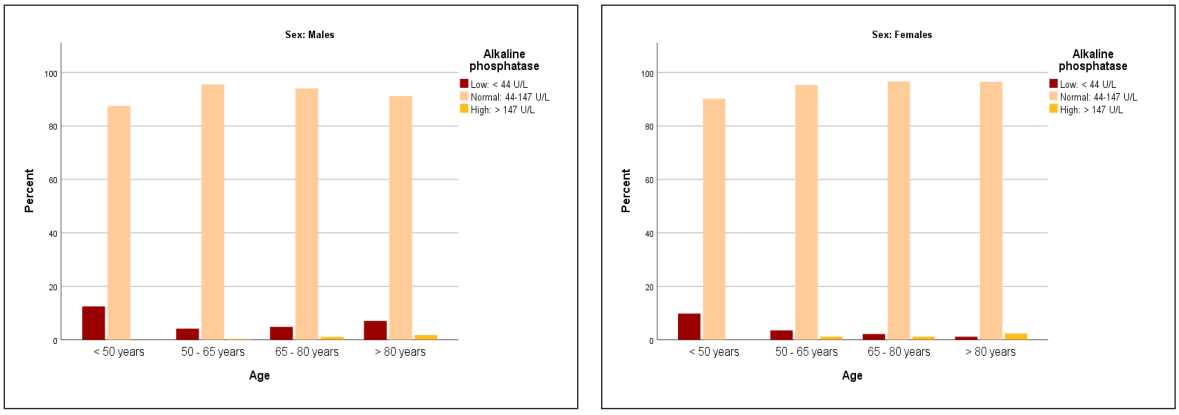
Figure 7.10: Percentage of NICOLA participants with serum levels of rheumatoid factor, above / below 20 IU/mL, by age group and sex.



Alkaline phosphatase

The levels of alkaline phosphatase in serum were normal (44 - 147 U/L) in the majority of the NICOLA participants, with median values of 73 U/L (Figure 7.11).

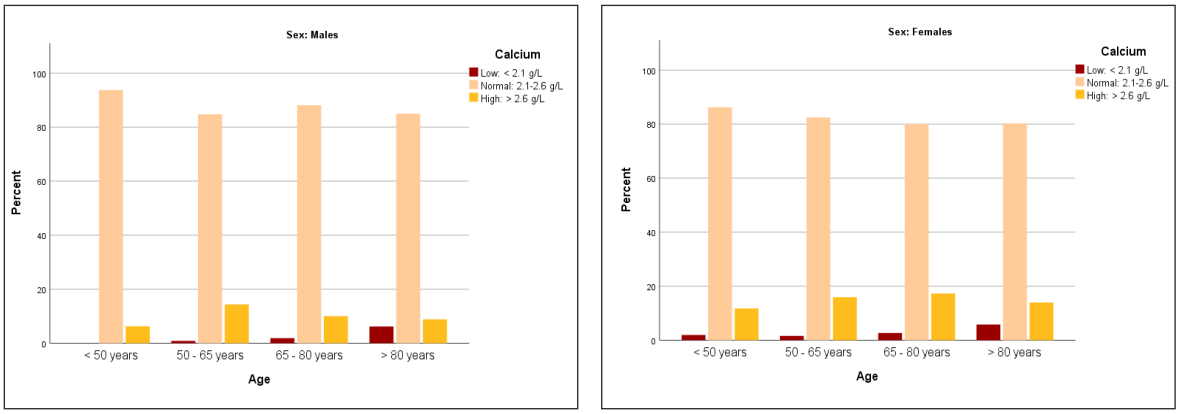
Figure 7.11: Percentage of NICOLA participants with low / normal / high serum levels of alkaline phosphatase, by age group and sex.



Calcium

Serum levels of calcium were normal in over 80% of the NICOLA participants, across ages and gender (Figure 7.12). Median level of serum calcium was 2.4 g/L.

Figure 7.12: Percentage of NICOLA participants with low / normal / high serum levels of calcium, by age group and sex.



7.5 Hormonal Biomarkers

Neoplasms, with a worldwide prevalence of 100.5 million (1.4% of total burden of disease) and an incidence of 24.4 million in 2017, represents one of the major concerns in public health, being responsible of 17.1% of all global deaths (9.6 million) in the same year (1,2).

SHBG is a glycated homo-dimeric plasma transport glycoprotein produced by hepatocytes, which binds and controls the levels of sex-hormones within the circulation (25). Its serum concentration is an indicator of the metabolic clearance of sex steroids and their access to target tissues. Serum SHBG levels have been significantly associated with increased risk of breast and prostate cancer, polycystic ovary syndrome (26), osteoporosis, obesity and metabolic syndrome (27).

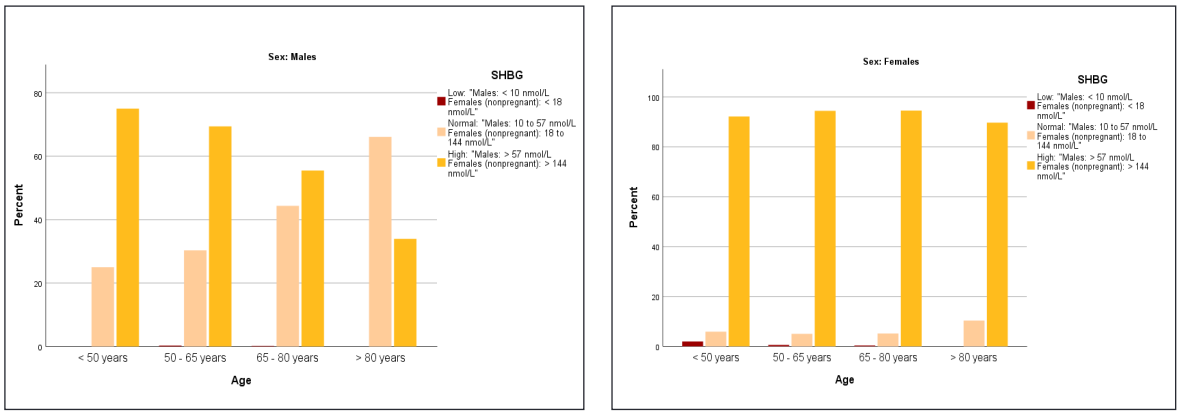
Testosterone, the major androgenic steroid hormone, is responsible for the development of secondary sexual characteristics in men. Most of the circulating testosterone is bound to the carrier protein SHBG. In women, high levels of testosterone in serum are associated with polycystic ovaries, ovarian cancer (28), adrenal tumours (29) and adrenal hyperplasia (27).

Oestradiol is a steroid hormone secreted mainly by the ovaries, although small amounts are produced by the adrenals and testis, hence present at low concentrations both in men and in post-menopausal women. Pathologically high values have been associated with neoplasms such as ovarian tumours (30), adrenal tumours (29) and testicular tumours (31), but also with other non-oncological conditions.

SHBG

Serum levels of SHBG in men were 50.3 nmol/L versus 67.9 nmol/L in women. In men, levels of SHBG gradually increased with age, from 43.4 nmol/L in men under 50 years to 66.3 nmol/L in men over 80 years (Figure 7.13).

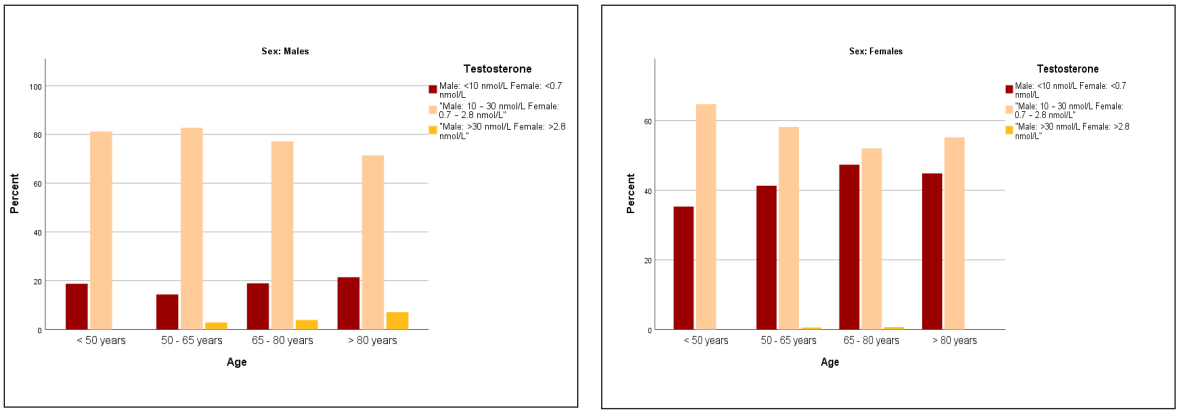
Figure 7.13: Percentage of NICOLA participants with low / normal / high serum levels of sex hormone-binding globulin, by age group and sex.



Testosterone

Testosterone levels in participants were normal in over 70% of men and 55% of women (Figure 7.14). Men had median serum levels of testosterone of 15.4 nmol/L, versus 0.75 nmol/L in women.

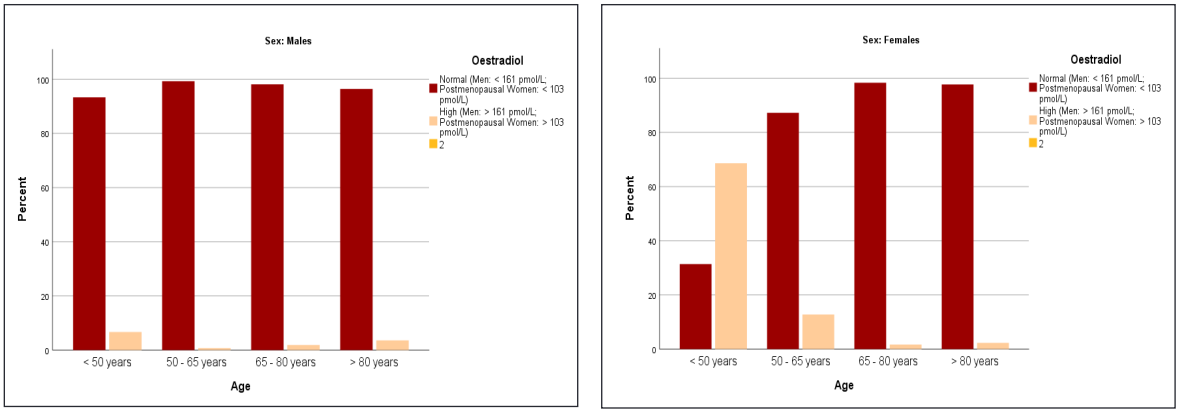
Figure 7.14: Percentage of NICOLA participants with low / normal / high serum levels of testosterone, by age group and sex.



