4. Cognitive impairment and dementia in older English adults: Risk factors and diagnostic algorithms

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Key points arising from this chapter are:

- With an increase in the number of older people living in the UK, early diagnosis of cognitive impairment and dementia are significant public health priorities.

- The Harmonised Cognitive Assessment Protocol (HCAP) is a sub-study of the English Longitudinal Study of Ageing (ELSA), administered to 1,273 individuals aged ≥65 years in 2018, including a comprehensive neuropsychological battery of cognitive tests.

- A diagnostic algorithm was developed to ascertain cognitive impairment and dementia in the ELSA-HCAP, which classified participants according to their medical records, overall cognitive performance, subjective memory complaints and functional impairments.

- In ELSA-HCAP, 43% of the sample was classified with cognitive impairment and 13% with dementia. These proportions are higher than in the general population aged 65 and older because people with low cognition were selectively recruited into the sub-study.

- We found an increased prevalence of neurocognitive disorders (cognitive impairment and dementia) with age and lower socioeconomic position.

- A cross-walk prediction algorithm was derived between ELSA-HCAP cognitive groups and ELSA wave 9 indicators (age, sex, education and all cognitive measures available). The highest probability score was selected for each participant, and a group diagnostic probability was assigned to each ELSA participant at wave 9.

- In ELSA wave 9, 72.4% of the diagnostic algorithm sample aged 60 and older ($N = 6,669$) was classified with no cognitive impairment, 23% with cognitive impairment and 4.6% with dementia.

- Participants classified with dementia and cognitive impairment were older than those with no cognitive impairment. Fewer than 30% of the older individuals (aged 80+) had no cognitive impairment at wave 9.

- A large proportion of those classified with cognitive impairment or dementia at wave 9 had no formal educational qualifications, and only a few had completed a degree.

- We examined the longitudinal association between emerging cardiovascular (high blood pressure, diabetes and physical inactivity), psychosocial (loneliness, depression) and socioeconomic/neighbourhood risk factors (geographical region) at wave 4 (2008/09) in relation to cognitive impairment and dementia at wave 9 (2018/19).

- A higher proportion of participants classified with cognitive impairment and dementia at wave 9 had worse health (high blood pressure, diabetes) and higher levels of both depressive symptoms and loneliness at wave 4.

- We found an increased risk for cognitive impairment at wave 9, for those with elevated depressive symptoms 10 years earlier.

- Physical inactivity at wave 4 was a strong determinant of dementia risk at wave 9.

- Greater loneliness at baseline was predictive of an increased risk of cognitive impairment and dementia almost a decade later.

- The longitudinal structure of ELSA allows medical and psychosocial risk factors to be assessed many years before neurocognitive disorders develop, and demonstrate that these factors precede the occurrence of cognitive impairment and dementia.

4.1 Introduction

The UK population is ageing, and projections by the Office for National Statistics (2015) estimate that by 2050 one in four people will be aged 65 years and over. With this demographic change indicating an increase in the number of older people, neurocognitive disorders such as dementia constitute a public health challenge in the UK (Department of Health and Social Care, 2019). Dementia can be defined as an umbrella term for a variety of conditions characterised by severe deterioration of the brain, resulting in memory loss, changes in behaviour and communication problems. The most common forms of dementia are Alzheimer's disease (AD) and vascular dementia (VaD) (Prince et al., 2016). Despite being a prominent global challenge, dementia is often underdiagnosed, since its identification can be challenging. With age being amongst the key determinants, there is a grey area between the 'normal ageing process' and 'Mild Cognitive Impairment' (MCI) – an intermediate phase between the normal cognitive ageing and abnormal neuropathological changes associated with dementia (Petersen, 2004; Langa and Levine, 2014). MCI is often considered a prodromal stage of AD, and an important target for early diagnosis and therapeutic interventions. Recent studies show that individuals with MCI tend to progress to probable AD at a rate of approximately 10–15% per year, compared with controls who develop dementia at a rate of 1–2% per year (Petersen et al., 2014). Early detection of MCI is of paramount importance for possible delay of the transition from MCI to AD. Still, questions can be raised regarding the diagnostic criteria and diagnostic algorithms for MCI. The

importance of risk reduction across the life course is crucial for delaying the onset and the progression of cognitive impairment and dementia. Indeed, prevention techniques and tailored interventions have been estimated to have the potential to delay or prevent up to 40% of dementia cases (Livingston et al., 2020). Population policies previously targeted at some of these risk factors may explain why certain countries, including the UK, have found a lower incidence of dementia than predicted from previous projections (Wu et al., 2016). With these key policy priorities in mind: (1) early diagnosis of cognitive impairment and dementia and (2) increased awareness about the modifiable risk factors which could improve brain health, we explored data drawn from wave 9 of the English Longitudinal Study of Ageing (ELSA) (Steptoe et al., 2013) to provide further clarity about this public health priority.

In this chapter, we aim to examine the prevalence of cognitive impairment and dementia in England using data drawn from a sub-study of ELSA, named the Harmonised Cognitive Assessment Protocol (HCAP). Section 4.2 describes the HCAP sub-study and the algorithm for estimating MCI and dementia. In Section 4.2.2, we describe the prevalence of MCI and dementia in ELSA-HCAP in relation to age, gender and education. Section 4.3 explains how the results from the HCAP sub-study were extrapolated to the rest of the ELSA study sample and details the levels of MCI and dementia in wave 9 of ELSA based on these calculations. Finally, in Section 4.4 we examine the longitudinal associations between predictors of cognitive impairment and dementia status at wave 9, linking factors measured in wave 4 (2008/09) with cognitive function in 2018/19. We endeavoured to confirm the association between several well-established behavioural and intermediate-risk factors, as described by the Blackfriars Consensus, e.g. smoking, poor diet, physical inactivity, excessive alcohol intake, raised blood pressure, blood cholesterol and diabetes (Lincoln et al., 2014). In addition, we also examined the association between cognitive impairment and dementia with a number of social and psychosocial risk factors for which there is emerging evidence (depression, social isolation, loneliness, social support, socioeconomic risk factors).

4.2 HCAP and dementia diagnosis algorithm

Identifying individuals with cognitive impairment and dementia is crucial for early intervention, care planning and treatment. From the early 2000s, there has been a growing focus on prioritising the study of prodromal stages of the neurodegenerative disease before dementia syndromes emerge (i.e., mild cognitive impairment). While the current decade has seen a significant improvement in terms of imaging techniques and biomarker assessment to characterise preclinical stages of the disease, the diagnostic criteria remain controversial in population-based studies.

The HCAP is linked to the family of studies associated with the Health and Retirement Study (Sonnega et al., 2014) and offers an opportunity for investigating harmonised measures relevant to dementia diagnosis including cognitive and sensory performance, as well as psychological well-being and functional abilities in large representative population samples of older adults in both high and middle-income countries. The overall aim of HCAP was to ascertain and investigate MCI and dementia across general populations

worldwide. The HCAP employed multiple cognitive and other tests to evaluate the prevalence of neurocognitive disorders in individuals aged 65 years and older within each participating country. By being embedded within the ongoing longitudinal studies of ageing, HCAP has provided the potential to improve the understanding of the evolution of cognition and day-to-day function as people live and age in vastly diverse settings. The design and administration of the HCAP protocol within the English Longitudinal Study of Ageing (ELSA) are described elsewhere (Cadar et al., 2020). In this section, we explain the derivation of MCI and dementia using a diagnosis algorithm based on the HCAP battery of tests.

4.2.1 Methods

HCAP data

Data are from the Harmonised Cognitive Assessment Protocol (HCAP), a sub-study of the ELSA, administered to 1,200 individuals aged ≥65 years in 2018. This sub-study was implemented between waves 8 (2016/17) and 9 (2018/19) of the ELSA. The HCAP includes an in-person interview with the ELSA-HCAP study member, which lasted approximately one hour, and a second interview with an informant nominated by the respondent, which lasted about 20 minutes. Invitations to participate were stratified on the basis of cognitive performance in earlier waves of ELSA, so as to oversample people with moderate or low cognition.

Study variables

The ELSA-HCAP respondent interview consisted of a neuropsychological test battery which was implemented objectively to measure a wide range of critical cognitive domains that are known to be sensitive to the ageing process. These include memory, language, attention, executive function and processing speed. The full description of the tests included is presented in the Appendix.

HCAP global score

A summary global cognition score was derived from all the standardised cognitive tests included in the HCAP battery presented above, except the Mini-Mental State Examination (MMSE). Trail Making A and B scores were log-transformed to improve normality.

