COGNITIVE FUNCTION AND HEALTH IN OLDER ADULTS

by

EMMA LOUISE SUTTON

A thesis submitted to

The University of Birmingham

for the degree of

DOCTOR OF PHILOSOPHY

School of Psychology

College of Life and Environmental Sciences

University of Birmingham

July 2023

UNIVERSITY OF
BIRMINGHAM

University of Birmingham Research Archive

e-theses repository

This unpublished thesis/dissertation is copyright of the author and/or third parties. The intellectual property rights of the author or third parties in respect of this work are as defined by The Copyright Designs and Patents Act 1988 or as modified by any successor legislation.

Any use made of information contained in this thesis/dissertation must be in accordance with that legislation and must be properly acknowledged. Further distribution or reproduction in any format is prohibited without the permission of the copyright holder.

Abstract

Ageing is characterised by changes to many aspects of health, such as cognition, mental wellbeing, physical functioning, and serological markers of health. A background to relevant ageing literature is detailed in **Chapter 1**. **Chapter 2** was an amendment to the original research plan due to the COVID-19 pandemic. Cross-sectional findings suggest that during the pandemic, older adults that worried about their cognitive health also reported poorer mental and physical wellbeing. A person-centred approach (latent profile analysis) in **Chapter 3** established characteristics of individuals based on physical, mental, and serological markers of health. Results suggest that good physical functioning is not always associated with good mental wellbeing, and it is therefore important to not just look at individual health markers but to build a profile of overall health for more detailed information. **Chapter 4** used a rigorously designed randomised controlled intervention to assess the benefits of a commercially available brain training programme. Results report no transferable cognitive benefits in healthy older adults. Finally, **Chapter 5** summarises key findings from each empirical chapter and discusses further implications. Overall, the findings from this thesis demonstrate that there is a complex relationship between cognitive function and health in older adults, and that it is important to consider multiple aspects of health when assessing healthspan.

This thesis is dedicated to my grandparents:

Nanna, Grandpa, Nutty, and Grandad

Without whom I wouldn't be here

Acknowledgements

First and foremost, I would like to thank my supervisors, Dr Jonathan Catling, Dr Katrien Segaert, and Dr Jet Veldhuijzen van Zanten. I know I am truly lucky to have such supportive supervisors in every sense of the word, and I can't thank you enough for everything you have done. Jon, I can't believe it's been almost 10 years since I was one of your tutees – I think it's testament to your kindness and encouragement that we are still working together. Katrien, you have been a joy to work with ever since we met (only two years after Jon!), and I have learnt so much from you. Thank you for always encouraging me to improve and develop, and for your pep talks and hugs when needed. And finally, Jet, thank you for joining our team. You are so enthusiastic and knowledgeable, and it has been such a pleasure getting to know you. A special thank you for letting me test out my newly learnt phlebotomy skills on your arm…

To all of those at UoB: Roxy; we started our PhDs together and I will be forever grateful for all the laughs, rubber ducking, and (many, many) coffee breaks. We have come so far since 2019 – I don't think you realise quite how amazing you are. And to the more recent starters in our office: Amélie, Monica, Rupali, and Salma. You have made Roxy and I's quiet COVID office into a bubbly and social place to be, and I can't wait to see how you get on. Rich, I'm so grateful for your patient teaching and for your guidance for all things phlebotomy. Finally, I can't write this without acknowledging my original Psychology postgrads: Al, Mel, Sean, and Tom. Our Masters were so long ago now, but I know that you are still always available for a chat (likely with a bottle of wine).

I thank the Economic and Social Research Council (ESRC) Midlands Graduate School (MGS) Doctoral Training Partnership (DTP) for funding the research presented here, and for giving me the amazing opportunity to visit Australia at the end of 2022.

To friends, near and far, who have supported me over the last few years: thank you always being at the end of a phone or train journey and for reminding me that life is bigger than a PhD. A special thank you to Beth and Jonny for our regular dinner parties and impromptu pub trips (being known as the Aperol spritz table is our finest achievement). You never fail to make me laugh and have made staying in Birmingham such a joy.

To Paddy, I cannot thank you enough for your never-ending love and support. You have seen this PhD through all its highs – celebrating big successes with fried chicken and Champagne is something I hope to carry on forever – but also its lows, for which you would always manage to bring me out of. I am so excited for our new chapter of us (finally) entering the big wide world of work.

Last but definitely not least, I would like to thank my family. To Mum, Dad, and Laura; thank you for your unwavering love. Laura: I am so proud of the person you have become, and I hope that you get everything you want in life, because you truly deserve it. Mum and Dad: you have always encouraged me to do whatever I set my mind to and have cheered me on in every step of this very long academic journey. Thank you all for allowing me to natter on about psychology, even when you didn't understand what I was talking about! I would not be here today without your support, and for that, I thank you with all my heart.

List of publications

Below lists published work included in this thesis and outlines author contributions for each:

Sutton, E., Catling, J., Segaert, K., & Veldhuijzen van Zanten, J. (2022). Cognitive health worries, reduced physical activity and fewer social interactions negatively impact psychological wellbeing in older adults during the COVID-19 pandemic. *Frontiers in Psychology*, *13*, 382. https://doi.org/10.3389/fpsyg.2022.823089

Author contributions: ES, JC, KS, and JVvZ: conception and design of the study. ES: data acquisition. ES, JC, and JVvZ: data analysis. All authors contributed to the data interpretations and drafting and final approval of the manuscript.

The above publication forms the entire body of the work presented in **Chapter 2**.

Sutton, E., Catling, J., Veldhuijzen van Zanten, J., & Segaert, K. Computerised brain training has limited cognitive benefits in healthy ageing. Manuscript submitted for publication in Aging, Neuropsychology, and Cognition.

Author contributions: ES, JC, JVvZ, and KS: conception and design of the study. ES: data acquisition. ES, JC, JVvZ, and KS: data analysis. All authors contributed to the data interpretations and drafting and final approval of the manuscript.

The above publication forms the entire body of the work presented in **Chapter 4**.

Table of Contents

List of tables *8*

List of figures *9*

Chapter 1 - INTRODUCTION *10*

1 Introductory statement 11

1.1 Ageing 11

1.1.1 Cognitive ageing 13

1.1.2 Physical ageing 15

1.1.3 Changes to mental wellbeing 17

1.1.4 Changes to serological markers of health 19

1.2 Cognitive training 22

1.2.1 Cognitive training in healthy ageing 23

1.2.2 Brain training 24

1.2.3 Methodological issues in brain training 26

1.2.4 Best practice for training research 27

1.2.5 Summary 28

1.3 Thesis aims 29

1.3.1 The COVID-19 pandemic 30

Chapter 2 - COGNITIVE HEALTH WORRIES, REDUCED PHYSICAL ACTIVITY AND FEWER SOCIAL INTERACTIONS NEGATIVELY IMPACT PSYCHOLOGICAL WELLBEING IN OLDER ADULTS DURING THE COVID-19 PANDEMIC *35*

2.1 Abstract 36

2.2 Introduction 36

2.3 Methods 42

2.4 Results 49

2.5 Discussion 54

Chapter 3 - PROFILES OF PHYSICAL FUNCTIONING, MENTAL WELLBEING, AND INFLAMMATION IN HEALTHY OLDER ADULTS, AND THEIR ASSOCIATIONS WITH COGNITIVE FUNCTION: A PERSON-CENTRED APPROACH *60*

3.1 Abstract 61

3.2 Introduction 61

3.3 Methods 67

3.4 Results 77

3.5 Discussion 83

Chapter 4 - COMPUTERISED BRAIN TRAINING HAS LIMITED COGNITIVE BENEFITS IN HEALTHY AGEING **.......... 89**

4.1 Abstract 90

4.2 Introduction 90

4.3 Methods 97

4.4 Results 108

4.5 Discussion 117

Chapter 5 - GENERAL DISCUSSION **.......... 122**

5.1 Summary of aims 123

5.2 Summary of findings 123

5.3 Key findings and theoretical implications 124

5.4 Overall strengths and limitations 131

5.5 Overall conclusions and implications 133

References **.......... 135**

Appendices **.......... 157**

LIST OF TABLES

Chapter 2:

2.1	Demographic information	43
2.2	Mean (SD) wellbeing outcomes for different groups of cognitive health worries and results of one-way ANOVA	50
2.3	Descriptive statistics for variables	50
2.4	Correlation matrix and descriptive statistics for continuous variables	53

Chapter 3:

3.1	Demographic information	68
3.2	Fit indices for latent profile analysis using Model 1, estimating 1-4 profiles	79
3.3	Results of one-way MANOVA validating LPA profiles	81
3.4	Results of one-way MANCOVA assessing cognitive ability between profiles, with age as a covariate.	82

Chapter 4:

4.1	Baseline demographics for intervention and active control groups	108
4.2	Mean (SD) pre- and post-intervention Peak scores for participants in the intervention group	110
4.3	Pre-intervention and post-intervention scores in intervention and active control groups for cognitive outcome measures	111
4.4	Summary of the best fitting models for cognitive data analysed using linear mixed models	113
4.5	Summary of regression models for cognitive data analysed using linear regression	115

LIST OF FIGURES

Chapter 1:

1.1	Graphical representation of empirical chapters within this thesis	34

Chapter 3:

3.1	Figure showing standardised mean value for each indicator included in the LPA, split by final profile	80

Chapter 4:

4.1	Participant flow chart	98
4.2	Pre- and post-intervention scores for Peak games, demonstrating practice effects within the intervention	110
4.3	Pre- and post-intervention scores for outcome measures split by condition, demonstrating a lack of transfer effects to cognitive measures	116

Chapter 1 - INTRODUCTION

1 Introductory statement

This thesis aims to add to the current literature on older adult health. The three aims of the thesis are as follows:

1. Investigate the cognitive, mental, and physical wellbeing of older adults during the COVID-19 pandemic via an online survey (**Chapter 2**)
2. Establish the relationship between cognitive, mental, physical, and serological markers of health, in a cross-sectional sample of healthy older adults (**Chapter 3**)
3. Determine the effectiveness of a commercially available computerised brain training programme on cognitive performance in a sample of healthy older adults, in a randomized and controlled intervention design (**Chapter 4**)

This introductory chapter will first discuss literature surrounding age-related changes to cognitive, mental, physical, and serological markers of health (which relates to **Chapters 2**, **3**, and **4**). It will then discuss the effects of cognitive training (relating to **Chapter 4**), and finally the effects of the COVID-19 pandemic on older adults (relating to **Chapter 2**).

1.1 Ageing

Humans are living longer now than ever before. Life expectancy has increased consistently since the 1900's, driven by both decreased infant mortality and advances in healthcare (Roser et al., 2013). With adults living longer, the general population is ageing, and the proportion of older adults compared to other age groups is growing steadily. The percentage

of those over 65 in the United Kingdom is expected to reach 24.7% in 2046, up from 15.9% in 2006 (Randall, 2017).

This thesis will centre on aspects of health that decline with age during ‘healthspan’, that is, the number of years in which someone is ‘healthy’ or without disease (Garmany et al., 2021). Healthy ageing is related to declines across physical and cognitive health, and extending the time before this deteriorates is beneficial to reducing costs to care and health services. For example, the prevalence of dementia doubles every five years after the age of 65, so much so that an estimated 1 in 6 of 80+ year olds have some form of dementia (Alzheimer's Society, 2016). Dementia cost the UK an estimated £37.4 billion in 2019, 40% of which was through unpaid care (Wittenberg et al., 2019). A third of over 65s and 50% of over 80s suffer from yearly falls, which is estimated to cost the NHS £2.3 billion every year (National Institute for Health and Care Excellence, 2013). Overall, an estimated two fifths of NHS budget is spent on adults over 65 and this is expected to increase with our ageing population (Robineau, 2016).

Age-related changes are seen throughout the body and brain. As we are living longer, finding ways of staying healthy for longer is imperative, not only for our overall health but to minimise costs to health and care services. This has therefore been the basis for much research into healthy ageing. The following sections will discuss the different aspects of ageing, namely changes to cognitive health, physical functioning, mental wellbeing, and serological markers of health.

1.1.1 Cognitive ageing

A number of things change in our cognitive system with age. Some cognitive abilities begin to decline, with "fluid" abilities such as explicit memory, processing speed, and reasoning showing steady declines from as early as in our 20s (Salthouse, 2010). Older adults have a reduced capacity for new learning due to a decline in working memory ability, and executive function deficits may result in older adults struggling with new or complex tasks that require problem solving or planning (Murman, 2015). Conversely, "crystallised" abilities (semantic memory, memory for facts and information, and vocabulary) seem to remain stable or even improve as we age (Salthouse, 2010).

These declines in performance have been linked to changes in brain structure and function. Brain volume and weight reliably decline in healthy ageing, a finding partially attributed to neuronal cell death (Svennerholm et al., 1997). However, the brain does not deteriorate at the same rate across all brain regions. The prefrontal cortex (PFC) and hippocampus are most vulnerable to deterioration in healthy ageing, with both regions showing significant synaptic loss (Morrison & Baxter, 2012). Many higher cognitive functions rely on these areas (working memory and executive function for the PFC, and memory on the hippocampus) and so it is not surprising that ability declines in healthy ageing. Indeed, hippocampal deterioration is reliably shown as a marker for Alzheimer's disease, which itself is characterised by loss of memory (Gosche et al., 2002).

However, despite these relatively stable age-related changes to the brain, cognitive performance can range significantly between older adults. There are three main theoretical frameworks that have been proposed to explain these individual differences; cognitive reserve,

maintenance, and compensation (Cabeza et al., 2018). *Cognitive maintenance* refers to the preservation of neural resources throughout life (Cabeza et al., 2018), and relates to the brain repairing itself as cells die naturally or through damage. The model proposes that as we get older, the repair process becomes imbalanced, and more brain cells die than can be repaired or replaced.

Cognitive compensation refers to the recruitment of additional neural resources to cope with increased task demand. A common model associated with compensation is the Compensation-Related Utilization of Neural Circuits Hypothesis (CRUNCH; Reuter-Lorenz & Cappell, 2008). It proposes that older adults are less efficient at processing due to general age-related declines, and so during low task demand, they require more neural resources to reach the same level of performance as younger adults. At high task demand however, the neural resources have already been depleted, older adults are unable to recruit any more resources, and so performance crashes. CRUNCH proposes that training cognitive abilities allows cognitive processes to be made more efficiently and rely on fewer neural resources, and so improve performance at higher task demands (Reuter-Lorenz & Cappell, 2008).

Finally, *cognitive reserve* refers to a gradual improvement in neural resources, which allows the brain to compensate for age-related neural decline (Cabeza et al., 2018). This improvement or reserve accumulates over a matter of years and has been linked to a number of factors, most frequently education, but also stimulating occupation and lifestyle choices during adulthood such as mental, social, or leisure activities (Clare et al., 2017). Research has shown that those with high cognitive reserve are able to tolerate more neuropathology from dementia before starting to show symptoms, and high cognitive reserve significantly reduces the

incidence of dementia (Valenzuela & Sachdev, 2006). Indeed, incidence rates of dementia are highest in those with low education and occupational attainment (Stern et al., 1994). However, what has also been shown in the literature is a different prognosis after symptoms of dementia begin to show behaviourally. Researchers have found that while those with higher initial cognitive reserve can tolerate more pathology in the brain and that this results in a reduced risk of Alzheimer's prevalence, when symptoms do appear, the deterioration seen is often faster and more severe (Wilson et al., 2010; Wilson, Scherr, et al., 2007).

Cognitive maintenance, compensation and reserve are separate processes. However, older adults who have higher levels of education would, according to the reserve hypothesis, have higher levels of cognitive *reserve*, allowing them to maintain higher levels of performance on cognitive tasks. Higher levels of education may also mean they maintain these resources better, through cognitive *maintenance*, but also that they may have more *compensatory* resources to draw on, when performance declines. This shows that the three theoretical frameworks can be intrinsically linked and that not one theory can explain cognitive ageing as a whole (Cabeza et al., 2018).

1.1.2 Physical ageing

Perhaps the most obvious changes to humans with age are physical ones. Older adults see decline in muscle mass and bone density (Goodpaster et al., 2006). Metabolism rates slow down, resulting in an increase in fat mass and weight gain (Johannsen & Ravussin, 2010). Maintaining fitness in later life is important for overall health, but research shows a reduction in physical activity with age (NHS Digital, 2019). Cardiorespiratory fitness levels also decline with age, a finding commonly shown by differences in VO_2max scores between young and old

(e.g., Segaert et al., 2018). Studies have shown that poor cardiorespiratory fitness predicts higher risk of mortality in older adults (Sui et al., 2007). Another important factor is grip strength, which is a measure of body function and has been termed an 'indispensable biomarker' for older adults (Bohannon, 2019). This is not only for overall strength but for numerous other factors including falls, cognitive impairment, sleep, diabetes, quality of life, and malnutrition (Bohannon, 2019).

Research has shown that declines in physical activity are causally linked with declines in mobility (Visser et al., 2002). Age-related changes such as musculoskeletal pain, obesity, and sensory impairment can exacerbate mobility declines further (Rantakokko et al., 2013). Importantly, those that are limited in mobility are more reliant on others for daily activities and as a result lose independence (Hirvensalo et al., 2000). Alongside mobility changes, with increasing age comes an increased risk of falling. Risk factors include gait variability (Hausdorff et al., 2001) and balance issues (Tinetti et al., 1986), and conditions such as dementia can further increase the risk of falling (Shaw et al., 2003).

1.1.2.1 Relating physical health to cognitive functioning

The aspects of physical health mentioned above have been linked with cognitive functioning. For example, physical exercise can benefit cognition as it significantly reduces the risk of dementia and brain ageing (Law et al., 2020), by stimulating growth, reducing the immune response, and reducing exposure to neurotoxins (Cheng, 2016). Keeping cognitively active can also help, by increasing the connectivity between brain regions and improving neural plasticity (Cheng, 2016). Physical activity is suggested to help protect the brain 'hardware' by increasing brain mass and integrity, while cognitive activity protects the 'software' by

strengthening the connections within the brain (Cheng, 2016). Higher cardiorespiratory fitness is predictive of better cognitive wellbeing (Pentikainen et al., 2019), and research has found that exercise training is beneficial to executive function (Chen et al., 2020), cognitive flexibility (Mekari et al., 2020), as well as memory and processing speed (Erickson et al., 2019) in older adults.

Despite being a simple behavioural marker, grip strength has been associated with cognitive impairment (Bohannon, 2019) and cognitive performance (Sternang et al., 2016) in older adults. Finally, fall risk and gait variability have been shown to relate to cognition. Research has argued that age-related declines in cognition, particularly executive function, are partially responsible for an increased risk of falls (Kearney et al., 2013). Indeed, intervention studies that have trained executive function and speed of processing saw improvements to gait (Shimada et al., 2018) and performance on fall risk measures (Smith-Ray et al., 2015). As falls are so costly both to the individual's quality of life and the healthcare system, cognitive interventions that could reduce fall risk would appear to be an imperative area of research.

1.1.3 Changes to mental wellbeing

Alongside changes to physical and cognitive health, older adults may see changes to their mental wellbeing. There are a multitude of factors that may impact this: career changes (e.g., retirement) lead to a reduction in regular activities and social interactions; declines in mobility may affect how much physical activity one is able to do; and older adults may be affected by the death of close family and friends. Mental health in older adults is therefore an important factor to consider when researching this population. Of particular importance are depression, anxiety, and loneliness. Depression affects up to 25% of older adults in the UK, but

they receive significantly less support than younger adults (Age UK, 2016). Anxiety disorders affect around 5% of older adults (Bryant et al., 2008), but symptoms increased significantly during the COVID-19 pandemic, with a third of over 60s reporting increased anxiety (Age UK, 2020b). Finally, recent research has found up to 25% of older adults experience high levels of loneliness (Chawla et al., 2021).

Half of older adults with major depression experience their first episode in later life (Fiske et al., 2009). Late onset depression has been associated with a number of risk factors including drugs commonly taken in later life (e.g., beta blockers, corticosteroids, or respiratory or gastrointestinal medication), dementia, diabetes, poor sleep, and stressful life events (Fiske et al., 2009). Depression and anxiety are often comorbid and as a result, anxiety shares many of the same risk factors in older adults (Vink et al., 2008). Risk factors specific to anxiety may include traumatic events, being childless, and personality traits (Vink et al., 2008).

Experiences of negative mental health symptoms can be exacerbated by a number of physical health factors. In older adults, a lack of physical activity is regularly associated with poor mental health, and exercise is an effective intervention for reducing mental health symptoms (Fox, 1999). Further, individuals with both poor cardiorespiratory fitness and grip strength have an increased risk for anxiety and depression (Kandola et al., 2020). Similarly, maintaining physical functioning is important to one's mental health. Older adults with mobility issues have been found to report more symptoms of depression (Lampinen & Heikkinen, 2003), a poorer quality of life (La Grow et al., 2013), and lower social engagements (Rosso et al., 2013). Social isolation has been associated with significantly higher risk of dementia, heart

disease, and stroke, which can lead to further mobility declines (National Academies of Sciences & Medicine, 2020).

1.1.3.1 Relating mental health to cognitive functioning

The mental health symptoms mentioned above have been related to cognitive wellbeing. Research has found links between increased social activity and global cognition (Kelly et al., 2017), and emotional support is a significant predictor of better cognitive function in older adults (Seeman et al., 2001). Research has also found that social isolation and loneliness are associated with cognitive decline, with participants over 50 who reported high levels of isolation and loneliness scoring lower on measures of verbal fluency and working memory (Lara et al., 2019). A further study indicating that long term loneliness is detrimental to cognitive health is one longitudinal study that found loneliness to be a predictor of Alzheimer's disease (Wilson, Krueger, et al., 2007). Similarly, research has shown that in older adults, depressive symptoms are associated with poorer cognitive performance (Shimada, Park, et al., 2014). However, research is inconclusive as to whether cognitive impairments that are often seen alongside depression or anxiety are a cause or consequence of the symptoms (Beaudreau & O'Hara, 2008; Ganguli, 2009). Despite this, there are clear associations between poor mental health and cognition (Shimada, Park, et al., 2014) and physical functioning (Lampinen & Heikkinen, 2003) which may affect healthspan in older adults.

1.1.4 Changes to serological markers of health

Another way to assess overall health is by examining serological markers of health, which are reflective of different physiological systems. There is evidence that with ageing, various serological markers of health change. Two markers that are particularly relevant to

ageing and this thesis are an inflammatory marker (interleukin-6; IL-6) and a growth factor (brain-derived neurotropic factor; BDNF).

Inflammation is how the body responds to infection, and interleukin 6 (IL-6) plays a key role in the inflammatory response. IL-6 is a cytokine, which act as cell-to-cell communication throughout the body, signalling to other cells what response should be taken (Reeh et al., 2019). An acute IL-6 response to infection or injury is beneficial as it informs organs to prepare for a response to help fight infection. However, issues can arise when IL-6 production is increased for an extended period of time (Narazaki & Kishimoto, 2018). IL-6 has been implicated in the immune response, stimulating T- and B-cells (which can lead to chronic inflammation) and has been associated with a number of inflammatory diseases such as rheumatoid arthritis, Crohn's disease, and psoriasis (Gabay, 2006).

With age, the body goes through a process of 'inflammageing' (Franceschi et al., 2007). Inflammageing is a low-grade systemic increase in pro-inflammatory markers, such as an increase in circulating levels of IL-6 (Wei et al., 1992). While inflammageing is a normal process of ageing, it can have negative health consequences. Inflammageing has a marked impact on physical disability and frailty, as well as overall morbidity and mortality (Ferrucci & Fabbri, 2018). Inflammation has also been shown to be a risk factor for the development of cardiovascular diseases (Sorriento & Iaccarino, 2019), Alzheimer's disease (Huberman et al., 1995) and cancer (Ferrucci & Fabbri, 2018).

A second key biological marker for this thesis is brain-derived neurotrophic factor (BDNF). BDNF is a protein that has an important role in brain health, specifically in neuronal

survival and growth, and neuroplasticity (Bathina & Das, 2015). It is closely related to learning and memory, with high expression in the hippocampus (Miranda et al., 2019). With age, circulating BDNF declines, which has further been linked with smaller hippocampal volume and worse memory performance in older adults (Erickson et al., 2010).

Both IL-6 and BDNF have been associated with mental and physical health. High levels of IL-6 have been associated with symptoms of loneliness (K. J. Smith et al., 2020) and depression (Baune et al., 2012) in later life. BDNF has been implicated in depression, with one review providing evidence that anti-depressant treatment increases BDNF expression in clinically depressed patients (Brunoni et al., 2008). Further, IL-6 and BDNF levels can be improved through physical activity. Exercise has been shown to reduce levels of systemic inflammation (Woods et al., 2012), and similarly, aerobic exercise can boost BDNF levels and therefore improve brain health (Huang et al., 2014). However, with BDNF, whether these benefits are maintained in ageing populations is inconclusive due to a lack of research (Walsh et al., 2020). Despite this, the theory behind the benefits of physical activity on BDNF levels in older adults is promising for future research (Walsh et al., 2020).

1.1.4.1 Relating serological markers of health to cognitive functioning

Research has linked serological markers of health and cognitive decline. Low levels of BDNF have been associated with mild cognitive impairment (Shimada, Makizako, et al., 2014) as well as Alzheimer's, Huntington, and Parkinson's disease (Miranda et al., 2019). Interestingly, some research has suggested that a computerised brain training paradigm can improve BDNF levels in healthy older adults (Ledreux et al., 2019), though it is important to note that other studies have not found corroborating results (Roheger et al., 2020).