Oestradiol

The majority of men in NICOLA had normal levels of serum oestradiol, across all ages, with a median value of 18 pg/mL (66 pmol/L) (Figure 7.). Women under 50 years showed mostly pre-menopausal levels (47.0 pg/mL or 172 pmol/L) versus post-menopausal levels over 50 years old, stabilised in a median of 10 pg/mL (37 pmol/L) (Figure 7.15).

Figure 7.15: Percentage of NICOLA participants with low / normal / high serum levels of oestradiol, by age group and sex.



7.6 Renal Biomarkers

Chronic kidney disease (CKD) has a prevalence up to 17.3% in adult European populations (32), and is a global public health problem (33) and a leading cause of death (1). Globally, approximately 697.5 million people had CKD in 2017, and 19.7 million were newly diagnosed. Annually, 11.2 million people die from CKD, which

represents 2.2% of all global deaths (1,2). The worldwide prevalence of individuals with CKD is steadily increasing (2), being predicted to become the fifth leading cause of death worldwide by 2040 (34).

The 2012 Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline developed by the Kidney Disease Outcomes Quality Initiative (KDOQI) of the National Kidney Foundation (NKF), recommends the use of estimated glomerular filtration rate (eGFR) in the evaluation, classification, and stratification of CKD (35). The most widely used eGFR equation, recommended by the KDOQI guidelines for initial assessment of kidney function (36), is based on serum creatinine, taking account of sociodemographic variables (age, gender and ethnicity). A second equation, based on the measurement of serum cystatin C (36), offers an alternative to the serum creatinine equation in situations where the latter is less accurate, such as in elderly individuals with low muscle mass and in those with extreme body mass index values (37).

Total protein in serum represents a combination of serum albumin (≈60%) and □ 1, □2, □ and □ globulins (≈40%). Increased levels of total protein may be an indicator of dehydration but also of disorders that course with abnormally high production of protein, like inflammatory or oncologic conditions. Decreased levels of serum total protein are makers of conditions that interfere with production of albumin or globulin proteins, such as malnutrition or severe liver disease; increase the breakdown or loss of protein, such as kidney disease (nephrotic syndrome) or increase or expand the volume of plasma, such as congestive heart failure.

Urea, formed in the liver, is the nitrogen-containing end product of protein metabolism and the urea cycle. The kidneys eliminate about 85% of urea whereas the rest is excreted via the gastrointestinal tract. Although increased serum urea is usually an indicator of conditions where renal clearance decreases, like acute and chronic kidney disease, it may also increase in other conditions not related to renal diseases such as upper gastrointestinal bleeding, dehydration, catabolic states, and high protein diets. Low-protein diets and severe liver disease may lead to decreased urea concentrations in serum. Despite serum creatinine being a more accurate assessment of renal function, urea is usually increased earlier in kidney disease.

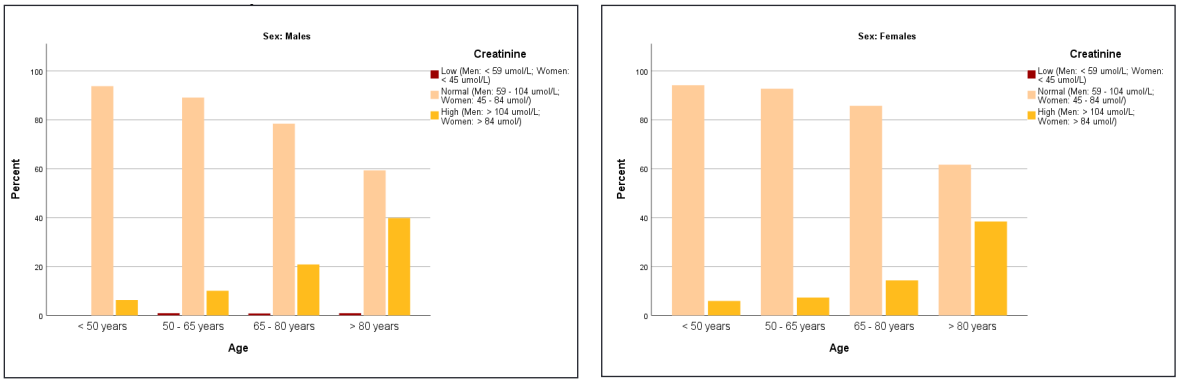
Hyperphosphatemia is associated with significant pathophysiology in CKD, which could contribute to increased mortality (38). Systemic oxidative stress associated with the dysregulation of iron and phosphate is a critical determinant of morbidity and mortality in CKD patients, especially those with concomitant CVD (39). High phosphate levels have been associated with an increased risk for infection in dialysis patients (40).

Hyperuricemia, defined by high concentration of serum urate, is common in people with CKD and is associated with adverse cardiovascular outcomes and progression of CKD (41–44).

Creatinine

Creatinine is the most commonly used endogenous marker for assessment of glomerular function. Serum creatinine levels were within normal range (50 – 120 µmol/L) in over 90% of NICOLA participants across all age groups and sex (Figure 7.16). Median value for serum creatinine was 73.4 µmol/L.

Figure 7.16: Percentage of NICOLA participants with low / normal / high serum levels of creatinine, by age group and sex.

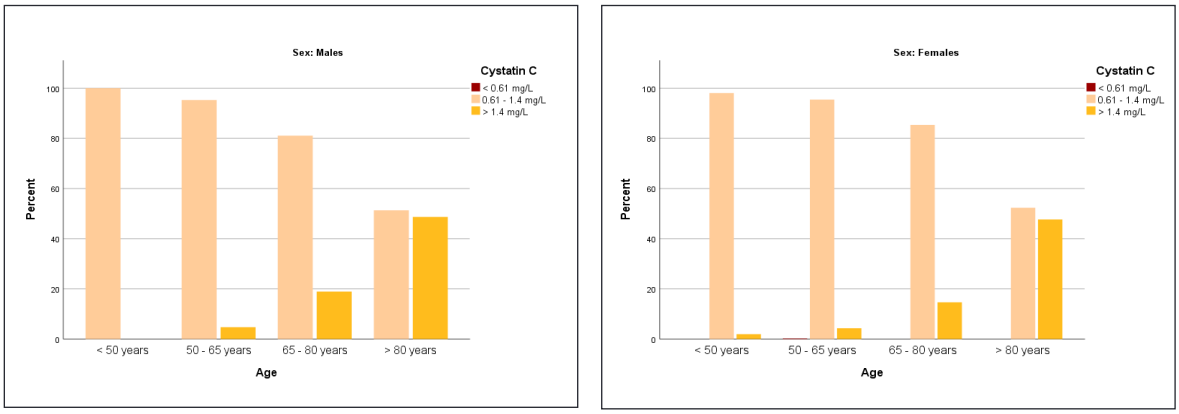


Cystatin C

Cystatin C is a low-molecular-weight protein formed at a constant rate and freely filtered by the kidneys, which functions as a protease inhibitor and is produced by all nucleated cells in the body.

Serum levels of cystatin C steadily increased with age in both men and women, with the majority of those aged 80 years and above having high levels (1 mg/L) (Figure 7.17). Median values in men increased from 1.03 (< 50 years) to 1.40 mg/L (> 80 years) and from 0.91 (< 50 years) to 1.40 mg/L (> 80 years) in women.

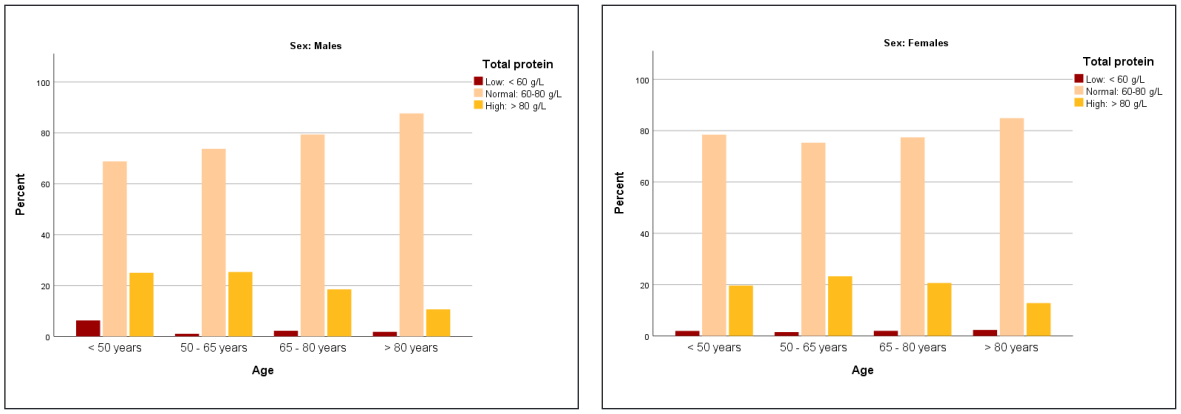
Figure 7.17: Percentage of NICOLA participants with low / normal / high serum levels of cystatin C, by age group and sex.



Total protein

The median serum levels of total protein in the NICOLA participants was 74.9 g/L, with around 80% of them within normal levels (60 - 80 g/L) (Figure 7.18).

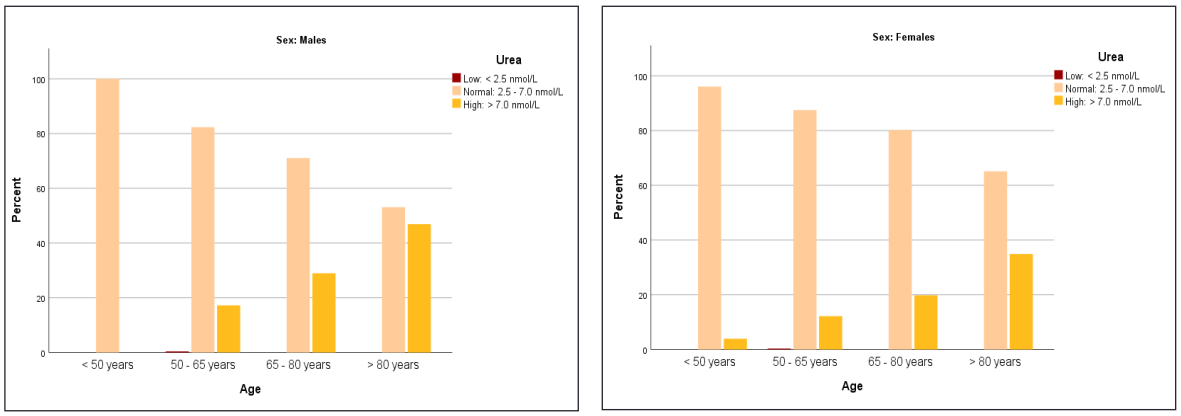
Figure 7.18: Percentage of NICOLA participants with low / normal / high serum levels of total protein, by age group and sex.