Functional impairment

Functional impairment was defined as at least two self-reported limitations on either 'Basic Activities of Daily Living' (ADL) and 'Instrumental Activities of Daily Living' (IADL). ADL included six activities: dressing, walking across a room, bathing or showering, eating, getting in or out of bed, using the toilet. IADL included seven activities: using a map to get around in a strange place, preparing a hot meal, shopping for groceries, making telephone calls, taking medications, doing work around the house or garden and managing money. ADL and IADL were both measured in ELSA-HCAP and each ELSA wave.

Informant Questionnaire on Cognitive Decline in the Elderly

The Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) (Jorm and Jacomb, 1989) uses informant reports to measure the change in

cognitive abilities (e.g. memory) based on the pre-morbid level of functioning. Each item was scored on a 1 (much improved) to 5 (much worse) range. The validity of this scale was previously examined, and the threshold used has both high specificity (0.84) and sensitivity (0.82).
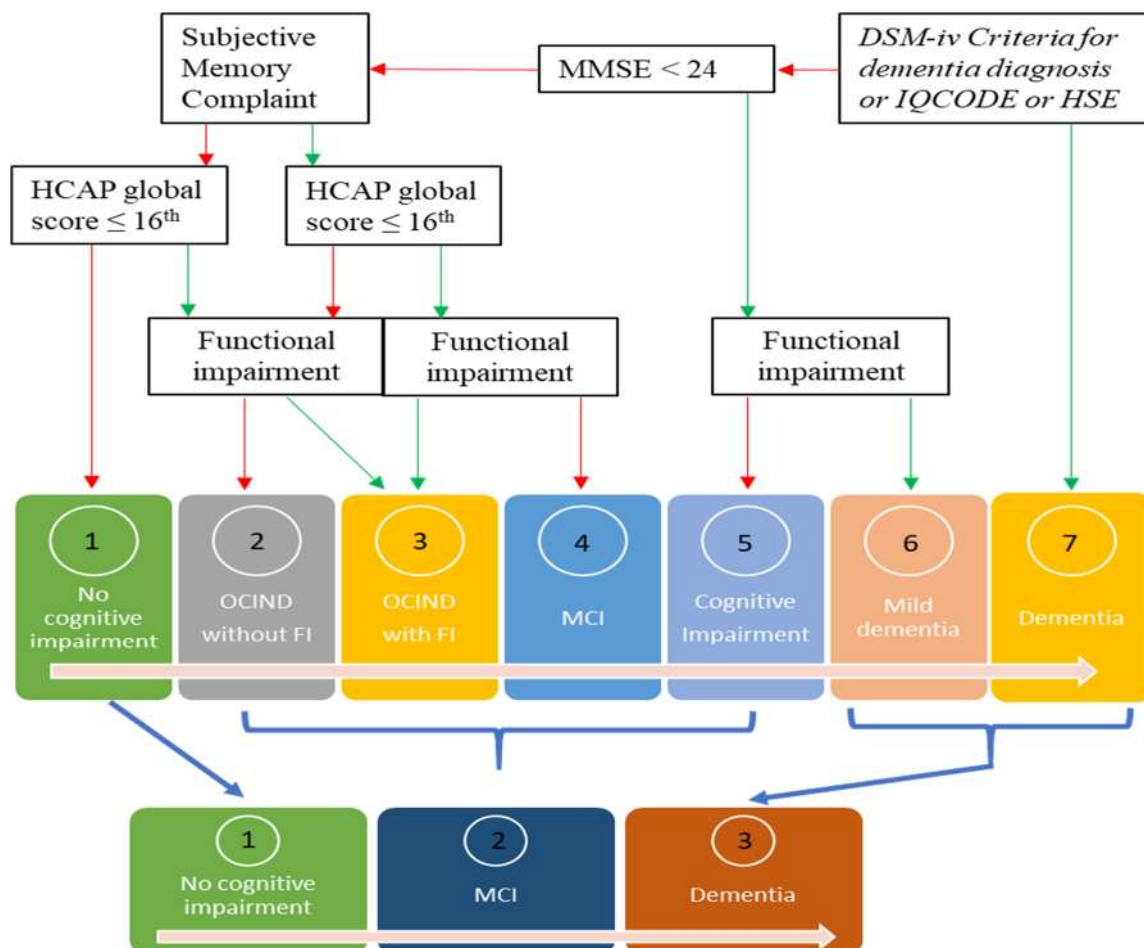
HCAP sample groups and weights

A weighting procedure was derived for the ELSA-HCAP sub-study in order to adjust for the low response rate of individuals identified with low cognition at the previous ELSA wave 8 (2016/17). The weighting procedure combined three different components: (i) design weights, (ii) non-response weights and (iii) a calibration procedure to account for differential selection probabilities and to adjust for non-response. The weights were calibrated by age and sex within each sample selection cognition group and by housing tenure, education, ethnicity, and marital status across groups. The HCAP sample selection groups procedure was based on cognitive performance (wave 8, or 7 if missing at the latest wave) on various tests contributing to the modified Telephone Interview Cognitive Screening (mTICS) (Brandt et al., 1988; Welsh et al., 1993) and/or a diagnosis of Alzheimer's disease or dementia reported in previous ELSA interviews. Three sampling cognition groups were defined using the following thresholds on the mTICS 27-item scale (Crimmins et al., 2011): Group 1: low cognition (≤6 mTICS27 score) and/or a previously reported diagnosis of Alzheimer's disease or dementia; Group 2: moderate cognition (7–11 mTICS27 score) and had never reported a diagnosis of Alzheimer's disease or dementia; Group 3: normal cognition (≥ mTICS27 score) or unknown for those with missing data on mTICS scores at ELSA wave 8 or 7. Reports of physician diagnosis of Alzheimer's disease or dementia were taken from the previous ELSA waves 1–8. Any eligible study member who had ever reported a diagnosis of Alzheimer's disease or dementia was assigned to group 1 (low cognition), regardless of their score on mTICS. The overall calibration adjustment for ELSA-HCAP was minimal, meaning that the distributions of other variables used in the non-response weighting were very close to population estimates.

Dementia diagnosis algorithm

Cognitive impairment and dementia were ascertained using scores on the MMSE, subjective memory evaluation, low performance on a global score of cognitive functioning derived from the sum of all the objective cognitive tests included in the HCAP battery, and functional impairment on ADL and IADL. The diagnosis algorithm to ascertain MCI and dementia implemented in the ELSA-HCAP was based on the diagnostic algorithm implemented in the Cognitive Functioning and Ageing Study (CFAS) (Richardson et al., 2019). This algorithm was designed to classify the entire cognitive spectrum of cognitive function from normal cognition, through mild cognitive impairment and dementia, taking into consideration the subjective memory complaints and the level of functional disability according to Diagnostic and Statistical Manual (DSM) criteria. To achieve this, we categorised the overall HCAP sample into seven categories: no cognitive impairment, MCI (defined using consensus criteria), other cognitive impairment no dementia (OCIND) without functional impairment, OCIND with functional impairment, cognitive impairment (MMSE <24 and no functional impairment), mild dementia (MMSE <24 and functional impairment) and dementia using a triangulation method based on

three sources (physician diagnosis of dementia or Alzheimer's disease, a score equal or higher than 3.38 on the IQCODE, and a dementia record from the Hospital Episode Statistics (HES)), either before or at the time of the HCAP study. Figure 4.1 describes the algorithm used to derive each cognitive outcome.

Figure 4.1. Flow chart describing diagnostic criteria used in ELSA-HCAP for each cognitive spectrum outcome

4.2.2 Prevalence of MCI and dementia in ELSA-HCAP

The weighted prevalence of cognitive impairment and dementia in ELSA-HCAP are presented by age groups, gender and education in an overall sample of 1,270 participants with data available. Of these, 560 individuals (44%) were classified with no cognitive impairment, 545 (43%) with cognitive impairment and 165 (13%) with dementia.

Figure 4.2 shows the percentages of respondents within each cognitive status by age groups in 2018. Around 70% of all participants aged 65–69 had no cognitive impairment, and only 6% of them were classified with dementia. Half of those aged 70–79 had no cognitive impairment, 38% were cognitively impaired, and 12% had dementia. The majority (63%) of older participants (aged 80+) were classified with cognitive impairment, and 20% with dementia at the time of the ELSA-HCAP sub-study.