High levels of IL-6 have been associated with cognitive decline in healthy older adults (memory, reasoning and verbal fluency), demonstrating that increased inflammation can be detrimental to cognition *without* clinical impairment (Singh-Manoux et al., 2014). A longitudinal study with over 3,000 participants over 10 years found that regular use of non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen was significantly associated with a lower risk of all-cause dementia and Alzheimer's disease (Szekely et al., 2008). Similarly, a review suggested that Rheumatoid Arthritis (RA) patients (RA being an inflammatory autoimmune disease) were up to six times less likely to develop Alzheimer's disease, a finding that was attributed to the common prescription and prolonged use of anti-inflammatory drugs (McGeer et al., 1996). However, NSAIDs have *not* been found to be an effective treatment for Alzheimer's patients (Aisen et al., 2003; Rogers et al., 1993; Scharf et al., 1999). Therefore, it may protect those with little or no brain deterioration, rather than improving symptoms of those with an advanced disease prognosis.

1.2 Cognitive training

As a result of the number of changes adults go through as they age, research has focused on ways to mitigate age-related cognitive decline. This section will first discuss traditional cognitive training programmes in healthy ageing populations. I will then discuss commercially available brain training programmes, the controversy that surrounds the field, followed by issues in the cognitive training literature and recommendations for best practise. For the purposes of this thesis, cognitive training will refer broadly to any intervention that seeks to strengthen cognitive performance through guided practice or strategies, while brain training will refer specifically to the subset of available cognitive training programmes, provided by

companies and organisations that offer the public cognitive interventions aiming to improve cognitive performance (Nguyen et al., 2022).

Note that for the most part I will discuss cognitive training in relation to healthy populations, rather than those with cognitive impairment or dementia. Research has not found convincing evidence that cognitive training can improve cognitive performance in mild to moderate dementia (Bahar-Fuchs et al., 2013), and only small to moderate effects in patients with mild cognitive impairment (Hill et al., 2017). This arguably reiterates the need to focus on cognitive therapies that slow decline rather than attempting to treat cognitive impairment after diagnosis.

1.2.1 Cognitive training in healthy ageing

The use of cognitive training programmes to improve cognition in older adults has been extensively researched. Arguably the most common cognitive functions examined in cognitive training are working memory and executive function. Working memory is theorised to be a central cognitive function closely linked with other cognitive abilities including executive function (Heinzel et al., 2016), and both are key to other higher cognitive functions, such as fluid intelligence, reasoning and multitasking (Sandberg et al., 2014). Theoretically, improving these processes would result not only in improvements to the specific functions but also to untrained cognitive abilities as they are so closely linked. Indeed, cognitive training programmes targeting working memory and executive functions have resulted in transfer to other cognitive tasks (see Karbach & Verhaeghen, 2014 for a review), albeit inconsistently (Melby-Lervåg et al., 2016). Both working memory and executive function performance

decline significantly in healthy ageing (Salthouse, 2010) and so provide a promising starting point to improve cognition in older populations.

One of the key pieces of research that assesses computerised cognitive training in ageing is the large-scale intervention ACTIVE trial by Ball et al. (2002). Over 2,800 participants aged 65 and above took part in a computerised cognitive training programme which focused on speed of processing, reasoning, or memory. All training groups saw an improvement in the cognitive function that was trained, and a booster session after one year led to the effects being maintained for two years (Ball et al., 2002), and five years (Willis et al., 2006) after the initial training programme. This was one of the landmark studies that showed that CT can improve cognitive ability in older adults, but also that these improvements can be maintained over an extended period of time.

1.2.2 Brain training

In recent years, an increasingly popular method of training cognition is to utilise commercially available brain training programmes such as Lumosity, Peak, or BrainHQ. These programmes are tailored to the user's performance, adapting in difficulty (which is key for brain training to work, Brehmer et al., 2012), and target a wide range of cognitive abilities through short, game like tasks. Brain training applications are advertised as programmes that are designed by "scientists" (Lumosity, 2023), can improve "neuroplasticity" (Peak, 2023), and "exercise your brain" (BrainHQ, 2023). However, research is inconclusive as to whether these brain training programmes work. In 2014, a large group of scientists published an open letter arguing that computerised brain training has little benefit to cognition, and that the marketing from brain training companies is frequently exaggerated and misleading (Allaire et al., 2014).

Two months later, an equally large group published a response, countering that there *is* a substantial body of evidence that cognitive training programmes can improve cognitive functioning (Alescio-Lautier et al., 2014).

Peer-reviewed research is just as contentious. Brain training websites often cite peer-reviewed publications that show positive effects of their programme, and there is research that suggests brain training in healthy populations improves auditory processing and memory (Anderson et al., 2013), sustained visual attention (Savulich et al., 2019), and improves executive functions (Meltzer et al., 2023), among others. However, there are also many cases where no significant effects have been found (e.g., Kable et al., 2017; Stojanoski et al., 2018). This is all the more important in older populations. Research has shown that older adults have higher expectations about how well these programmes work compared to younger counterparts (Rabipour & Davidson, 2015), and arguably, older adults can benefit more from the programmes (if they are effective). However, meta-analyses both support (Lampit et al., 2014) and disagree (Nguyen et al., 2022) with their benefits in healthy older adults.

A key benefit that brain training programmes aim for are transfer effects. Transfer effects refer to how similar outcome measures are to the trained cognitive domain (Sala et al., 2019). They can be near or far – near transfer referring to the training generalising to similar domains (e.g., if training working memory transfers to related, but untrained, working memory tasks), while far transfer being that the programme transfers to wider, unrelated tasks (e.g., working memory training transferring to improvements in language or attention). Transfer effects are key to a successful and wide-reaching brain training programme; however, they are elusive, especially in ageing research. Often, reports of significant transfer are for near transfer rather

than far, limiting any effects to similar cognitive processes (H. K. Lee et al., 2020), or no evidence is seen at all (Kable et al., 2017; Stojanoski et al., 2018). Importantly, even in the popular ACTIVE study (Ball et al., 2002), cognitive benefits were limited to the type of cognitive training given to each participant and did not transfer to untrained outcome measures.

1.2.3 Methodological issues in brain training

As has been shown, the field is fraught with controversy. A major reason for this is that there are many methodological differences in the brain training literature which lead to inconsistent findings. A paper by von Bastian and Oberauer (2014) suggests that there are two factors at hand explaining the lack of consistency in cognitive training research: training differences and individual differences. Interventions vary hugely, in terms of training length, training intensity, sample size, whether the training is adaptive, and the training tasks themselves (von Bastian & Oberauer, 2014). To emphasise, a literature review investigated methodological differences and found large ranges in sample size and study duration (Noack et al., 2014). Sample sizes ranged from 20 to almost 2,500, but 90% included fewer than 100 participants. Similarly, training duration also varied, with 50% of studies reported 8 hours and 20mins of training or less, and the majority (90%) reporting less than 20 hours in total. Individual differences are also a significant issue in cognitive training research; older adults show large variability in both baseline performance and training gains (Buitenweg et al., 2012). This variability can come from factors such as age (Brehmer et al., 2012) or motivational differences (Buitenweg et al., 2012) which often makes it difficult to compare or generalise results.

A further issue in cognitive training research is the choice of control group. Reviews have shown that not all studies in this field use active control groups (Simons et al., 2016). An active control group is favoured as they control for general effects of taking part in an intervention (e.g., the routine of practicing tasks each day, or the social aspects of interacting with peers as part of the training), test re-test effects of completing the outcome measures more than once, or expectancy effects that taking part in the intervention will result in positive results (Cech & Martin, 2011). Conversely, passive or no-contact control groups are unable to distinguish whether positive results are from the training programme, placebo effects, or other confounding variables. The tricky part for researchers is to decide on a control condition that is as close to the intervention in terms of engagement, time, and energy intensity, but that theoretically will not result in improved cognitive performance.

1.2.4 Best practise for training research

Factors to improve methodological design have been suggested by numerous reviews. One recommendation is to use an appropriate and comprehensive test battery to assess cognitive outcomes (Green et al., 2014). This review argued that small test batteries cannot accurately assess cognitive outcomes and transfer effects. The outcome measures need to be comprehensive enough to assess changes across cognitive functions, rather than in specific tasks (Green et al., 2014). For example, assessing executive functioning through one task is not enough, as executive function is made up of three smaller processes (inhibition, shifting and updating; Sandberg et al., 2014). If an intervention leads to improvements on multiple executive function tasks, this is a much more reliable indicator that the intervention improved executive functioning *as a whole*.

A notable review that focusses specifically on brain training is one by Simons et al. (2016). It gave recommendations for best practice for assessing the efficacy of brain training programmes. The gold standard, as in much clinical practice, is a *double-blind*, *placebo-controlled*, *randomised* clinical trial. *Double-blind* studies, where both participant and researcher are blinded to the participants condition, remove any potential social or expectation biases. *Placebo-controlled* studies (using an active control condition) can control for placebo effects, but they are more difficult to implement in brain training research compared to a drug trial. Active control groups are gold standard, but appropriate active control conditions can be difficult as it is challenging to blind participants to their condition. The review found that many published studies use passive or no-contact controls, which cannot account for placebo effects, increases in motivation, or potential social benefits of completing the programme (Simons et al., 2016). They concluded that where possible, studies should include an active control condition that is as similar to the intervention as can be, while excluding the 'active' brain training element. Finally, studies should include a large sample size with *randomised* allocation to condition. Including these features in study design, when used appropriately, can allow causal inferences to be made about the brain training programme in question (Simons et al., 2016).

1.2.5 Summary

Cognitive training programmes have been widely utilised to train or improve cognitive health in healthy populations. As commercially available brain training programmes become more accessible to the general population, it is important to assess them in rigorous studies. Brain training companies will often cite positive benefits of their applications, but evidence that they improve untrained cognitive functions is limited, especially in ageing populations. Papers and reviews have made a number of methodological recommendations to combat issues from

study design and individual differences. There is a need for robust studies with randomised samples, active control conditions that can control for motivation and placebo effects, and large enough test batteries to assess improvements across cognitive functions, rather than just to the task or measure.

1.3 Thesis aims

Ageing is associated with changes across the body and throughout the brain. This chapter has detailed how ageing leads to declines in cognitive functioning, as well as changes to physical, mental, and serological health, and how they relate to cognition. These changes are intrinsic; they interact with one another and therefore require thorough investigation. What is missing in the literature is research that investigates the interactions between these aspects of health, doing so using person-centred approaches that can identify relationships between variables. This introduction has also shown that there is some evidence that computerised cognitive training can benefit cognitive performance (Ball et al., 2002), with some evidence that it can transfer to wider cognitive abilities (Karbach & Verhaeghen, 2014). The literature surrounding commercial brain training programmes is less conclusive and highly controversial, with many inconsistencies in the field that need addressing (Simons et al., 2016). There is therefore a need for robust research that overcomes the limitations identified in previous research, to thoroughly assess the effectiveness of brain training programmes.

Two original aims of this thesis (which can be viewed visually in Figure 1) were as follows:

- Establish the relationship between cognitive, mental, physical, and serological markers of health, in a cross-sectional sample of healthy older adults (**Chapter 3**)
- Determine the efficacy of a commercially available computerised brain training programme on cognitive performance in a sample of healthy older adults, in a three-month randomised and controlled intervention design (**Chapter 4**)

We had originally planned to study potential long-term benefits of the brain training programme in a follow-up session three months post-intervention. However, as a result of the COVID-19 pandemic, all human-based research was paused, which caused a delay of the intervention. Because of time restrictions, the original third aim of this research was not possible. COVID-19 restrictions were ongoing during 2020 and 2021, and at the time, very little research had been published on how COVID-19 could affect older adults. Therefore, the research plan was adapted to explore the impact of COVID-19 restrictions on older adult wellbeing, using an online questionnaire-based design.

1.3.1 The COVID-19 pandemic

The COVID-19 pandemic had a marked and drastic impact on the lives of billions of people across the world. Older adults were impacted significantly by the disease; they are more vulnerable to serious illness and complications due to the virus and accounted for 9 out of 10 deaths at the height of the first lockdown in the UK in 2020 (ONS, 2020b). As such, they were a vulnerable population who were instructed to stay at home and reduce social interactions for longer than many.

A wealth of research has now been published on the effects of the COVID-19 pandemic on mental and physical wellbeing across the lifespan. Social distancing and stay-at-home guidelines were put in place to protect the public, especially vulnerable populations (including older adults). This led to a significant reduction in physical activity or movement for all ages, subsequently increasing sitting time and sedentary behaviour and declining fitness levels (Oliveira et al., 2022). This undoubtably reduced the risk of older adults catching the virus, but it potentially harmed their psychological wellbeing (M. L. Smith et al., 2020). There were some ways to mitigate potential negative effects; research has shown that older adults who maintained levels of physical activity during COVID-19 lockdowns and social distancing guidelines reported fewer depressive symptoms (Callow et al., 2020) and more resilience (Carriedo et al., 2020). Similarly, those that co-habited with others rather than lived alone, and those that reported higher levels of social support, reported fewer loneliness symptoms (Groarke et al., 2020).

There has been a large focus on the impact of the pandemic on mental wellbeing. Studies show differing patterns with how older and younger adults were affected; for example, some research suggests older adults displayed smaller increases in rates of depression and anxiety compared to young adults and adolescents (Garcia-Portilla et al., 2020; Gonzalez-Sanguino et al., 2020). Nevertheless, older adults have seen significant changes to mental wellbeing. In England, a study with a large representative sample of older adults (N=5,146) reported significant deteriorations in depression, loneliness and quality of life symptoms at multiple times during the pandemic (Zaninotto et al., 2022). The researchers reported that depression symptoms saw the steepest increase, with a probability of depression rising from 12.5% before the pandemic to 28.5% at the end of 2020. Interestingly, the study showed that prevalence of

anxiety did not rise as much as depression or loneliness, rising from 9.4% to 10.9% from the first to second lockdown in 2020, but the effect was still significant. Researchers found significant sex differences too, with females reporting worse mental health symptoms for depression, loneliness, and anxiety (Zaninotto et al., 2022).

Cognitive decline during the pandemic is arguably under researched compared to changes to physical and mental health. This is surprising, given that research shows both mental wellbeing and physical health (which we know were affected by the pandemic) also relates to cognitive function. For example, as mentioned, physical exercise can reduce the risk of brain ageing (Ahlskog et al., 2011), and more social activity is associated with better global cognition (Kelly et al., 2017). However, arguably, cognition was more difficult to assess during the pandemic; for example, during lockdowns, healthcare professionals had to adapt cognitive assessments to telephone or video measures, meaning cognitive performance was more difficult to assess (Hantke & Gould, 2020).

Despite this, some research investigated changes to cognitive health in older adults during COVID-19. Pre-pandemic research shows that social isolation is predictive of cognitive decline in older adults (Lara et al., 2019), and with extended periods of social distancing, it is easy to imagine the pandemic having an effect. However, not all research implies this. One large scale study only found 8% of older adults reporting a decline in cognitive wellbeing during the pandemic, and these results were particularly related to depression symptoms (De Pue et al., 2021). Another study reported only 5.7% of healthy older adults developed cognitive impairment during the pandemic, a result partially mediated by whether participants were socially isolated (Noguchi et al., 2021). However, this longitudinal study was only over six

months (March to October 2020), and cognitive impairment was measured through subjective self-report questionnaires. Using more objective cognitive measures, one longitudinal study compared cognitive decline pre-pandemic to during pandemic in non-cognitively impaired older adults (at baseline) and found that the rate of cognitive decline was significantly steeper compared to pre-pandemic (Amieva et al., 2022). This has been corroborated in a recent study of participants with dementia which also found steeper declines in cognition (as measured by the mini mental state examination; MMSE) during the pandemic compared to before the pandemic (Matsui et al., 2023).

One alternative way of thinking about cognition during the pandemic is to look at subjective cognitive concerns. Concern or anxiety about COVID-19 is well-reported, with older adults reporting more COVID-19 concerns than their younger counterparts (Hyland et al., 2020). Similarly, older adults may worry about cognitive decline. Also termed dementia worry, this refers to the amount that older adults worry about developing cognitive impairment or dementia, and is widespread in older adult populations (Bowen et al., 2019). Worrying about cognitive decline has been associated with an increase in mental health symptoms such as stress and depression (Cutler & Bragaru, 2017) and even with poorer executive function performance (Caughie et al., 2021). Therefore, even if measuring memory concerns are often subjective rather than objective, they may indicate underlying mental health problems and poorer cognitive ability.

Although some research argues older populations were less negatively impacted than younger (Garcia-Portilla et al., 2020), it is clear that this population was affected physically (Oliveira et al., 2022), cognitively (Amieva et al., 2022), and mentally (Zaninotto et al., 2022).

It felt appropriate to investigate this during the pandemic to assess how older adults fared in terms of their mental wellbeing, health behaviours and worries about their cognitive health. At the time of data collection, little had been published on the effects of the COVID-19 pandemic on older adult health, in particular on subjective cognitive concerns. Therefore, to replace the original third aim, the first empirical chapter in this thesis (which can be viewed visually in Figure 1) is as follows:

- Investigate the cognitive, mental, and physical wellbeing in older adults during the COVID-19 pandemic via an online survey (**Chapter 2**)

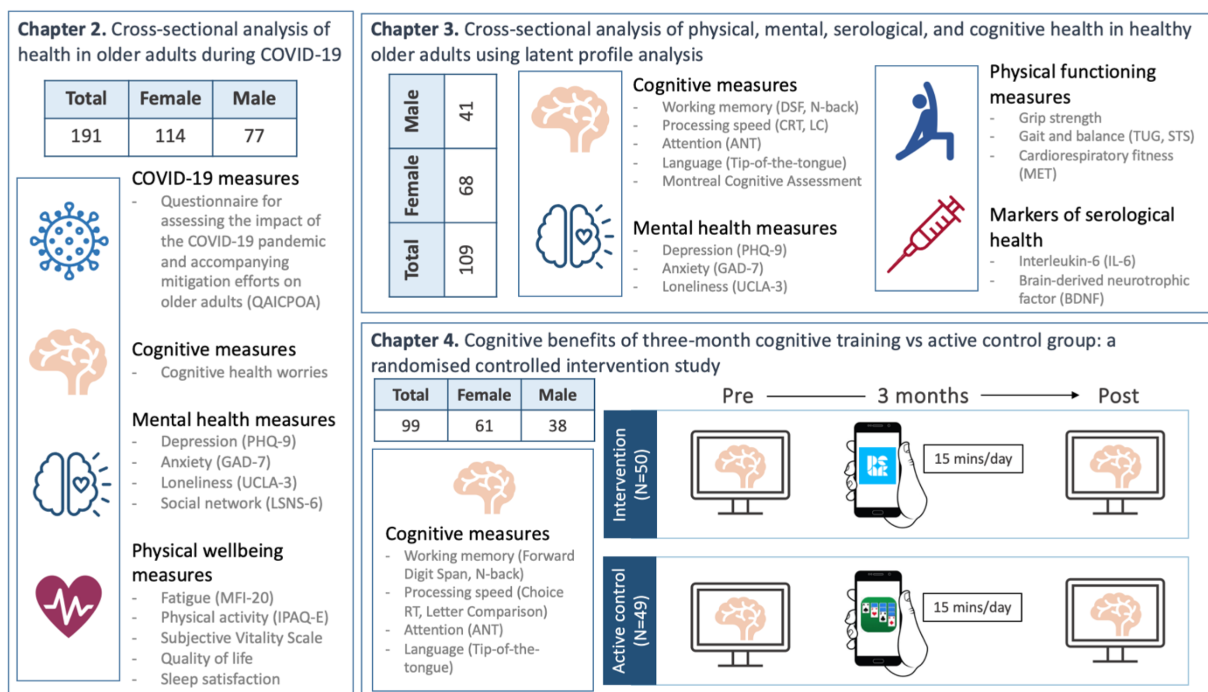

Figure 1.1. Graphical representation of empirical chapters within this thesis

CHAPTER 2 - COGNITIVE HEALTH WORRIES, REDUCED PHYSICAL ACTIVITY AND FEWER SOCIAL INTERACTIONS NEGATIVELY IMPACT PSYCHOLOGICAL WELLBEING IN OLDER ADULTS DURING THE COVID-19 PANDEMIC

2.1 Abstract

The Coronavirus pandemic has significantly affected psychological wellbeing in older adults, with cases of depression, anxiety and loneliness rising in the general population. Cognitive health has also potentially been affected, as social isolation can lead to cognitive decline. Worrying about cognitive health can be damaging to psychological wellbeing and is especially relevant to explore in the context of the Coronavirus pandemic. The objective of the present study was to explore the associations between cognitive health worries and wellbeing, and to investigate whether physical activity and social contact can mitigate negative effects of the pandemic on psychological wellbeing. Older adults (N=191, 114 female, *M*age 70.5, SD 6.4) completed an online survey which included measures of cognitive health worries, depression, anxiety, loneliness, social isolation, fatigue, impact of the Coronavirus pandemic, quality of life, subjective vitality, and physical activity. Analyses indicated that cognitive health worries, lower levels of physical activity and smaller amounts of social interaction were associated with poorer psychological and physical wellbeing. Results showed that worrying about cognitive health is associated with poorer wellbeing, and so interventions are needed to encourage positive cognitive functioning in times of social isolation. Promoting physical activity and social interaction is also beneficial, as results show that exercise and social contact are linked with improved wellbeing.

2.2 Introduction

The ongoing Coronavirus (COVID-19) pandemic has had a profound effect on peoples' lives across the world. Older adults in particular are more at risk of serious illness, further complications, and death as a result of COVID-19; over 65s account for more than 9 out of 10

COVID-19 related deaths in the United Kingdom (ONS, 2020b). As such, older adults were some of the first people to be advised to stay at home, 'shielding' themselves from the disease.

While this social isolation may have protected them from COVID-19, it directly disrupted activities that many older adults take part in, such as seeing family or friends, volunteering, and everyday physical exercise routines. Shielding and social distancing has undoubtedly protected older adults from catching the virus, but the resulting social isolation has potentially harmed their physical and psychological wellbeing (M. L. Smith et al., 2020). Furthermore, extended periods of isolation are known to harm cognitive health (Lara et al., 2019) and worrying about cognitive decline can be common in older populations (Bowen et al., 2019).

Research completed during the pandemic shows a significant impact on psychological wellbeing; rates of depression and anxiety are reported to be between 16-28% of the general population (Rajkumar, 2020). The percentage of UK adults reporting moderate or severe symptoms of depression has almost doubled from July 2019 (9.7%) to June 2020 (19.2%), with 12.9% of adults reporting that these symptoms developed during the pandemic (ONS, 2020a). Social isolation appears to be a contributing factor to poor mental health, with the prevalence of loneliness now at 27% of the population (Groarke et al., 2020). Those who are especially socially isolated seem to be the worst affected; one study found that older adults who live alone were twice as likely to report symptoms of loneliness, and that when shielding (staying at home and minimising face-to-face contact with others), 50% reported a decline in quality-of-life, and 40% a decline in mobility (Bailey et al., 2021). Higher loneliness scores have been found to correlate positively with symptoms of depression and anxiety (Robb et al., 2020), and another

study found that increased loneliness scores predicted scores of depression in older adults (Krendl & Perry, 2021). Sleep also seems to be related; research showed that in older adults during lockdown, sleep problems were associated with higher COVID-19 related loneliness Grossman et al. (2021). Research has similarly found that physical activity levels decreased in older adults during the COVID-19 pandemic, and that a decline in physical activity along with a change in sleep quality, significantly predicted a decline in psychological wellbeing (Trabelsi et al., 2021).

Recent research has looked at possible protective factors that might limit these negative effects. Physical activity is associated with better psychological wellbeing (Deslandes et al., 2009). This has continued during the pandemic: older adults who managed to meet the recommended guidelines for physical activity during the pandemic reported fewer depressive symptoms and higher positive affect compared to those who did not meet guidelines (Carriedo et al., 2020). Social contact is known to be another protective factor in both mental (Schwartz & Litwin, 2019) and cognitive (Crooks et al., 2008) health. Co-habiting and living with other people seem to help psychological wellbeing, particularly loneliness (Groarke et al., 2020). It is evident that staying physically active helps to mitigate some of the negative mental health effects of social isolation during the pandemic. Similarly, regular contact with loved ones appears to be a buffer against declines in psychological wellbeing. In this sense, older adults can still feel connected socially, despite following social distancing measures (Damiot et al., 2020). The present study aimed to investigate the benefits of physical activity and social contact on psychological wellbeing, in a sample of older adults during the COVID-19 pandemic.

Being concerned about the pandemic, termed 'COVID-related anxiety' (Shevlin et al., 2020) may also have an impact on psychological wellbeing and social isolation. Compared to younger participants, older adults report higher levels of anxiety about COVID-19 (Hyland et al., 2020; Shevlin et al., 2020), and higher levels of COVID-related anxiety have been shown to be predictive of poorer psychological wellbeing in a sample of 18–49-year-olds (Aslam et al., 2021). This poorer mental wellbeing can be counteracted by physical activity, emphasising the benefits of keeping physically active in the pandemic (Wright et al., 2021). However, to our knowledge, there is no research looking at the effects of COVID-related anxiety on psychological wellbeing in adults over 60.

We know that in older adults there is a natural decline in cognitive functioning (e.g., Salthouse, 2010). However, this decline can be moderated by lifestyle factors such as physical activity (Cheng, 2016) and social interaction (Bzdok & Dunbar, 2020; Kuiper et al., 2015). Accurate measures of cognitive ability are more difficult to obtain in online or remote psychological studies. However, remote versions of validated cognitive tools, such as the telephone version of the Mini-Mental State Examination, have been used for some time and have been utilised specifically during the pandemic to the same success as in-person versions (e.g., Quattropani et al., 2021).