Urea

The percentage of NICOLA participants who had serum urea within normal levels (2.5 - 7.0 nmol/L) decreased with age in both men and women from 100% to ≈60% (Figure 7.19). The median values in men increased from 5.13 (< 50 years) to 6.80 mg/L (> 80 years) and from 4.47 nmol/L (< 50 years) to 6.35 nmol/L (> 80 years) in women.

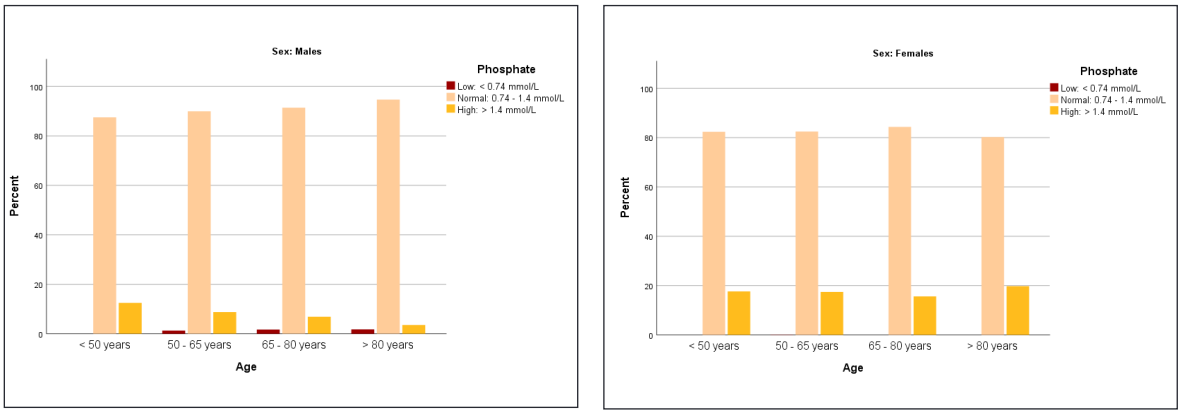
Figure 7.19: Percentage of NICOLA participants with low / normal / high serum levels of urea, by age group and sex.



Phosphate

Over 80% of NICOLA participants had serum levels of phosphate within the normal range (0.74 - 1.4 mmol/L) (Figure 7.20). The median levels were 1.2 mmol/L.

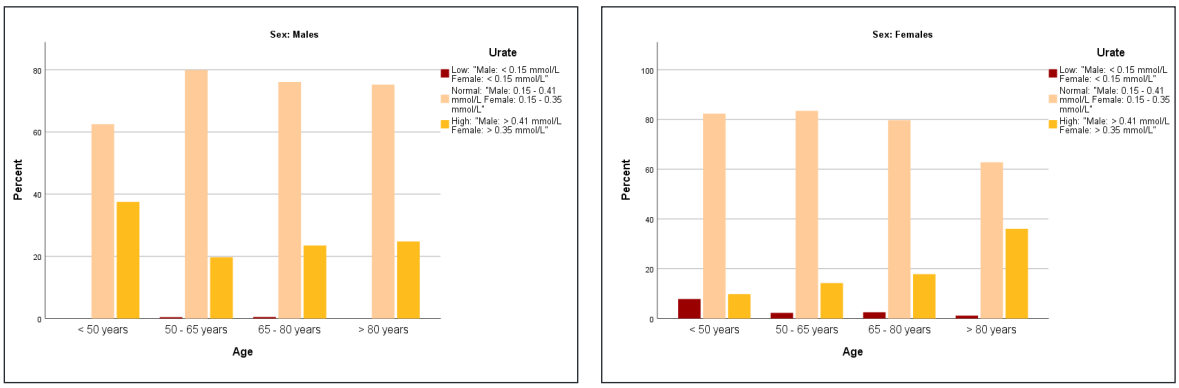
Figure 7.20: Percentage of NICOLA participants with low / normal / high serum levels of phosphate, by age group and sex.



Urate

Between 60 - 80% of men and women in the NICOLA cohort had serum urate levels within the normal range, with a median value of 0.307 mmol/L (Figure 7.21).

Figure 7.21: Percentage of NICOLA participants with low / normal / high serum levels of urate, by age group and sex.



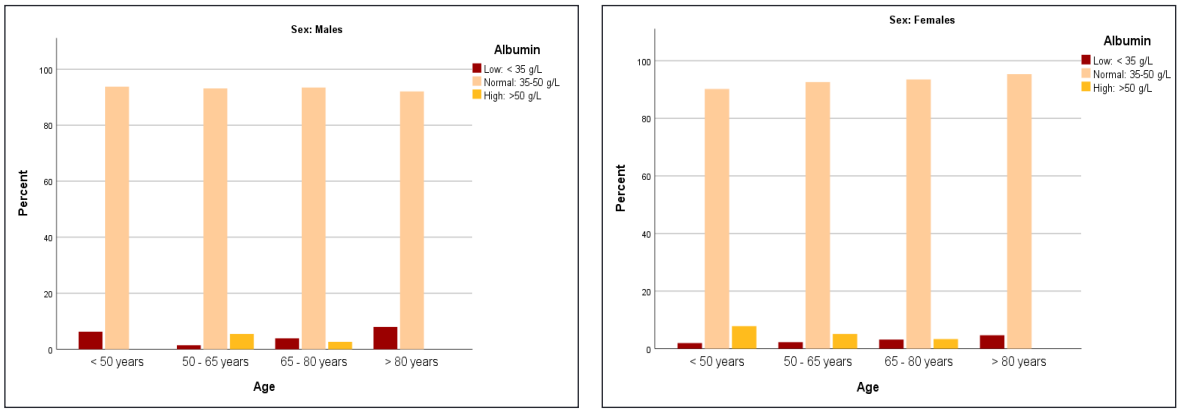
7.7 Liver Biomarkers

Approximately 1500.6 million people were living with cirrhosis and other chronic liver diseases in 2017, 5.2 million new cases were diagnosed and 1.3 million died from the disease, which represents 2.4% of all global deaths (1,2). Human serum albumin accounts for 50% of the plasma proteins, involved in the transport of various metal cations such as copper and zinc as well as poorly water-soluble molecules such as cholesterol, bilirubin, and thyroxine. Lower levels of albumin in serum have been associated with liver disease (45).

Albumin

Most of the NICOLA participants had serum albumin levels within the normal range (35 - 50 g/L) regardless of age and sex, with a median value of 42.6 g/L (Figure 7.22).

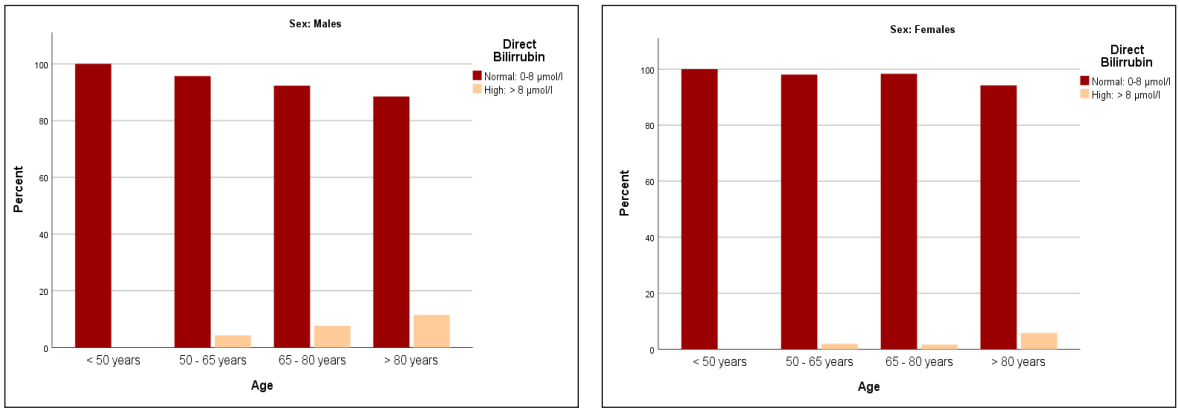
Figure 7.22: Percentage of NICOLA participants with low / normal / high serum levels of albumin, by age group and sex.



Direct Bilirubin

Most of the NICOLA participants showed normal levels of direct bilirubin (0 - 8 µmol/L), with median levels of 3.53 µmol/L (Figure 7.23).

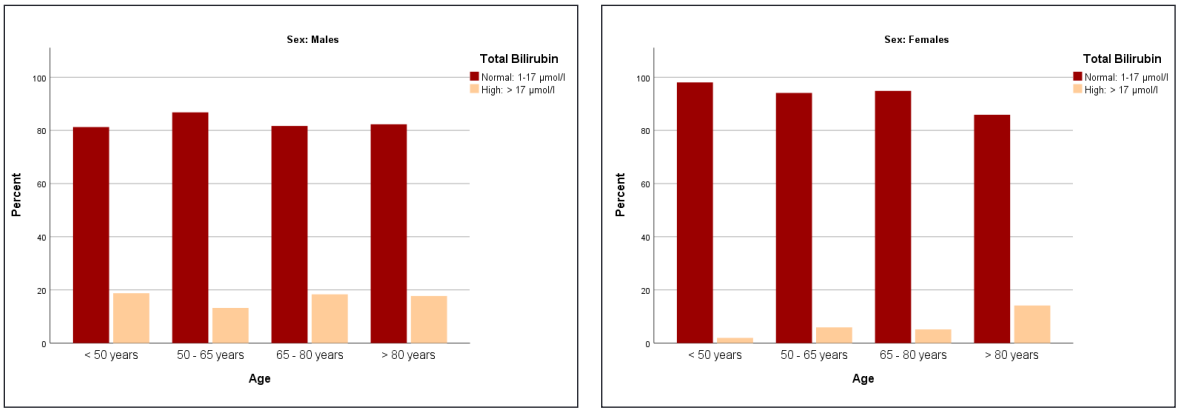
Figure 7.23: Percentage of NICOLA participants with serum levels of direct bilirubin, above / below 8 µmol/L, by age group and sex.



Total Bilirubin

Over 80% of men and almost all women in the NICOLA cohort had serum total bilirubin levels within the normal range (1 - 17 µmol/L) (Figure 7.24) (47). The median levels in men were 10.94 µmol/L and 8.39 µmol/L in women.