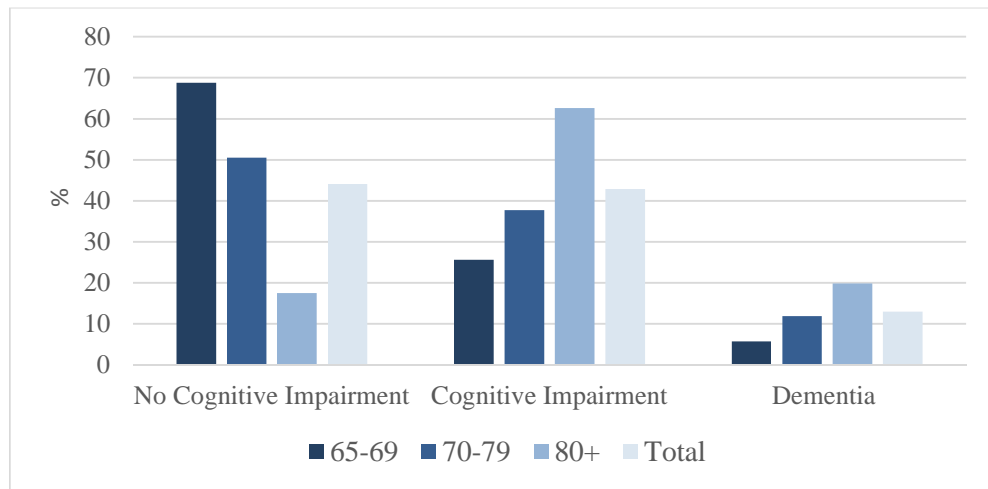**Figure 4.2. Cognitive status in ELSA-HCAP by age groups**

Figure 4.3 shows the percentages of ELSA-HCAP respondents within each of the three cognitive groups by gender. Among men, 45% had no cognitive impairment, 43% were cognitively impaired, and 13% had dementia. The proportion of women with no cognitive impairment was similar to those classified with cognitive impairment (43%), and 14% of them were classified with dementia. The lack of gender difference was not related to age.

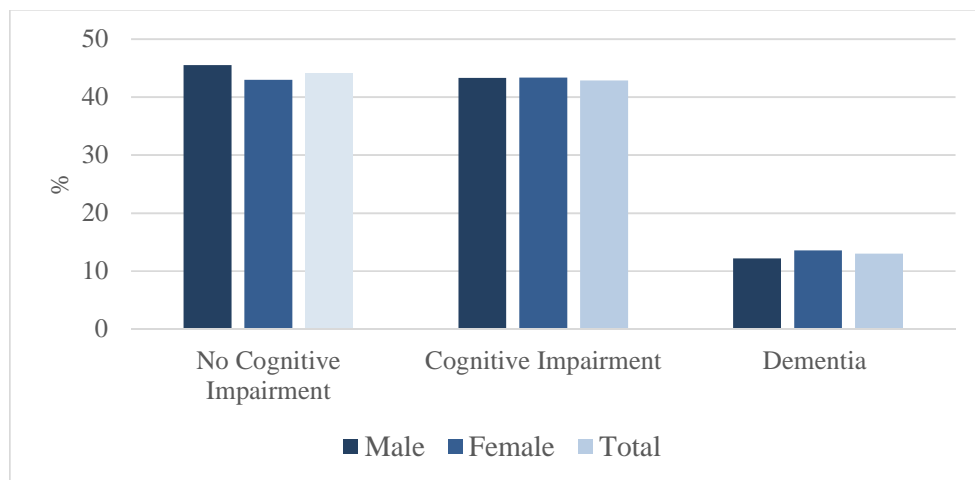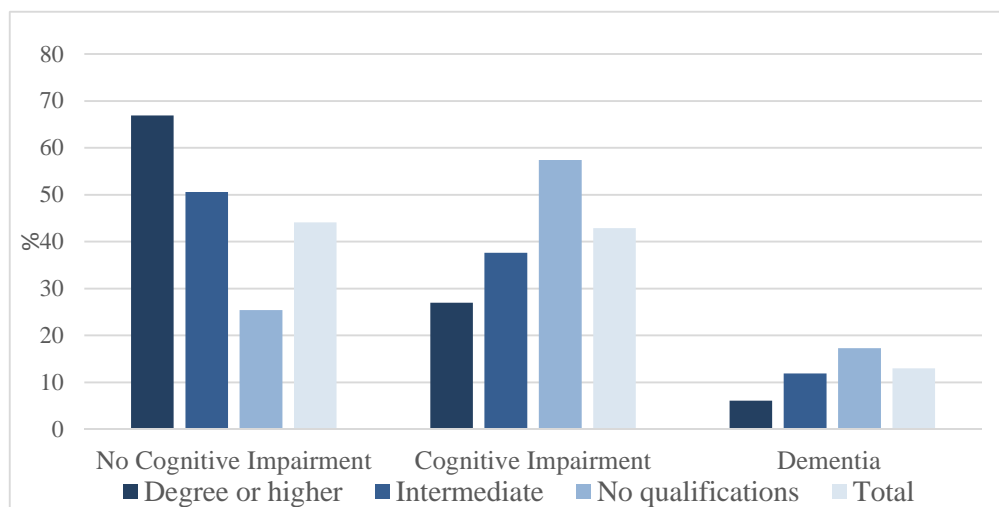**Figure 4.3. Cognitive status in HCAP by gender**

Figure 4.4 shows the percentages of respondents within each cognitive group by their highest educational qualification. Most of the participants with a higher degree (67%) had no cognitive impairment, 27% were classified with cognitive impairment, and 6% with dementia. Half of those with intermediate levels of education showed no cognitive impairment, 37% were cognitively impaired, and 12% had dementia. Of those with no formal qualifications, more than half (57%) were classified with cognitive impairment and 17% with dementia.

Figure 4.4. Cognitive status in HCAP by education groups

Our analyses confirm an increased prevalence of neurocognitive disorders (cognitive impairment and dementia) with age and lower socioeconomic position, as indicated by the increased prevalence of cognitive impairment and dementia in those with no formal educational qualification.

4.2.3 Strengths and limitations

The diagnostic algorithm used for these analyses was derived from a published protocol implemented in CFAS that took into account a detailed examination of both objective and subjective measures of cognition, as well as the level of functional disability according to DSM criteria. However, a diagnosis of MCI or dementia has profound psychological, social and financial impacts, not only on the individual but also on their family and friends. Therefore, it is important to note that diagnostic algorithms such as the one used here cannot replace clinical diagnoses and that they carry a risk of false positive or false negative conclusions. Nonetheless, they are useful in the context of population studies, and these estimates enable international comparisons of the prevalence of cognitive impairment and dementia around the world.

4.2.4 Conclusions

In this section, we identified and described the prevalence of cognitive impairment and dementia in the ELSA-HCAP sample. The results indicated that 43% of this sub-study population aged 65 and older were classified with cognitive impairment and 13% with dementia. Our findings support existing epidemiological evidence that age is an important factor in neurocognitive disorders. More than half of the participants aged 80 and over were classified with cognitive impairment, and we also observed the highest prevalence of dementia in this age group. There were no significant gender differences in these results. However, we found a protective association with education which is thought to be a marker of cognitive reserve, building brain resilience to neurodegenerative damage at older ages. It is notable that most of the participants with a university degree had no cognitive impairment, while the

highest prevalence of neurocognitive disorders was observed in those with lower levels of education.

4.3 HCAP – Wave 9 cross-walk diagnosis

The ELSA-HCAP sub-study was carried out with a relatively small number of participants, but the data can be used as a basis for extrapolation to the entire ELSA population. Reliable national data on incidence and prevalence of dementia and cognitive decline are vital for service planning, the prediction of future needs, estimating the costs of dementia care, and understanding the impact of these conditions on individuals and their families. Although the number of people with dementia is increasing throughout the world because of the demographic shift towards rising numbers of older people, estimates of future prevalence are complicated by the assumptions underlying different modelling methods (Norton et al., 2013). Indeed, there is evidence that prevalence has remained stable or even declined over recent decades in the USA and Europe (Manton et al., 2005), with strong indications of an apparent decline in prevalence in England reported by ELSA (Ahmadi-Abhari et al., 2017) and the two phases of the CFAS (Matthews et al., 2013).

4.3.1 Methods

ELSA wave 9 data

Data from wave 9 (2018/19) of ELSA were used as the basis for extrapolation. By linking the cognitive groups derived with the dementia algorithm in the ELSA-HCAP sub-study to the standard demographics (age, sex and education) and cognitive tests completed in wave 9 of ELSA, we calculated a probability score that linked the diagnosis of mild cognitive impairment and dementia in HCAP to the full ELSA sample.

Study variables

We used the range of cognitive measures administered at wave 9, which included tests of memory, orientation, language, attention, and executive function. The cognitive measures used for this cross-walk diagnostic algorithm are presented below.

Self-reported memory

This measure provides a self-evaluation of memory. Participants were asked to rate their memory at the present time as excellent, very good, good, fair or poor. They were also asked to say whether compared with two years ago, their memory is now better, the same, or worse than it was then.