Other studies conducted during the pandemic have explored self-reported memory complaints as a way of reporting cognitive functioning. Only a small percentage of older participants (8%) report that their cognitive functioning had declined as a result of COVID-19 (De Pue et al., 2021), with another study finding that while young participants' subjective memory complaints have increased compared to pre-pandemic, older adults were low and

remained stable (Fiorenzato et al., 2021). A mediating factor may be the amount of social isolation participants report. A recent longitudinal study found that older adults who were isolated both before *and* during the pandemic, and older adults who became isolated *as a result* of the pandemic, were significantly more likely to self-report cognitive decline compared to those that remained non-isolated (Noguchi et al., 2021). These subjective declines in cognitive functioning due to the pandemic appear to have a significant relationship with depression (De Pue et al., 2021; Fiorenzato et al., 2021) and anxiety (Fiorenzato et al., 2021) symptoms, indicating that those who are worried about their cognitive abilities may be concerned to the point of it impacting their psychological wellbeing.

An alternative way to think about cognitive health may be to look at self-reported worries about brain health. These cognitive health worries have mainly been used in the context of developing dementia, otherwise known as 'dementia worry'. Dementia worry can be widespread in the general population, ranging from 26-60% of reported populations (Bowen et al., 2019; Kessler et al., 2012), and can be exacerbated further by genetic exposure to dementia (G. J. Lee et al., 2020). Interestingly, research shows a reverse-U shaped relationship with age, with dementia worry peaking at 70 years old (Bowen et al., 2019).

Cognitive health worries have been associated with poorer psychological wellbeing. A study exploring worries about cognitive functioning and concerns about developing dementia found that participants who were more concerned about their cognitive health had higher levels of depression and stress, and poorer life satisfaction scores (Cutler & Bragaru, 2017). Participants who worry about developing dementia tend to report poorer cognitive functioning (Cutler & Hodgson, 1996), and high scores of dementia worry have been linked to poorer

cognitive functioning, shown by significantly lower scores of executive functioning (Caughie et al., 2021). While asking participants if they are worried about their cognitive health does not objectively measure cognitive ability, it does relate to cognitive performance and can negatively impact psychological wellbeing (Caughie et al., 2021; Cutler & Bragaru, 2017).

These cognitive health worries have yet to be explored in the context of the pandemic. As mentioned above, extended periods of social isolation can lead to cognitive decline (Lara et al., 2019; Noguchi et al., 2021; Yu et al., 2021) and so it may be reasonable to theorise that these cognitive worries have increased in the last 12 months. Older adults are hesitant to return to their normal day-to-day lives (Age UK, 2020a) and this extended isolation could lead to further declines in cognitive and psychological wellbeing.

The first aim of the current study was to examine whether cognitive health worries were associated with poorer psychological and physical wellbeing in older adults during the COVID-19 pandemic. A second aim was to corroborate previous findings conducted during the pandemic, specifically that greater levels of physical activity and social contact are associated with better mental health. A final aim was to expand research into COVID-related anxiety and its impact on wellbeing.

We hypothesised that first, worrying about one's cognitive health would have a significant negative association with psychological and physical wellbeing. Second, we hypothesised that higher levels of physical activity and social contact would be significantly correlated with better psychological wellbeing. Finally, we hypothesised that concern about COVID-19 would have a negative association with psychological wellbeing.

2.3 Methods

Participants

A total of 191 participants (75 male, 114 female, 2 prefer not to answer), recruited through social media, local community groups, and word of mouth, completed the entire questionnaire. A further 51 participants started the questionnaire but did not complete all questions and were therefore not included in the present analyses. All participants were over 60 years of age and lived in the UK, with a mean age of 70.5 years (SD 6.4, age range 60-88). The majority (N=183) identified as White, married (N=141) and described their living arrangements as living with a partner or spouse (N=126). Full demographics are shown in Table 2.1.

Procedure

The study was approved by the Science, Technology, Engineering, and Mathematics (STEM) Ethical Review Committee for the University of Birmingham (Ethics Approval Number: ERN_19-1176). Data was collected between February and April 2021, at a time where the UK was in its third national lockdown, with restrictions beginning to ease from March (Cabinet Office, 2020). All participants accessed the online questionnaire (hosted on SmartSurvey) and gave electronic informed consent before completing the study, following ethical guidelines outlined by the British Psychological Society.

Table 2.1. Demographic information

Demographic category	Frequency	Percentage
Education level		
Primary school	4	2.1
GCSEs, O Levels or equivalent	41	21.5
A-Levels or equivalent	26	13.6
University undergraduate programme (e.g., BSc, BA)	54	28.3
University postgraduate programme (e.g., MSc, MA)	54	28.3
Doctoral degree (e.g., PhD)	4	2.1
Other	7	3.7
Prefer not to answer	1	0.5
Ethnicity		
White	183	95.8
Mixed/Multiple Ethnic groups	3	1.6
Asian Chinese/Asian Indian/Asian Pakistani or Bangladeshi/Asian Other	1	0.5
European	1	0.5
Prefer not to answer	3	1.6
Marital status		
Married	141	73.8
Widowed	20	10.5
Divorced	15	7.9
Single (never married)	11	5.8
Legally separated	2	1.0
Prefer not to answer	2	1.0
Living arrangements		
Live with partner or spouse	126	66.0
Live with family members	28	14.7
Live alone	25	13.1
Live alone but part of a support bubble [a]	11	5.8
Prefer not to answer		0.5

Note: [a] – a support bubble in this instance referred to the UK Government definition of the term, in which those who lived alone were allowed to form a 'bubble' with another household to ease the negative effects of isolation (Department of Health and Social Care, 2020).

Materials

The following measures were included in the study:

Questionnaire for assessing the impact of the COVID-19 pandemic and accompanying mitigation efforts on older adults (QAICPOA)

The QAICPOA (Cawthon et al., 2020) is a newly developed questionnaire that aims to assess the impact of the COVID-19 pandemic on the lives of older adults. It is formed of 17

questions, including the UCLA 3-item loneliness scale (Hughes et al., 2004) which is described in more detail below. The QAICPOA includes items on COVID-19 diagnosis and symptoms, actions taken in response to the pandemic (e.g., social distancing measures) and changes to frequency of communication with others. In addition to this questionnaire, we asked participants if they had received a COVID-19 vaccine, and if so, how many and when their last vaccination was.

Cognitive health worries

To establish levels of cognitive health worry, participants were asked the question 'Are you worried about your cognitive health (abilities such as remembering things, communicating, doing and planning simple tasks)?'. This question used 'Yes, a lot', 'Yes, a little', 'Not really worried' and 'Not at all worried' as potential answers.

Multidimensional Fatigue Inventory (MFI-20)

The 20-item MFI (Smets et al., 1995) was used to assess five different aspects of fatigue: general fatigue, mental fatigue, physical fatigue, reduced activity, and reduced motivation. Items such as 'I feel fit' and 'I tire easily' are rated on a scale from 1 – 'Yes, that is true' to 5 – 'No that is not true'. Scores can range from 5-20 per aspect of fatigue (possible total value of 100) with a higher score indicating higher levels of fatigue. Scores were calculated for each subscale, recoding negatively formulated items, giving five scores per participant. The scale has been shown to be a valid measure of fatigue (Smets et al., 1995).

Subjective Vitality Scale

The six-item version of the Subjective Vitality Scale (Ryan & Frederick, 1997) was used to measure levels of vitality. Respondents are asked to rate how true they believe statements to be in their general lives. Each item (for example 'I have been feeling alive and vital' and 'I nearly always feel alert and awake') is rated on a six-point scale (from 1 – not at all true to 6 – very true). Scores are added up (out of 36) and calculated as an average of the six questions, with the highest score being 6. The scale demonstrates good levels of reliability in reported populations (Castillo et al., 2017). Higher scores indicate higher subjective vitality.

Patient Health Questionnaire-9 (PHQ-9)

The PHQ-9 (Kroenke et al., 2009) is a nine-item questionnaire assessing symptoms of depression. Participants are asked 'Over the past 2 weeks, how often have you been bothered by any of the following problems?'. Participants then score statements, such as 'Feeling down, depressed, or hopeless' or 'Poor appetite or overeating' on a 4-point scale ranging from 0 – 'Not at all', to 3 – 'Nearly every day', resulting in a possible score of 27. Higher scores indicate more depressive symptoms. Scores of 5, 10, 15 and 20 indicate mild, moderate, moderate-severe, and severe depressive symptoms, respectively (Urtasun et al., 2019). It has been validated in clinical settings (Gilbody et al., 2007) and the general population (Martin et al., 2006).

Generalised Anxiety Disorder-7 (GAD-7)

The GAD-7 (Spitzer et al., 2006) is a seven-item questionnaire on anxiety symptoms. It asks participants to rate how often in the past 2 weeks they have been bothered by the following problems. Items such as 'Not being able to stop or control worrying' or 'Becoming easily annoyed or irritable' are scored on a 4-point scale from 0 – 'Not at all', to 3 – 'Nearly every

day', giving a possible score of 21. Higher scores indicate higher levels of anxiety, with cut off points of 5, 10, and 15 indicating mild, moderate, and severe anxiety, respectively (Spitzer et al., 2006). The scale shows high validity and reliability when used with the general population (Lowe et al., 2008).

UCLA 3-item Loneliness scale (UCLA-3)

The UCLA-3 (Hughes et al., 2004) was included to measure levels of loneliness. The three included questions, 'How often do you feel that you lack companionship?', 'How often do you feel left out?', and 'How often do you feel isolated from others?' were taken from the original, non-abbreviated scale (Russell, 1996) and have good internal consistency (Hughes et al., 2004). The questions are scored on a 3-point scale ranging from 1 – 'Hardly ever' to 3 – 'Often', giving a maximum score of nine. A score of six or above has been used to classify participants as 'lonely' (Steptoe et al., 2013).

Lubben Social Network Scale (LSNS-6)

The LSNS-6 (Lubben et al., 2006) is a 6-item questionnaire that measures social isolation in older adults by quantifying the frequency of social contact the respondent has from both friends and family, and the perceived support they get from these interactions. Questions include 'How many relatives do you see or hear from at least once a month?' and 'How many friends do you feel at ease with that you can talk about private matters?'. Each item is scored from 0 – 'None', to 5 – 'Nine or more', with a score of 12 or fewer indicating respondents being possibly at-risk of social isolation. The scale has been validated in older populations (Lubben et al., 2006).

Quality of life and sleep

Participants were asked 'How would you rate your quality of life?' (rated on a 5-point Likert from 1 – 'Very poor' to 5 – 'Very good'), taken from the World Health Organisation Quality of Life Questionnaire (WHO, 2012), and 'How would you rate your quality of sleep overall?' (rated on a 5-point Likert from 1 – 'Very poor to 5 – 'Very good) taken from the Pittsburgh Sleep Quality Index (Buysse et al., 1989).

The International Physical Activity Questionnaire modified for the elderly (IPAQ-E)

The IPAQ-E is a modified short version of the International Physical Activity Questionnaire (Craig et al., 2003). Participants are asked how often in the last week they spent sitting, walking, doing moderate physical activity and doing vigorous physical activity. Answers were given in days, and more specifically hours and minutes. Scores were converted into a continuous score of total MET (metabolic equivalent) per week as per scoring guidelines (Forde, 2018). Both the original IPAQ and the IPAQ-E have shown good levels of validity in reported populations (Hurtig-Wennlöf et al., 2010; Rubio Castañeda & Aznar, 2017).

Data Reduction and Analysis

In addition to the measures above, we asked participants about their sitting activities, pain levels, sleep satisfaction and duration, health satisfaction, and information on social interaction and language use while doing physical activity. However, these measures were not included in the present analysis. Further questions about perceived cognitive health, including data on current and previous use of cognitive training methods, were also excluded.

Data were analysed using SPSS v26. Independent one-way ANOVAs were conducted to examine differences in wellbeing measures across levels of cognitive health worry. Next, Pearson correlations were conducted to look at relationships between all continuous variables (measures of depression, anxiety, loneliness, social isolation, age, fatigue, subjective vitality, physical activity). Kruskal-Wallis tests were completed to examine differences in loneliness scores across living arrangements, and to examine the differences between COVID-19 concern and wellbeing measures.

2.4 Results

Cognitive health worries

In total, 2 (1%) participants were worried a lot about their cognitive health, 46 (24.1%) were a little worried, 73 (38.2%) were not really worried and 70 (36.6%) were not at all worried. For analysis and in all future reference to this question, ‘Yes, a lot’ and ‘Yes, a little’ were recoded into one group (‘Yes, worried’).

A series of independent one-way ANOVAs using cognitive health worries as the independent variable (groups being ‘Yes, worried’, ‘Not really worried’ and ‘Not at all worried’) were conducted to investigate differences in wellbeing. Significant group differences were found in scores for depression, anxiety, general fatigue, subjective vitality, loneliness, sleep quality, and quality of life. Physical fatigue, reduced activity, mental fatigue and reduced motivation (subsets of the MFI-20) are not included in this reported analysis, but all had similar significant group differences. Results, including individual group differences, are summarised in Table 2.2. Overall, participants who were worried about their cognitive health had poorer psychological wellbeing, were more fatigued, and less satisfied with sleep, health, and quality of life. Tukey post-hoc analyses were completed for all significant results (see Table 2.2).

Table 2.2. Mean (SD) wellbeing outcomes for different groups of cognitive health worries and results of one-way ANOVA

	Cognitive health worries				
Outcome measure	**Yes, worried (N=48)**	**Not really worried (N=73)**	**Not at all worried (N=70)**	*F*-value	*P*-value
Depression (PHQ-9)	5.87 (4.79)	3.45 (4.10) a	1.58 (2.39) a, b	18.13	<.001
Anxiety (GAD-7)	4.29 (4.36)	2.42 (3.29) a	0.99 (2.19) a, b	14.36	<.001
General fatigue (MFI-20)[1]	12.26 (4.15)	10.24 (4.27) a	7.83 (3.63) a, b	17.68	<.001
Subjective vitality (SVS)	3.18 (1.24)	3.75 (1.21) a	4.70 (1.26) a, b	23.26	<.001
Loneliness (UCLA-3)	5.19 (1.89)	4.45 (1.63) a	4.03 (1.55) a	6.81	.001
Sleep quality	3.13 (1.00)	3.33 (1.00)	3.72 (0.80) a, b	6.41	.002
Quality of life	3.63 (0.73)	3.95 (0.83)	4.16 (0.83) a	6.18	.003

Note: Data presented as mean (SD). DF = 184, 2. Statistical analyses were conducted using a one-way ANOVA. a – significantly different from 'Yes, worried' group, b – significantly different from 'Not really worried' group.

Table 2.3. Descriptive statistics for variables

Variable	**Possible scores**	**Mean (SD)**
Age	60-88	70.56 (6.41)
Sleep quality	1-5	3.42 (0.96)
MFI General Fatigue	4-20	9.84 (4.36)
MFI Physical Fatigue	4-20	9.72 (4.61)
MFI Reduced Activity	4-20	9.30 (4.32)
MFI Mental Fatigue	4-20	7.83 (3.77)
MFI Reduced Motivation	4-20	7.67 (3.14)
SVS	1-7	3.96 (1.37)
PHQ-9	0-27	3.37 (4.10)
GAD-7	0-21	2.38 (3.50)
UCLA-3	0-9	4.48 (1.72)
LSNS-6	0-30	16.70 (4.98)
IPAQ-E total MET	-	2871.18 (2657.74)
Sleep quality	1-5	3.42 (.96)
Quality of life	1-5	3.94 (.83)

Psychological and physical wellbeing

The sample mean scores for the wellbeing questionnaires are reported in Table 2.3. Using clinical cut-off points mentioned above, 51 participants (26.8%) classified as lonely, and 41 (22.3%) participants were at risk of social isolation. Forty-four (23.5%) participants had

mild depression, 8 (4.3%) moderate and 4 (2.1%) moderate-severe depression, while 27 (14.4%) scored mild anxiety, 10 (5.4%) moderate, and one (0.5%) severe anxiety.

Pearson correlations were run on all continuous variables (see Table 2.4). A Bonferroni adjusted alpha level of .00125 was used. Overall, psychological wellbeing (depression, loneliness and anxiety) was negatively correlated with physical activity, sleep quality and social network, and positively correlated with fatigue. More physical activity (in the IPAQ-E) was negatively correlated with all five facets of fatigue and depression (all $p < .001$), and positively correlated with subjective vitality. The size of social network was negatively correlated with loneliness and depression ($p < .001$), with bigger social networks being better for psychological health. Sleep quality was negatively correlated with fatigue, depression, and anxiety, and positively correlated with subjective vitality (all $p < .001$).

To further investigate the associations between loneliness and social isolation and wellbeing, participants were recoded into three groups of living arrangements: living alone (N=25), living alone but in a support bubble (N=11) and living with others, including family, spouses, etc. (N=154). Because participant numbers were uneven across groups, a Kruskal-Wallis test was performed. Using living arrangements as the independent variable, the test revealed a significant difference between groups in scores of loneliness, $\chi^2(2) = 16.46$, $p = <.001$. Post-hoc Dunn comparisons (using a Bonferroni adjusted *p*-value of 0.017) revealed that scores on the UCLA-3 item loneliness scale were significantly lower for participants who lived with other people (Mdn = 4) compared to those who lived alone (Mdn = 5, $p = 0.007$) and those who lived alone but were in a support bubble (Mdn = 5, $p = 0.009$). No significant difference was found between participants who lived alone and those who were part of a support bubble

($p = .464$). No other significant differences in psychological wellbeing scores were found (all $p > .05$).

COVID-19 concern

In answer to the question 'How concerned are you about the COVID-19 pandemic?' taken from the QAICPOA (Cawthon et al., 2020), five participants were 'not at all concerned', 81 were 'somewhat concerned' and 104 'very concerned'. Due to uneven group sizes, a non-parametric Kruskal-Wallis test was completed to assess differences in groups. Using COVID-19 concern as the independent variable, results revealed a significant difference for General Fatigue (MFI-20) scores, $\chi^2(2) = 6.41$, $p = .041$, but after adjusting for multiple comparisons it was no longer significant. No significant differences were found in any other psychological wellbeing measures (PHQ-9, GAD-7, LSNS-6, UCLA-3, SVS, MFI-20; all p-values $> .05$).

Table 2.4. Correlation matrix and descriptive statistics for continuous variables

	Age	Sleep quality	MFI General Fatigue	SVS	PHQ-9	GAD-7	UCLA-3	LSNS-6	IPAQ-E total MET
Age	-								
Sleep quality	-.051	-							
MFI General Fatigue	.146	-.550**	-						
SVS	-.136	.499**	-.623**	-					
PHQ-9	-.061	-.606**	.667**	-.645**	-				
GAD-7	-.101	-.389**	.455**	-.491**	.722**	-			
UCLA-3	-.086	-.162	.297**	-.432**	.421**	.357**	-		
LSNS-6	-.033	.151	-.143	.193	-.258**	-.145	-.299**	-	
IPAQ-E total MET	-.044	.215	-.310**	.337**	-.256**	-.048	-.011	.067	-

*Note: * p < .001. MFI Physical Fatigue, Reduced Activity, Mental Fatigue and Reduced Motivation subscales are not included in this table, but all showed similar significant relationships.*

2.5 Discussion

The present study investigated factors that are associated with wellbeing in the context of the COVID-19 pandemic in a sample of older adults in the UK. The main aim was to establish whether increased concern about cognitive abilities was related to poorer psychological and physical wellbeing. We further aimed to corroborate previous research undertaken during the pandemic that showed that higher levels of social contact and physical activity are associated with better psychological and physical wellbeing. Our final aim was to establish whether COVID-19 concern was associated with poorer psychological wellbeing. Our results showed that cognitive worries were significantly related to poorer psychological and physical wellbeing, while higher levels of physical activity and social contact were related to better wellbeing scores. Results also showed that psychological wellbeing scores did not differ between those that were very concerned about the COVID-19 pandemic and those that were not or somewhat concerned.

Cognitive health worries

Out of our sample, 25.1% were at least somewhat concerned about their cognitive health. This is consistent with previous studies that have reported dementia worry at 26-60% of people in the population (Bowen et al., 2019; Kessler et al., 2012). Previous research has associated dementia worry with poorer wellbeing in the form of depression, stress, and life satisfaction (Cutler & Bragaru, 2017). Our results demonstrate that not only do cognitive health worries relate to psychological health in the form of depression, anxiety, and loneliness scores, but this extends to physical wellbeing. Participants who worried about their cognitive health were significantly more fatigued and reported poorer sleep quality and poorer self-reported quality of life.

We have shown a clear distinction between those who are worried about their cognitive health and those that are not, in terms of both psychological and physical wellbeing. Assuming there is a causal relationship between cognitive health worries and psychological wellbeing, finding ways of reducing these cognitive health worries will benefit wellbeing in this population. For example, a modified cognitive behavioural therapy (CBT) programme has been used successfully to reduce dementia worry in a sample of older adults (An et al., 2020), but it did not include measures of wellbeing. A potential alternative could be a cognitive training programme; hypothetically, improving cognitive functioning could lessen cognitive health worries, if the participant believes that the cognitive training is working. While the present study was not able to assess this due to the nature of the online study, a future cognitive training study plans to investigate this further. By exploring how cognitive worries change after a cognitive training programme and looking into how these relate to psychological and physical wellbeing, we may be able to determine a causal link between cognitive training, cognitive health worries, and wellbeing. We may also be able to determine whether cognitive worries are directly related to cognitive performance. This is important given that subjective cognitive health worries do not necessarily map onto objective cognitive performance. Some research has shown that increased dementia worry is associated with poorer cognitive performance (Caughie et al., 2021), but to our knowledge this has not been measured in an interventional design.

Physical activity and social interaction

Results show that participants who completed more physical activity reported significantly lower depression and fatigue scores. Similarly, participants with bigger social networks and had more regular contact with friends and family scored lower on depression and

loneliness scales. This is in line with previous research conducted during the pandemic showing positive associations of physical activity (Carriedo et al., 2020) and social contact (Groarke et al., 2020) on mental health. Encouraging physical activity and social contact is therefore beneficial to promote during periods of social isolation.

Clinical cut-offs would suggest that 29.9% of our population were mild to moderately-severely depressed, 20.3% were mild to severely anxious, and that 26.8% classified as lonely (Spitzer et al., 2006; Steptoe et al., 2013; Urtasun et al., 2019). This is consistent with rates of mental health disorders in previous research conducted during the pandemic (Groarke et al., 2020; Rajkumar, 2020). Loneliness scores did not significantly differ between participants who lived alone and those that lived alone but were in a support bubble. Furthermore, both groups had higher loneliness scores than those who lived with other people. This supports research conducted during the pandemic that showed people who co-habit report lower levels of loneliness (Groarke et al., 2020). It suggests that while support bubbles may be valuable for some aspects of psychological wellbeing, they do not necessarily help to reduce feelings of loneliness. Lockdown loneliness has become prevalent during the pandemic (Shah et al., 2020) and so methods are needed to help combat this. Our results show that physical activity and social contact are related to better wellbeing scores, so guidelines and programmes that encourage physical activity with other people would be helpful to combat the negative effects of social isolation.

COVID-19 concern

Concern about the COVID-19 pandemic was not related to any significant differences in scores of psychological wellbeing scores; participants who were very concerned about the

pandemic did not score higher on scores on anxiety or depression, as has been found previously (Aslam et al., 2021). This could be due to several contextual factors. Recruitment took place during easing of the UK lockdown (February to April 2021). While speculative, it may be that our sample felt positive as cases and deaths in the UK were declining at the time of recruitment (Riley et al., 2021), and only one participant reported to have been diagnosed with the virus. Importantly, all participants had received at least one vaccine at the time of recruitment; recent research has shown that participants who have had a COVID-19 vaccine show lower anxiety and depression symptoms compared to before being vaccinated (Perez-Arce et al., 2021). As all our participants had been vaccinated, we were not able to compare psychological wellbeing symptoms to unvaccinated participants to confirm this hypothesis.

Limitations

The sample was primarily (95.8%) White. Black, Asian, and minority ethnic (BAME) groups are disproportionately affected by COVID-19 and see higher rates of infection and death (Iacobucci, 2020). Some disparities in mental health symptoms have already been found when comparing BAME to White British individuals during the pandemic, particularly for men (Proto & Quintana-Domeque, 2021). Future research could focus on older adult BAME communities to see whether these disparities remain.

Second, the sample size was relatively low compared to some large-scale studies investigating wellbeing in the pandemic (e.g., Robb et al., 2020; Shevlin et al., 2020), and we did not achieve the full number and representation of participants that we were originally aiming for. Approximately 20% of participants (51) were removed from our analysis due to incomplete survey responses, in an effort to reduce the risk of bias on results. Furthermore, our sample

included a low number of oldest-old (80+ years) participants compared to youngest-old. Research has shown that in a sample of adults over 50, the risk of reporting worsening depression and anxiety symptoms as a result of the pandemic *decreases* with age, in that youngest-old participants report poorer wellbeing compared to oldest-old (Robb et al., 2020). Future research would benefit by examining age differences in psychological wellbeing in older adults during the COVID-19 pandemic, in a large, representative sample.