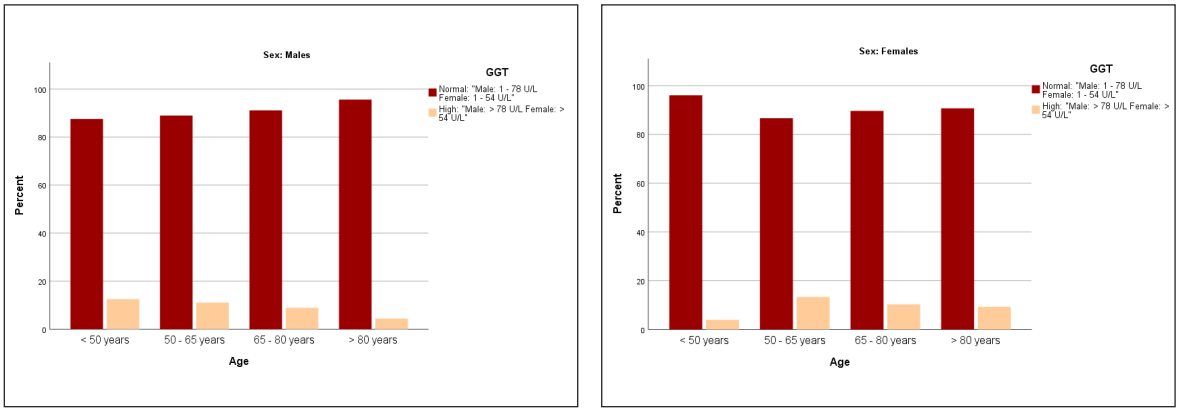
Figure 7.24: Percentage of NICOLA participants with serum levels of total bilirubin, above / below 17 µmol/L, by age group and sex.



Gamma Glutamyltransferase

Between 80 – 100% of NICOLA participants had normal levels of GGT regardless of sex or age (Figure 7.25). Women had a median GGT of 23.6 U/L versus 31.3 U/L in men.

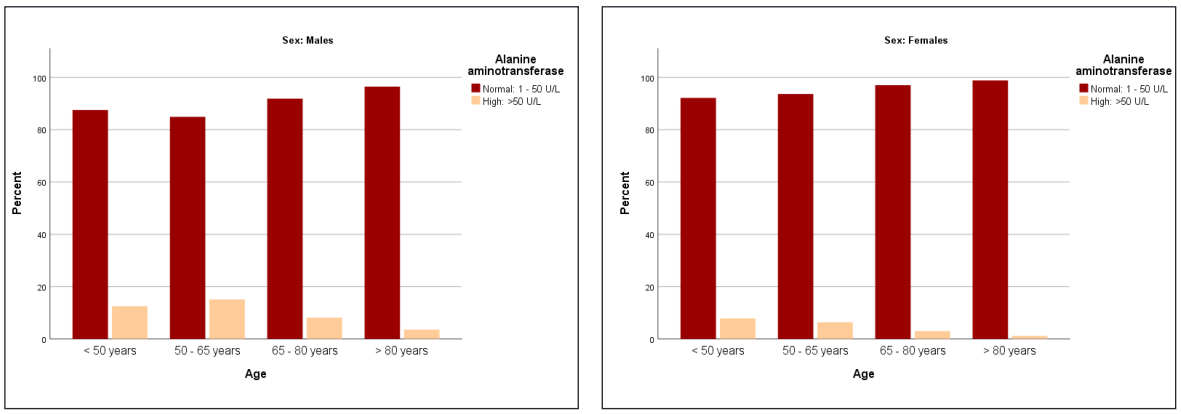
Figure 7.25: Percentage of NICOLA participants with serum levels of gamma glutamyltransferase (GGT), above / below 78 U/L (men) and 54 U/L (women), by age group and sex.



Alanine aminotransferase

Over 80% of NICOLA participants showed normal levels of serum ALT activity, with a median value of 25 U/L (Figure 7.26).

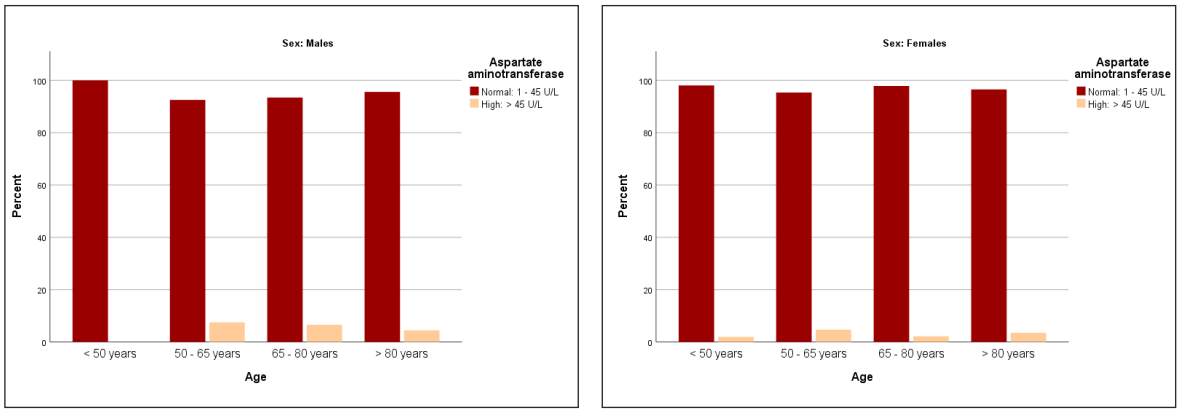
Figure 7.26: Percentage of NICOLA participants with serum levels of alanine aminotransferase, above / below 50 U/L, by age group and sex.



Aspartate aminotransferase

The activity of the AST enzyme in serum was normal (1 - 45 U/L) in the majority of the NICOLA participants with a median value of 27 U/L (Figure 7.27).

Figure 7.27: Percentage of NICOLA participants with serum levels of aspartate aminotransferase, above / below 45 U/L, by age group and sex.



7.8 Derived clinical variables based on biochemistry data

The eGFR equations derived for serum creatinine, cystatin C and the combined formula, along with CKD, CKD stage and ESRD variables, described in the 7.6 Renal Biomarkers section were calculated by Dr Marisa Cañadas-Garre and Dr Laura Smyth within the QUB Molecular Epidemiology and Public Health research team, funded by the Science Foundation Ireland-Department for the Economy (SFI-DfE) Investigator Program Partnership Award (15/IA/3152) and the Economic and Social Research Council (ES/L008459/1). All equations are based on those defined by the KDIGO2021 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. The values of the eGFR equation based on serum creatinine, serum cystatin C and both serum creatinine and cystatin C are presented in Table 7.2. Both men and women aged under 80 years old in the NICOLA cohort had eGFR in the normal range (over 60 mL/min/1.73m2) (35).

Table 7.2: Estimated glomerular filtration ratio, based on serum creatinine, cystatin C or both, according to the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation, by age and sex. Units in mL/min/1.73m2.

Equation	Age (yrs)	Males	Females
		Median [IQR]	Median [IQR]
$eGFR^{EPI}_{Creatinine}$	< 50	102.1 [94.4-106.0]	95.5 [87.2-103.5]
	50 - 65	91.4 [78.2-98.3]	87.1 [78.9-94.8]
	65 - 80	79.0 [64.8-89.1]	77.2 [68.2-85.6]
	> 80	64.3 [51.0-77.6]	63.8 [46.8-74.5]
$eGFR^{EPI}_{CystatinC}$	< 50	78.4 [66.1-92.8]	86.1 [77.8-93.7]
	50 - 65	73.7 [64.6-84.3]	74.8 [63.6-85.6]
	65 - 80	59.5 [50.3-70.5]	60.1 [49.9-70.3]
	> 80	45.3 [36.9-53.2]	43.0 [33.3-54.1]
$eGFR^{EPI}_{CreatinineCystatinC}$	< 50	87.2 [80.4-99.7]	90.9 [82.3-97.3]
	50 - 65	81.4 [72.1-89.8]	79.7 [69.9-88.6]
	65 - 80	68.8 [58.4-78.8]	67.4 [58.6-76.1]
	> 80	53.3 [44.1-64.0]	51.7 [39.9-61.8]

Abbreviations: eGFR: estimated glomerular filtration rate, according to the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation.

Values are presented as median [interquartile range]

CKD

Among the NICOLA participants, 13% of men (n = 194) and 10% of women (n = 159) had CKD, defined as eGFREPI < 60 mL/min/1.73m2, according to the KDIGO guidelines (35).

CKD Stage

The KDIGO guidelines establish the classification for the staging of CKD according to the eGFREPI (35). The distribution of the NICOLA participants according to their CKD stage are presented in Table 7.3.

Table 7.3: Stages of Chronic Kidney Disease (CKD) in the NICOLA participants

Stage	Definition	Males	Females	Total
		n (%)	n (%)	n (%)
G1	eGFR ≥ 90 mL/min/1.73m2	517 (35.3)	450 (27.8)	967 (31.4)
G2	90 > eGFR ≥ 60 mL/min/1.73m2	753 (51.4)	1007 (62.3)	1760 (57.1)
G3a	60 > eGFR ≥ 45 mL/min/1.73m2	142 (9.7)	116 (7.2)	258 (8.4)
G3b	40 > eGFR ≥ 30 mL/min/1.73m2	42 (2.9)	36 (2.2)	78 (2.5)
G4	30 > eGFR ≥ 15 mL/min/1.73m2	8 (0.5)	6 (0.4)	14 (0.5)
G5	eGFR < 15 mL/min/1.73m2	2 (0.1)	1 (0.1)	3 (0.1)

Abbreviations: eGFR: estimated glomerular filtration rate, according to the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation; n: number.

Values presented are unweighted.

ESRD

Only two men (n = 2; 0.1%) and one woman (n = 1; 0.1%) from the NICOLA cohort had ESRD according to the KDIGO definition (eGFREPI < 15 mL/min/1.73m^2) (35).