Self-reported mental abilities

This measure provides a self-evaluation of their overall mental abilities. Participants were asked to rate their overall mental abilities at the present time as excellent, very good, good, fair or poor. They were also asked to say whether compared with two years ago, their mental ability is now better, the same, or worse.

Orientation in time

Time orientation was assessed by standard questions about the date (day, month, year) and the day of the week. These questions are also part of the Mini-Mental State Examination (MMSE), which was used in the ELSA-HCAP.

Verbal memory

The word list learning and recall task is a verbal memory test in which ten common words were presented aurally by a computer, using a taped voice. The participants were asked to recall them both immediately and after a short delay during which other cognitive tests were administered.

Backwards count

Backwards digit recall is often employed as a measure of working memory. In this test, the participants were asked to count backwards for 10 consecutive numbers beginning with the number 20.

Serial subtraction

Serial 7's or serial subtraction test is also a test of mental processing. The interviewer asked the respondent to subtract 7 from 100 and continue subtracting 7 from each subsequent number for a total of five trials.

Cross-walk diagnostic algorithm

The cross-walk diagnostic algorithm between ELSA-HCAP and ESLA wave 9 was computed using a multinomial logistic regression model, which predicted the probability of participants belonging to each diagnostic group within the cognitive spectrum derived in ELSA-HCAP (e.g. normal cognition, MCI and dementia). For this cross-walk prediction algorithm, we used a weighted multinomial logistic regression in which we predicted the HCAP cognitive groups by age, sex, education, all the cognitive measures available at wave 9. The highest probability group was then selected for each participant, and a group diagnostic probability was assigned to each ELSA participant at wave 9, taking into consideration any previous or new dementia diagnosis at wave 9, using the three sources available in ELSA (physician diagnosis of dementia or Alzheimer's disease, a score equal or higher than 3.38 on the IQCODE and a dementia record from the Hospital Episode Statistics (HES)). The physician diagnosis or HES took precedent in this diagnostic algorithm, and corrections ($n = 37$) were made for any misclassifications generated by the probability score diagnostic algorithm.

4.3.2 Prevalence of MCI and dementia in ELSA wave 9

The weighted prevalence of cognitive impairment and dementia at wave 9 were calculated for an overall sample of 6,669 participants aged 60 and older with data available for all the measures presented in Section 4.3.1. Of these, 4,829 were classified as having no cognitive impairment (72.4%), 1,532 as having a cognitive impairment (23%) and 308 individuals were classified with dementia (4.6%). The prevalence of cognitive impairment and dementia are presented below by age groups, gender and education. Although these factors were used as demographic inference tools in our diagnostic prediction algorithm, they

were also investigated in this context as a method of validation that the prediction model yielded sensible results.

Figure 4.5 shows the percentages of ELSA respondents within each cognitive status at wave 9 by age groups. The majority (93%) of younger participants (65–69 years) had no cognitive impairment, 5% were cognitively impaired, and 1.4% were classified with dementia at wave 9. Among the 70–79 age group, 73% had no cognitive impairment, 23% were classified as cognitively impaired, and 4% with dementia. Among the older participants (80+ years), 58% were classified as cognitively impaired, and 13% with dementia.

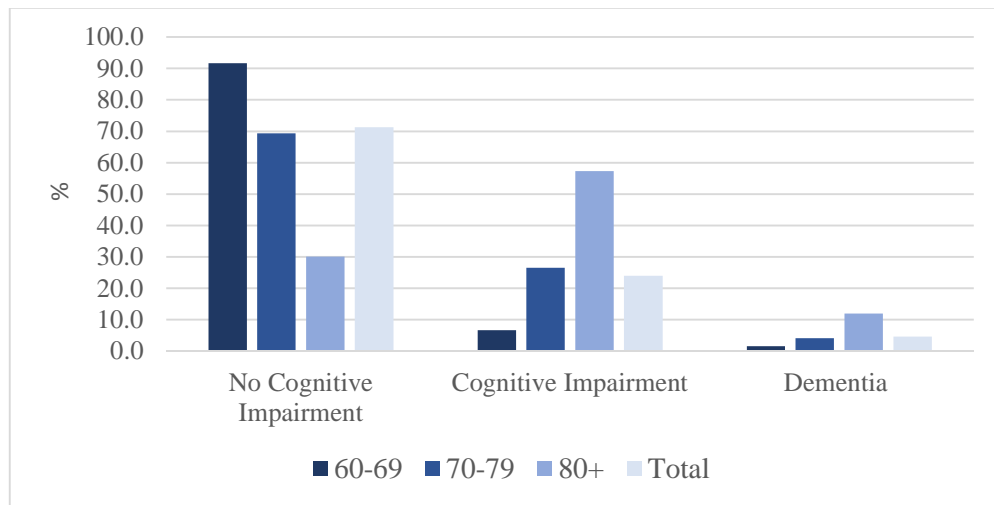**Figure 4.5. Cognitive status at wave 9 by age groups**

Figure 4.6 presents the percentages of ELSA respondents at wave 9 within each cognitive group by gender. Among men, 75% had no cognitive impairment and 21% were cognitively impaired. Among women, 71% had no impairment and 25% were classified as cognitively impaired. The percentage of men of women classified with dementia was similar (4.7%).

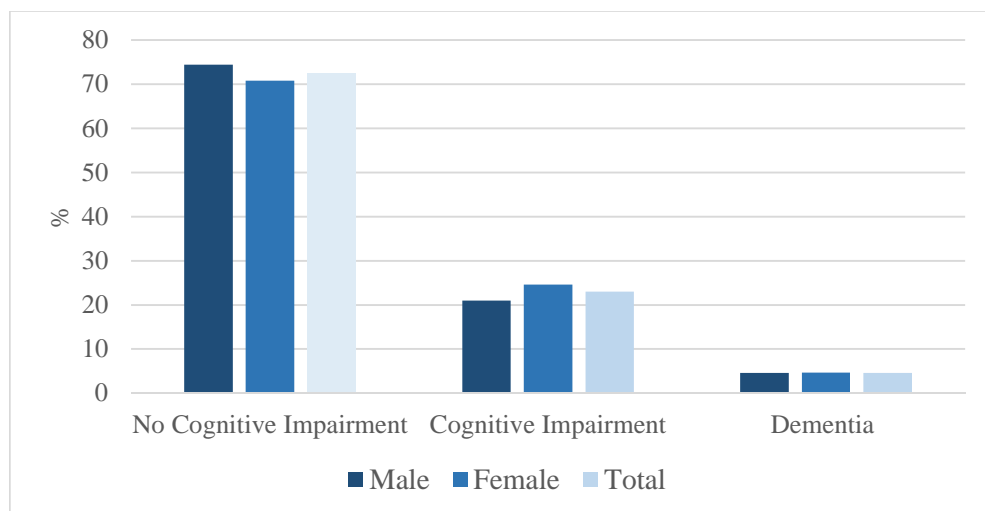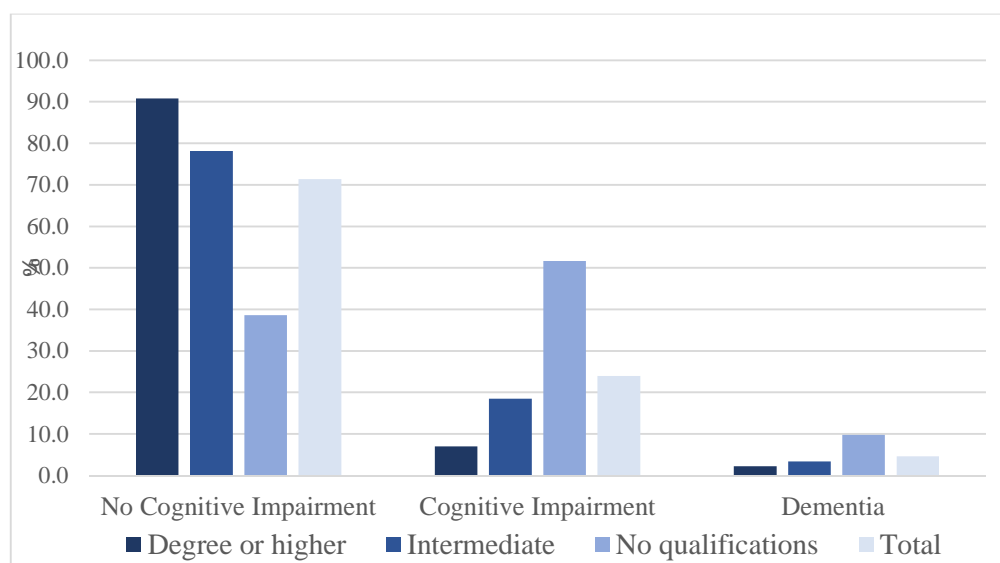**Figure 4.6. Cognitive status at wave 9 by gender**

Figure 4.7 shows the percentages of ELSA participants at wave 9 in each cognitive group by the level of education. Among those with higher education or educated to degree level, a large proportion (90%) had no cognitive impairment, 7% were classified with cognitive impairment and 3% with dementia. For those with intermediate levels of education, 76% had no impairment, 20% were classified as cognitively impaired, and 4% with dementia. In contrast, among those with no formal qualification, half of the participants were classified as cognitively impaired, and almost 10% were classified with dementia.