Finally, the study is cross-sectional, meaning that inferences cannot be compared over different time points. Recruitment took place almost 12 months into the pandemic, by which time the UK had gone through three national lockdowns. However, when recruitment started, the UK Governments 'roadmap' out of lockdown had been published (Cabinet Office, 2020), restrictions were beginning to ease, and as mentioned above, cases were declining (Riley et al., 2021). This period is associated with a general improvement in psychological wellbeing scores in the UK general population, with scores fluctuating over time, coinciding with the number of restrictions in place and the number of cases in the UK (Daly & Robinson, 2021). Comparing findings with data collected when restrictions were toughest would be particularly interesting, to see whether cognitive health worries follow the same pattern.

Conclusion

Results from the present study showed that cognitive health worries are associated with poorer psychological and physical wellbeing, across a range of measures. We also found that higher levels of physical activity and social contact are related to better psychological wellbeing, supporting previous research conducted during the pandemic. Results appeared to

show no association between COVID-19 concern and any wellbeing measures, though this may be explained by vaccine status.

This research shows we need to continue to consider the role of regular physical activity and social contact on wellbeing, especially in those populations that may feel uneasy about re-entering society. It also highlights we need to focus resources on those who are worried about their cognitive health. By encouraging activities that can enhance cognitive functioning, perhaps we can lessen this concern.

Reflection on Chapter 2

This chapter was an adaptation of the original research plan due to the COVID-19 pandemic. It allowed my PhD research to continue, albeit remotely, and allowed me to gain a grounding in the literature of an ever-changing topic. Findings showed that subjective cognitive worries are associated with poorer psychological wellbeing. This links to Chapter 3, where cognition is measured using computerised cognitive tasks. This means the link between psychological wellbeing and cognition can be assessed more objectively. Results also showed distinct associations between physical activity and social interaction on psychological wellbeing. This is explored further in Chapter 3, which used a person-centred analytical approach (compared to traditional, variable-centred approaches used in Chapter 2) to explore whether there are subgroups within a population. Chapter 3 therefore expands on the findings from the current chapter by delving deeper into the associations between cognition, psychological wellbeing, and physical health.

CHAPTER 3 - PROFILES OF PHYSICAL FUNCTIONING, MENTAL WELLBEING, AND INFLAMMATION IN HEALTHY OLDER ADULTS, AND THEIR ASSOCIATIONS WITH COGNITIVE FUNCTION: A PERSON-CENTRED APPROACH

3.1 Abstract

The present study aimed to investigate age-related health changes using a person-centred approach (latent profile analysis; LPA). LPA identified subgroups in a sample of 109 healthy older adults based on physical functioning, mental wellbeing, and serological markers of health. MANCOVAs then established whether there were significant differences in cognitive functioning between profiles. LPA indicator variables included physical functioning measures (estimated cardiorespiratory fitness, grip strength, 8-foot up-and-go, 30-second sit-to-stand), mental health questionnaires (depression, anxiety, loneliness), and serological markers of health (IL-6 and BDNF). Analyses revealed three profiles: *Optimally ageing, Challenged physical health but good mental health,* and *Average physical health but challenged mental health*. This study then explored the associations between these functional and health outcomes with cognitive function (working memory, processing speed, attention, and language functioning). Despite not finding associations with cognitive function, the results suggest that subtle but important differences in physical and mental wellbeing may be present in subpopulations of older adults.

3.2 Introduction

Ageing is characterised by changes to physical function, mental wellbeing, serological health, and cognition. Often, these changes are evaluated individually, however, this method risks missing potential interactions between variables. In the present study, we investigate these changes in a more holistic manner. We use a person-centred approach (latent profile analysis; LPA) to group individuals with distinct characteristics and relationships between multiple indicator variables. We included physical function measures, mental health questionnaires, and

serological markers of health to establish the latent profiles in a sample of healthy older adults. These profiles were then used to assess whether groups of healthy older adults, based on physical function and health, are also characterised by different cognitive function outcomes.

Ageing is often associated with changes to physical functioning such as declines in gait and mobility (Cruz-Jimenez, 2017). This can be indicative of fall risk (Hausdorff et al., 2001), which affects a third of over 65s and 50% of over 80s (National Institute for Health and Care Excellence, 2013). Grip strength has been proposed as a functional marker not only for overall strength but also for a range of other factors, including cognitive function, bone density, and quality of life (Bohannon, 2019). Physical activity also tends to decline with age, which is associated with declines in mobility (Visser et al., 2002). Those who sustain higher amounts of physical activity into later life are healthier overall (Hamer et al., 2014), with *low* levels of physical activity being predictive of all-cause mortality, recurrent falls, cognitive decline, and depression (Cunningham et al., 2020).

Several physiological markers have been suggested to contribute to the decline seen with ageing. Low-grade systemic inflammation takes place, whereby levels of pro-inflammatory markers increase with age. This is a process known as 'inflammageing' (Ferrucci & Fabbri, 2018). Higher levels of inflammation (for example interleukin-6; IL-6) have been associated with cardiovascular disease, cognitive decline, and mental health disorders (Ferrucci & Fabbri, 2018; Kivimäki et al., 2014; Singh-Manoux et al., 2014). In particular for mental wellbeing, high IL-6 has been related to increased symptoms of depression in older adults (Baune et al., 2012). Inflammageing can partially be mediated by physical exercise, with regular, moderate exercise leading to lower levels of inflammatory markers, in turn reducing

negative effects of inflammation (Woods et al., 2012). Another serological marker known to change with age is brain-derived neurotrophic factor (BDNF), a neurotrophic protein linked to cognitive function (Walsh et al., 2020). BDNF levels decline with age and have been associated with cognitive decline and mild cognitive impairment in older populations (Shimada, Makizako, et al., 2014), as well as lower levels of BDNF being implicated in clinical depression (Brunoni et al., 2008). Like IL-6 and other inflammatory markers, BDNF production can be affected by physical activity, with aerobic exercise being associated with increased concentrations of BDNF (Huang et al., 2014).

Ageing is not limited to physical changes; older adults also see changes to mental wellbeing. Mental health symptoms are relatively common, with up to 25% of older adults meeting diagnoses for depression (Age UK, 2016), and loneliness (Chawla et al., 2021). Anxiety symptoms substantially increased during the recent COVID-19 pandemic, with 33% of over 60s reporting higher levels of anxiety (Age UK, 2020b). However, while 50% of younger adults with depression are referred to treatment, only 6% of older adults seeking medical help receive the same referrals (Burns & Warner, 2015). Further, older adults are six times more likely to be on medication for mental health problems but have five times fewer opportunities for talking therapies such as cognitive behavioural therapy (Burns & Warner, 2015). Mental health problems are therefore arguably widely undertreated in older adult populations. Further, there may be subtle differences in mental health symptoms in older populations. Research often cites a lifelong 'U-shaped' pattern regarding experiences of mental health symptoms, with depression levels declining from early adulthood and then rising again into later life (Sutin et al., 2013). However, there can be individual differences, with a number of protective factors (e.g., emotion regulation and a close social network) and risk factors (e.g.,

activity curtailment after retirement and cognitive impairment) that affect an individual's likelihood of depression in later life (Fiske et al., 2009). Therefore, there may be more complex patterns to investigate.

Another aspect related to ageing is a decline in cognitive function. Cognitive health during ageing has been shown to be related to all factors mentioned above. Cognitive performance, particularly poor executive functioning, has been linked with increased fall risk and poor gait (Kearney et al., 2013), and overall cognitive functioning is improved in older adults who maintain regular physical activity (Lautenschlager & Almeida, 2006). Similarly, social isolation and poor mental wellbeing have been linked with age-related cognitive decline. Particularly relevant due to the recent COVID-19 pandemic, social isolation and loneliness has been associated with cognitive decline (Lara et al., 2019). Depression and anxiety are regularly linked with cognition, both subjectively and objectively. Subjective worries about cognitive wellbeing have been associated with poor mental health in older adults (Sutton et al., 2022), and cognitive deficits are often a secondary symptom of depression (Austin et al., 2001), but causation is unclear. There are arguments for cognitive impairment caused by anxiety and depression as well as cognitive decline leading to co-morbid depressive or anxiety symptoms (Beaudreau & O'Hara, 2008; Ganguli, 2009). Finally, high levels of inflammation and low levels of BDNF are related to poorer cognitive health in both healthy older adults (Gunstad et al., 2008; Yaffe et al., 2003) and clinically diagnosed cognitive impaired adults (Huberman et al., 1995; Shimada, Makizako, et al., 2014). The present study assessed a wide range of cognitive functions known to change with ageing, to investigate whether profiles established using LPA may impact cognitive performance.

The variables listed above encompass a wide range of changes that occur in ageing and are intrinsically linked; however, few studies assess such a range of outcome measures using person-centred approaches. The present study aimed to use latent profile analysis (LPA) to identify relationships between variables in older adults, before assessing group differences in cognitive functioning. LPA can be described as a person-centred approach that identifies relationships between variables that might otherwise be missed in variable-centred approaches such as ANOVAs. It works by analysing quantitative data, forming clusters or profiles based on the distribution of data (Spurk et al., 2020). It assumes unobserved population heterogeneity, that profiles can only be established by analysing the data and cannot be assumed a priori (Spurk et al., 2020). Once profiles have been created, the profiles can be used to establish differences between outcome variables. In short, once participants have been assigned a profile based on probability of profile membership, these groups are used as categorical independent variables in further statistical analyses. LPA has been used to group participants in a variety of settings, from patient experience of care management (Wannheden et al., 2022), to physical exercise and mental health (Park et al., 2017), and mindfulness and emotional outcomes (Pearson et al., 2015). A relevant study to the present research is one that conducted LPA in an older adult population using physical health measures as indicator variables, subsequently investigating differences in mental health (Park et al., 2019). Their results demonstrated that the profile that displayed better physical health also displayed fewer anxiety and depression symptoms compared to the poorer physical health profile (Park et al., 2019). The present study will include both physical and mental wellbeing measures into the LPA, extending it to also include serological markers of health and subsequently investigating differences between profiles in cognitive outcomes.

The present study thus utilised a person-centred approach with a sample of healthy older adults in a cross-sectional design. LPA was used to create profiles based on four measures of physical function (estimated fitness, grip strength, 8-foot up-and-go, 30-second sit-to-stand), three mental wellbeing questionnaires (depression, anxiety, loneliness), and two serological markers of health (IL-6 and BDNF). Profiles were established by creating clusters (or profiles) of people with similar scores on our indicator variables. This allows for a more holistic approach, considering all variables and allowing the possibility of subgroups within a given population. These profiles were then used to investigate differences in cognition, using a comprehensive test battery of cognitive outcome measures known to change with age: working memory (Forward Digit Span and N-back task), processing speed (Choice Reaction Time Task and Letter Comparison Task), attention (Attention Network Task), and language functioning (tip-of-the-tongue task). To our knowledge, no study has incorporated such factors into LPA and further analysis. Our aims were exploratory in nature; first, to identify profiles using LPA of physical functioning, mental wellbeing, and serological markers of health. Second, to apply these profiles to investigate whether significant differences were present in terms of performance on a range of cognitive tasks.

3.3 Methods

Participants and study protocol

One hundred and nine participants were recruited and ranged in age from 60-84 years old (M = 70.8, SD = 5.52). Recruitment took place through existing participant databases and social media advertisements. Demographics are shown in Table 3.1. Inclusion criteria was as follows: over 60 years old, monolingual native English speaker, normal or corrected to normal hearing and vision, able to walk short distances unaided, and up to date on COVID-19 vaccinations at the time of visit. Exclusion criteria was as follows: a diagnosis of cognitive impairment (e.g., mild cognitive impairment, Alzheimer's disease), a diagnosis of mental health disorder (e.g., depression, anxiety), a diagnosis of dyslexia (specifically for the tip-of-the-tongue task), or currently taking medication known to interact with cognitive function or inflammation (e.g., medication for arthritis, anti-depressants). The Montreal Cognitive Assessment (Nasreddine et al., 2005) was used to assess cognitive impairment. A revised cut-off of 23 out of 30 (rather than 26 out of 30) has been found to provide fewer false positives for mild cognitive impairment (Carson et al., 2018). No participants were excluded based on this cut-off point.

All participants were screened on inclusion/exclusion criteria and gave written informed consent before participation. The testing session took around two hours in total, and consisted of computerised cognitive measures, followed by physical functioning assessments, an online questionnaire with mental health measures and demographic information (age, gender, ethnicity, highest educational qualification, postcode, and regular medication), and finally, a blood sample. All measures were completed in one session, but breaks were available when

needed. The study was approved by the University Ethics Committee (ERN_19-1176). Participants received monetary compensation for their visit.

Table 3.1. Demographic information

	N	% Total
Gender		
Female	68	62.4
Male	41	37.6
Ethnicity		
White	105	96.3
Mixed/Multiple Ethnic Groups	2	1.8
Other	2	1.8
Highest educational qualification		
GCSEs, O Levels or equivalent	8	7.3
A-levels or equivalent	23	21.1
University undergraduate (e.g., BSc, BA)	30	27.5
University postgraduate (e.g., MSc, MA)	23	21.1
Doctoral degree (e.g., PhD)	4	3.7
Other	20	19.3

Materials

Cognitive health: Working memory

Forward Digit Span: The Forward Digit Span task is a well-established measure of working memory. In this task, participants were presented with a sequence of single digits (0-9) one at a time, 1000ms apart, on a computer screen. Once the full sequence had been presented, participants were asked to type the digits in the order they appeared using a computer keyboard. Trials began with three digits, up to a possible ten-digit sequence, with three trials in each level. Participants moved up a level if they correctly answered two out of three trials, and the task automatically ended if there were two incorrect trials within a level. Maximal digit span was taken from the last level participants completed two out of three trials correctly.

N-back task: A visual N-back task (with both 1-back and 2-back conditions) was used. A 3 x 3 grid was displayed on a computer screen, and a square appeared one at a time at regular 1000ms intervals in one of the nine boxes. Participants were asked to press the Space key

whenever the target matched the location either 1 or 2 steps before. The task consisted of 12 practice 1-back trials with feedback at the end of the practice (score out of 12). There were then two blocks, a 1-back and a 2-back, with 60 trials in each. RT was measured in milliseconds, with performance being calculated by a d' score which accounts for correct hits, misses, correct rejections, and false alarms (Harvey, 1992; Macmillan & Creelman, 2004). A higher d' score indicates better performance and sensitivity to the targets. The final d' was calculated as follows:

Z-score Hit Rate [#Hits / (#Hits + #Misses)] minus Z-score False Alarm Rate [#False Alarms / (#False Alarms + #Correct Rejections)]

Cognitive health: Processing speed

Choice RT task: This task measured the speed in which participants responded to one of four options. Participants rested index and middle fingers on the Z, X, N, and M keys on a standard keyboard, which corresponded to an empty box on a computer screen. An X appeared in one of the four boxes and participants were asked to press the corresponding key as quickly and accurately as possible. Intertrial intervals (ITIs) were between 1000 and 2500ms at 250ms intervals, target locations and ITIs were counterbalanced, and trials were randomised. The task consisted of eight practice trials with feedback for each trial, followed by 32 trials with no feedback. Response was measured in milliseconds.

Letter Comparison task: This task assessed reaction times to three- or six-letter strings. After a fixation cross, two strings of letters were displayed on the screen, one above and one below the fixation cross. Participants were instructed to decide as quickly and accurately as possible whether the letter strings were the same (e.g., JRT and JRT) using the Z key or different

(e.g., JRT and QRT) using the M key. Reaction time is measured in milliseconds. During the task there were eight practice trials (all three-letter strings) with feedback after each trial, followed by 48 randomised trials of either three or six letter strings. Trials were presented at even intervals. Reaction times were measured in milliseconds, split by condition.

Cognitive health: Attention

The Attention Network Task, combining a flanker and spatial attention task, can accurately measure three aspects of attention: alerting, orienting, and executive control. After a fixation cross (400ms), a horizontal row of five arrows appeared on the screen, each either facing left or right, and either at the top or bottom of the screen. Using the left and right arrow keys on the keyboard, participants were asked to decide which direction the centre arrow pointed, as quickly and accurately as possible. The task included conditions for both targets and cues. There were three target conditions: congruent (flanker and centre arrows point in the same direction), incongruent (centre arrow pointing in the opposite direction to the flanker arrows) or neutral (centre arrow surrounded by squares instead of arrows). There were also four cue conditions, as the stimuli could sometimes be cued with an asterisk (*). In the spatial cue condition, the asterisk appeared either above or below the fixation, cueing where the target stimulus will appear. There were then three ambiguous cue conditions: centre cue (asterisk appeared in the centre of the screen), double cue (two asterisks appeared simultaneously, one above and one below the fixation cross) or no cue (no asterisk/cue is shown). After 12 practice trials with feedback for each trial, there were three blocks of 96 trials (total of 288).

Performance was measured by calculating cost scores for alerting, orienting, and executive control. Response time was measured in milliseconds, and each cost score only included correct trials. Alerting score was calculated from the no cue response time minus the

double cue response time. Orienting score was measured from the centre cue response time minus spatial cue response time. Executive control was calculated from incongruent trials minus congruent trials. Better performance was indicated from higher scores for alerting and orienting, and lower scores for executive control.

Cognitive health: Language functioning

Language functioning was assessed through a computerised task that measured tip-of-the-tongue (TOT) occurrences. In each trial, participants were presented with a definition of a word. They were asked whether they could name the word the definition was describing, with three possible responses: 'Yes, I know the word' (if the participant selected this, the answer was displayed on the screen and participants were asked if that was the word they had in mind), 'No, I don't know the word' (task moved onto the next trial) or 'tip-of-the-tongue' (described to the participant as 'you know the word but can't bring it to mind just now, or you could think of it with more time'). During potential TOT occurrences, participants were then given prompt questions (free type response on the keyboard) asking how many syllables the word had, or if they could recall any sounds or letters in the word. The correct answer was then displayed, with two possible answers for if this was the word they had in mind: 'Yes' was recorded as a true TOT response, 'No' was a false TOT. True TOT score out of 60 was recorded. Two lists of 60 words were used and counterbalanced across participants.

Physical health: Grip strength

A standard analogue Takei hand grip dynamometer was used to measure grip strength. Grip strength was chosen as a measure of physical health as it can be predictive of other conditions such as frailty (Syddall et al., 2003), fall risk (Cardon-Verbecq et al., 2017) and

mortality in old age (Chua et al., 2020). The Takei dynamometer shows high criterion validity and reliability (Espana-Romero et al., 2010). Participants were asked to stand upright and hold the dynamometer in one hand, elbow fully extended, arm stretched to 180° above their head. They were then asked to bring their arm down, keeping it straight, and grip as hard as they could. Two measurements were taken from both the dominant and non-dominant hand, with the best score out of four taken for later analysis.

Physical health: Mobility

8-foot up-and-go: Participants were asked to sit on a chair, and when instructed, stand up, walk as fast as possible (without running) to a point eight feet away, turn around, walk back, and sit down on the chair. Performance was measured by time in seconds and milliseconds, with longer timings indicating worse mobility. Research has found it to be both a reliable and valid measure to assess functional mobility (Rolenz & Reneker, 2016), and is a predictor of fall risk (Rose et al., 2002) in older adults.

30-second sit-to-stand test: Participants were seated in a chair. They were asked to stand up and sit down unaided as many times as possible in 30 seconds. Performance was measured by how many correct stands were completed within the 30 seconds. It has been shown to be a reliable and valid measure of motor agility and dynamic balance in older adults (Rikli & Jones, 1999), as well as an accurate predictor of fall risk (Applebaum et al., 2017). Lower scores indicate higher fall risk.

Physical health: Estimated cardiorespiratory fitness

Cardiorespiratory fitness (CRF) was estimated based on gender (female = 0, male = 1), age, body mass index (BMI, weight in kg / height in m^2, measured objectively using scales),

resting heart rate (in beats per minute), and self-reported physical activity levels (Jurca et al., 2005). This information was used to estimate metabolic equivalent (MET) without the participant having to complete any form of exercise (Jurca et al., 2005). The equation has been found to be as valid as field test equivalents that assess maximal oxygen uptake (VO_2max; Mailey et al., 2010). The equation is as follows:

$$MET = [(\text{gender coefficient} \times 2.77) - (\text{age} \times 0.1) - (\text{BMI} \times 0.17) - (\text{resting heart rate} \times 0.03) + (\text{physical activity score}) + 18.07]$$

Physical activity score was derived based on the self-reported level of physical activity: *Level 1*, inactive or little daily activity (score of 0.00). *Level 2*, regular participation in low levels of exercise for at least 10 minutes a day, 5 days a week (score of 0.32). *Level 3*, 20 to 60 minutes a week of aerobic exercise such as swimming, cycling, jogging, or other activities with similar exertion levels (score of 1.06). *Level 4*, 1 to 3 hours a week of aerobic exercise, or other activities with similar exertion levels (score of 1.76). *Level 5*, over 3 hours a week of aerobic exercise, or other activities with similar exertion levels (score of 3.03).

Mental health: Depression

The Personal Health Questionnaire (PHQ-9) was used to assess self-reported symptoms of depression (Kroenke et al., 2009). The measure includes nine statements asking participants how frequently over the last two weeks participants have been bothered by a number of problems (e.g., ‘Feeling down, depressed or hopeless’) and is measured on a 4-point Likert scale from 0 – ‘Not at all’ to 3 – ‘Nearly every day’. Scores can range from 0 to 27, with higher scores indicating more depression symptoms. The PHQ-9 is well-established within research

and health settings and has high sensitivity and specificity when testing in clinical settings (Gilbody et al., 2007). Internal reliability for this measure was α = 0.72.

Mental health: Anxiety

The Generalised Anxiety Disorder (GAD-7) questionnaire was used to measure self-reported symptoms of anxiety (Spitzer et al., 2006). The GAD-7 is made up of seven statements asking participants 'Over the last 2 weeks, how often have you been bothered by the following problems? (e.g., 'Worrying too much about different things'). The GAD-7 can range from 0-21, with higher scores indicating more anxiety. The measure has high validity and reliability in both patient populations (Kroenke et al., 2007) and the general population (Lowe et al., 2008). The GAD-7 demonstrated good internal reliability at α = 0.79.

Mental health: Loneliness

The UCLA 3-item Loneliness Scale (UCLA-3) was used to measure self-reported symptoms of loneliness (Russell, 1996). The scale contains three questions ('How often do you feel that you lack companionship?', 'How often do you feel left out?', and 'How often do you feel isolated from others?') measured on a three-point scale ('Hardly ever', 'Sometimes', and 'Often'). The UCLA-3 demonstrates good reliability and convergent validity (Russell, 1996). Scores range from 3 to 9, with higher scores indicating more feelings of loneliness. Internal reliability was good for this measure at α = 0.84.

Serological markers of health

For analysis of serological markers, a venous blood sample (6ml EDTA vacutainer) was collected by a trained phlebotomist. Plasma was collected by centrifugation and stored at -80°C

in freezers until analysis. Samples were analysed for IL-6 (HS600C, HS Quantikine R&D) and BDNF (DY248, Duoset R&D) using enzyme-linked immunosorbent assays according to manufacture instructions. Seven-point standard curves were generated, and sample concentrations were quantified using 4-PL logistic regression. Samples are reported in picograms per millilitre (pg/mL).

Data reduction and analysis

Raw data were cleaned and prepared for analysis using Python 3.7. Reaction time outliers for cognitive measures (N-back, Choice RT, Letter Comparison, and ANT tasks) were detected 2±SD from the mean, per participant per condition, and removed from the dataset. Average response times and accuracy rates were calculated for each condition of each task where appropriate. Outliers for other measures (mental health questionnaires, physical functioning measures and levels of biomarkers) were identified 3±SD from the mean within SPSS v29 and removed. There was some missing data in the LPA dataset (N=2 for PHQ-9 and GAD-7, N=1 for UCLA-3, N=22 for IL-6, N=33 for BDNF). Little's MCAR test revealed missing data for the nine LPA indicator variables were missing at random ($\chi^2 = 33.57$, df = 28, $p = .215$). Missing data for LPA indicator variables were therefore inputted using expectation maximisation to allow all datapoints to be included, as is required in LPA analysis.

After data cleaning and preparation, latent profile analysis was conducted to identify profiles in the sample using the physical functioning, mental wellbeing, and serological markers of health mentioned above. LPA was conducted in R Studio (RStudio Team, 2020) using the *tidyLPA* package (Rosenberg et al., 2018), which is an extension of *mclust* (Scrucca et al., 2016). There are six possible LPA models which differ in how variances and covariances are treated

within the model. See Appendix 1 for variance-covariance matrix. Running LPA within R limits analysis to models 1, 2, 3, and 6, as models 4 and 5 are not available in R. Once the best fitting model and number of profiles were established, profile information was exported into SPSS with the original dataset. MANOVAs were used to validate profiles (i.e., to confirm that profiles had significantly different values for each indicator/predictor). Finally, one-way MANCOVAs (including age as a covariate) were conducted to identify significant differences between profiles on cognitive performance.

3.4 Results

Latent profile analysis

Nine variables were included as indicator variables within the LPA. These were measures of physical health (estimated cardiorespiratory fitness, grip strength, 8-foot up-and-go, and 30-second sit-to-stand), mental health (depression, anxiety, and loneliness), and serological markers of health (IL-6 and BDNF). First, all models were compared using fit indices such as Bayesian information criterion (BIC), Akaike information criterion (AIC), sample-size adjusted Bayesian information criterion (SABIC), Entropy and bootstrapped likelihood ratio test (BLRT) p-value. Lower BIC, AIC, and SABIC values, and a higher Entropy value, indicate better model fit. Research typically reports an Entropy value of 0.8 or above is acceptable (Tein et al., 2013), however Entropy alone should not determine the final model choice in latent mixture models (Weller et al., 2020). A significant BLRT *p*-value indicates the model is significantly better than the one preceding it.