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8 Molecular Biomarkers

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Key Findings

- NICOLA has a strong focus on molecular biomarkers so there is complementary genetic, epigenetic and transcriptomic data available for a subset of individuals.
- We inherit much of our DNA from our parents while a small amount of this material changes as we get older. In NICOLA we have 551,839 directly genotyped and 18,148,478 imputed Single Nucleotide Polymorphisms (SNPs) currently available for 2969 participants.
- Summary statistics for the association of these gene polymorphisms with ~30 phenotypes were generated.
- Epigenetics provides a link between our inherited DNA and environmental influences from a person's diet, medication and lifestyle. NICOLA has the epigenetic quality controlled profiles of 1984 individuals arising from variations in DNA methylation at 862,927 genetic sites.
- Transcriptomics (i.e. measures of the expression of genes) may help explain how genetic and epigenetic changes lead to disease, and we have complementary gene expression data for a subset of individuals. Reference data for men and women at different ages has been generated, enabling the cohort to contribute to international collaborations focussing on a range of conditions including renal and eye disease.

8.1 Introduction

Multiple biomarker studies have been performed using this early baseline data with biological material safely stored for future molecular biomarker studies (Table 8.1). This chapter presents the findings from the molecular analysis of the samples and is divided into several complementary sections - Genetic biomarkers, Epigenetic biomarkers, and Transcriptomic biomarkers. The chapter describes the genotyping and quality control (QC) procedures applied to the genotype data in the first two batches of the NICOLA data release, which contains 3,266 unique samples genotyped at 551,839 single nucleotide polymorphisms (SNPs). We also describe characteristics of the generated genotype data, both in terms of content and quality. This document is relevant to researchers accessing and using the genotype data available in the NICOLA resource.

Table 8.1: Overview of genetic, epigenetic and transcriptomic biomarkers and derived phenotypes currently available in the NICOLA cohort.

Biomarker	Derived variables
Infinium CoreExome-24 Array	Imputation to the 1KGP3 reference panel Imputation to the HRC reference panel Clinically actionable variants
	Annotated and Filtered VCF files (Batches 1 & 2; 1KGP3 & HRC Panels): VCF files with only polymorphic variants Lists of monomorphic variants after imputation Quality Control information of the imputation process VCF files with polymorphic variants annotated with RS VCF files with polymorphic variants with R2>0.3 VCF files with polymorphic variants with R2>0.3 and MAC≥5 VCF files with polymorphic variants with R2>0.3 and MAC≥5 annotated with RS and gene
	Kinships for relatedness in association analysis: Kinship matrix for autosomes, 1KGP3 reference panel Kinship matrix for chrX, 1KGP3 reference panel Kinship matrix for autosomes, HRC reference panel Kinship matrix for chrX, HRC reference panel
	Software specific files (Batches 1 & 2; 1KGP3 & HRC Panels): Concatenated VCF files with polymorphic variants for kinship generation Concatenated VCF files with polymorphic variants and duplicated SNPs removed for clumping pgen files for input in PLINK 2.00 alpha

	Individual Genome-Wide Association Summary statistics for: Total cholesterol HDL-cholesterol LDL-cholesterol Non-HDL cholesterol Triglycerides Height Body mass index Waist-to-hip ratio Early age-related macular degeneration eGFR Serum creatinine Chronic kidney disease Serum urea Subretinal drusenoid deposits (reticular pseudodrusen) Subretinal drusenoid deposits (reticular colour) Macular pigment: peak height Macular pigment: peak volume Naevi Arterial calibre Venular calibre Arteriovenous ratio Arteriolar fractal dimension Venular fractal dimension Arteriolar tortuosity Venular tortuosity
	Lists of dosage information on SNPs provided for candidate SNPs and Genetic Risk Score projects: 55 SNPs previously associated with age-related macular degeneration 64 SNPs previously associated with arsenic levels
	Genome-Wide Association Meta-Analysis Summary statistics for: Subretinal drusenoid deposits (reticular pseudodrusen) Subretinal drusenoid deposits (reticular colour) Macular pigment: peak height Macular pigment: peak volume Naevi Arterial calibre Venular calibre Arteriovenous ratio Arteriolar fractal dimension Venular fractal dimension Arteriolar tortuosity Venular tortuosity

	Beta values (□)
	M values
	Proportional cell counts
	Epigenetic clocks
	Summary statistics for: Alcohol consumption Body-mass index Education level eGFR Naevi Physical activity Risk preference Serum urate Smoking Socioeconomic status Subretinal drusenoid deposits (reticular pseudodrusen) Subretinal drusenoid deposits (reticular colour) Time preference
	Gene expression counts
	Summary statistics for: Renal phenotypes
Abbreviations: 1KGP3: 1000 Genomes Phase3 v5; chr: chromosome; eGFR: estimated glomerular filtration ratio; HDL: High-density lipoproteins; HRC: Haplotype Reference Consortium; LDL: Low-density lipoproteins; VCF: Variant Call Format.	

8.2 Measurement of molecular biomarkers

Blood samples were collected from participants in EDTA tubes and processed within Belfast City Hospital to separate plasma and buffy coats. DNA was extracted from buffy coats with DNA quantified using PicoGreen and normalised to 200 ng/uL aliquots with 0.1 TE in 2D and readable barcode tubes. DNA was stored in multiple aliquots at -80°C to minimise freeze/thaw cycles and maximise the utility of high molecular weight DNA for molecular studies.

Samples were genotyped by Eurofins Scientific (Eurofins Genomics: https://www.eurofinsgenomics.eu). Genotype data (n = 551,839 markers directly typed) was generated using the Illumina Infinium CoreExome-24 for high-throughput screening on an iScan for two batches composed of 2799 and 467 participants respectively. For the purposes of analysis, each batch was processed separately. GenomeStudio® Genotyping Module was used as calling algorithm, using the Genome Reference Consortium Human Build 37 (GRCh37). Each SNP is analysed independently to identify genotypes. Seven control individuals, blinded to the genotyping lab, were included for internal QC. The Infinium CoreExome-24 BeadChip is a customizable

array designed to be used in large-scale genotyping studies which includes all the tag (SNPs) found on the Infinium Core-24 BeadChip, plus over 240,000 markers from the Infinium HumanExome BeadChip (1). The Infinium CoreExome-24 BeadChip can be used to obtain baseline sample data sets for various downstream applications quickly and easily. These applications include common variant, mitochondrial DNA (mtDNA), ancestry, sex confirmation, loss of-variant, and insertion/deletion (indel) detection studies.

Quality Control and Imputation

QC of the genotyped data was performed in PLINK 1.90 beta (2). QC included removal of samples with a call rate < 95%, heterozygosity (> median + 3 x interquartile range) and principal component (PC) analysis outliers; gender mismatches and duplicates or up to second-degree related individuals were also removed, by eliminating one individual from each pair with an Identity By Descent (IBD) value > 0.1875, which is halfway between the expected IBD for third- and second-degree relatives (3,4). Variants with a call rate ≥ 98%, Hardy-Weinberg equilibrium p>10-6 and Minor Allele Frequency (MAF) < 0.0001 were removed.

Files were prepared for imputation using the "HRC/1KG Imputation Preparation and Checking Tool", developed by Will Rayner (5), and then imputed to the 1000 Genomes Phase3 v5 (1KGP3) and Haplotype Reference Consortium (HRC) r1.1 2016 reference panels using the Michigan Imputation Server (6). A minor allele cut-off of 5 and imputation quality of 0.3 was applied to imputed files; monomorphic markers were removed.

Two empirical genomic relationship matrices (kinship matrix), one for the set of autosomes and one for the hemizygous region of X chromosome, were generated using rvtests, for each reference panel (7). Kinship matrices are used in association analyses to account for familial relatedness, cryptic relatedness, and population stratification. The matrices were created using the imputed VCF files after removing monomorphic markers.

Quality Control of directly genotyped SNPs

The NICOLA batch 1 consisted of 2799 individuals and batch 2 was composed of 467 individuals, after filtering by a minimum 94% sample call rate as a pre-QC control step in GenomeStudio. After QC, 2560 samples (352,061 SNPs) for batch 1 and 402 (307,743 SNPs) for batch 2 passed filters (Table 8.2).

Table 8.2: Genotyping Quality Control exclusions for NICOLA batches 1 and 2

	NICOLA Batch	
QC Step	**1**	**2**
Individuals (n)	**2799**	**467**
Sex Discordance	9	16
Sample Call Rate < 95%	63	11
Exclusion of heterozygosity > median ± 3 x IQR	73	34
Related Individuals (IBD < 0.185)	78	
Ancestry Outliers	21	
Final	**2560**	**402**
SNPs	**551,839**	**551,839**
Hardy-Weinberg Equilibrium p > 10-6	797	94
SNP Call Rate ≥ 98%	22,633	33,101
Minor Allele Frequency < 0.00001	176,210	210,793
No chromosome designation	138	108
Final	**352,061**	**307,743**
Abbreviations: IBD: Identity By Descent. IQR: interquartile range. SNP: single nucleotide Polymorphism		

Imputation

The number and nature of variants after imputation to the reference panels and removal of monomorphic markers in the imputed datasets are detailed in Table 8.3. These are the variants used to construct the kinship matrices to be used in association analysis to account for cryptic relatedness.

Table 8.3: Number and nature of polymorphic variants in autosomes and X chromosome after imputation to reference panels used to construct the kinship matrices. *Others refers to a variation of any other type, for example a symbolic allele or a complex substitution.

	NICOLA Batch			
	1		**2**	
Reference Panel	**1KGP3**	**HRC**	**1KGP3**	**HRC**
number of samples	2,567	2,567	402	402
number of SNPs	16,083,011	18,148,478	12,313,319	12,860,489
number of indels	1,747,078	0	1,453,645	0
number of others*	14,804	0	11,124	0
Total	**17,844,893**	**18,148,478**	**13,778,088**	**12,860,489**
Abbreviations: SNP: single nucleotide Polymorphism. 1KGP3: 1000G Phase3 Reference Panel. HRC: Haplotype Reference Consortium				

After applying QC filters for quality of imputation and minor allele count, the total number of SNPs for the 1KGP3 panel are detailed on Table 8.4. These are the variants used for association analyses.

Table 8.4: Number and nature of polymorphic variants in autosomes and X chromosome after filtering by quality of imputation (R2 > 0.3) and minor allele count ≥ 5 to reference panels to be used in association analyses. *Others refers to a variation of any other type, for example a symbolic allele or a complex substitution.

	NICOLA Batch			
	1		2	
Reference Panel	**1KGP3**	**HRC**	**1KGP3**	**HRC**
number of samples	2,567	2,567	402	402
number of SNPs	11,168,920	11,955,381	8,866,368	8,629,476
number of indels	1,325,292	0	1,159,263	0
number of others*	9,348	0	7,265	0
Total	**12,503,560**	**11,955,381**	**10,032,896**	**8,629,476**

Abbreviations: SNP: single nucleotide Polymorphism. 1KGP3: 1000G Phase3 Reference Panel. HRC: Haplotype Reference Consortium

Derived variables

To enhance NICOLA's bioresource, the majority of derived variables have been returned to the main dataset and are available for researchers within our data access agreements.