Figure 4.7. Cognitive status at wave 9 by education groups

4.3.3 Conclusions

Based on the most recent wave of data collection in ELSA, we found that among individuals aged 60 years and above, the prevalence of cognitive impairment was 23% while dementia was present in 4.6%. The prevalence of dementia in CFAS II was somewhat higher (Matthews et al., 2013), with age-standardised estimates of 4.9% in men and 7.7% in women. There may be several reasons for this. The fieldwork for CFAS II was carried out between 2008 and 2011, whereas our data were collected in 2018–19. Differences may, therefore, reflect trends of decline in dementia prevalence. Moreover, the CFAS II was carried out in three areas – Cambridgeshire, Nottingham and Newcastle – while the ELSA sample comes from all regions of England. However, the percentage of ELSA participants that were institutionalised is very small (under 1%), and therefore our findings are only representative of the English population aged 60 and older, living in the community.

4.4 Determinants of cognitive impairment and dementia at wave 9

Biological and psychosocial risk factors, particularly those that are malleable across the life course, are important determinants of neurocognitive health in later life. There has been increased interest in identifying which modifiable risk factors to target since potential treatments of dementia will not reduce the need for effective prevention. The longitudinal nature of ELSA presents several opportunities for the investigation of precursors and consequences of neurocognitive disorders spanning over 16 years of data from wave 1 to wave 9.

In this section, we conduct a longitudinal investigation of a number of risk factors in relation to neurocognitive impairment ascertained at wave 9. We examine a range of predictors, selected to represent determinants from several domains of risk factors including cardiovascular risk factors (high blood pressure, diabetes, and physical inactivity), psychosocial determinants (loneliness, depression) and socioeconomic/neighbourhood risk factors (geographical region). These factors were measured in wave 4 (2008/09), 10 years before the ascertainment of dementia and cognitive impairment.

4.4.1 Determinants of neurocognitive health

High blood pressure (Biomarkers)
High blood pressure is a known risk factor for cardiovascular diseases (e.g. heart disease and stroke) and has been found to be associated with dementia in later life (Prince et al., 2014). Potential biological mechanisms for this association include cerebral small vessel disease that is linked with vascular dementia (Coca et al., 2016). It has been suggested that the critical time for treatment of hypertension to reduce risk of dementia and improve brain health is midlife (Livingston et al., 2017, 2020), but raised blood pressure is a significant risk factor across the life course.

Type 2 diabetes (Pre-existing medical conditions)
Type 2 diabetes is a chronic disease that causes an increase in the risk of cardiovascular diseases and dementia among the older population aged 65 and older (Winblad et al., 2016; Livingston et al., 2017, 2020). Raised glucose levels could damage small blood vessels that contribute to the risk of vascular dementia. In addition, vascular dysfunction may interrupt blood flow to the brain, contributing to AD (Prince et al., 2014).

Physical inactivity (Lifestyle factors)
Dementia risk is known to be influenced by physical activity, particularly in older age (Norton et al., 2014; Winblad et al., 2016; Livingston et al., 2017, 2020), although it has been suggested that this relationship is not due to a protective effect of physical activity (Sabia et al., 2017). However, the relationship may be indirect, with physically inactive people having a higher risk for vascular risk factors in older age (Livingston et al., 2020). Factors like atherosclerosis and endothelial dysfunction could mediate the relationship between physical activity and dementia risk (Rovio et al., 2005).

Loneliness (Social engagement)

Evidence is growing that a lack of social contact in later life may be a risk factor for dementia. The relationship may be indirect, through increasing the risk of cardiovascular problems such as hypertension (Holt-Lunstad and Smith, 2016). However, there is also evidence that reduced social contact, and especially loneliness, is directly associated with poorer cognitive functioning and an increased risk of dementia (Shankar et al., 2013; Rafnsson et al., 2020).

Depression (Mental health)

Depressive symptoms in later life have been found to be associated with risk of dementia (Dotson et al., 2010; Saczynski et al., 2010). Several plausible, biological mechanisms for this association have been suggested, such as stress hormones, neuronal growth factors, and hippocampal volume (Alexopoulos, 2003). However, the direction of the association is unclear, and studies have suggested that depressive symptoms could be an early symptom of the disease progression (Singh-Manoux et al., 2017).

Regional variation and neighbourhood deprivation (Socioeconomic)

It has been suggested that there are regional variations across the UK in dementia prevalence and diagnosis (Matthews et al., 2013; Walker et al., 2017). Furthermore, socioeconomic inequalities have been observed in the UK for both dementia risk and dementia-related mortality (Sharp and Gatz, 2011; Russ et al., 2013). For example, living in an area or neighbourhood with high levels of deprivation is associated with poorer cognitive function in later life (Lang et al., 2008). Furthermore, an association between other indicators of socioeconomic position, such as household wealth and risk of dementia has been found, even after educational status is taken into account (Cadar et al., 2018).

4.4.2 Methods

Cognitive status at wave 9 (Outcome)

To examine the longitudinal association between predictors of cognitive impairment and dementia, we used a sample of 4,639 older people who had participated in both wave 4 (2008/09) and wave 9. Exclusions were made for those who reported a doctor diagnosis of dementia at wave 4, those who had missing data on predictors at wave 4 and those who were younger than 60 years of age at wave 9.

As described in Section 4.3.1, cognitive status at wave 9 was categorised into three diagnostic groups (e.g. normal cognition, MCI and dementia) using a cross-walk diagnostic algorithm between ELSA-HCAP and ELSA wave 9. This cross-walk was carried out using a multinomial logistic regression model, which used age, sex, education and all the cognitive measures available at wave 9 to predict the probability of participants belonging to each diagnostic group.

Covariates in ELSA (wave 4)

High blood pressure/hypertension: defined as doctor-diagnosed hypertension or directly measured blood pressure, with systolic blood pressure/diastolic blood pressure ≥140/90 mmHg. Systolic (SBP) and diastolic (DBP) blood pressure was measured using standardised methods.

Physical activity: measured using responses to questions about the frequency of vigorous, moderate and light leisure-time physical activities. In this analysis, we used a binary variable to indicate whether the participants had once a week participated in any vigorous or moderate physical activity. Those who had not were counted as having low levels of physical activity.

Long-term conditions: respondents were asked whether a physician had ever told them that they suffered from any of the following conditions: diabetes, coronary heart disease (angina or myocardial infarction), stroke; which were recoded to indicate a history of cardiovascular disease (CVD).

Depressive symptoms: assessed using the eight-item version of the Centre for Epidemiologic Study Depression (CES-D) scale administered in the face-to-face interview (Radloff, 1977). We used a binary variable to define a high level of depressive symptoms as those reporting four or more (White et al., 2016).

Loneliness: assessed by three items of the UCLA loneliness scale (lack companionship, feeling left out, feeling isolated), with a response for each item from 'hardly ever or never', 'some of the time' or 'often' (Hughes et al., 2004). The total score ranges from 3 to 9, with higher scores indicating greater loneliness and a binary variable to indicate a high level of loneliness (>5) was used.

Geographical region: the regional indicators used in this chapter divide England into nine regions: North East, North West, Yorkshire and the Humber, East Midlands, West Midlands, East of England, London, South East, and South West. The small number of households in the ELSA sample who live outside England (either Scotland or Wales) were excluded from the analyses. These were firstly recoded into seven regions, which match the NHS England regions. However, due to a small number of participants in certain areas, these regions were grouped into four categories based on the mean household wealth (excluding pension wealth) of each region in 2006–08: (1) North East/Yorkshire/North West (<£190k); (2) East/West Midlands (£190k–£225k); (3) East of England/London (£226–£255k); (4) South West/South East (£255k+) (Office for National Statistics, 2008).

Educational level: ascertained with the participant's highest reported educational qualification at wave 4; grouped into five categories: (1) Degree or equivalent, (2) A-level or equivalent, (3) O-level or equivalent, (4) CSE/other, (5) No qualifications.

Household wealth: assessed with an overall measure that includes savings, investments, and value of property or business assets, but excludes pension assets.