Models 2 and 6 failed to converge, likely due to our relatively small sample size. Models 1 and 3 were investigated, but Model 1 (which allows variances to be equal across profiles, while covariances are restricted to zero) was ultimately selected due to a better model and conceptual fit. This model was then estimated from one to four profiles to ensure satisfactory profile sizes. Final model selection was based on fit indices identified in the analysis, as well as the size of profiles and how meaningful each profile was (Marsh et al., 2009). Model fit improved significantly between one to two profiles, and from two to three profiles ($p = 0.01$). Adding further profiles did not add meaningful improvement to the data, so three profiles was selected for the final model. This final model is visualised in Figure 3.1, with the datapoints representing the standardised mean score for each indicator. Fit indices are displayed in Table

3.2 (full fit indices for all models are available in Appendix 2). The established profiles were as follows.

Profile 1: Average physical health but challenged mental health (N=22), was the smallest group. Participants showed average physical functioning scores and levels of serological markers, but their mental health scores were significantly above average (i.e., they showed high depression, anxiety, and loneliness symptoms compared to the other profiles). This group, while showing average physical health, displayed unusually high levels of mental health symptoms, the worst of the three identified profiles. N=14 (63.6%) of this sample were female, and the groups mean age was the youngest at 68.6 years.

Profile 2: Optimally ageing (N=53) made up just under half of the sample. Participants displayed above average performance on the four physical function measures, their mental health scores were below the mean (i.e., they showed fewer depressive, anxiety, and loneliness symptoms), and they showed good levels of serological markers (low IL-6 and above average BDNF). This profile is therefore both physically and mentally healthy, according to our indicator variables. N=23 (43%) of this sample were female, and the group mean age was 70.6 years old.

Profile 3: Challenged physical health but good mental health (N=34) was the next largest group. Participants demonstrated poor physical functioning and poor levels of serological markers (i.e., their estimated cardiorespiratory fitness scores, grip strength, 8-foot up-and-go, 30-second sit-to-stand and both IL6 and BDNF were the poorest of the three groups) however their mental health scores were at or below the mean, with scores very similar to that

of Profile 2. Therefore, despite evidence of poor physical health, mental health symptoms were low (i.e., good) in this group. This sample had the highest proportion of females (91%, N=31), as well as the highest mean age (72.6 years).

Table 3.2. Fit indices for latent profile analysis using Model 1, estimating 1-4 profiles

No. of profiles	AIC	BIC	SABIC	Entropy	prob_min	prob_max	n_min	BLRT_p
1	2810.92	2859.36	2691.91	1.00	1.00	1.00	1.00	-
2	2763.89	2839.25	2676.93	0.72	0.88	0.95	0.40	0.01
3	**2709.79**	**2812.06**	**2617.87**	**0.81**	**0.85**	**0.97**	**0.20**	**0.01**
4	2715.23	2844.41	2610.79	0.82	0.85	0.95	0.12	0.55

Note: AIC = Akaike's Information Criterion; BIC = Bayesian Information Criterion; SABIC = sample-size adjusted Bayesian Information Criterion; Entropy = measure of classification certainty; prob_min = smallest probability of most likely profile membership; prob_max = largest probability of most likely profile membership; n_min = proportion of the sample in the smallest group; BLRT_p = p-value for bootstrapped likelihood ratio test. Note: selected final model is highlighted in bold.

Profile validation

To validate that the three profiles were significantly different from one another, one-way MANOVAs were completed using the LPA indicators (N=9) as dependent variables. After adjusting for multiple comparisons (new $p = 0.0055$), results showed significant differences between groups for all indicator variables apart from BDNF, indicating that the LPA identified successful latent profiles of participants in terms of physical health (estimated cardiorespiratory fitness, grip strength, 8-foot up-and-go, and 30-second sit-to-stand), mental wellbeing (depression, anxiety, and loneliness), and IL-6. Values are displayed in Table 3.3.

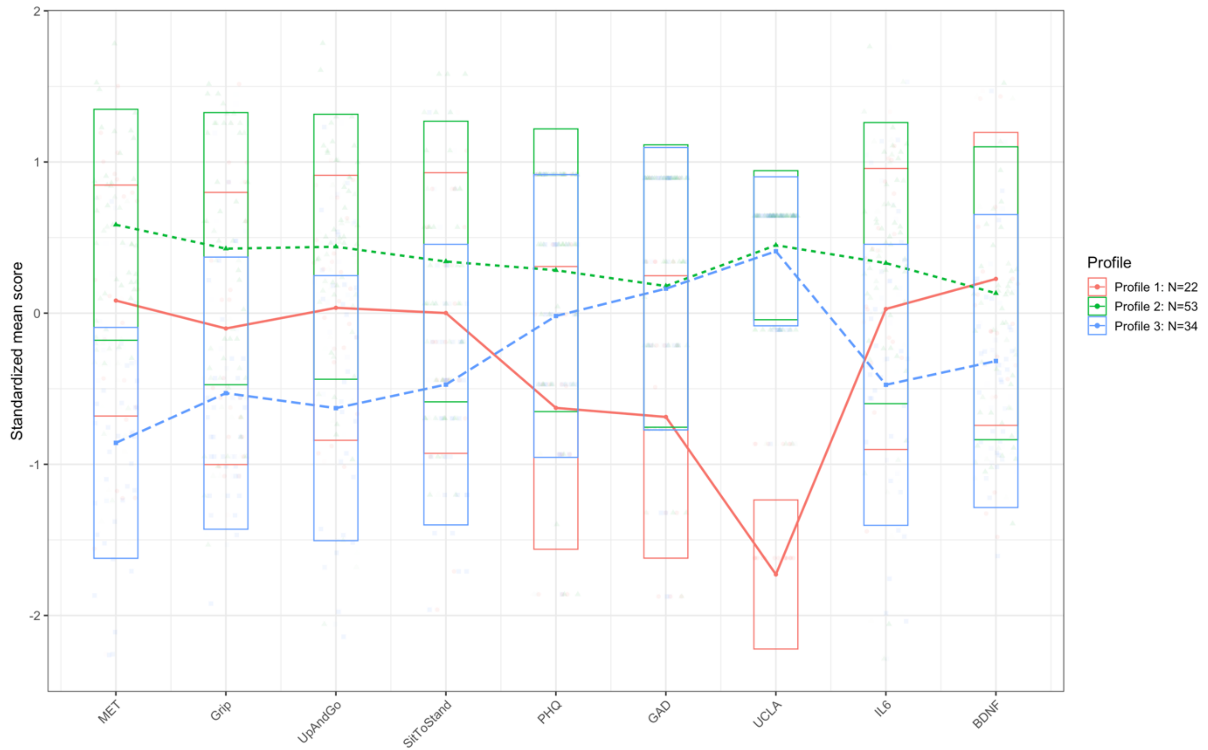

Figure 3.1. Figure showing standardised mean value for each indicator included in the LPA, split by final profile. *Note: Raw datapoints are plotted as dots. Boxes show +/-1SD around the mean. Values over 2SD outside the mean for each indicator were removed from this visualisation for illustrative purposes. MET = estimated cardiorespiratory fitness; Grip = grip strength; UpAndGo* = 8-foot up-and-go; SitToStand = 30-second sit-to-stand; PHQ* = PHQ-9 (depression); GAD* = GAD-7 (anxiety); UCLA* = UCLA-3 (loneliness); IL6* = interleukin-6; BDNF = brain-derived neurotrophic factor. * Items reverse-coded for illustrative purposes.*

Table 3.3 Results of one-way MANOVA validating LPA profiles.

Health measure	Indicator variable	LPA profiles			*F*-value	*P*-value
		Profile 1 (N=22)	Profile 2 (N=53)	Profile 3 (N=34)		
Physical functioning	Estimated cardiorespiratory fitness (MET)	7.43 (1.85)	8.49 (1.40) $_a$	5.27 (1.33) $_{a, b}$	49.35	**<.001**
	Grip strength (kg)	28.41 (6.19)	32.59 (7.82)	24.81 (5.93) $_b$	13.13	**<.001**
	8-foot up-and-go (seconds)	6.44 (0.82)	5.90 (1.14)	7.49 (1.71) $_{a, b}$	15.55	**<.001**
	30-second sit-to-stand (N)	14.68 (3.73)	16.15 (3.92)	12.62 (3.19) $_b$	9.61	**<.001**
Mental wellbeing	Depression (PHQ-9)	3.36 (2.66)	1.32 (1.84) $_a$	2.12 (1.86)	7.99	**<.001**
	Anxiety (GAD-7)	2.89 (2.02)	1.35 (1.67) $_a$	1.21 (1.51) $_a$	7.77	**<.001**
	Loneliness (UCLA-3)	6.14 (1.04)	3.24 (0.52) $_a$	3.32 (0.54) $_a$	166.38	**<.001**
Serological markers of health	IL-6 (pg/mL)	1.56 (0.89)	1.34 (0.59)	1.96 (0.79) $_b$	7.06	**.001**
	BDNF (pg/mL)	6.55 (3.35)	6.29 (2.76)	4.84 (1.65) $_b$	4.05	.020

Note: data presented as mean (SD). DF = 106, 2. Bonferroni adjusted p-values were used based on N=9 comparisons (p = 0.0055). Significant effects that remained after correcting are highlighted in bold. Statistical analyses were conducted using one-way MANOVAs. $_a$ *- significantly different from Profile 1,* $_b$ *- significantly different from Profile 2.*

Differences in cognitive ability between profiles

Age is known to be a significant predictor of cognitive performance (Park et al., 2002). A one-way ANOVA indicated that there were significant group age differences ($F(2,106) = 4.199$, $p = .019$) so age was added in as a covariate for further analyses. A one-way MANCOVA using profile (1, 2, or 3) as the independent variable and age as a covariate was conducted to investigate whether profile was associated with differences in cognitive performance. Cognitive performance measures included measures of working memory (Forward Digit Span: maximal digit span; N-back task: 1-back d', 2-back d'), processing speed (Choice RT task: average RT; Letter Comparison task: 3-letter average RT, 6-letter average RT); attention (ANT: alerting score, orienting score, conflict score); and tip-of-the-tongue (% tip-of-the-tongue occurrences). After adjusting for age, the MANCOVA was not significant; $F(20,174) = 1.057$, $p = .400$, Wilks' $\Lambda = .795$, partial $\eta^2 = .108$, indicating there were no significant differences between groups in terms of cognitive performance after controlling for age (see Table 3.4).

Table 3.4 Results of one-way MANCOVA assessing cognitive ability between profiles, with age as a covariate

Health measure	Indicator variable	LPA profiles			*F*-value	*P*-value
		Profile 1 (N=22)	Profile 2 (N=53)	Profile 3 (N=34)		
Working memory	Digit Span	6.00 (1.30)	5.85 (1.47)	5.64 (1.03)	.14	.866
	1back d’	3.80 (.49)	3.76 (.44)	3.76 (.50)	.48	.619
	2back d’	2.70 (.82)	2.55 (1.05)	2.23 (.94)	.60	.552
Processing speed	CRT average RT (ms)	.57 (.13)	.58 (.10)	.62 (.12)	1.57	.212
	LC 3 letter RT (ms)	1.05 (.14)	1.01 (.13)	1.13 (.17)	5.22	.007
	LC 6 letter RT (ms)	1.58 (.30)	1.52 (.26)	1.67 (.23)	2.35	.10
Attention	ANT alerting	4.55 (21.82)	2.99 (19.47)	-6.01 (23.08)	1.56	.216
	ANT orienting	24.45 (18.90)	23.45 (24.09)	20.60 (28.14)	.09	.918
	ANT executive control	131.41 (60.97)	120.53 (47.25)	149.78 (78.58)	2.57	.082
Language functioning	TOT states (%)	4.75 (4.81)	3.55 (3.25)	4.34 (5.27)	.72	.492

Note: CRT: Choice Reaction Time. LC: Letter Comparison. ANT: Attention Network Task. TOT: Tip-of-the-tongue. Data presented as mean (SD). DF = 174, 20. Bonferroni adjusted p-values were used based on N=10 comparisons (p = 0.005). Statistical analyses were conducted using one-way MANCOVAs, using age as a covariate.

3.5 Discussion

The present study utilised a person-centred approach to establish health profiles in a sample of healthy older adults and relate profiles to potential differences in cognitive performance. To do this, we used latent profile analysis (LPA) with a wide range of indicator variables, including physical functioning (estimated cardiorespiratory fitness, grip strength, 8-foot up-and-go, 30-second sit-to-stand), mental wellbeing (depression, anxiety, loneliness), and serological markers of health (IL-6, BDNF). Note that BDNF scores did not significantly differ between groups after adjusting for multiple comparisons, so when discussing serological markers of health, we will be referring to IL-6. LPA identified three latent profiles: *Optimally ageing*, *Average physical health but challenged mental health*, and *Challenged physical health but good mental health*. Surprisingly, despite our three profiles significantly differing from each other in terms of our LPA indicator variables, we found no differences between these profiles with respect to their cognitive performance. To our knowledge, this was the first study to use LPA based on these types of variables to explore differences in cognitive function.

The LPA identified three distinct profiles with differing patterns of physical functioning, mental wellbeing, and systemic inflammation. The largest profile, *Optimally ageing* (Profile 2) made up just under half of the sample. This profile had the best overall health profile, including the best performance on grip strength, 8-foot up-and-go, 30-second sit-to-stand, and estimated cardiorespiratory fitness out of the three groups. They displayed the lowest scores on the depression, anxiety, and loneliness questionnaires, and had the lowest amounts of systemic inflammation as shown by low IL-6 levels. The smallest group was Profile 1: *Average physical health but challenged mental health*. This group showed average scores for grip strength, 8-foot up-and-go, 30-second sit-to-stand, estimated cardiorespiratory fitness, and systemic

inflammation (IL-6). However, they were significantly different in terms of mental wellbeing, reporting the highest scores on our three mental wellbeing measures, depression, anxiety, and loneliness (note that high scores here mean poor mental health). Our final group was Profile 3, *Challenged physical health but good mental health.* This group displayed interesting characteristics. They were the profile that showed poorest physical health in both physical functioning measures and systemic inflammation, displaying the lowest scores for grip strength, mobility measures, estimated cardiorespiratory fitness, and IL-6. However, they reported average or above average mental health, with very similar scores to our *Optimally ageing* group. This was particularly noteworthy, given that these two profiles had opposite scores for all physical functioning variables. Our *Challenged physical health but good mental health* group therefore had good mental wellbeing *despite* their poor physical functioning and IL-6 levels.

Our findings partially support previous research. Our *Optimally ageing* profile echoes previous person-centred research that suggests better physical functioning is related to better mental wellbeing (Park et al., 2019). However, our other two profiles do not necessarily follow past research, particularly our *Challenged physical health but good mental health* profile. It makes an important distinction and an interesting possibility, that there may be some protective factor not measured in the present study that protects some older adults from potential mental health declines. Indeed, past research has suggested a wide variety of protective factors in the development in older adults. One review suggested three themes: resources to draw upon (physical, cognitive, and socioeconomic), life experiences teaching strategies to manage stressors, and meaningful engagement such as volunteering, religion, or social activities (Fiske et al., 2009). Future research could investigate these three themes using similar person-centred approaches to establish profiles based on both health and behavioural measures.

The three profiles were significantly different from one another for the most part, when validating our profiles by comparing group means of our indicator variables. An unanticipated result was that we did not find meaningful group differences in cognitive performance. One might have expected our *Optimally ageing* group to perform best on cognitive measures such as working memory, processing speed, and attention, as past research has shown clear links between good physical health and cognitive ability in healthy older adults (Northey et al., 2018). Further, research has linked aerobic fitness with language functioning in older populations (Segaert et al., 2018), so theoretically it would have been expected that this group would perform better on the tip-of-the-tongue task as well. However, we did not find differences in cognitive scores between our *Optimally ageing* group compared to our other profiles. The lack of significant findings may be due to a lack of statistical power (Johnson, 2021) or there not being enough variance between groups in cognitive functioning. An alternative argument is that using a person-centred approach such as LPA allows an important incorporation of multiple indicators and allows the possibility of subpopulations within a given sample, which variable-centred approaches are unable to do (Howard & Hoffman, 2017). Evidence shows clear associations between physical health, inflammation, and mental health individually with cognitive performance (Lara et al., 2019; Lautenschlager & Almeida, 2006; Yaffe et al., 2003), but in our study at least, these patterns do not persist once the variables are integrated and viewed holistically. Person-centred approaches acknowledge how these variables are combined *within* people instead of looking at characteristics in isolation, which is useful given that individuals present with a combination of these variables.

There are some limitations of LPA. The process of selecting the best LPA model might appear to some to be a ‘statistical fishing expedition’ (Johnson, 2021), and person-centred

approaches such as LPA have limited generalisability and replicability (Ullrich-French & Cox, 2020). However, person-centred approaches overcome limitations of variable-centred approaches (e.g., a typical ANOVA or regression) as they allow the possibility of subgroups *within* a population that might have differing characteristics (Howard & Hoffman, 2017). They therefore give more specificity than variable-centred approaches, as each subpopulation is described independently rather than looking at outcomes separately. This study has further strengths in its comprehensive testing battery. To our knowledge, no study has incorporated physical functioning, mental wellbeing, and serological markers of health into latent profile analysis, or assessed group differences in such a wide range of cognitive functions in older adults. The cognitive outcome measures span a wide range of abilities, allowing analyses across cognitive functions rather than within tasks. We utilised three commonly used mental wellbeing questionnaires, assessing distinct symptoms known to interact with ageing. Our physical functioning measures too spanned a wide range of measures, and the inclusion of serological markers of health was a way of incorporating immunological health into a behavioural setting.

The main limitation with the present study is its relatively small sample size, however a number of previously published papers have successfully conducted LPA on smaller samples (Arnett & Flaherty, 2022; Park et al., 2017; Terhune, 2015). Importantly, we limited the number of potential profiles to four, to ensure that our group sizes would be sufficient (Kleitman et al., 2021). There could arguably be subsequent latent profiles that we could not identify due to our sample size, so this is the most pressing direction for future research. Another limitation is the ethnically homogenous nature of our sample - most of our sample were White, which does limit the generalisability of our findings. Both the size of our sample and the nature of our sample of healthy older adults may have limited findings in the second step of our analysis. While each

profile was significantly different from each other in terms of the LPA indicator variables, no differences were found in cognitive performance after adjusting for age. This may be for two reasons; as explained above, our sample size may not have been large enough for sufficient power (Johnson, 2021), or because our sample had limited variance. In particular, our sample displayed relatively good mental health scores (i.e., fewer depression, anxiety, or loneliness symptoms) compared to the rates cited in the introduction (Age UK, 2016, 2020b). There are a range of socio-cultural variables that could account for mental health symptomology, meaning patterns are not consistent across cultural settings (Kiely et al., 2019; Lee & Lee, 2011). Future research with a larger sample size and a wider population (be it a wider range of socioeconomic status, ethnicity, or the inclusion of old-old participants over the age of 85) may help in identifying profiles as well as differences in cognitive performance. A further direction for future research would be to assess how these profiles change over time, through the use of latent profile transition analysis (Johnson, 2021).

In sum, the present study utilised a novel person-centred approach in a healthy ageing population. Latent profile analysis identified meaningful differences between groups in terms of physical, mental, and serological markers of health, but did not find differences in cognitive performance between profiles. Latent profile analysis, when used in this way, is a relevant way of looking at an overall profile of someone rather than just one aspect of wellbeing at a time. It differs from traditional variable-centred approaches in this way and offers an alternative view of wellbeing. We have shown that there may be subtle but important distinctions between mental and physical health in some populations, suggesting that for public health initiatives, researchers may need to look at the whole profile of an individual to target interventions where

needed. The present study can be used as a base for future research conducting LPA on larger and more diverse samples of older adults to investigate these differences further.

Reflection on Chapter 3

Chapter 3 explored associations between facets of older adult health using a person-centred analytic approach. It identified three subgroups within the population who displayed differing patterns of psychological, physical, and serological health. However, results from the second step of the latent profile analysis did not find significant associations between profile and cognitive performance. Given that in this population, cognitive performance was not impacted by psychological, physical, or serological health, Chapter 4 looked to assess whether an external intervention could impact cognitive ability. Chapter 4 therefore expands on Chapter 3 by exploring cognition in older adults in more depth, assessing whether cognitive ability changes over time using a training intervention.

CHAPTER 4 - COMPUTERISED BRAIN TRAINING HAS LIMITED COGNITIVE BENEFITS IN HEALTHY AGEING

4.1 Abstract

Whether brain training programmes are effective and have transferable benefits to wider cognitive abilities is controversial, especially in older adult populations. We assessed, in a randomised controlled intervention study, whether a commercially available brain training programme led to cognitive improvements in a sample of healthy older adults (N=103). Participants completed a three-month intervention of either an adaptive brain training programme or active control. Cognition was measured through a comprehensive battery of tasks pre- and post-intervention to assess working memory, processing speed, attention, and language functioning. Analyses were conducted using mixed models and linear regressions. Despite participants in the intervention group significantly improving on all tasks within the brain training programme, there was no evidence of any transfer benefits to cognitive outcome measures (as compared to the active control group). Our results indicate that benefits of brain training programmes appear to be limited to practice effects, while no evidence is found for transfer effects.

4.2 Introduction

Cognitive processes such as working memory, processing speed, attention, and language functioning all decline during healthy ageing (Reuter-Lorenz et al., 2021; Salthouse, 2010; Segaert et al., 2018). As life expectancy in developed countries continues to increase (Roser et al., 2013), mitigating age-related cognitive decline has become a field of research paid much attention to. In the present study, we examined whether computerised brain training improves performance across multiple domains of cognition.

A recently popular method of delivering cognitive training has been to use commercially available brain training programmes. Applications such as Lumosity (Lumosity, 2023), Peak (Peak, 2023) and BrainHQ (BrainHQ, 2023) are commercially advertised as training programmes that will improve cognitive ability and delay cognitive decline. These applications are easy to use, relatively affordable, adaptive (increasing in difficulty with improved performance, which is key for cognitive training programmes to work, Brehmer et al., 2012) and include training games that cover a variety of cognitive processes such as short-term memory, language, attention, and processing speed. Research suggests some promising support for the use of these brain training applications; company websites often cite peer-reviewed publications that show effects of their programme: BrainHQ for example references over 100 publications (BrainHQ, n.d.). Brain training applications have been tested with healthy populations and have been suggested to improve auditory processing and memory (Anderson et al., 2013), sustained visual attention (Savulich et al., 2019), and improve executive functions (Meltzer et al., 2023), to name a few.

However, there are some inconsistencies in the brain training literature. There is evidence from meta-analytic studies that computerised cognitive training or brain training leads to small but significant improvement in skills such as working memory, processing speed, and visuospatial skills in healthy older adults (Kueider et al., 2012; Lampit et al., 2014). Conversely, a recent meta-analysis has found no convincing improvement after accounting for publication bias (Nguyen et al., 2022). Older adults have higher expectations of brain training compared to younger adults (Rabipour & Davidson, 2015), and they could arguably benefit most from their use, if effective. Whether brain training programmes lead to tangible improvements in cognitive abilities in healthy older adults therefore warrants further investigation.

Some of the inconsistencies found in cognitive training research more broadly can be attributed to methodological differences, which have been identified in various papers and reviews (Green et al., 2014; Noack et al., 2014; Simons et al., 2016). Sample sizes vary wildly and are often limited; 50% of studies in a 2014 review of transfer effects in cognitive training studies had fewer than 20 participants in each group (Noack et al., 2014), and 90% had fewer than 45 in each group. Training duration is also often limited; 50% of studies reported 8 hours and 20mins of training or less, with the majority (90%) reporting less than 20 hours in total (Noack et al., 2014). Another concern is the size and content of the test battery (Green et al., 2014). Many studies, especially early studies when cognitive training was in its infancy, used a small test battery (i.e., one test per cognitive function) to assess cognitive outcome measures. However, to assess valid training benefits, the outcome measures need to be chosen such that they assess changes across the construct rather than the individual tasks. For example, executive function cannot be assessed by a single measure, the function itself is made up of three smaller processes (inhibition, shifting and updating, Sandberg et al., 2014), so one outcome measure that focuses on one of those processes is not enough to encompass executive function as a whole. Moreover, if cognitive training includes a specific task that trains, for example, working memory (e.g., an n-back task), then its benefits can only truly be assessed through performance on a different task which measures skills within this domain (a task which also assesses working memory such as a digit span task). A final consideration is the choice of control group (Simons et al., 2016). The gold standard is to use an active control group that mimics the intervention as closely as possible, while leaving out the 'active ingredient' of the training. However, the very nature of cognitive training programmes makes this difficult. The type of control groups in published studies therefore varies, often including passive control groups, and not always

accounting for placebo effects, motivation, or cognitive demands (Simons et al., 2016). Active control groups can be divided further; into 'active-ingredient' controls and 'similar-form' controls (Masurovsky, 2020). 'Active-ingredient' control groups are identical in every aspect apart from the 'active' ingredient, but these are difficult to implement and in practice are rarely used. 'Similar-form' active controls are much more common, mimicking aspects of the training but differing in a few ways. 'Similar-form' control groups are still considerably more suitable than passive or no-contact control groups (Masurovsky, 2020).