Imputation dosages

Imputation from directly genotyped SNPs was conducted using the Michigan Imputation Server for the 1000 Genomes Phase3 v5 (1KGP3) and Haplotype Reference Consortium (HRC) r1.1 2016 reference panels.

Kinship Matrices

Four kinship matrices (two sets, one for each reference panel, composed of one kinship for the autosomes and one for the hemizygous region of X chromosome) (Table 8.5) were created to be used to account for relatedness in association analyses (7).

Annotated and Filtered VCF files

Different sets of VCF files, containing the genotyped and imputed SNPs, filtered according to quality parameters (polymorphic variants; R2 > 0.3; minor allele count ≥ 5, see Table 8.5) and annotated with RS information of SNPs and gene information added have been created to be used in subsequent association analysis. Lists of monomorphic variants were also created.

Software specific files

The VCF files containing the genotyped and imputed SNPs have been converted into formats to work with software specific for genome-wide association studies (Table 8.5), such as concatenated VCF files for kinship calculations and generation using rvtests (8), concatenated VCF files with duplicated SNPs removed to be used for clumping with PLINK 1.90 beta and pgen files for input in PLINK 2.00 alpha (2,9).

Summative data

The projects undertaken with the genotyped and imputed biomarkers of NICOLA Batches 1 & 2 have generated summary statistics for their genome-wide association analysis with different phenotypes, detailed in Table 8.5. Summary statistics for genome-wide association meta-analysis for different phenotypes have also been generated (Table 8.5).

Table 8.5: Summary statistics generated for the genome-wide association analysis of the genotyped and imputed biomarkers of NICOLA Wave 1.

Trait	Units	Transformation	Sub-cohort	Genotyping Batch	Chr	Reference Panel	Analysis	Covariates	Lead Consortia	NICOLA Contact	Analyst
Total cholesterol	mg/dL	raw	All Men Women	1	chr1-chr22 chrX	1KGP3 HRC	Linear regression	Age Age^2 Sex (only in 'All') 4 first PCs	GLGC	AJM	MCG LJS
		inverse normal		1		1KGP3 HRC			GLGC	AJM	MCG LJS
HDL-cholesterol	mg/dL	raw	All Men Women	1	chr1-chr22 chrX	1KGP3 HRC	Linear regression	Age Age^2 Sex (only in 'All') 4 first PCs	GLGC	AJM	MCG LJS
		inverse normal		1		1KGP3 HRC			GLGC	AJM	MCG LJS
LDL-cholesterol	mg/dL	raw	All Men Women	1	chr1-chr22 chrX	1KGP3 HRC	Linear regression	Age Age^2 Sex (only in 'All') 4 first PCs	GLGC	AJM	MCG LJS
		inverse normal		1		1KGP3 HRC			GLGC	AJM	MCG LJS
Non-HDL cholesterol	mg/dL	raw	All Men Women	1	chr1-chr22 chrX	1KGP3 HRC	Linear regression	Age Age^2 Sex (only in 'All') 4 first PCs	GLGC	AJM	MCG LJS
		inverse normal		1		1KGP3 HRC			GLGC	AJM	MCG LJS
Triglycerides	mg/dL	natural log	All Men Women	1	chr1-chr22 chrX	1KGP3 HRC	Linear regression	Age Age^2 Sex (only in 'All') 4 first PCs	GLGC	AJM	MCG LJS
		natural log inverse normal		1		1KGP3 HRC			GLGC	AJM	MCG LJS

Trait	Units	Transformation	Sub-cohort	Genotyping Batch	Chr	Reference Panel	Analysis	Covariates	Lead Consortia	NICOLA Contact	Analyst
Height	cm	raw	All Men	1	chr1-chr22	1KGP3 HRC	Linear regression	Age 4 first PCs	GIANT	AJM	MCG LJS
Body mass Index	kg/m2	raw inverse normal	Women	1	chrX	1KGP3 HRC		Age Age^2 4 first PCs	GIANT	AJM	MCG LJS
Waist-to-hip ratio		raw unadjusted inverse normal	All Men Women	1	chr1-chr22 chrX	1KGP3 HRC	Linear regression	Age Age^2 4 first PCs	GIANT	AJM	MCG LJS
		adjusted by BMI inverse normal		1		1KGP3 HRC		Age Age^2 4 first PCs BMI	GIANT	AJM	MCG LJS
Early age-related macular degeneration	Yes / No	-	All	1	chr1-chr22	1KGP3	Logistic Regressio	Age 2 first PCs	IAMDGC	RH/ AJM	MCG
eGFR	mL/min/1.73m2	natural log inverse normal	All	1/2	chr1-chr22 chrX	1KGP3 HRC	Linear regression	Age Sex 10 first PCs		AJM	MCG LJS
Serum Creatinine	mg/dL	natural log inverse normal	All	1/2	chr1-chr22 chrX	1KGP3 HRC	Linear regression	Age Sex 10 first PCs		AJM	MCG LJS

Trait	Units	Transformation	Sub-cohort	Genotyping Batch	Chr	Reference Panel	Analysis	Covariates	Lead Consortia	NICOLA Contact	Analyst
Chronic Kidney Diseasn	Yes / No	-	All	1/2	chr1-chr22 chrX	1KGP3 HRC	Logistic Regressio	Age Sex 10 first PCs		AJM	MCG LJS
Serum Urea	mmol/L	raw	All	1/2	Set of 2,527 unique autosomal genes chrMT	1KGP3 HRC	Linear regression	Age Sex		AJM	RC
eGFR	mL/min/1.73m2	natural log inverse normal	All	1/2	Set of 2,527 unique autosomal genes chrMT	1KGP3 HRC	Linear regression	Age Sex		AJM	RC
eGFR	mL/min/1.73m2	natural log quantile-normalized	All	1/2	Set of 2,527 unique autosomal genes chrMT	1KGP3 HRC	Linear regression	Age Sex 10 first PCs		AJM	MCG
Chronic Kidney Disease	Yes / No	-	All	1	Set of 2,527 unique autosomal genes chrMT	1KGP3 HRC	Logistic Regressio	Age Sex 10 first PCs		AJM	MCG

Trait	Units	Transformation	Sub-cohort	Genotyping Batch	Chr	Reference Panel	Analysis	Covariates	Lead Consortia	NICOLA Contact	Analyst
Serum Creatinine	mg/dL	natural log quantile-normalized	All	1	Set of 2,527 unique autosomal genes chrMT	1KGP3 HRC	Linear regression	Age Sex 10 first PCs		AJM	MCG
eGFR	mL/min/1.73m2	natural log quantile-normalized	All	1	mitochondrial haplotypes	-	Linear regression	Age Sex 10 first PCs		AJM	MCG
Serum Creatinine	mg/dL	natural log quantile-normalized	All	1	mitochondrial haplotypes	-	Linear regression	Age Sex 10 first PCs		AJM	MCG
Chronic Kidney Disease	Yes / No	-	All	1	mitochondrial haplotypes	-	Logistic Regressio	Age Sex 10 first PCs		AJM	MCG
eGFR	mL/min/1.73m2	natural log inverse normal	Men	1/2	chrY	-	Linear regression	Age Sex 10 first PCs		AJM	KA/ MCG
Serum Creatinine	mg/dL	natural log inverse normal	Men	1/2	chrY	-	Logistic Regressio	Age 10 first PCs		AJM	KA/ MCG
Chronic Kidney Disease	Yes / No	-	Men	1/2	mitochondrial haplotypes	-	Logistic Regressio	Age 10 first PCs		AJM	MCG

Trait	Units	Transformation	Sub-cohort	Genotyping Batch	Chr	Reference Panel	Analysis	Covariates	Lead Consortia	NICOLA Contact	Analyst
SDD - reticular pseudodrusen	Yes / No	-	All	1/2	chr1-chr22 chrX	1KGP3 HRC	Logistic Regressio	Age Age2 4 first PCs		AJM	MCG
SDD - reticular colour	Yes / No	-	All	1/2	chr1-chr22 chrX	1KGP3 HRC	Logistic Regressio	Age Age2 4 first PCs		AJM	MCG
Macular pigment: peak height		natural log quantile-normalized	All	1/2	chr1-chr22 chrX	1KGP3 HRC	Logistic Regressio	Age Age2 4 first PCs		RH/ AJM	MCG
Macular pigment: peak volume		natural log inverse normal	All	1/2	chr1-chr22 chrX	1KGP3 HRC	Logistic Regressio	Age Age2 4 first PCs		RH/ AJM	MCG
Naevi	Yes / No	-	All	1/2	chr1-chr22 chrX	1KGP3 HRC	Logistic Regressio	Age Age2 4 first PCs		RH/ AJM	MCG
Arterial calibre		raw	All	1/2	chr1-chr22 chrX	1KGP3 HRC	Logistic Regressio	Age Sex MABP		GMK/ AJM	MCG
Venular calibre		raw	All	1/2	chr1-chr22 chrX	1KGP3 HRC	Logistic Regressio	Age Sex MABP		GMK/ AJM	MCG
Arteriovenous ratio		raw	All	1/2	chr1-chr22 chrX	1KGP3 HRC	Age Sex 10 first PCs	Age Sex MABP		GMK/ AJM	MCG
Arteriolar fractal dimension		natural log inverse normal	All	1/2	chr1-chr22 chrX	1KGP3 HRC	Age Sex 10 first PCs	Age Sex MABP		GMK/ AJM	MCG

Trait	Units	Transformation	Sub-cohort	Genotyping Batch	Chr	Reference Panel	Analysis	Covariates	Lead Consortia	NICOLA Contact	Analyst
Venular fractal dimension		natural log inverse normal	All	1/2	chr1-chr22 chrX	-1KGP3 HRC	Logistic Regressio	Age Sex MABP		GMK/ AJM	MCG
Arteriolar tortuosity		natural log inverse normal	All	1/2	chr1-chr22 chrX	1KGP3 HRC	Logistic Regressio	Age Sex MABP		GMK/ AJM	MCG
Venular tortuosity		natural log inverse normal	All	1/2	chr1-chr22 chrX	1KGP3 HRC	Logistic Regressio	Age Sex MABP		GMK/ AJM	MCG
Clinically relevant variants		Based on ACMG and pharmacoge-netically active SNPs	All	1/2	chr1-chr22 chrX	1KGP3 HRC	No association performed	-		AJM	CB
		Lists of dosage information on SNPs provided for the analysis of candidate gene polymorphisms or genetic risk scores									
Age-related macular degeneration	-	-	All	1/2	Set of 55 SNPs	-	-			RH/ AJM	MCG
Arsenic Levels	-	-	All	1/2	Set of 64 SNPs	-	-			JW/ AJM	MCG

Abbreviations: 1KGP3: 1000 Genomes Project Phase3 Reference Panel; AJM: Amy Jayne McKnight; CB: Caitlin Bailie; chr: chromosome; eGFR: estimated glomerular filtration ratio; HDL: High-density lipoproteins; HRC: Haplotype Reference Consortium; KA: Kerry Anderson; GMK, Gareth McKay; JW, Jayne Woodside; LDL: Low-density lipoproteins; LJS: Laura Smyth; MCG: Marisa Cañadas-Garre; MT: mitochondrial; PCs: Principal components; RC: Ruaidhri Cappa; RH: Ruth Hogg; SDD: subretinal drusenoid deposits; SNPs: single nucleotide polymorphisms.