Mobility status: respondents were asked to report any difficulty with the following mobility-related activities: walking 100 yards, sitting for two hours, getting up from a chair after sitting for long periods, climbing one flight of stairs, climbing several flights stairs, stooping, kneeling or crouching, reaching or

extending arms above shoulder level, pulling or pushing large objects, lifting or carrying weights over 10 pounds, and picking up a five-pence coin from a table.

Statistical analysis

Firstly, we present the prevalence (percentages) of each predictor at wave 4 by cognitive status at wave 9. We used multinomial regression models to examine the association between each potential determinant at wave 4 and cognitive status at wave 9. Multinomial logistic regression can be used to model outcome variables which consisted of more than two categories. We present relative risk ratios (RRR) which can be interpreted as the ratio of the probability of being classified with one of the outcome categories (dementia or cognitive impairment) over the likelihood of being classified as being in the reference category (no cognitive impairment) for a unit change in the predictor variable. We estimate three models: The first model includes each predictor and age, age^2, gender, education, and household wealth, as these demographic factors may influence both cognitive status and also many of these socially patterned risk factors. The second model also takes into account mobility status, as physical functioning in later life is associated with both cognitive status and also several of these predictors. The final model takes a history of cardiovascular disease into account as well, because lifestyle factors and social engagement may be particularly affected by these underlying health conditions.

4.4.3 Distribution of predictors (wave 4) by cognitive status at wave 9 (2018/19)

Table 4.1 shows the prevalence of each of the predictors used in the longitudinal analysis by the cognitive status groups in wave 9 (normal cognition, cognitive impairment and dementia). Overall, there were fewer men than women in the sample, although there was a similar proportion of men in each of the three cognitive status groups. Those classified with dementia and cognitive impairment were older than those with no cognitive impairment at wave 9. The cognitive impairment and dementia groups also included a higher proportion of people with worse health (high blood pressure, diabetes) and higher levels of both depressive symptoms and loneliness. However, among those not classified with cognitive impairment or dementia at wave 9, a lower percentage reported no formal educational qualifications at baseline. There was also some evidence of geographical variation, with fewer dementia cases in the South West of England and a higher number of dementia cases in the Midlands. However, it is also clear that in this analytical sample, capturing geographical regions divided into seven categories reveals results in small cell numbers (<20).

Table 4.1. Prevalence of predictors at wave 4, by cognitive status at wave 9

Predictors *N* (%)	Normal cognition (*N* = 3,199)	Cognitive impairment (*N* = 1,242)	Dementia (*N* = 198)	Total (*N* = 4,639)
Age; mean (SD)	60.6 (6.6)	69.0 (6.1)	70.9 (7.5)	63.2 (7.6)
Sex (% male)	1,454 (45.5%)	487 (39.2%)	87 (43.9%)	2,028 (43.7%)
Hypertension (Yes)	1,475 (46.1%)	755 (60.8%)	131 (66.2%)	2,361 (50.9%)
Physical activity (Low)	247 (7.7%)	172 (13.9%)	45 (22.7%)	464 (10.0%)
Diabetes (Yes)	192 (6.0%)	123 (9.9%)	22 (11.1%)	337 (7.3%)
Depressive symptoms (High)	312 (9.8%)	172 (13.9%)	30 (15.2%)	514 (11.1%)
Loneliness (High)	571 (17.9%)	254 (20.5%)	54 (27.3%)	879 (18.9%)
Education (No qualifications)	374 (11.7%)	534 (43.0%)	72 (36.4%)	980 (21.1%)
Wealth (Lowest quintile)	330 (10.3%)	209 (16.8%)	41 (20.7%)	580 (12.5%)
Geographical region				
North East/Yorkshire	502 (15.7%)	233 (18.8%)	35 (17.7%)	770 (16.6%)
North West	360 (11.3%)	112 (9.0%)	20 (10.1%)	492 (10.6%)
Midlands	680 (21.3%)	268 (21.6%)	56 (28.3%)	1,004 (21.6%)
East of England	456 (14.3%)	168 (13.5%)	24 (12.1%)	648 (14.0%)
London	282 (8.8%)	102 (8.2%)	15 (7.6%)	399 (8.6%)
South West	536 (16.8%)	207 (16.7%)	23 (11.6%)	766 (16.5%)
South East	383 (12.0%)	152 (12.2%)	25 (12.6%)	560 (12.1%)

4.4.4 Association between predictor wave 4 and cognitive status wave 9

In Table A.4.1, the results of the multinomial regression models are presented. We have estimated each predictor separately, adjusting for the covariates discussed. The results are presented as relative risk ratios (RRR); these indicate the risk of an adverse outcome when exposed to a risk factor versus the risk when not exposed. In general, an RRR > 1 indicates that the outcome is more likely in the group with the risk factor. The results for the high blood pressure results in Model 1 show the RRR for having raised blood pressure in a model which takes into account age, age^2, gender, education and wealth. The relative risk ratio for having elevated blood pressure was 1.25 (0.90, 1.72) of being classified with dementia compared to those with no cognitive impairment. In other words, the expected risk of being in the dementia group at wave 9 was higher for those who have raised blood pressure at wave 4. This effect size is slightly smaller than reported elsewhere for the relative risk of hypertension for dementia (Norton, 2014; Livingston et al., 2020). However, due to the restrictions of this sample, we were not able to distinguish between midlife and later life hypertension, known to be a noteworthy difference for this particular risk factor.

There is an association between physical inactivity and an increased risk of dementia, but not cognitive impairment in this sample. In Model 3 when the estimates have been adjusted for demographic characteristics, mobility status and also cardiovascular disease history, those who report low levels of physical activity were more likely to be in the dementia group (RRR = 1.61 (CI 95%; 1.04, 2.49)). This effect size is similar to the RRR for physical inactivity and dementia reported elsewhere (Livingston et al., 2020). The relative risk for reporting diabetes (RRR = 1.46 (0.89, 2.42)) was also a similar size to that reported elsewhere (Norton, 2014), although we cannot rule out a null effect

size. The magnitude of this effect was attenuated when mobility status and cardiovascular disease history were taken into account.

We also found an association between reporting a high number of depressive symptoms and risk for both cognitive impairment and dementia 10 years later at wave 9. The risk of dementia for individuals with higher depressive symptoms was again similar to those reported elsewhere (Norton, 2014), although these were attenuated when models were adjusted for mobility and cardiovascular disease. However, the risk of a high level of depressive symptoms for cognitive impairment remained in the final model (RRR = 1.53 (0.96, 2.44)). There was also an association between a high level of loneliness and the risk of cognitive impairment (RRR = 1.38 (1.12, 1.71)) and dementia (RRR = 2.01 (1.40, 2.87)). These effects remained significant when other markers of physical functioning and cardiovascular health were taken into account. We also saw some indications that the risk of dementia was greater for those living in regions with a lower mean household wealth (North East/Yorkshire/North West) and East/West Midlands when compared to those living in the East of England/London., This was independent of individual household wealth which was accounted for the in the analysis, suggesting that other factors may be involved. However, the small numbers of dementia cases in each region resulted in wide confidence intervals.

4.5 Conclusions

In this chapter, we introduced the Harmonised Cognitive Assessment Protocol (HCAP), which was implemented in 1,200 ELSA participants aged 65 and older. This specialised sub-study offered for the first time an opportunity to examine in detail the full spectrum of cognition from normal functioning to cognitive impairment and dementia. Capitalising on this new battery of neuropsychological tests, we developed a research diagnostic algorithm, which classified the overall HCAP sample into various diagnostic groups such as dementia, mild dementia, cognitive impairment, MCI, OCIND with and without functional impairment and no cognitive impairment. This initial categorisation was regrouped into no cognitive impairment, cognitive impairment, and dementia. In ELSA-HCAP, we found that a significant proportion (43%) was classified with cognitive impairment, and 13% with dementia. These estimates are somewhat higher than expected in the general population, and the reason for this is that we oversampled individuals with low cognitive performance prior to this specific sub-study.

In the second section of this chapter, we presented the population prevalence of cognitive impairment and dementia in ELSA at wave 9, by extrapolating the diagnosis algorithm derived in the HCAP sub-study to the rest of the ELSA sample using a prediction algorithm. Using this algorithm, we predicted the probability of participants belonging to each HCAP cognitive group. We calculated these probabilities using education levels, basic demographics, and cognitive performance on all the available measures at wave 9. Here we present the first population-based prevalence estimate, ascertained in a representative sample of the English population aged 60 and older ($N = 6,669$). From this overall sample, 23% were classified with cognitive impairment and 4.6% with

dementia. These prevalences are slightly lower than those reported by CFAS II, where 6.6% of their overall sample were classified with dementia; however, their study population ($N = 7,762$) were aged 65 and older at the recruitment in 2011 and involved only three areas of the country (Richardson et al., 2019).