We note that in above set of issues, a key concern, but one most often overlooked, is the need to establish evidence of *transfer* effects (the benefits of the training 'transferring' to other, un-trained, cognitive tasks), as opposed to practice effects (improvements within the training, or same tasks, itself). Transfer effects can be categorised by how similar they are to the trained cognitive domain (Sala et al., 2019). Near transfer refers to skills generalising to similar domains (e.g., working memory training transferring to other, related but untrained, working memory tasks), while far transfer relies on the cognitive domain being weakly related, or not related at all, to the trained domain e.g., working memory training to language, or executive control (Sala et al., 2019). The more shared features there are between domains, the nearer the transfer effects (Sala et al., 2019). This is the ultimate aim of brain training programmes, that regular training of specific cognitive processes leads to improvements across cognitive domains (Stojanoski et al., 2018). There is some evidence that brain training can lead to transfer effects (McDougall & House, 2012), however, there are also cases where no transfer benefits are found at all (Kable et al., 2017; Stojanoski et al., 2018). Even when papers report significant positive effects of brain training programmes on cognition in healthy older populations, the effects are often driven by improvements on very near transfer tasks (H. K. Lee et al., 2020), and show

little to no evidence of far transfer. Furthermore, a recent meta-analysis of brain training randomised controlled trials with older adults found small but significant transfer to some cognitive domains, however most effects were no longer significant once publication bias was taken into account (Nguyen et al., 2022). There are also cases where previously reported effects have perhaps been exaggerated. Brain training research sometimes describes improvements in trained effects (improvement in performance within the programme) and report this as an improvement in cognitive ability (Bonnechere et al., 2021). Instead, these are in fact just practice effects and do not necessarily entail improvements in cognitive function, since transfer effects (near or far) are missing or were not assessed. Transfer effects are essential if a training programme is going to be effective and wide-reaching, especially in ageing populations, but concrete evidence for them is often lacking.

Due to these inconsistencies and the controversy surrounding brain training programmes and their effects, there is a need for robust and rigorous research to assess its efficacy. An extensive review paper has given recommendations for how research into brain training programmes should be conducted and published (Simons et al., 2016). The researchers recommended a large sample size with random allocation to groups, with blinding of conditions if possible. An appropriate active control group should be utilised, meaning a control group that correctly mimics the level of engagement of the intervention, but that theoretically will not result in improved cognitive performance. This allows for placebo effects to be controlled for, and any effects to be attributed to the 'active' ingredient of the training programme (Simons et al., 2016). Furthermore, interventions need to control for expectations and motivations of both groups to ensure they are not different. The researchers finally recommend using appropriate

outcome measures and a sufficient test battery by using multiple tasks to measure each construct. Our study has incorporated each of these key recommendations.

To assess the possible cognitive benefits of the training we measured cognition across a wide range of domains. Among various possible cognitive functions of interest, working memory stands out as a commonly reported function. This is not only due to its consistent decline with age (Salthouse, 2010) but also because it serves as a foundation for many other cognitive abilities. Working memory training has shown convincing improvements in memory skills in older adults in recent years (Karbach & Verhaeghen, 2014). Another cognitive skill that exhibits consistent decline with age is processing speed, which has been effectively trained in older adults. The well-known ACTIVE study demonstrated significant and sustained improvements over a two-year period in processing speed.(Ball et al., 2002). Although findings on attention skills are not always consistent, they do undergo changes with age, and deficits in attention can impact daily life (Glisky, 2007), making it a worthwhile line of enquiry. Finally, language skills, specifically word finding difficulties, increase with age (Maylor, 1990) and are commonly reported by older adults as deficits they notice in older age (Segaert et al., 2018).

Cognitive training is an important field of research that needs methodologically sound experiments to assess whether brain training programmes are effective. The aim of the current study was to do just that; assess the efficacy of a commercially available adaptive brain training programme (Peak) on a range of cognitive domains, in a randomised controlled study with healthy older adults. We aimed to include a larger sample size than has been used in many previous cognitive training studies (Noack et al., 2014) and an appropriate active control group. We assessed cognitive functions known to decline with healthy ageing and used tasks that are

commonly used in ageing research. These included working memory (Forward Digit Span task and visual N-back task), processing speed (Choice Reaction Time task and Letter Comparison task), attention (Attention Network Task) and language functioning (tip-of-the-tongue task). We hypothesised that we would find significant improvements within the training games (practice effects) for our intervention group. Whether we would find transfer effects from the brain training to other cognitive abilities was unclear, but we anticipated any transfer effects would be to similar cognitive tasks (near transfer) rather than to dissimilar tasks (far transfer).

4.3 Methods

Participants

One hundred and nine participants were initially recruited through existing participant databases at the University of Birmingham (Birmingham 1000 Elders) and online social media advertisements. Six participants dropped out and did not complete the post-intervention measures; 103 completed both pre- and post-intervention sessions. Our sample size was not informed by power analysis but guided by previous research (Noack et al., 2014). Our aim was for 100 people to complete the intervention with roughly 10% attrition rate. Participants ranged from 60 to 84 years old (M = 70.57, SD = 5.5). The Montreal Cognitive Assessment (Nasreddine et al., 2005) was used to check for impaired cognition. A recent meta-analysis suggested that a cut off score of 23 out of 30 for mild cognitive impairment (rather than the original 26/30) provides fewer false positives and better diagnostic accuracy (Carson et al., 2018); no participants were excluded based on this cut-off point. Participant flow chart is in Figure 4.1.

Inclusion criteria required participants to be over 60 years of age, a monolingual native English speaker, have normal or normal to corrected hearing and vision, access to a smartphone or tablet, and be able to walk short distances unaided. Participants were also required to be up to date on COVID-19 vaccinations at the time of visit. Exclusion criteria were criteria that might be confounded by cognitive ageing: a diagnosis of cognitive impairment (mild cognitive impairment, Alzheimer's disease, Lewy body dementia, vascular dementia, frontotemporal dementia), a diagnosis of mental health disorder (depression, anxiety, schizophrenia, bipolar disorder, post-traumatic stress disorder, psychosis, obsessive compulsive disorder), a diagnosis of dyslexia (this specifically related to the tip-of-the-tongue task), or currently taking

medication known to interact with cognitive function or inflammation (medication for arthritis, anti-depressants, anti-anxiety).

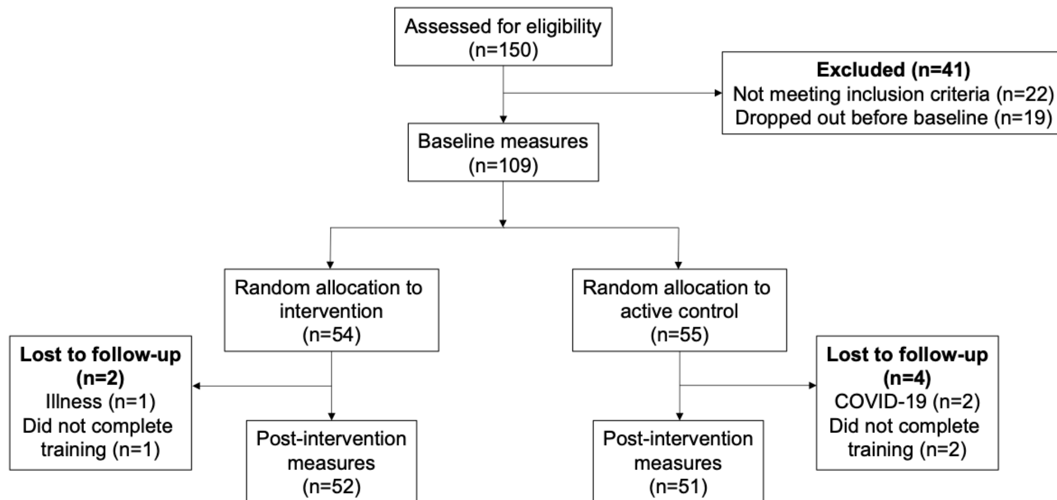

Figure 4.1. Participant flow chart.

Intervention

Cognitive training intervention

The present study used Peak (Peak, 2023), a commercially available brain training application, as the intervention. A total of 48 games based on neuroplasticity train seven different cognitive functions: Language, Problem Solving, Memory, Focus, Mental Agility, Emotion, and Coordination. The app tracks progress, comparing your scores to personal previous scores and to other players of a similar age group. Scores are given out of a possible 1000 and are updated for each category every time a game or 'brain workout' is played. Games are adaptive, increasing in difficulty with improved performance. Participants in this group were asked to use the pre-made 'daily brain workouts' to ensure a wide range of cognitive abilities were trained. The daily workouts took around 15 minutes, after which participants were

told they could explore the app and use other games as they wished. Peak has been reported by others to improve everyday functioning and improve measures of processing speed in younger adults with depression (Motter et al., 2019), however to our knowledge, no research to date has investigated the efficacy of Peak on cognition in healthy ageing.

Active control group

Active control groups, matched to the intervention as best as possible on training intensity, motivation, and engagement, are the gold standard in intervention studies (Green & Bavelier, 2012). Active control groups are crucial to establish that any effects found are a direct result of the intervention itself, rather than social impacts, expectation effects of training, or the repetition or structure of completing a daily or regular task (Green et al., 2014). Following the justification of an active control group given by Kable et al. (2017), the control group was chosen to mimic and control for any effects of cognitive stimulation. The choice of training was a 'similar-form' control group (Masurovsky, 2020), a readily available free mobile application, Cardgames.io (Cardgames.io, 2023), that includes 42 card and board games, such as Hearts, Rummy, Yahtzee, and Solitaire. Similar to Kable et al., participants were not restricted in terms of what games they played but were encouraged to try a variety of them, as long as it was for at least 15 minutes per day, to match training intensity. Crucially, game difficulty was not adaptive to user performance, and the variety of games ensured novelty and engagement.

Cognitive outcomes measured pre- and post-intervention

Working memory

Working memory was assessed through two computerised tasks: the Forward Digit Span task, and N-back task.

Forward Digit Span: Single digits (0-9) are presented to participants one at a time on a computer screen at 1000 ms intervals. Trials begin with three-digit sequences up to a possible ten-digit sequence. After the sequence has been presented, participants are asked to type the digits in the order they were presented using the computer keyboard, using the Enter key to confirm. Feedback is given after each trial. There are three trials in each level, and participants must get two trials correct to move up to the next level. The task automatically ends after two incorrect answers within a level. The participant's digit span is taken from the highest level in which participants get two trials correct. Measuring working memory using Digit Span tests is common in psychological experiments such as these and has been established within ageing literature (Grégoire & Van der Linden, 1997). This task takes approximately 5 minutes.

N-back task: This task consists of a visual N-back task. Participants view a 3 x 3 grid on a computer screen, in which squares appear in one of the nine possible places (presented regularly at 1000 ms intervals), one at a time. Participants are asked to respond by pressing the 'Space' key whenever the target matches the location shown N steps before. There are two blocks of 60 trials, a 1-back and a 2-back, with 16 targets in the 1-back block, and 12 in the 2-back. Participants have a practice 1-back block of 12 trials and receive feedback on their performance at the end of the practice. No feedback is given for rest of the task. This task is well established and has been validated as an effective working memory measure (Jaeggi et al., 2010) RT is measured in milliseconds and a performance is measured by calculating a d' score from the four outcomes of each trial: hit (correct button press in response to the target), miss (no button press when the target appears), correct rejection (participant correctly does not press button) and false alarm (participant incorrectly presses button when no target appears). A higher score indicates better performance or better sensitivity to the target. The task takes approximately 10 minutes. The final score, d', is calculated as follows:

Z-score Hit Rate [#Hits / (#Hits + #Misses)] minus Z-score False Alarm Rate [#False Alarms / (#False Alarms + #Correct Rejections)]

Processing speed

Processing speed was assessed through two computerised tasks, the Choice RT task, and Letter Comparison task.

Choice RT task (CRT): Four empty squares are displayed on the computer screen, which correspond to the Z, X, N, and M keyboard keys. Participants rest index and middle fingers on these keys. Intertrial intervals ranged from 1000 and 2500ms (at 250ms increments), after which an X appears in one of the four squares. Participants are asked to press the Z, X, N, or M key for which box the X appears in, as fast and accurately as possible. The task consists of 8 practice trials, followed by 32 test trials. Feedback is only given after each practice trial. Target locations and intertrial intervals are counterbalanced, and trials are randomised. RT is calculated in milliseconds. This task is well established when assessing processing speed (Deary et al., 2010). The CRT takes approximately 2 minutes.

Letter Comparison task (LC): A fixation cross is displayed in the middle of the screen. Two sequences of letters are then displayed at equal distances above and below the fixation cross, and participants are asked to decide whether the letter sequences are the same or different. Participants are asked to do this as fast and accurate as possible. The Z arrow key is pressed for the same letters, M for different. The task consists of eight practice trials of three letter sequences, followed by one block of 48 trials, consisting of three-letter and six-letter strings. Trials are presented at even intervals (1000ms between trials, fixation cross for 500ms, blank for 100ms, letters presented until response) and are randomised. RT is calculated in

milliseconds. This task is a well-known measure of processing speed in ageing populations (Salthouse & Babcock, 1991). The task takes approximately 5 minutes to complete.

Attention

Attention Network Task (ANT): The Attention Network Task was used to measure attention. The computerised task allows assessment of orienting, alerting and executive control through the combination of a flanker (Eriksen & Eriksen, 1974) and spatial attention task (Posner & Cohen, 1984). During each trial, a fixation cross is displayed for 400ms before a stimulus appears. The stimulus is a row of five arrows, each pointing left or right. Participants are asked to report, using the left and right arrow keyboard keys, which direction the centre arrow points. They are asked to do this as fast and accurate as possible. The centre arrow can be congruent (points the same direction as the flankers) or incongruent (points in the opposite direction to the flankers). The stimuli can appear above or below the fixation cross and can be cued with an asterisk (*) or not cued. There are three cue conditions: spatial cue (cue appears either above or below the fixation cross), centre cue (asterisk appears in the centre of the screen), or double cue (cue appears both above and below the fixation cross). Only the spatial cue indicates where the stimulus will appear, the location of the stimuli is ambiguous for the centre and double cue. Participants have a practice trial of 12 trials followed by three blocks of 96 trials (total of 288 trials). Feedback is only given during the practice trials. The ANT has been used in older adults to detect changes in attention compared to younger adults (Jennings et al., 2007).

RT is measured in milliseconds. Alerting is measured by the no cue response time minus the double cue response time for correct responses only. Orienting is measured by the centre cue response time minus the spatial cue response time for correct responses only. Executive

control is measured by response time in the incongruent flanker condition minus response time in the congruent condition. High scores for alerting and orienting, and low scores on executive attention, indicate better performance. The task took approximately 10 minutes to complete.

Tip-of-the-tongue

Tip-of-the-tongue (TOT) instances were measured through a computerised task. In 60 trials, participants are shown a written definition of a word and are asked whether they can name the word the definition is referring to. There are three available responses: 'Yes, I know the word' (participant is given the answer and is asked whether that was the word they had in mind), 'No, I don't know the word' (move onto next trial) or 'tip-of-the-tongue' (described to the participant as 'you know the word but can't bring it to mind just now, or you could think of it with more time'). In TOT instances, participants are then asked if they can recall how many syllables the word has, or if they can remember any of the sounds in the word. Both answers are typed on the keyboard. They are then shown the answer and are asked whether that was the word they had in mind. A 'Yes' response at this stage is recorded as a true TOT instance, and a TOT score out of 60 is recorded for analysis. This TOT task has been used in previous research with older adults and was found to be related to cardiovascular health (Segaert et al., 2018). There were two 60-word lists for this task, which were counterbalanced across participants. The TOT task takes approximately 20 minutes.

Procedure

All participants were screened on the inclusion and exclusion criteria and gave informed consent before being allocated to the intervention or active control group. Groups were allocated using stratified randomisation (split by sex), to ensure equal sex distribution.

Participants completed a baseline assessment of all outcome measures which took around two hours as well as a questionnaire to record demographic information. Age, sex, ethnicity, highest educational qualification, and regular medication were all recorded. Cognitive measures were coded and administered using PsychoPy (Peirce et al., 2019).

The researcher then downloaded either the intervention application (Peak) or control application (Cardgames.io) onto the participant's smartphone or tablet. Participants were shown how the applications work and were instructed to train for at least 15 minutes each day for the duration of the intervention period (three months). This training intensity and duration was based on a previous report which found that 50% of studies had less than 8hrs 20mins of training in total (Noack et al., 2014). If adhered to correctly, our intervention would result in at least 22.5hrs of training. While more training could in theory be more beneficial to our outcomes, we wanted to choose a duration and intensity that would be feasible and achievable for our chosen population. Adherence to the training programme was measured by asking participants to keep a training diary, which they reported through weekly emails detailing how much training they had completed that week (in minutes per day), what their Peak brain scores were (intervention) and what games they had played (active control). This also controlled for the amount of researcher contact both groups received.

Participants repeated the series of outcome measures immediately after the three-month intervention, to assess any direct effects of the training. At post-intervention, additional questions were asked about motivation ('How motivated were you to complete the training?') and enjoyment ('How much did you enjoy the training?') on a 7-point Likert scale from 1- 'Not motivated' / 'I did not enjoy it', to 7 – 'Extremely motivated' / 'I really enjoyed it'. Adherence

to the training was determined by asking participants how many days of training they missed per week.

The study was randomised, controlled, and a single blinded intervention: participants were randomly allocated and both groups were told the study aimed to investigate the effects of computerised smartphone apps on cognitive health, to ensure the same level of expectation effects (Kable et al., 2017). The assessor for both sessions was not blinded to whether participants were part of the intervention or control group, but, while in theory this might introduce bias (Kendall, 2003), it is important to note that all cognitive outcome measures were computerised which should mitigate potential limitations. The study was approved by the University of Birmingham Ethics Committee (ERN_19-1176) and complied with ethical considerations outlined in the British Psychological Society Code of Human Research Ethics (BPS, 2021). The study was performed in accordance with all relevant guidelines and regulations. Participants received monetary compensation for the in-person visits.

Data reduction and analysis

Before analysis, data were cleaned to identify outliers, using Python 3.7. Outliers for RT data (for N-back, CRT, LC, and ANT tasks) were detected and removed from 2±SD from the mean, per participant per condition. This removed around 1% of RT responses. Individual responses were excluded from analysis if the % accuracy was below 50% for that task (this removed one participant's response for CRT, four for the Letter Comparison task, four from the N-back task, four from the ANT, and two from the ToT task).

Pre- vs post-intervention cognitive scores were analysed in R Studio (RStudio Team, 2020). For those tasks where outcome variables had repeated observations over trials and/or participants (CRT task, Letter Comparison task, and tip-of-the-tongue task), we ran linear mixed models using the *lme4* (Bates et al., 2015) and *report* (Makowski et al., 2023) packages. Linear mixed models are extensions of regressions that are increasingly popular in psychological research (Bono et al., 2021) as a way of analysing data while being able to account for variability within factors such as item or participant (Judd et al., 2012). For each model, we attempted to include a maximal random-effects structure (Barr et al., 2013). We included participant and item as random intercepts (as there may be variance between items or individual differences in participants) and attempted to include as many random slopes (random adjustments to the fixed effects) as the model would allow. For other tasks, where the outcome measure is a single value (i.e., N-back d', maximal digit span, or ANT cost score), linear regressions were conducted using the *dplyr* package (Wickham et al., 2023).

For the CRT task, 3-letter condition, and 6-letter condition of the Letter comparison task, we fitted separate linear mixed models predicting reaction time, including session (pre vs post) and condition (intervention and control) as fixed effects. Random intercepts were included for participants and items. Random slopes for items were not included in the final models as they did not converge (Barr et al., 2013). These models were estimated using REML (Corbeil & Searle, 1976) and used nloptwrap optimizer. ToT data was analysed by a generalised linear mixed effects model, as the dependent variable (tip-of-the-tongue occurrence) was binomial (ToT response was either a 0 – no ToT, or 1 – ToT). ToT occurrence was predicted by fixed effects of session, condition, and the number of phonemes in each item (Segaert et al., 2018), as well as including random intercepts for item and participant. Random slopes were again not

included in the final model due to non-convergence. ToT models were estimated using maximum likelihood and BOBYQA optimizer, with the logit link function. Maximal digit span, 1-back d', 2-back d', and alerting score, orienting score, and executive control score from the ANT were all investigated using session and condition as predictor variables in a linear regression model. As less than 5% of data was missing, missing data was not estimated (Jakobsen et al., 2017; Roth & Switzer III, 1995; Schafer, 1999). All continuous variables were scaled prior to analysis. As we were assessing many outcome variables and conducting multiple statistical analyses (N=10), a Bonferroni adjusted *p*-value was calculated (new *p*-value = 0.005). 95% Confidence Intervals (CIs) and *p*-values were computed using a Wald t-distribution approximation.

4.4 Results

Demographics

Table 4.1 reports demographic information for the 103 participants who completed both pre- and post-intervention assessment sessions. There were no significant differences between groups at baseline in terms of age, gender, or MoCA score (all $p > .05$). Participants were excluded from further analyses if total training was less than 80% (less than 18 hours in total). Four participants (N=2 intervention, N=2 control) were excluded due to low training, meaning a total of 99 participants (N=50 intervention, N=49 active control) were included in analysis. It is worth noting that, following Intent to Treat principles (Montori & Guyatt, 2001), we also ran analyses on the full dataset (N=103). Overall effects did not change for any reported analyses.

Table 4.1. Baseline demographics for intervention and active control groups.

	Intervention (n = 52)	**Active control (n = 51)**	**p value**
Age – years (SD)	70.7 (5.5)	70.5 (5.6)	.84
MoCA score – M (SD)	28.3 (1.3)	28.5 (1.5)	.45
Sex - N			.94
Female	31	30	
Male	19	19	
Ethnicity - N			.99
White	48	47	
Mixed/Multiple Ethnic Groups	1	1	
Other	1	1	
Highest educational qualification - N			
GCSEs, O-levels or equivalent	4	2	
A-levels or equivalent	7	15	
University undergraduate (e.g., BSc, BA)	13	14	
University postgraduate (e.g., MSc, MA)	8	13	
Doctoral degree (e.g., PhD)	4	0	
Other	13	5	

Note: MoCA = Montreal Cognitive Assessment.

Adherence to training

Overall adherence to both intervention and active control was high. Participants were asked to train for at least 15 minutes per day on their respective programmes for three months. The expected training time was a minimum of 22.5hrs. On average, participants trained for 42.22hrs (SD = 26.28) and missed 4.5 days of training between baseline and follow-up during the three-month intervention. Total hours of training were calculated per participant by time trained across the three months, multiplying by the number of days participants trained for. Total training hours did not differ between intervention (M = 41.34, SD = 28.05) and active control (M = 43.13, SD = 24.59), $t(97) = .336$, $p = .369$.

Motivation and enjoyment

Motivation to complete the training and enjoyment of the training were measured through questions post-intervention. There were no significant differences between intervention and active control in terms of motivation ($p = .118$) or enjoyment ($p = .895$) of the respective training programmes. Intervention and active control groups were therefore matched well in terms of motivation and enjoyment.

Intervention group practice effects: Peak performance pre- vs post-intervention

Repeated measures analysis of variance (ANOVAs) were conducted to compare first and last reported scores for the intervention group, for each of the seven Peak categories. Results were significant for all measures (all $p < .001$), indicating that participants in the intervention group improved significantly in their performance within the app. Descriptives and results can be found in Table 4.2. Visual representations are shown in Figure 4.2.

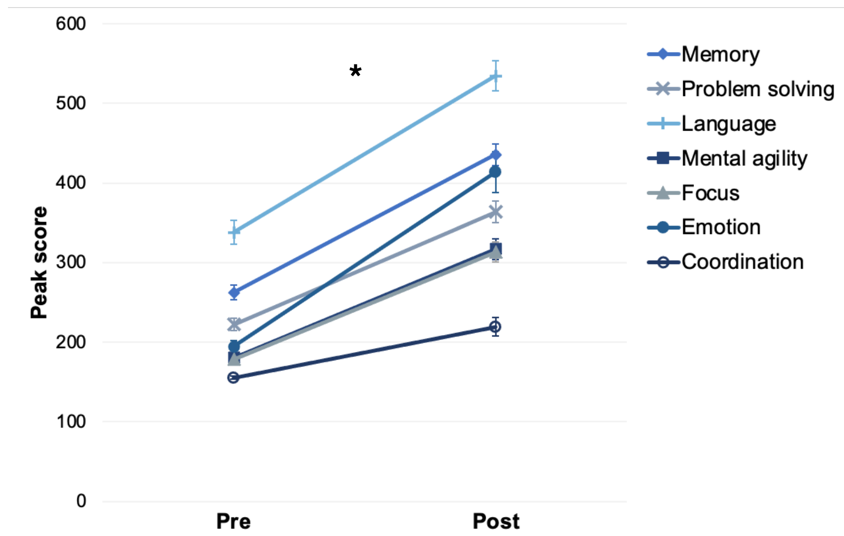

Figure 4.2. Pre- and post-intervention scores for Peak games, demonstrating practice effects within the intervention. *Note: Error bars reflect standard error. Peak scores are out of 1000.*

Table 4.2. Mean (SD) pre- and post-intervention Peak scores for participants in the intervention group.

	M (SD) pre-intervention	M (SD) post-intervention	ANOVA result
Memory	262.47 (63.08)	435.49 (94.44)	$F(1,50) = 206.08, p < .001, \eta^2 = .81$
Problem solving	222.12 (55.01)	363.51 (95.28)	$F(1,50) = 121.77, p < .001, \eta^2 = .71$
Language	338.00 (107.48)	534.37 (133.22)	$F(1,50) = 175.03, p < .001, \eta^2 = .78$
Mental agility	180.61 (29.63)	317.00 (93.55)	$F(1,50) = 126.20, p < .001, \eta^2 = .72$
Focus	178.61 (26.38)	313.35 (89.67)	$F(1,50) = 144.82, p < .001, \eta^2 = .74$
Emotion	194.41 (53.64)	413.45 (184.92)	$F(1,50) = 98.56, p < .001, \eta^2 = .66$
Coordination	155.14 (14.34)	219.39 (85.02)	$F(1,50) = 33.06, p < .001, \eta^2 = .40$

Note: Peak scores are out of 1000.