8.3 Epigenetic-based biomarkers

This section describes the epigenetic analysis applied to the DNA methylation data generated from Wave 1 NICOLA and the derived variables. This section is relevant to researchers accessing and using the epigenetic data available in the NICOLA resource.

Methods

Blood samples were collected from participants in EDTA tubes and processed within Belfast City Hospital to separate plasma and buffy coats. DNA was extracted from buffy coats with DNA quantified using PicoGreen and normalised to 200 ng/uL aliquots with 0.1 TE in 2D and readable barcode tubes. DNA was stored in multiple aliquots at -80°C to minimise freeze/thaw cycles and maximise the utility of high molecular weight DNA for molecular studies. This is particularly important for epigenetic analysis where the DNA storage methods often have a major impact on DNA methylation levels.

Samples were processed by Eurofins Scientific who extracted the DNA from the buffy coats and quantitated each sample using PicoGreen. The-derived DNA for all individuals was quantitated before a concentration of 800 ng per sample was bisulphite treated (BST) using the EZ DNA Methylation™ Kit (Zymo Research, USA) using the manufacturer's instructions. All samples were analysed together, in the same laboratory.

To assess the methylation status of the CpG sites, the Infinium MethylationEPIC BeadChip array (Illumina, USA) was used following the manufacturer's instructions. This array quantitatively targets 862,927 CpG sites across the genome. Participant samples were randomly distributed across each array. This high throughput platform evaluated individual methylation levels (▯ values) for each CpG site, ranging from 0 for unmethylated to 1 for complete methylation. ▯ values provide a more intuitive biological interpretation. M values are also generated which are more statistically valid for conducting differential methylation analyses (10). For replication purposes, DNA is available for a further independent ~1,500 individuals within the NICOLA cohort. Several significant EWAS associations from microarray data have been validated in-house using bisulfite treated targeted next generation sequencing or Sequenom EpiTYPER.

Quality Control

Raw methylation data was assessed for dye bias and quantile normalised as previously reported (11). Quality control (QC) included evaluation of the bisulphite treatment conversion efficiency, dye specificity, hybridisation, and staining. This was assessed using GenomeStudio v2011 and BeadArray Controls Reporter software platforms (both Illumina). Data was extracted from GenomeStudio using the Partek plugin and analysed using both beta and M values. Alternatively, .idat files were analysed

directly in R packages, paying careful attention to pre-processing and quality control measures if using this approach.

Proportional white cell counts (WCCs) were estimated following the Houseman method (12) using the raw .idat files output from the iScan machine. The minfi Bioconductor (v3.10) package was utilised. Estimation of six WCCs, CD8+ T, CD4+ T and CD19+ B lymphocytes, CD56+ natural killer cells, CD14+ monocytes and CD15+ granulocytes was performed using the estimateCellCounts function.

MethylationEPIC analysis was performed using Partek® Genomics Suite® v7.19.1018 and R (13). Partek® Genomics Suite® was employed to complete Gene Ontology (GO) analysis and pathway enrichment analysis using the Kyoto Encyclopedia of Genes and Genomes (KEGG) database.

Results

In all, 1938 NICOLA participants who consented to DNA methylation analysis passed the QC threshold and were included in downstream analyses (Table 8.6).

Table 8.6: Summary statistics for NICOLA population included in the epigenetic analysis (DNA methylation)

Variable	n (%)
Gender	
Males	952 (49.1)
Females	986 (50.9)
Age group (yrs)	
50 - 59	668 (34.5)
60 - 69	716 (36.9)
70 - 79	423 (21.8)
80 +	131 (6.8)

Proportional WCCs were determined for the whole population (Table 8.7).

Table 8.7: Average proportional white cell counts for the NICOLA population and both males and females individually

Average	CD8T	CD4T	NK	BCELL	Mono	Gran
Males	0.0246	0.1867	0.0773	0.0457	0.0858	0.5771
Females	0.0460	0.2040	0.0707	0.0474	0.0677	0.5591
Total Population	0.0355	0.1955	0.0739	0.0466	0.0766	0.5679
Abbreviations: BCELL: CD19+ B lymphocytes; CD4T: CD4+ T cells; CD8T: CD8+ T cells; GRAN: CD15+ granulocytes; MONO: CD14+ monocytes; NK: CD56+ natural killer cells.						

Summative data

The projects undertaken with the methylation data from NICOLA was generated from a single batch of data generation. This has also provided summary statistics for methylation association analysis with different phenotypes, summarised in Table 8.8. by Dr Laura Smyth within the QUB Molecular Epidemiology and Public Health research team, funded by the Northern Ireland Kidney Research Fund, the Medical Research Council (MC_PC_15025) and the Public Health Agency R&D Division (STL/4760/13), Science Foundation Ireland (SFI15/US/B3130), NIH R01_DK105154, a Science Foundation Ireland and the Department for the Economy, Northern Ireland US partnership award 15/IA/3152 and the Economic and Social Research Council (ES/L008459/1).

Table 8.8: Summary statistics generated for the epigenetic DNA differential methylation analysis of NICOLA Wave 1.

Trait	Software	Sub-cohort	Lead Consortia	NICOLA Lead	Analyst
Alcohol consumption	PGS and R	1,929 individuals	Lifepath	GMK/AJM	GM/LJS
BMI	PGS and R	1,929 individuals		AJM	LJS
BMI	PGS and R	1,929 individuals	Lifepath	GMK/AJM	GM/LJS
CKD	PGS	1,984 individuals		AJM	RC/LJS
Education level	PGS and R	1,929 individuals		AJM	LJS
Education level	PGS and R	1,929 individuals	Lifepath	GMK/AJM	GM/LJS
Epigenetic clocks	R	19,29 individuals		AJM	AJM/LJS
eGFR	PGS	1,984 individuals		AJM	RC/LJS
eGFR	PGS	1,097 individuals between the ages of 60 and 79		AJM	LJS
Naevi	PGS	1,887		RH/AJM	LJS
Physical activity	PGS and R	1,929 individuals	Lifepath	GMK/AJM	GM/LJS
Risk preference	PGS and R	1,656 individuals		FK/AJM	LJS
Serum Urate	R	1,870 individuals	CKDGen	AJM	LJS/SH
Smoking	PGS and R	1,929 individuals	Lifepath	AJM	GM/LJS
Smoking	PGS and R	1,929 individuals	Lifepath	GMK/AJM	GM/LJS
SDD-reticular pseudodrusen	PGS	1,887 individuals		RH/AJM	LJS
SDD-reticular colour	PGS	1,887 individuals		RH/AJM	LJS
Time preference	PGS	1,648 individuals		FK/AJM	LJS

Abbreviations: AJM: Amy Jayne McKnight; BMI: body-mass index; eGFR: estimated glomerular filtration rate; FK: Frank Kee; GMK: Gareth McKay; LJS: Laura Jane Smyth; PGS: Partek Genomics Suite; RC: Ruaidhri Cappa; RH: Ruth Hogg; SDD: subretinal drusenoid deposits; SH: Sophia Halliday.

8.4 Transcriptomic-based biomarkers

This section describes transcriptomic analysis applied to the RNA generated from Wave 1 NICOLA and the derived variables.

Methods

Blood samples (n ~3,800) were collected from participants in PAXgene® blood RNA tubes. RNA was extracted using a proprietary approach by Eurofins Scientific who quantitated and normalised the RNA. An extraction quality of RIN≥8 as measured by a bioanalyser 2100 was required for further analysis. Analysis was conducted in-house for RNA-Seq on a subset of NICOLA including Ambio® ERCC spike-in controls; further samples are still undergoing RNA-seq. Libraries were prepared using the RiboMinus Eukaryote System v2 for whole transcriptome sequencing on a subset of samples, while the AmpliSeq RNA approach was cost-effectively selected for the majority of samples. Sequencing was conducted using Ion Torrent next generation sequencing on an S5XL or Ion Gene Studio S5 system. Sequence alignment was performed using Torrent Suite and Ion Reporter, Partek Flow and Partek Genome Studio, and R packages.

Data available

Sequence data is available, but is subject to our rare variant limitations within NICOLA. Gene counts and exome-based (from RNA) SNP files have been generated, with further data analysis underway. To date, transcriptome-based data has been used to provide support for EWAS results and as a population control for renal phenotypes – this was conducted by LJS and AJM.

8.5 Conclusion

The availability of rich multiomic data within NICOLA's bioresource provides a powerful landmark resource representing our Northern Ireland population aged 50 years and older. A key motivation of NICOLA to generate genetic-epigenetic-transcriptomic data, linked to biochemical biomarkers and extensive phenotype information, was to facilitate a wide spectrum of research. In the first two years, NICOLA's bioresource has been used to identify multiple biological markers associated with more than 30 different phenotypes. NICOLA has also contributed to developing innovative new approaches for multi-omic analyses, critically highlighting the importance of careful DNA and RNA storage for robust experimental studies. Early detection of declining health, particularly in the asymptomatic stages, is very important to facilitate early interventions that promote health and minimise loss of function; NICOLA is identifying novel biomarkers for cardiovascular, eye, and kidney-related outcomes. Our valuable bioresource facilitates exploration of how health and social experiences may lead to increased biological stress and therefore has potential to identify biomarkers for biomedical and biosocial research. Current studies using NICOLA's bioresource involve multiple phenotypes, with a strong focus on cognitive decline, age-related diseases, and socioeconomics. Working with our international colleagues for global studies of ageing we are working to promote health, support research, and inform policymakers.