In the final section of this chapter, we examined the longitudinal associations between predictors of cognitive impairment and dementia status at wave 9, by looking at various social and psychosocial risk factors for which there is emerging evidence (depression, social isolation, loneliness, social support, socioeconomic risk factors). Our findings provide further support for evidence on the impact of the psychosocial risk factors on neurocognitive disorders in later life. We found positive prospective associations between increased loneliness or depressive symptoms at wave 4 in relation to subsequent cognitive impairment and dementia at wave 9. These risk factors are amongst those where the evidence is less well established (Lincoln et al., 2014), and it is unclear whether these represent early symptoms of cognitive impairment or causal risk factors. The longitudinal structure of ELSA allows medical and psychosocial risk factors to be assessed almost a decade before neurocognitive disorders would develop and demonstrate that these factors precede the occurrence of cognitive impairment and dementia. The role of social isolation and loneliness in elevating dementia risk (Rafnsson et al., 2020) has been described previously with significant implications for shorter life expectancy and mortality (Holt-Lunstad et al., 2010). Moreover, the evidence regarding depression is somewhat mixed, suggesting that it may represent a risk factor associated with cognitive impairment, but the relationship could also be bidirectional, and therefore depression may constitute a prodromal stage of the clinical manifestation of the neurocognitive disorders.

Previous ELSA work has confirmed some of the associations presented in this chapter, such as depressive symptoms (Zheng et al., 2018) and loneliness (Yin et al., 2019) in relation to cognitive performance and changes in cognitive performance over time. Moreover, a large body of evidence conducted in ELSA has shown significant variability in the modifiable risk factors associated with dementia, such as socioeconomic differentials (Cadar et al., 2018), social support (Khondoker et al., 2017), loneliness (Rafnsson et al., 2020), social and cultural engagement (Fancourt et al., 2018), cognitive reserve (Almeida-Meza et al., 2020), and obesity (Ma et al., 2020) despite the fact that these studies were based on a less precise and comprehensive assessment of cognitive impairment and dementia than the ones developed here.

The findings reported in this chapter support previous evidence on the common risk factors linking the cardiovascular, metabolic and psychiatric risk factors, via socioeconomic status and social context, smoking, and sedentary behaviours, and extend some of these effects in relation to cognitive impairment. It is important to acknowledge that many of these modifiable risk factors co-exist or are part of the same pathways, as in the case of stroke and microvascular infarcts for both vascular dementia and AD. Our findings confirm the direction and effect size of several well-established risk factors (high blood pressure, low levels of physical activity, diabetes), which suggests that the cross-walk groups established for wave 9 cognitive status were satisfactory.

We also noted some variation by geographical region. However, these geographic and neighbourhood characteristics may not be independent of individual-level socioeconomic factors, which are known to be significant predictors of cognition status in later life.

4.5.1 Study strengths and weaknesses

There are numerous strengths in the context of the present analyses, including the specialised neuropsychological HCAP assessment that allowed the development of a diagnostic algorithm to ascertain cognitive impairment and dementia, which further permitted extrapolation to the rest of ELSA. Given the harmonisation framework of these data, there are several opportunities for cross-cohort investigations of cognitive impairment or dementia prevalence in different countries around the world. In addition, the wide range of data collected in ELSA, capturing various domains including biological, psychological, physical, cognitive, economic, social, and behavioural factors, opens up possibilities for fruitful longitudinal investigations of the determinants and outcome of cognitive impairment. Our analyses also have limitations. The operationalisation of diagnostic criteria for the ever-changing concepts of MCI and dementia, as well as their diagnostic boundaries, are varied. There is a lack of standardised diagnostic criteria for the ascertainment of neurocognitive disorders in population studies. More work is needed to further explore the agreement between self-reported physician diagnosis of dementia, the records from Hospital Episode Statistics, and routinely collected clinical data. The sample of participants selected in this study was relatively small, and any HCAP analyses must be weighted using the sample weights in the data set in order to make the findings more representative of the English population. Furthermore, we were not able to investigate dementia subtypes (Alzheimer's disease, vascular dementia).

4.5.2 Policy implications

The current work suggests important avenues for developing appropriate public health messages and policy implications in terms of early identification and dementia prevention.

The cognitive performance data collected every two years since 2002 in ELSA, coupled with the ELSA-HCAP sub-study, have allowed us to develop algorithms for the identification of cognitive impairment and possible dementia at the population level. These assessments confirm that many cases in the community are not identified through current clinical channels. Underdetection could be related to the availability of specialised services in various geographical areas, the waiting times for clinical consultations, to the reluctance of older people to come forward with problems, or lack of awareness (for example, thinking that impairments are part of normal ageing). Other challenges of developing policy in this context are related to our limited knowledge of the biological mechanisms underlying vascular causes of cognitive impairment and its clinical manifestations in those at risk or prodromal stages.

With respect to dementia prevention, several actions are supported by this study: notably maintaining physical activity, preventing and treating cardiovascular risk factors (e.g., hypertension, diabetes mellitus, smoking) and remaining

socially and intellectually engaged in order to avoid loneliness. This is consistent with international evidence about these risk processes (Livingston et al., 2020). It has been estimated that the potential for Alzheimer's disease prevention through modification of seven risk factors – diabetes, hypertension in midlife, midlife obesity, smoking, depression, low educational attainment, and physical inactivity – is around 30% (Norton et al., 2014). The reality is that it will take some time for these risk factors to be fully incorporated into public awareness and policy, though a vigorous evidence-based public health awareness campaign could accelerate this process. The future provision of modifiable interventions and care will require a national response and integration across all societal levels, taking into consideration the marked socioeconomic differentials in risk.

4.6 Acknowledgements

Appendix

Cognitive tests included in the HCAP sub-study

Self-reported Memory

This measure provided an indication of whether the respondent was worried about their memory. Participants were asked to rate their memory at the present time as excellent, very good, good, fair or poor. They were also asked to say whether compared with two years ago, their memory is now better, the same, or worse.

Mini-Mental State Examination

The Mini-Mental State Examination (MMSE) or Folstein test (Folstein et al., 1975) is a 30-point questionnaire that is used extensively in clinical and research settings to measure cognitive impairment. This is a multipart test and includes questions that assess multiple cognitive domains such as memory, language, repetition, and orientation to time and place, registration, attention and calculation. The maximum MMSE score of 30 is computed by assigning one point for each correct response for orientation to time (5 points), orientation to place (5 points), registration (3 points), attention to calculation (5 points), recall (3 points), language (2 points), repetition (1 point) and complex demands (6 points).

People and Objects Naming (Telephone Interview for Cognitive Status)

The HRS-TICS (Telephone Interview for Cognitive Status) is a very brief global mental status test based on a set of questions, which are similar to those in the MMSE, that has been adapted from the full Telephone Interview for Cognitive Status (Brandt et al., 1988). This provides information about language and factual knowledge. In ELSA-HCAP, the test included questions to identify two words, e.g. scissors, cactus (vocabulary) and naming the Prime Minister of the United Kingdom (factual knowledge). The score for HRS-TICS recorded in the ELSA-HCAP data was computed by assigning one point for each correct response with scores ranging from 0 to 3.

CERAD Word List Learning and Recall

This is a simple memory test comprised of three distinct parts, testing immediate recall, delayed recall and recognition as described below.

CERAD Word List Immediate Recall: The respondent was shown ten words in the CERAD flipbook and was asked to read them aloud in turn. They were then asked to immediately recall as many of the ten words as they could. They were shown the same words in a different order and asked to read them aloud in turn, and they were asked again to recall the words. They were shown the words in a different order a third time and asked again to read them aloud and then remember them (making a total of three immediate recalls). The immediate recall score was computed by summing the total number of words correctly recalled for each of the three trials with a maximum score of 30.

CERAD Word List Delayed Recall: After completing several other tests that were part of the HCAP interview (Animal naming, Ps and Ws Letter Cancellation, Backwards Counting, and Naming Items (10/66)), the respondent was asked to recall as many of the ten words as they could. The Delayed Recall score was the number of words correctly recalled after the delay, with a maximum score of 10.

CERAD Word List Recognition: This was a recognition trial of the CERAD 10-word list, in which the respondent was visually presented with a series of 20 words including 10 from the original list and 10 that were not part of that list. Participants were asked whether they could recognise each word from the original list (Yes/No). The task was administered after completing another test of the HCAP interview (Story recall – immediate recall). The Recognition score was computed by summing the number of words that were correctly identified as from the original 10-word list, with a maximum score of 20.

Verbal Fluency (Animal Naming)

This is a typical neuropsychology test of retrieval fluency that was also administered in the ELSA Core survey. Respondents were asked to name as many animals as they could think of in 1 minute. The score for verbal fluency was computed by subtracting the estimated number of incorrect or repeated responses (if applicable) from the total number of responses provided.