Cognitive benefits of the intervention: pre- vs. post-intervention cognitive outcomes

We investigated pre- versus post-intervention cognitive outcomes using a mixture of mixed models (where there were repeated observations over participants and/or items) and linear regressions (where the outcome variable was one value). Raw pre- and post-intervention scores can be found in Table 4.3. Detail on best fitting models can be found in Table 4.4 (mixed

models) and Table 4.5 (linear regressions). Visual representations can be found in Figure 4.3. Alpha level (α) was adjusted for multiple comparisons (0.05 / 10 = .005).

Table 4.3. Pre-intervention and post-intervention scores in intervention and active control groups for cognitive outcome measures.

Cognitive function	Measure	Group	Pre intervention [95%CI]	Post intervention [95%CI]
Working memory	**Digit Span**	Intervention	5.65 [5.27, 6.03]	6.00 [5.67, 6.33]
		Active control	5.84 [5.46, 6.22]	6.06 [5.73, 6.40]
	1back d'	Intervention	3.817 [3.69, 3.95]	3.914 [3.84, 3.99]
		Active control	3.706 [3.57, 3.84]	4.090 [4.02, 4.17]
	2back d'	Intervention	2.415 [2.14, 2.69]	3.045 [2.83, 3.26]
		Active control	2.632 [2.35, 2.91]	2.724 [2.50, 2.95]
Processing speed	**CRT average RT (ms)**	Intervention	0.602 [0.57, 0.64]	0.547 [0.52, 0.58]
		Active control	0.597 [0.56, 0.63]	0.540 [0.51, 0.57]
	LC 3 letter RT (ms)	Intervention	1.061 [1.02, 1.10]	1.052 [1.02, 1.09]
		Active control	1.052 [1.01, 1.10]	1.020 [0.99, 1.06]
	LC 6 letter RT (ms)	Intervention	1.595 [1.52, 1.67]	1.635 [1.57, 1.70]
		Active control	1.569 [1.49, 1.65]	1.537 [1.47, 1.60]
Attention	**ANT alerting**	Intervention	-2.19 [-8.27, 3.87]	2.18 [-2.96, 7.31]
		Active control	4.91 [-1.16, 10.98]	5.09 [-0.04, 10.23]
	ANT orienting	Intervention	21.14 [14.31, 27.97]	27.10 [20.25, 22.95]
		Active control	22.01 [15.17, 28.84]	22.12 [15.27, 28.97]
	ANT executive control	Intervention	128.00 [110.02, 145.98]	122.59 [104.24, 140.94]
		Active control	147.42 [129.44, 165.39]	137.44 [119.09, 155.97]
Language functioning	**TOT states (%)**	Intervention	4.17 [2.93, 5.40]	3.13 [1.93, 4.33]
		Active control	3.50 [2.25, 4.75]	3.30 [2.09, 4.51]

Note: CRT: Choice Reaction Time. LC: Letter Comparison. ANT: Attention Network Task. TOT: Tip-of-the-tongue

CRT task

We fitted a linear mixed model to predict reaction time from session (pre and post) and condition (intervention and active control). The model included item and participant ID as random effects. The total effect of both fixed and random factors (conditional R^2) was 0.38, and the variance explained by the fixed effects alone (marginal R^2) was 0.03. The main effect of session was significant ($t(6058) = -10.63$, $p < .001$), but we found no main effect of condition ($p = 0.492$) or interaction between session and condition ($p = 0.907$). Overall, RTs got faster

post-intervention regardless of condition, after accounting for variability in items and participants.

Letter Comparison task – 3-letter condition

We fitted a linear mixed model to predict reaction time for the 3-letter condition of the Letter Comparison task from session (pre and post) and condition (intervention and active control). The model included item (each letter string) and participant ID as random effects. The variance of fixed and random factors together (conditional R^2) was 0.42, and the variance explained by the fixed effects alone (marginal R^2) was 0.003. The model showed a main effect of session ($t(4399) = -4.29$, $p < .001$) but no significant effect of condition ($p = 0.917$) or interaction between session and condition ($p = 0.007$), once Bonferroni adjusted p-values were accounted for. Similar to the CRT, after accounting for variance between item and participant, RTs got faster post-intervention, regardless of condition.

Letter Comparison task – 6-letter condition

We fitted a linear mixed model to predict reaction time for the 6-letter condition of the Letter Comparison task from session (pre and post) and condition (intervention and active control). The model included item (each letter string) and participant ID as random effects. The variance of fixed and random factors together (conditional R^2) was 0.45, and the variance explained by the fixed effects alone (marginal R^2) was 0.005. After correcting for multiple comparisons, there was no significant effect of time ($p = 0.01$) or condition ($p = 0.922$) but there was a significant interaction between session and condition ($t(3778) = 3.98$, $p < .001$). Results showed that post (compared to pre) intervention, the control group significantly reduced their reaction times (i.e., they got faster), compared to the intervention group.

ToT

We fitted a logistic mixed model to predict ToT occurrences per trial with session, condition, and number of phonemes per item as fixed effects, as an increase in phonemes has been associated with increased ToT occurrences (Segaert et al., 2018). The model included item (each word) and participant ID as random effects. The variance of fixed and random factors together (conditional R^2) was 0.33, and the variance explained by the fixed effects alone (marginal R^2) was 0.01. After correcting for multiple comparisons, the model did not show significant effects of session (p = 0.373), condition (p = 0.356), number of phonemes (p = 0.05) or an interaction between session and condition (p = 0.006).

Table 4.4. Summary of the best fitting models for cognitive data using linear mixed models.

Task (outcome)	**Predictor**	**Coefficient**	**95% CI**	**SE**	**t- or z-value**	***p***
CRT task (RT)	Intercept	0.02	-0.03, 0.07	0.028	0.731	0.497
	Session	**-0.055**	**-0.07, -0.05**	**0.005**	**-10.63**	**<0.001**
	Condition	0.013	-0.02, 0.05	0.019	0.687	0.493
	Session*Condition	0.0008	-0.01, 0.02	0.0007	0.117	0.907
Letter Comparison – 3 letter (RT)	Intercept	0.018	-0.03, 0.06	0.023	0.776	0.439
	Session	**-0.033**	**-0.05, -0.02**	**0.008**	**-4.295**	**<0.001**
	Condition	-0.003	-0.06, 0.05	0.028	-0.104	0.917
	Session*Condition	0.03	0.00, 0.05	0.011	2.72	0.007
Letter Comparison – 6 letter (RT)	Intercept	0.01	-0.07, 0.09	0.043	0.224	0.824
	Session	-0.035	-0.06, -0.00	0.014	-2.558	0.011
	Condition	0.004	-0.08, 0.09	0.045	0.098	0.922
	Session*Condition	**0.077**	**0.04, 0.12**	**0.019**	**3.977**	**<0.001**
ToT occurrence (0/1)	**Intercept**	**- 3.780**	**-4.15, -3.41**	**0.191**	**-19.787**	**<0.001**
	Session	0.119	-0.14, 0.38	0.134	0.891	0.373
	Condition	0.219	-0.25, 0.69	0.238	0.922	0.356
	Nb Phonemes	0.098	0.00-0.20	0.050	1.960	0.050
	Session*Condition	-0.541	-0.92, -0.16	0.195	-2.770	0.006

Note. This analysis was conducted on N=99 participants who completed more than 80% of minimum training hours. Following Intent to Treat principles (Montori & Guyatt, 2001), we also ran analyses on the full dataset (N=103), including four participants who completed <80% of the training. Overall effects did not change. Bonferroni adjusted p-values were used based on N=10 comparisons (p = 0.005). Significant effects that remained after correcting are highlighted in bold. T- values are used for CRT and Letter Comparison task. Z-value is used for ToT task.

Linear regressions

A linear regression predicting 1-back d' was statistically significant and explained a moderate proportion of variance ($F(3, 190) = 9.97$, $p < .001$, adj. $R^2 = 0.12$). There was a main effect of session ($t(190) = 2.97$, $p = 0.003$; Std. $\beta = 0.57$), but condition ($p = 0.101$) and interaction between session and condition ($p = 0.658$) were not significant. Results show that participants in both conditions improved performance in the post-intervention session compared to pre-intervention.

A linear regression predicting 2-back d' was statistically significant ($F(3, 188) = 4.49$, $p = 0.005$, adj. $R^2 = 0.05$). However, after correcting for multiple comparisons (new $p = 0.005$), main effects of session ($p = 0.739$), condition ($p = 0.232$), and interaction between session and condition ($p = 0.023$) were not significant.

Linear regression predicting digit span from session (pre and post) and condition (intervention and control) was conducted. The model was not significant and explained little of the variance ($F(3, 193) = 1.11$, $p = 0.344$, adj. $R^2 = 0.002$). There were no significant effects of session ($p = 0.378$), condition ($p = 0.437$) or an interaction between the two ($p = 0.704$). Participant performance did not change as a result of session or condition.

Similarly, linear regression predicting alerting score from session and condition was not significant ($F(3, 191) = 1.23$, $p = 0.301$, adj. $R^2 = 0.003$). Results showed no significant effects of session ($p = 0.843$), condition ($p = 0.083$) or interaction between session and condition ($p = 0.409$). A linear regression predicting orienting score from session and condition was also not significant ($F(3, 191) = 0.88$, $p = 0.455$, adj. $R^2 = -0.001$). Results showed no significant effects of session ($p = 0.96$), condition ($p = 0.861$) or interaction between session and condition ($p =$

0.305). A final linear regression predicting executive control from session and condition was also not significant ($F(3, 191) = 1.02$, $p = 0.383$, adj. $R^2 = 0.0003$). Results showed no significant effects of session ($p = 0.493$), condition ($p = 0.149$) or interaction between session and condition ($p = 0.45$). Results showed no effects of time or condition for any of the ANT cost scores.

Table 4.5. Summary of regression models for cognitive data analysed using linear regression.

Outcome	Predictor	Coefficient	95% CI	SE	t-value	*p*
1-back d'	**Intercept**	**-0.187**	**-0.29, -0.08**	**0.053**	**-3.505**	**<.001**
	Session	**0.226**	**0.08, 0.38**	**0.076**	**2.972**	**0.003**
	Condition	0.124	-0.02, 0.27	0.075	1.650	0.101
	Session*Condition	0.047	-0.16, 0.2	0.107	0.443	0.658
2-back d'	Intercept	-0.067	-0.32, 0.18	0.126	-0.533	0.595
	Session	0.059	-0.29, 0.41	0.178	0.333	0.739
	Condition	-0.212	-0.56, 0.14	0.177	-1.200	0.232
	Session*Condition	0.571	0.08, 1.06	0.250	2.286	0.023
Digit Span	Intercept	-0.046	-0.40, 0.31	0.180	-0.259	0.796
	Session	0.224	-0.28, 0.73	0.254	0.884	0.378
	Condition	-0.197	-0.70, 0.30	0.253	-0.778	0.437
	Session*Condition	0.135	-0.57, 0.84	0.358	0.378	0.706
ANT: Alerting score	Intercept	2.767	-2.92, 8.46	2.884	0.959	0.339
	Session	-0.807	-8.81, 7.20	4.058	-0.199	0.843
	Condition	-7.110	-15.16, 0.94	4.079	-1.743	0.083
	Session*Condition	4.741	-6.55, 16.03	5.725	0.828	0.409
ANT: Orienting score	Intercept	- 1.261	-8.12, 5.60	3.478	- 0.363	0.717
	Session	- 0.244	-9.90, 9.41	4.893	-0.050	0.960
	Condition	- 0.868	-10.57, 8.83	4.918	- 0.176	0.860
	Session*Condition	7.104	-6.51, 20.72	6.902	1.029	0.305
ANT: executive control score	Intercept	12.259	-6.45, 30.97	9.486	1.292	0.198
	Session	- 9.174	-35.50, 17.15	13.347	- 0.687	0.493
	Condition	- 19.420	-45.88, 7.04	13.415	- 1.448	0.149
	Session*Condition	8.419	-28.72, 45.56	18.828	0.447	0.655

Note. This analysis was conducted on N=99 participants who completed more than 80% of minimum training hours. Following Intent to Treat principles (Montori & Guyatt, 2001), we also ran analyses on the full dataset (N=103), including participants who completed <80% of the training. Overall effects did not change. Bonferroni adjusted p-values were used based on N=10 comparisons (p = 0.005). Significant effects that remained after correcting are highlighted in bold.

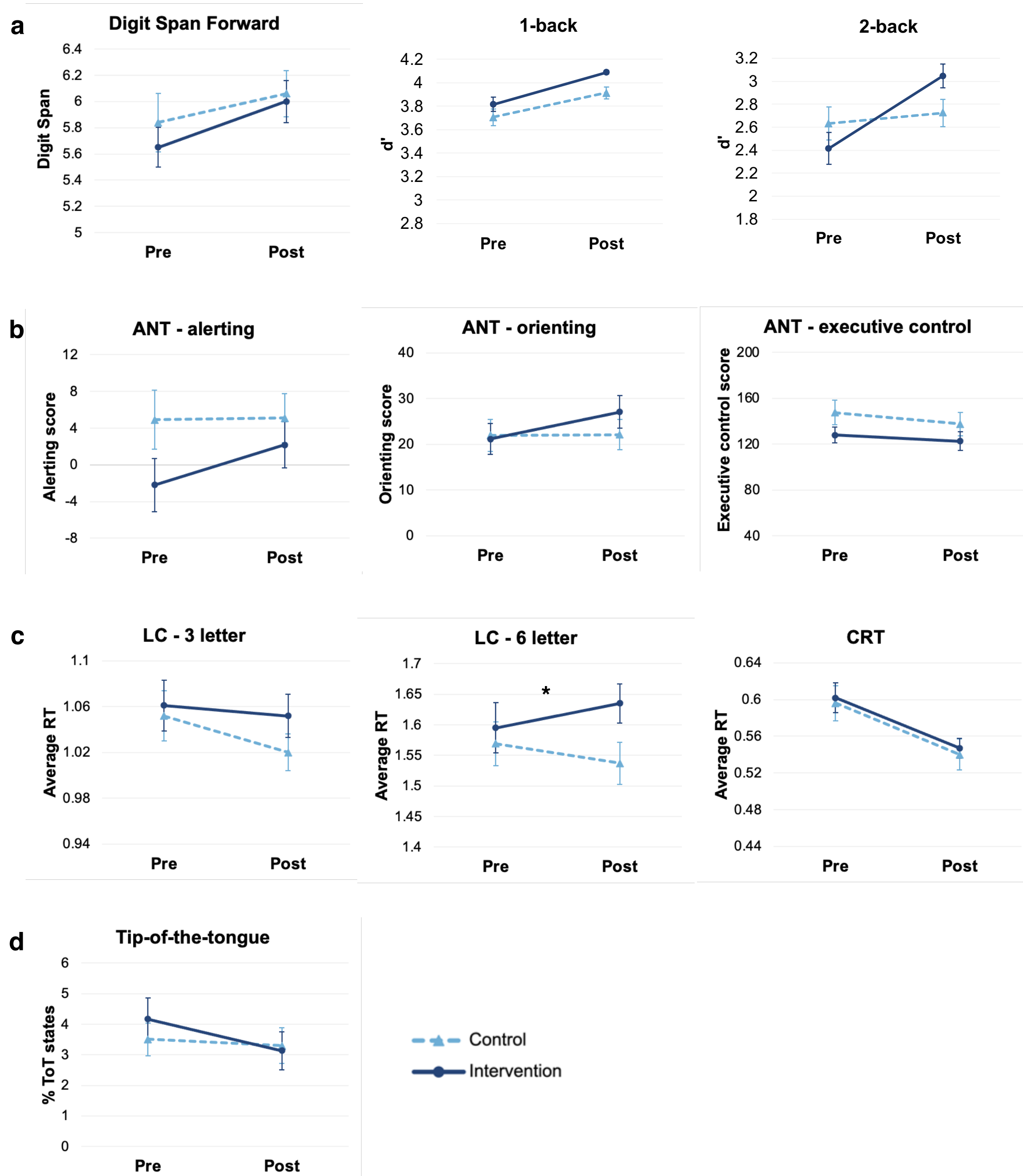

Figure 4.3. Pre- and post-intervention scores for outcome measures split by condition, demonstrating a lack of transfer effects to cognitive measures. **a**: scores for working memory measures, analysed using linear regression. Higher scores represent better performance. **b**: scores for attention measures, analysed using linear regression. Higher performance for alerting and orienting, and lower scores for executive control, represent better performance. **c**: scores for processing speed measures, analysed using mixed models. Lower scores represent better performance. **d**: score for tip-of-the-tongue measure, analysed using mixed models. Lower scores represent better performance. *Note: Asterisks (*) represent significant time by condition interaction. Error bars reflect standard error*

4.5 Discussion

This study explored the benefits of Peak, a commercially available adaptive brain training programme, on cognitive abilities in a sample of older adults. In line with recommendations for evaluating the effectiveness of these programmes, we used a randomised controlled intervention study design, with a sufficiently large sample of healthy older adults, a blinded active control group, and assessed potential cognitive benefits using a comprehensive test battery. In line with our hypothesis, we found practice effects in the intervention group, specifically observing significant improvements on the Peak training games. However, we found no evidence of transfer to untrained tasks. While some previous research had suggested promising effects of brain training programmes (Anderson et al., 2013; Meltzer et al., 2023; Savulich et al., 2019), the literature is mixed and many other studies, alongside our own, find little to no transfer effects (Guye & von Bastian, 2017; Stojanoski et al., 2018).

Our data demonstrated that participants in our intervention condition significantly improved their scores for all seven of Peak's categories: Memory, Problem Solving, Language, Mental Agility, Focus, Emotion, and Coordination. Practice effects are shown regularly in brain training studies, so this was not unexpected. We also found some test re-test effects where both our intervention and active control group improved in performance on our cognitive outcome measures. Test re-test effects (which are well documented in the literature, Scharfen et al., 2018) as well as improvements within the training programme are unlikely to indicate true improvements in cognitive abilities, but merely learning effects of being able to do the training task. The key aim for the present study was to assess whether brain training leads to transferable benefits to wider cognitive abilities.

We did not find any evidence of transfer effects. The only session by condition interaction we found, after accounting for variability in items and participants, was for the 6-letter condition of the Letter Comparison task. Data showed that reaction times got faster in the active control group compared to the intervention group post vs. pre-intervention. This finding is slightly unexpected, but the finding that a control group improves more than a cognitive training group has previously been shown (Hardy et al., 2015; van Muijden et al., 2012). Further, the effect is marginal, with the average RT in the intervention group increasing by 40ms, while the control group decreasing by 32ms. Nevertheless, there are potential issues with our choice of active control; it is a similar-form control rather than an active-ingredient control (Masurovsky, 2020), and arguably our control group could have differed in terms of the choice of games. These reasons may have led to the significant improvement in RTs compared to the intervention group in the 6-letter condition of the Letter Comparison Task.

However, our active control group, who played computer games on a free smartphone application, was similar regarding the novelty and variety of tasks. We found no significant differences between our intervention and active control groups in terms of motivation or enjoyment. This is important as research has shown these factors can affect intervention success (Green & Bavelier, 2008). Furthermore, there were no significant differences between groups in how much time participants trained for. This shows that the active control group was a suitable match for the experimental condition – they were comparable in these important factors, but their training did not include the brain training element. Note that our study design is comparable to a cognitive training study that used Lumosity to assess improvements in executive function in younger adults (Kable et al., 2017). Similar to our study, they used an active control group that was matched to the intervention group in terms of engagement, motivation and novelty (Kable et al., 2017). In line with our findings, they found practice

effects but did not find any evidence of transfer effects from the brain training programme to any cognitive outcome measures. We have both corroborated the findings from this study and extended the research to an older population.

We did not find any evidence that brain training significantly improved cognitive performance in the intervention group when comparing to the active control. As mentioned in the introduction, transfer effects are few and far between in existing brain training literature, and it is possible that 'transfer effects' in published research are sometimes misinterpreted practice effects instead. For example, one recent study reported transfer effects for a composite of memory measures, however these were driven solely by improvements in N-back training (H. K. Lee et al., 2020). Upon closer examination, the cognitive training programme administered in the intervention group (BrainHQ) involved an N-back style game, and therefore any suggested transfer is arguably due to a practice effect.

It is important in this field to closely scrutinise previous research, as the terms practice effects and transfer effects are sometimes not fully explained. For example, one recent study analysed retrospective data from Peak and suggested that from a sample of 12,000 users, processing speed increased after 100 sessions of Peak training (Bonnechere et al., 2021). While this finding is impressive at face value, what is important here is that the authors' measure of processing speed was performance on the trained games and thus should be interpreted as practice effects. Our data show practice benefits do indeed take place during brain training, but in the present study at least, this does not transfer to other measures of the same cognitive constructs, or to different cognitive constructs. Results such as these should therefore be interpreted with caution.

Although our data suggest there are no direct benefits of brain training on cognitive performance in this population, there may be indirect benefits. There is rarely a negative impact of using these programmes, and perhaps a belief of these applications working might lead to improvements in wellbeing, which itself is helpful. For example, worries about cognitive health has been associated with poorer psychological wellbeing (Sutton et al., 2022) and have even been linked with poorer cognitive performance (Caughie et al., 2021). Therefore, even if these applications do not directly improve general cognitive ability, if they reduce worry about cognitive decline in older adults this is still beneficial. This is a possible avenue for future research. There may be factors not analysed in the present study that may have mediated training effects. For example, higher baseline cognitive performance has been shown to result in smaller training effects in brain training studies (Harvey et al., 2020), so theoretically this could impact cognitive improvements. Similarly, while groups did not differ in total amount of training, there were individual differences in the *amount* of training that may have impacted potential gains in cognitive performance. While outside the scope of the present study, this is something future research could investigate.

Limitations of the present study include that the sample consisted of mainly White participants, which limits the generalisability of the findings. A positive of our sample however is that the sample size was larger than 90% of previous cognitive training studies (Noack et al., 2014). One could argue that the flexibility participants were afforded in training duration is a limitation of our study design. Indeed, there were large differences in how long participants trained for; some maintained the minimum 15 minutes a day, but many went above and beyond. While we designed this intervention to be controlled and robust, we also wanted it to be enjoyable and not too restrictive for the participants. A small pilot study found limiting training to 15 minutes a day was difficult due to participants enjoyment of the training, so we removed

this requirement for the study presented here. Importantly, training duration did not significantly differ between the intervention and the control group, so this is unlikely to have impacted results. Future research would benefit from including more than one language task (such as verbal fluency). Finally, future studies would benefit from the inclusion of non-cognitive outcomes (such as mental health symptoms), a further assessment or booster training sessions to investigate potential longer-term benefits, as well as a double-blind design in which both the participant and researcher were blinded to participant condition.

Researchers and consumers alike should look closely at the terms used in publications and on company websites, as we have shown that making a clear distinction between transfer and practice effects is important. This has implications in the brain training market as consumers should be aware of the differences and what they mean in terms of real-life results. A recent meta-analysis concluded that at present there is no convincing empirical evidence to suggest brain training programmes lead to tangible transfer effects in older adults (Nguyen et al., 2022). Our data is in line with this and suggests that commercial brain training leads to practice effects, without convincing evidence of transfer to cognitive abilities beyond the practiced tasks. In short, in our sample of healthy older adults, practice makes perfect, but it does not transfer to wider cognitive benefits.

CHAPTER 5 - GENERAL DISCUSSION

5.1 Summary of aims

This thesis sought to contribute to knowledge of older adult cognitive, mental, physical, and serological markers of health, using a combination of cross-sectional and intervention studies. The aims of each chapter were as follows:

1. Investigate cognitive, mental, and physical wellbeing in older adults during the COVID-19 pandemic via an online survey (**Chapter 2**)
2. Explore, using a person-centred approach, the differences in cognitive performance in older adults based on profiles of physical, mental, and serological markers of health (**Chapter 3**)
3. Examine the efficacy of a commercially available computerised brain training programme for improving cognitive performance in a sample of healthy older adults, in a three-month randomised and controlled intervention design (**Chapter 4**)

5.2 Summary of findings

This thesis first assessed older adult wellbeing in a period of uncertainty, during the COVID-19 pandemic (**Chapter 2**). Results showed that worrying about cognitive health was associated with poorer mental and physical wellbeing, and that those who reported higher levels of social interaction and physical activity also reported better psychological wellbeing. Next, we used a person-centred approach, latent profile analysis (LPA), to establish profiles in older health based on physical, mental, and serological markers of health (**Chapter 3**). Results revealed three profiles: one who demonstrated good physical and mental wellbeing, a second who reported average physical functioning but poor mental wellbeing, and a third group who

reported good mental wellbeing but poor physical health. We then investigated whether there were differences in cognitive performance between the three groups but did not find meaningful group differences. Finally, **Chapter 4** assessed the effectiveness of a commercially available brain training programme for cognitive function in healthy older adults, in a controlled intervention study that overcame many methodological issues reported in previous research in this field. We found no transfer benefits of a three-month training programme compared to an active control group in relation to performance on cognitive functions known to be affected by ageing: working memory, processing speed, attention, or language functioning.

The following discussion highlights key findings from each empirical chapter, discusses overall strengths and limitations of the thesis, and suggests future directions for the field.