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9 Methodology

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Citation

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Summary

- The Wave 1 NICOLA health assessment took place between January 2014 and August 2018.
- All participants who undertook the Wave 1 CAPI interview were invited to attend for a Health Assessment at the Wellcome Trust-Wolfson Northern Ireland Clinical Research Facility (NICRF) in Belfast. A total of 3741 participants (44%) completed the Health Assessment.
- As part of the health assessment, participants were also asked to complete two additional questionnaires: i) a self-completion questionnaire (SCQ) which captured additional information that was not suitable to obtain via the face-to-face home CAPI interview; and ii) a food frequency questionnaire (FFQ) to capture dietary related information. Both questionnaires were completed in the participant's own time and returned by post in a pre-paid envelope. Fifty nine percent (n = 5032) completed the SCQ and 34% (n = 2919) completed the FFQ. The results from the SCQ are not included in this report.
- Wave 1 health assessments were primarily conducted at NICRF based at the Belfast City Hospital, Belfast. A nurse-led home assessment was offered to participants (n = 193, 5%) who were willing to undergo a health assessment but were unable to attend the NICRF in Belfast.

9.1 Wave 1 Health Assessment Methodology

Details of the sampling methods for Wave 1 have previously been reported in the Wave 1 Early Findings Report (1).

All participants who undertook the Wave 1 CAPI interview were invited to take part in the detailed Health Assessment and were given a Participant Information Leaflet which provided full details regarding the benefits of taking part in the Health Assessment and detailed all aspects of what was involved in the Health Assessment. Participants were also informed that if they had any questions, they could contact one of the NICOLA nurses for clarification, by telephone or face to face when attending the assessment.

Health Assessments were conducted at the Wellcome Trust-Wolfson Northern Ireland Clinical Research Facility (NICRF), based at the Belfast City Hospital in Belfast. Written consent was obtained from all participants prior to the Health Assessment. Each health assessment appointment took approximately 2 hours, during which a range of anthropometric, cardiovascular, cognitive and ophthalmic measurements were performed. Measures included blood pressure, lung function, cognition, physical measures, facial photograph, height and weight, waist-to-hip measurement, fat and muscle measurement, eye examination, non-fasting blood and urine samples. If participants were unable or unwilling to travel to the NICRF, they were offered a modified home-based health assessment. All assessments were conducted by fully qualified and trained research nurses and research assistants. The list of health assessment tests undertaken is provided in Table 9.1.

Following the health assessment, participants were given an FFQ (EPIC-Norfolk), to be completed and returned to the NICOLA research support team in a pre-paid envelope. The FFQ was designed to measures participants' usual food intake during the previous 12 month period. The first section of the FFQ asked participants to report the frequency of consumption (ranging from never or less than once per month to > 6 times per day) of 130 food items while the second section contained more open response questions relating to supplement use, special diets, food allergy, shopping and cooking.

Table 9.1: Overview of measures and tests included in the NICOLA Wave 1 health assessment, self-completion questionnaire and food frequency questionnaire

	Domain	Measures
Health Assessment	Neuropsychological	Montreal Cognitive Assessment (MOCA) (2); Mini Mental State Examination (MMSE) (3); Colour Trails 2; Animal Recall; Centre for Epidemiologic Studies Depression Scale (CES-D) (4); Warwick Edinburgh Mental Wellbeing Scale (WEMWS) (5)
	Cardiovascular	Blood pressure (systolic; diastolic; postural); heart rate; Spirometry
	Gait and physical function	Step test; Timed up and go; Grip strength (hand dynamometry)
	Sensory function	Visual Acuity; Vision (use of glasses/ eye diseases/ visits to optician); Hearing
	Anthropometry	Height; weight; waist circumference; hip circumference; percentage body fat (Bodystat)
	Facial characteristics	Facial photograph
	Biological samples	Blood (non-fasting); urine; saliva (sub-set only)
Self-completion questionnaire*	Computer and internet use	
	General health	GHQ-12
	Vision problems	
	Loneliness	UCLA Loneliness Scale (6)
	Disability	
	N. Ireland Troubles	Adapted from the 2012 Poverty and Social Exclusion (PSE) Survey (7)
	Religion	
	Trauma	
	Post-traumatic stress	17 item post-traumatic stress disorder checklist (8)
	Physical activity	Recent Physical Activity Questionnaire (RPAQ) (9-12)
	Leisure time activities in past 4 weeks	

	Risk preference, time and patience	(adapted from 13-15)
	Trust	(adapted from 13-15)
	Optimism	(adapted from 13-15)
	Personality	NEO Five Factory Inventory. Adapted and reproduced form the publisher, Psychological Assessment Resources (16)
Food frequency questionnaire	Frequency of intake of 130 food items (average use in past 12 months)	Never or less than once a month, 1-3 per month, once a week, 2-4 times a week, 5-6 times a week, once a day, 2-3 times per day, 4-5 times per day, 6+ times per day
	Type of cereal, milk, fats and oils	
	Consumption of fried, grilled, roasted food	
	Consumption of fast food/ takeaways	
	Use of salt/salt substitute	
	Food supplement and vitamin use	
	Food allergy / food avoidance	
	Special diets	
	Vegetarian / vegan	
	Food shopping	
	Food preparation / cooking	

* Findings of the SCQ are not included in this report

9.2 Health assessment response rates

Of the participants who completed the Wave 1 CAPI, 34% returned a food frequency questionnaire (n = 2919), while 44% took part in the health assessment (n = 3655). The majority of participants attended the clinical facility for the health assessment (95%, n = 3462), with the remainder taking place in the participants' home (5%, n = 193).

Response rates for the health assessment and FFQ varied across the age groups, gender and across region. The majority of participants who attended the health assessment were aged 65 - 74 years, had a high level of education (tertiary), were married, and were a non-smoker. Participants in the older age category i.e. age 75+ years, with a lower level of education, and single were less likely to take part in the health assessment.

Table 9.2: Completion rates of NICOLA Wave 1 health assessment

	Health Assessment			FFQ
Age group (yrs)	All	Clinical Research Facility	Home Based	
50 – 64	1977	1937	40	1505
65 - 74	1187	1125	62	952
75 +	491	400	91	397
Total	3655	3462	193	2919

9.3 Anonymity and security of data

Written consent was obtained from all participants prior to the health assessment being conducted. All participants were informed that their results would not be individually identified. Details of participants' contact details are held in a locked filing cabinet and kept separate from all other participant data, which is anonymised (by use of a unique study number). Anonymous participant data is held on University computers, which are encrypted and password protected. All blood, saliva and urine samples are anonymised (by use of a unique study number), and kept in locked, alarmed freezers, within secure University buildings.

9.4 Data availability

All data relating to the Wave 1 health assessment is currently located in the 'Safe Setting' within the Centre for Public Health at Queen's University Belfast. The application procedure to access the data is detailed on the NICOLA website and within the NICOLA Data Access Policy. A data dictionary detailing all the variables that are available can also be found on the NICOLA website (https://www.qub.ac.uk/sites/NICOLA/InformationforResearchers/). An anonymised dataset has also been archived at the UK Data Archive Service (https://www.data-archive.ac.uk/) while

the metadata can also be accessed via the Dementias Platform UK (https://www.dementiasplatform.uk/). NICOLA is also one of 19 longitudinal studies that has joined the CLOSER consortium (https://www.closer.ac.uk/), a hub of longitudinal studies spanning the UK, the aim of which is to maximise the use, value and impact of longitudinal studies and help improve understanding of key social and biomedical challenges.

9.5 Statistical tests

Within this report, we have only presented high level findings based on summary statistics. However, we do recognise that many other factors, not mentioned within this report, may have a bearing on the relationships and patterns observed. More detailed multivariate analysis are being conducted by our specialist research teams and will continue to form the subject of future NICOLA outputs which will be made available on the NICOLA website following publication.

The majority of results presented in this report reflect the proportion of adults within the following categories: age groups, sex, marital status, educational level, area deprivation, urban/rural, or other analysis criteria. Means (SD) or medians (IQR) are reported where appropriate. Estimates are also presented with 95% confidence intervals (CI). This is to account for inherent uncertainty in the derived estimates due to the random nature of the population sampling process. The 95% CI indicates that with repeated sampling, 95% of the CIs calculated would contain the true population parameter. The 95% CI can be interpreted as the range of values within which there is a 95% certainty that the true population parameter e.g. the mean, lies.

9.6 Weighting

Although NICOLA is nationally representative of the older community dwelling population in Northern Ireland, the patterns of response to specific parts of the study vary. As detailed above, not everyone invited to participate in the health assessment chose to do so. It is known that there are systematic differences in the types of people who agreed to take part and those who did not.

While it is difficult to adjust for these systematic differences in responses, we can apply weights to the data and the different analyses in order to account for differential non-responses and to make the sample estimates more representative of the population as a whole. Weighting ensures that, for the estimates calculated, the various population sub-groups are fairly represented. In effect, the weighting puts more emphasis on data from those participant groups who are known to have been underrepresented and less on those groups which are proportionally overrepresented. The net effect is to produce results that are more truly representative of the Northern Ireland population aged 50 years and over.

The weighting of the NICOLA Health Assessment was based on the following factors which were shown to affect the likelihood of attending the health assessment:

age, sex, education (3 categories, primary, secondary, tertiary), marital status (3 categories: married or living with partner; single; separated, divorced, widowed), self-reported health, smoking (cigarettes, cigars, cigarillos or pipe for a period of at least 1 year), alcohol status (current, ex or never), location (Belfast; city or town; rural) and income domain score (scored 1 - 5). Results were based on 8280 participants, aged over 50 years, who took part in the baseline CAPI.

The following steps were performed to generate a weighting for each individual:

1. A logistic regression analysis was conducted which generated a predicted value representing the probability of an individual taking part in the HA.
2. The reciprocal of the predicted value (i.e. 1/predicted value) was then calculated to generate a weight.
3. Resulting values were then rescaled into a new weight (called CAPIHAweight) by dividing each person's weight by the sum of the weights and multiplying by 8280 i.e the total CAPI population. This was to ensure that the weights of those included in the sample added up exactly to the CAPI population size.
4. A final HA weight was then calculated (called NIHAweight) by multiplying the new weight by the Gross weight provided by IPSOS MORI. This weight was rescaled by dividing each person's weight by the sum of the weights and multiplying by 572,196 (the population of NI aged over 50 years in 2011 according to figures taken by IPSOS MORI from census information).

The number of participants presented in this report are based on the number of participants who attended the Health Assessment, while the proportions (%) are presented as weighted values (NIHAweight) and thus provide an estimate based on the Northern Ireland population.

9.7 Software

All analyses in this report were conducted using SPSS version 25.0 or STATA v15.

9.8 Next steps

A follow-up health assessment will be conducted, pending continued funding.

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