Processing Speed (Letter Cancellation)

This is a timed test measuring attention and processing speed that was also administered in the ELSA Core survey. Respondents were asked to search a grid

of letters and cross out any 'Ps' or 'Ws' they saw, and then underline how far down the grid they got in the 1-minute time allowed. The score for the Letter Cancellation test was calculated from a combination of speed (how far through the grid they got in the time), and processing accuracy (the number of mistakes made, or letters missed).

Backwards Counting

The backwards counting span task is a mental tracking test, associated with working memory and executive function. The respondent was asked to count backwards from 100 as fast as possible, for 30 seconds. The interviewer recorded the number they get to in the time allowed and the number of mistakes they made. The score was calculated by subtracting from 100 the final number the respondent reached, taking into account the number of errors made.

Naming Items

These questions were initially derived from the 10/66, and Community Screening Interview for Dementia (CSI-D) surveys to assess cognitive impairment and dementia. The questions evaluate language, knowledge and the ability to follow directions. The respondent was asked four questions: to name an object the interviewer points to, to describe how to use an object, to explain how to get to a nearby shop, and to point to a window and then a door. The score was calculated by assigning one point for each correct response, with scores ranging from 0 to 4.

Logical Memory (Story recall)

This test involved the reading of two different stories ('Brave Man' and 'Anna Thompson' from the WMS-IV Logical Memory) and assessed the logical memory recall of various story points that the respondent could remember after hearing each story. The scores were based on the number of the story points correctly named. Three aspects of logical memory were examined as described below.

Immediate Recall: After reading the first story (Brave Man), the respondent was asked to recall as much detail about the story as they could, and the interviewer scored them on the details they remembered. The interviewer then read the second story (Anna Thompson) and again asked participants to recall as much detail about the second story as they could. Separate scores were computed as a sum of the information immediately recalled per each story, with respective maximum scores of 6 and 25.

Delayed Recall: After completing other tests of the HCAP interview (Word List Recognition, Shape Drawing (Constructional Praxis), Symbol Digit Modalities Test (SDMT), and Shape Drawing Recall), the respondent was invited to recall as much detail as they could about both stories. The delayed recall scoring was identical to the immediate recall.

Recognition: After the delayed recall of the two stories, the respondent was presented with a series of 15 statements about the second story (Anna Thompson). They were asked to confirm whether each statement was true or false, based on what they were able to remember and recognise as part of the original story. The recognition score was based on the number of correct responses given with a maximum score of 15.

CERAD Constructional Praxis (Shape Drawing)

The CERAD Constructional Praxis test involves drawing four geometric shapes, with each drawing assessed against specific criteria. The shapes were a circle, a diamond, two overlapping rectangles, and a 3D cube. Two aspects of constructional praxis were examined as described below.

Constructional Praxis – immediate: The respondent was given a worksheet containing the first geometric shape (the circle) and asked to copy the shape on the same sheet of paper. They were then given a worksheet containing the second geometric shape (the diamond) and again asked to copy the shape. This was repeated for the third (the overlapping rectangles) and fourth shape (the 3D cube). The final score represented the sum of various aspects that met the precision criteria set, with a maximum score of 11.

Constructional Praxis – recall: After completing one other test of the HCAP interview (Symbol Digit Modalities Test), the respondent was asked to redraw the shapes from memory on a blank piece of paper. The score was calculated based on the individual criteria used in the immediate score of constructional praxis.

Symbol Digit Modalities Test

The Symbol Digit Modalities Test (SDMT) measures processing speed and attention. The test was administered with the official SDMT paper form (a pre-printed carbon-backed worksheet) and required the respondent to substitute a number for randomised presentations of geometric figures. The respondent was presented with a set of number-symbol pairings at the top and a large grid of symbols underneath. The task was to accurately write down the corresponding number for each symbol on the grid. The respondent was given 90 seconds to complete as many of the symbols as they could. The score computed represents the number of attempted pairings minus the number of mistakes or skipped pairings.

Number Series

The Number Series measures problem-solving ability and numeric reasoning by presenting a set of six individual series of numbers, where one or two numbers in the series are missing. The interviewer read out a series of numbers with a gap for a missing number. The respondent was asked to write down the sequence of numbers and work out the missing number that would go in the gap. The task was not timed. Respondents were given a set of three number series questions of varying difficulty. Based on the number of correct responses in the first set of three (score range = 0 to 4), respondents were then assigned to the second set of three questions, for which the difficulty level was adapted on the number correct on the first set. There were two versions of the Number Series questions available, and each respondent was assigned to the version that had not been completed in a previous wave of ELSA (wave 8, 2016/17).

Raven's Standard Progressive Matrices

This is a general intelligence test that evaluates picture-based pattern reasoning of varying difficulty. The respondent was shown a matrix of shapes or patterns, with the final shape or pattern in the series being missing. The respondent was asked to indicate which of several options given underneath would be the next

shape or pattern in the series. ELSA-HCAP used only a subset of 17 questions out of the 60 from the full standard test, including one practice question. The test was not timed, and the score is calculated by summing the number of correct responses, with scores ranging from 0 to 17.

Trail Making (A and B)

This task requires the respondent to track numeric and alpha-numeric characters on a grid that looks like a dot-to-dot puzzle. The test was administered in two parts, A and B. Trail Making A involves numbered circles (from 1 to 18), and the respondent was asked to draw a line linking the circles in numeric order (1, 2, 3, etc.). Trail Making B involves numbered circles and circles containing letters, and the respondent was asked to draw a line linking the numbers and letters alternately (1, A, 2, B, 3, C, etc.). The task was timed. The interviewer watched the respondent as they were completing each task, and if they made a mistake, the interviewer stopped them and asked them to go back and correct the error made. The scores for A and B were based on the time it took to complete each task, with the time spent going back to correct mistakes included. The score represents the time that an individual took to finish the task in each test, with a higher score indicating a lower performance on these particular tests.

An assessment of depression (Center for Epidemiological Studies-Depression) and an olfaction test were also administered at the end of the ELSA-HCAP respondent interview, but these were not used as part of the dementia algorithm.

Table A.4.1. Multinomial logistic regression for the association between demographic characteristics and cognitive impairment

N = 4,853	Model 1		Model 2		Model 3	
	Cognitive impairment	*Dementia*	*Cognitive impairment*	*Dementia*	*Cognitive impairment*	*Dementia*
	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)
High blood pressure						
No	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Yes	1.10 (0.93, 1.30)	1.25 (0.90, 1.72)	1.08 (0.92, 1.28)	1.19 (0.86, 1.65)	1.07 (0.91, 1.27)	1.17 (0.84, 1.62)
Low physical activity						
No	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Yes	1.16 (0.89, 1.51)	2.09 (1.39, 3.12)	1.03 (0.78, 1.36)	1.60 (1.04, 2.48)	1.03 (0.78, 1.36)	1.61 (1.04, 2.49)
Diabetes history						
No	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Yes	1.30 (0.96, 1.75)	1.46 (0.89, 2.42)	1.24 (0.92, 1.67)	1.29 (0.78, 2.15)	1.21 (0.89, 1.64)	1.23 (0.74, 2.06)
Depression (case)						
No	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Yes	1.68 (1.30, 2.19)	1.93 (1.23, 3.02)	1.56 (1.19, 2.05)	1.54 (0.97, 2.46)	1.56 (1.19, 2.05)	1.53 (0.96, 2.44)
Loneliness (high)						
No	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Yes	1.38 (1.12, 1.71)	2.01 (1.40, 2.87)	1.33 (1.07, 1.65)	1.81 (1.26, 2.61)	1.33 (1.07, 1.64)	1.81 (1.26, 2.61)
Geographical region						
North East/Yorkshire/North West	1.15 (0.91,1.45)	1.30 (0.83, 2.03)	1.13 (0.89,1.42)	1.23 (0.79, 1.93)	1.12 (0.89,1.42)	1.23 (0.78, 1.93)
East/West Midlands	1.04 (0.81, 1.33)	1.48 (0.94, 2.32)	1.02 (0.80, 1.31)	1.40 (0.89, 2.21)	1.03 (0.80, 1.32)	1.41 (0.90, 2.22)
East of England/London	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
South West/South East	1.18 (0.94, 1.49)	1.03 (0.65, 1.63)	1.18 (0.94, 1.49)	1.02 (0.65, 1.62)	1.18 (0.93, 1.49)	1.03 (0.65, 1.63)

Model 1: predictor, age, age2, gender, education, and household wealth.
Model 2: Model 1 further adjusted for mobility status.
Model 3: Model 2 further adjusted for a history of cardiovascular disease.

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