5.3 Key findings and theoretical implications

1. **Worries about cognitive health may impact psychological and physical wellbeing**

Chapter 2 examined cross-sectional associations between cognitive health worries, psychological wellbeing, and physical health, in an online survey of older adults in the UK during the COVID-19 pandemic. This chapter was motivated by the COVID-19 pandemic and nationwide lockdowns. At the time of data collection, little had been published on how older adult wellbeing had been affected, and assessing worries about cognitive health was a way of investigating subjective concerns about cognition at the time. Results showed that compared to participants who did not worry about their cognitive health, those who did worry scored significantly higher on depression, anxiety, loneliness, and fatigue scales, and significantly

lower on sleep satisfaction, subjective vitality, and quality of life scales. Results furthermore supported what *had* been published in the literature and showed that participants who reported higher levels of physical activity and social interaction also reported better psychological (depression and loneliness) and physical (fatigue) wellbeing. Surprisingly, we found no significant differences in psychological wellbeing between participants who were concerned about the COVID-19 pandemic (COVID-19 worry) and those who were not.

The findings that cognitive health worries were significantly associated with both psychological and physical wellbeing extends previous research investigating dementia worry in older adults. Research has found dementia worry to be linked with depression, stress, and quality of life (Cutler & Bragaru, 2017), and with performance on executive functioning measures (Caughie et al., 2021). The cross-sectional findings from **Chapter 2** suggest negative effects of cognitive worries transcend mental wellbeing and can associate with poorer perceived physical health in terms of fatigue and sleep satisfaction. These findings perhaps suggest we need to pay more attention to the mechanisms behind dementia and cognitive health worry and identify potential interventions that can support cognitive performance in older adults. This may help to improve perceived physical health as a result.

Our findings partially support previous research conducted during the pandemic that utilised latent profile analysis (Maxfield & Pituch, 2022). The analysis established one profile that was characterised by high levels of dementia related worry, and participants in this profile also reported more anxiety, depression, and COVID-19 worry symptoms than those with low dementia related worry (Maxfield & Pituch, 2022). This partially supports our results that showed cognitive worries to be related to psychological wellbeing. However, we did not find associations between COVID-19 worry and negative psychological wellbeing. Data collection

for this study took place early in the pandemic (April to May 2020), so it may be that overall concerns were higher in the early stages compared to our data collection almost a year later (February to April 2021). Indeed, psychological wellbeing scores have been found to fluctuate over time in the UK during the pandemic, coinciding with the number of cases and strength of restrictions in place (Daly & Robinson, 2021). While speculative, this research, taken together with the findings from **Chapter 2**, suggests that there are clear associations between dementia worry and negative psychological wellbeing, but they do not always relate to COVID-19 concerns. Instead, COVID-19 concerns may be more related to the level of restrictions in place at time of data collection.

The findings that more physical activity and increased social interactions were associated with better psychological wellbeing is not necessarily surprising but was important to corroborate. Research conducted during COVID-19 broadly supports this finding and has shown that physical activity and social interactions are protective against negative mental health impacts of the pandemic (Carriedo et al., 2020; Groarke et al., 2020). Our findings therefore provide further support to the idea that in times of social isolation, keeping physically and socially active is important to mental wellbeing (Callow et al., 2020; Groarke et al., 2020).

Chapter 2 adds to the growing body of literature on how the COVID-19 pandemic has affected older adult health. It assessed cognition (albeit subjectively) at a time when laboratory-based cognitive assessments were difficult or not possible during nationwide lockdowns. It extends previous research investigating dementia related worries, finding that worrying about cognitive health relates to poorer psychological wellbeing as well as poorer physical health, affecting sleep and fatigue. The findings from this cross-sectional study have implications for future research, as interventions that can successfully reduce dementia worry may be able to

improve cognitive wellbeing. Further, these interventions could potentially have a positive indirect impact on their perceived physical health and overall quality of life.

2. **There are significant and interesting relationships between physical functioning, mental wellbeing, and serological markers of health in older adults, but these profile characteristics do not necessarily relate to cognitive performance**

Chapter 3 used a person-centred approach, latent profile analysis, to identify characteristics of populations based on their physical functioning, mental wellbeing, and serological markers of health. The LPA identified three distinct, but related profiles of people based on the distribution of data. Just under half of the sample were *Optimally ageing*, displaying good physical and mental health as well as low levels of inflammation. A second group of participants, *Average physical health but challenged mental health*, displayed physical functioning and inflammatory levels around the sample mean, but their mental health scores were high (i.e., poor). Our final group, *Challenged physical health but good mental health*, showed the poorest scores for physical functioning and inflammation, but their mental health scores were below the mean (i.e., good) and similar to our *Optimally ageing* group.

The characteristics of the *Optimally ageing* group reflects much previous research that shows good physical functioning to be related to good mental wellbeing (e.g., Park et al., 2019). However, the other two profiles, in particular the *Challenged physical health but good mental health* group, are perhaps more surprising given the associations between physical and mental wellbeing. The subtle differences in how mental and physical wellbeing related to each other therefore prove an interesting thought for potential protective factors in older adults. As reported in **Chapter 3**, research has found many protective factors against negative mental

health symptoms, including physical, cognitive, and socioeconomic resources one can draw one, strategies to manage life stressors, and meaningful engagement through volunteering or social activities (Fiske et al., 2009).

The second step of the analysis was to use these latent profiles as independent variables and to compare group differences in cognitive performance. We did not find significant differences between groups in terms of performance on working memory, processing speed, attention, or language functioning measures. This was surprising as research has shown links between physical, mental, and serological markers of health individually with cognitive performance (Lara et al., 2019; Lautenschlager & Almeida, 2006; Yaffe et al., 2003). The lack of significant differences here may be due to a lack of variance or power (Johnson, 2021), or that there were simply no differences to find in our sample of healthy older adults. Despite this, Chapter 3 can be used as a template for future research to examine older adult health in more detail, using person-centred approaches.

This chapter has theoretical implications in comparing variable- and person-centred approaches. Person-centred approaches such as LPA overcome limitations of variable-centred approaches by allowing the possibility of subpopulations within a given sample. Research shows that *generally*, good physical health is associated with good mental health, and our findings partially support this. However, the LPA also found smaller subgroups that show differing patterns of wellbeing. These findings show that it is important to not just look at individual markers of health, but that a profile based on multiple markers of health could provide more information. For example, it is possible that the negative effects of poor mental health on cognitive function could be compensated by good physical health in some individuals. This suggestion would need to be tested in further research.

3. **After controlling for a number of methodological inconsistencies found in the literature, practice makes perfect, but brain training does not improve wider cognitive performance**

Chapter 4 assessed the effectiveness of a commercially available brain training programme, Peak, in a randomised controlled intervention study with a sample of healthy older adults. This chapter was motivated by the reported potential benefits of brain training programmes (e.g., Kueider et al., 2012; Lampit et al., 2014) and sought to overcome many of the methodological issues that had been identified in previous reviews, as mentioned in the introduction of this thesis. We used a larger sample than many studies in the field (Noack et al., 2014), randomised participants to condition (stratified by sex to ensure equal sex distribution) and included an appropriate blinded active control group that matched the intervention on motivation and enjoyment as well as intensity and training duration. We furthermore assessed cognition and transfer effects comprehensively, including three measures for working memory, processing speed, and attention, which would allow assessment of improvements across cognitive functions rather than within specific tasks.

The results from **Chapter 4** indicate that there are no transferable benefits of a brain training programme on cognitive performance, in our sample of healthy older adults. We show that practice effects do indeed take place, as our intervention group significantly improved on all seven of Peak's categories. This is commonly shown in published research, with many studies showing improvements on the trained tasks (e.g., Owen et al., 2010; Stojanoski et al., 2018). However, we found no evidence of transfer to working memory, processing speed, attention, or language functioning. Our results are contrary to research that has found transfer

effects (McDougall & House, 2012), but do echo that of other training studies that find limited or no transfer to wider cognitive abilities (Booth et al., 2023; Kable et al., 2017; Ripp et al., 2022). The reasons for such inconsistencies in findings likely come down to the methodological differences between studies which have been identified in review papers (e.g., Simons et al., 2016). For example, one striking comparison involves two studies that examined effects of an adaptive, computerised working memory training programme. The studies were very similar in terms of study design, but either used a passive (Penner et al., 2012) or active control group (Booth et al., 2023). The study with a passive control group reported significant transfer to other cognitive tasks, while the study with an active control group reported no transfer. While this may not explain all the differences, it emphasises the importance of an active control group.

We also argue that better distinctions need to be made between practice and transfer effects, as published research sometimes does not make this clear. For example, a recent paper claimed that regular use of the Peak brain training app improves processing speed (Bonnechere et al., 2021). The conclusions from this large-scale retrospective observational study are arguably exaggerated, as their measure of processing speed was merely the games within the app. These 'effects' are therefore likely to be reflective of practice effects rather than true improvements in processing speed, as they show improvements within the trained task rather than training-induced gains seen in untrained tasks (Ripp et al., 2022).

The findings from **Chapter 4** add to the growing body of literature that investigates brain training programmes in a controlled manner. It emphasises the need to conduct rigorous trials where possible, and to include appropriate active control groups and a comprehensive test battery. It suggests that researchers should be careful not to overstate their findings or confuse practice and transfer effects as this has implications for consumers who may believe

in the benefits of these programmes. Importantly, research has shown that older adults have higher expectations of these programmes compared to younger adults (Rabipour & Davidson, 2015), but this chapter suggests limited benefits in terms of cognitive performance. These results therefore indicate that brain training programmes need to be evaluated rigorously, so consumers are aware of their true effects.

5.4 Overall strengths and limitations

This thesis has strengths in its broadness of topics and range of methodologies and analysis techniques. **Chapter 2** was an adaptation of the original research plan as a result of COVID-19 restrictions. However, it allowed research to continue during a global pandemic and as a result I gained a grounding in the literature surrounding COVID-19 and older adult wellbeing through an online observational survey. The person-centred approach in **Chapter 3** gave an alternative viewpoint to traditional variable-centred approaches, lending more specificity to our results. We included a wide range of variables in the LPA, allowing us to identify patterns across physical functioning, mental wellbeing, and serological markers of health. Combining both physiological and psychological variables meant we could assess an individual holistically rather than focusing on one aspect of health. While some LPA review papers suggest our sample size may restrict our results, I believe that this chapter can be used as a basis for future research investigating links between multiple aspects of health in later life. Finally, **Chapter 4** had strengths by overcoming methodological issues in past brain training research, adopting a single-blind randomised controlled intervention design. Double blinding was not possible due to the small research team, but single blinding is not often possible in cognitive training studies due to the nature of the training (Simons et al., 2016). The fact that participants were blinded to condition (intervention and control participants were told that the experiment was investigating different types of cognitive training) is therefore a strength of the

design. We included an active control condition that matched in terms of enjoyment, motivation, and intensity, making it appropriate for the intervention. We finally assessed both practice and transfer effects, clearly differentiating the two. These factors, alongside the comprehensive test battery, makes it more rigorous than many other studies in the field.

There are some limitations to be addressed. Following on from our findings in **Chapter 2** regarding cognitive health worries, we could have assessed worries about cognitive health (or dementia worry) in **Chapters 3** and/or **4** to allow a comparison across chapters. It would have been particularly interesting for the intervention in **Chapter 4**. Despite not finding any cognitive improvement as a result of the brain training, there could be an unmeasured placebo effect in which some participants (intervention *or* control) believed that the training was improving their cognitive health, and therefore reducing worries about their brain health. Indeed, some research suggests that dementia worry can be reduced by interventions, with one study successfully using group cognitive behavioural therapy (CBT) to reduce dementia worry in older adults (An et al., 2020). Other than this however, investigation on cognitive interventions to reduce dementia worry is limited and is a clear direction for future research.

A limitation that runs throughout the empirical chapters is the characteristics of the sample, as, for the most part, my participants were White and educated to at least undergraduate level. Research has found those who take part in ageing research are likely to be more educated, healthier and more motivated than the general population (Cabeza et al., 2005, p. 31). Therefore, wider samples are under-researched in the ageing literature. Furthermore, the diversity of the sample could arguably be affected by eligibility criteria for **Chapters 3** and **4**, which required participants to be monolingual native English speakers, due to the tip-of-the-tongue task being affected by bilingual performance (Gollan & Brown, 2006). Particularly

relevant to **Chapter 2**, recent research has shown non-White adults to be more negatively affected in terms of mental wellbeing during the COVID-19 pandemic and showed higher levels of unmet mental health care needs (Thomeer et al., 2023). Future research would benefit from including wider samples to assess age-related changes in a broader population.

5.5 Overall conclusions and implications

Adults over 65 years of age take up an increasingly large proportion of the general population (Randall, 2017), and with this comes a higher cost to health and care services (Robineau, 2016). Optimising healthspan before age-related decline (e.g., cognitive impairment or mobility issues) is therefore imperative to reduce these costs. This thesis contributes to the field by combining functions of ageing (across cognitive health, mental wellbeing, physical functioning, and serological markers of health) to gain a more holistic view of the ageing process. The empirical chapters have evaluated wellbeing during a global pandemic, used novel person-centred approaches, and conducted a robust efficacy intervention.

The results from this thesis provide many avenues for future research. Dementia worries could be investigated further to establish whether they can be reduced through cognitive interventions. Research could investigate protective factors against mental health declines *relative* to declines in physical health. Finally, research should ensure that any future interventions assessing the efficacy of brain training programmes are done rigorously. It is hoped that by conducting further research in these areas, our understanding of older adult health (and the relationships *between* different aspects of health) and how to extend healthspan are understood more clearly.

Taken together, the results from this thesis indicate that worrying about cognitive health may be detrimental to both psychological and physical wellbeing (**Chapter 2**). This chapter also suggests that more research needs to be undertaken to assess interventions to mitigate potential negative effects, especially in times of uncertainty such as a global pandemic. Second, this thesis shows that there may be subtle differences in patterns of physical functioning and mental wellbeing in older adults, and that poor physical health does not always associate with poor mental health (**Chapter 3**). This has implications for public health initiatives, in that interventions may need to be targeted to consider a holistic profile of an individual. Finally, it provides strong evidence that in a controlled intervention study, brain training programmes do not transfer to wider cognitive abilities in older adults, and that more needs to be done to separate practice and transfer effects for consumer benefit (**Chapter 4**).

REFERENCES

Age UK, A. (2016). Hidden in plain sight: The unmet mental health needs of older people. *Age UK, London*. www.ageuk.org.uk/brandpartnerglobal/wiganboroughvpp/hidden_in_plain_sight_older_peoples_mental_health.pdf

Age UK, A. (2020a, 16th October 2020). *Age UK research lays bare the drastic impact of the pandemic on our older population's health and morale*. Retrieved 18/11/21 from https://www.ageuk.org.uk/latest-press/articles/2020/10/age-uk--research-into-the-effects-of-the-pandemic-on-the-older-populations-health/

Age UK, A. (2020b, Dec 01 2020). *Worrying rise in anxiety and loss of motivation among older people*. Retrieved 04/06/2023 from https://www.ageuk.org.uk/latest-press/articles/2020/11/worrying-rise-in-anxiety-and-loss-of-motivation-among-older-people/

Ahlskog, J. E., Geda, Y. E., Graff-Radford, N. R., & Petersen, R. C. (2011). Physical exercise as a preventive or disease-modifying treatment of dementia and brain aging. *Mayo Clin Proc, 86*(9), 876-884. https://doi.org/10.4065/mcp.2011.0252

Aisen, P. S., Schafer, K. A., Grundman, M., Pfeiffer, E., Sano, M., Davis, K. L., Farlow, M. R., Jin, S., Thomas, R. G., Thal, L. J., & for the Alzheimer's Disease Cooperative, S. (2003). Effects of Rofecoxib or Naproxen vs Placebo on Alzheimer Disease Progression. *JAMA, 289*(21). https://doi.org/10.1001/jama.289.21.2819

Alescio-Lautier, B., Allen, M., Andersen, R., Ball, K., Banai, K., & Baniel, A. (2014). Cognitive Training Data Response Letter. https://www.cognitivetrainingdata.org/the-controversy-does-brain-training-work/response-letter/

Allaire, J., Bäckman, L., Balota, D., Bavelier, D., Bjork, R., Bower, G., & Zelinski, E. (2014). A Consensus on the Brain Training Industry from the Scientific Community. *Max planck institute for human development and stanford center on longevity*, (12/06/23). https://longevity.stanford.edu/a-consensus-on-the-brain-training-industry-from-the-scientific-community-2/

Alzheimer's Society, A. (2016). *Risk factors for dementia*.

Amieva, H., Retuerto, N., Hernandez-Ruiz, V., Meillon, C., Dartigues, J.-F., & Pérès, K. (2022). Longitudinal Study of Cognitive Decline before and after the COVID-19 Pandemic: Evidence from the PA-COVID Survey. *Dementia and geriatric cognitive disorders, 51*(1), 56-62.

An, Q., Wang, K., Sun, F., & Zhang, A. (2020). The effectiveness of modified, group-based CBT for dementia worry among Chinese elders. *J Affect Disord, 274*, 76-84. https://doi.org/10.1016/j.jad.2020.05.054

Anderson, S., White-Schwoch, T., Parbery-Clark, A., & Kraus, N. (2013). Reversal of age-related neural timing delays with training. *Proc Natl Acad Sci U S A, 110*(11), 4357-4362. https://doi.org/10.1073/pnas.1213555110

Applebaum, E. V., Breton, D., Feng, Z. W., Ta, A. T., Walsh, K., Chasse, K., & Robbins, S. M. (2017). Modified 30-second Sit to Stand test predicts falls in a cohort of institutionalized older veterans. *Plos One, 12*(5), e0176946. https://doi.org/10.1371/journal.pone.0176946

Arnett, A. B., & Flaherty, B. P. (2022). A framework for characterizing heterogeneity in neurodevelopmental data using latent profile analysis in a sample of children with ADHD. *J Neurodev Disord, 14*(1), 45. https://doi.org/10.1186/s11689-022-09454-w

Aslam, N., Shafique, K., & Ahmed, A. (2021). Exploring the impact of COVID-19-related fear, obsessions, anxiety and stress on psychological well-being among adults in Pakistan. *The Journal of Mental Health Training, Education and Practice, 16*(4), 313-321. https://doi.org/10.1108/jmhtep-10-2020-0074

Austin, M. P., Mitchell, P., & Goodwin, G. M. (2001). Cognitive deficits in depression: possible implications for functional neuropathology. *The British Journal of Psychiatry, 178*(3), 200-206.

Bahar-Fuchs, A., Clare, L., & Woods, B. (2013). Cognitive training and cognitive rehabilitation for mild to moderate Alzheimer's disease and vascular dementia. *Cochrane Database Syst Rev*(6), CD003260. https://doi.org/10.1002/14651858.CD003260.pub2

Bailey, L., Ward, M., DiCosimo, A., Baunta, S., Cunningham, C., Romero-Ortuno, R., Kenny, R. A., Purcell, R., Lannon, R., McCarroll, K., Nee, R., Robinson, D., Lavan, A., & Briggs, R. (2021). Physical and Mental Health of Older People while Cocooning during the COVID-19 Pandemic. *QJM*. https://doi.org/10.1093/qjmed/hcab015

Ball, K., Berch, D. B., Helmers, K. F., Jobe, J. B., Leveck, M. D., Marsiske, M., Morris, J. N., Rebok, G. W., Smith, D. M., Tennstedt, S. L., Unverzagt, F. W., & Willis, S. L. (2002). Effects of Cognitive Training Interventions With Older Adults A Randomized Controlled Trial. *JAMA, 288*(18), 2271-2281. https://jamanetwork.com/journals/jama/articlepdf/195506/joc21020.pdf

Barr, D. J., Levy, R., Scheepers, C., & Tily, H. J. (2013). Random effects structure for confirmatory hypothesis testing: Keep it maximal. *Journal of Memory and Language, 68*(3), 255-278.

Bates, D., Mächler, M., Bolker, B., & Walker, S. (2015). Fitting Linear Mixed-Effects Models Usinglme4. *Journal of Statistical Software, 67*(1). https://doi.org/10.18637/jss.v067.i01

Bathina, S., & Das, U. N. (2015). Brain-derived neurotrophic factor and its clinical implications. *Arch Med Sci, 11*(6), 1164-1178. https://doi.org/10.5114/aoms.2015.56342

Baune, B. T., Smith, E., Reppermund, S., Air, T., Samaras, K., Lux, O., Brodaty, H., Sachdev, P., & Trollor, J. N. (2012). Inflammatory biomarkers predict depressive, but not anxiety symptoms during aging: The prospective Sydney Memory and Aging Study. *Psychoneuroendocrinology, 37*(9), 1521-1530. https://doi.org/10.1016/j.psyneuen.2012.02.006

Beaudreau, S. A., & O'Hara, R. (2008). Late-life anxiety and cognitive impairment: a review. *The American Journal of Geriatric Psychiatry, 16*(10), 790-803.

Bohannon, R. W. (2019). Grip strength: an indispensable biomarker for older adults. *Clinical Interventions in Aging*, 1681-1691.

Bonnechere, B., Klass, M., Langley, C., & Sahakian, B. J. (2021). Brain training using cognitive apps can improve cognitive performance and processing speed in older adults. *Scientific Reports, 11*(1), 12313. https://doi.org/10.1038/s41598-021-91867-z

Bono, R., Alarcon, R., & Blanca, M. J. (2021). Report Quality of Generalized Linear Mixed Models in Psychology: A Systematic Review. *Front Psychol, 12*, 666182. https://doi.org/10.3389/fpsyg.2021.666182

Booth, S. J., Brown, L. J. E., Taylor, J. R., & Pobric, G. (2023). Experimental investigation of training schedule on home-based working memory training in healthy older adults. *Front Psychol, 14*, 1165275. https://doi.org/10.3389/fpsyg.2023.1165275

Bowen, C. E., Kessler, E. M., & Segler, J. (2019). Dementia worry in middle-aged and older adults in Germany: sociodemographic, health-related and psychological correlates. *Eur J Ageing, 16*(1), 39-52. https://doi.org/10.1007/s10433-018-0462-7

BPS, B. P. S. (2021). *BPS Code of Human Research Ethics*.

BrainHQ. (2023). Retrieved 21/02/23 from https://www.brainhq.com/

BrainHQ. (n.d.). *Hundreds of Published Studies*. Retrieved 08/02/2023 from https://www.brainhq.com/world-class-science/information-researchers/

Brehmer, Y., Westerberg, H., & Bäckman, L. (2012). Working-memory training in younger and older adults: Training gains, transfer, and maintenance. *Frontiers in Human Neuroscience*(MARCH 2012). https://doi.org/10.3389/fnhum.2012.00063

Brunoni, A. R., Lopes, M., & Fregni, F. (2008). A systematic review and meta-analysis of clinical studies on major depression and BDNF levels: implications for the role of neuroplasticity in depression. *Int J Neuropsychopharmacol, 11*(8), 1169-1180. https://doi.org/10.1017/S1461145708009309

Bryant, C., Jackson, H., & Ames, D. (2008). The prevalence of anxiety in older adults: methodological issues and a review of the literature. *J Affect Disord, 109*(3), 233-250. https://doi.org/10.1016/j.jad.2007.11.008

Buitenweg, J. I. V., Murre, J. M. J., & Richard Ridderinkhof, K. (2012). Brain training in progress: A review of trainability in healthy seniors. *Frontiers in Human Neuroscience*(JUNE 2012). https://doi.org/10.3389/fnhum.2012.00183

Burns, A. S., & Warner, J. (2015). Better access to mental health services for older people. *NHS England Blog*. https://www.england.nhs.uk/blog/mh-better-access/

Buysse, D. J., Reynolds III, C. F., Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Research, 28*(2), 193-213.

Bzdok, D., & Dunbar, R. I. M. (2020). The Neurobiology of Social Distance. *Trends Cogn Sci, 24*(9), 717-733. https://doi.org/10.1016/j.tics.2020.05.016

Cabeza, R., Albert, M., Belleville, S., Craik, F. I. M., Duarte, A., Grady, C. L., Lindenberger, U., Nyberg, L., Park, D. C., Reuter-Lorenz, P. A., Rugg, M. D., Steffener, J., & Rajah, M. N. (2018). Maintenance, reserve and compensation: the cognitive neuroscience of healthy ageing. *Nature Reviews Neuroscience, 19*(11), 701-710. https://doi.org/10.1038/s41583-018-0068-2

Cabeza, R., Nyberg, L., & Park, D. C. (2005). *Cognitive neuroscience of aging: Linking cognitive and cerebral aging*. Oxford University Press.

Cabinet Office, A. (2020, 22/02/2021). *COVID-19 Response - Spring 2021 (Summary)*. Retrieved 25/11/2021 from https://www.gov.uk/government/publications/covid-19-response-spring-2021/covid-19-response-spring-2021-summary

Callow, D. D., Arnold-Nedimala, N. A., Jordan, L. S., Pena, G. S., Won, J., Woodard, J. L., & Smith, J. C. (2020). The Mental Health Benefits of Physical Activity in Older Adults Survive the COVID-19 Pandemic. *Am J Geriatr Psychiatry, 28*(10), 1046-1057. https://doi.org/10.1016/j.jagp.2020.06.024

Cardgames.io. (2023). Retrieved 23/02/23 from https://cardgames.io

Cardon-Verbecq, C., Loustau, M., Guitard, E., Bonduelle, M., Delahaye, E., Koskas, P., & Raynaud-Simon, A. (2017). Predicting falls with the cognitive timed up-and-go dual task in frail older patients. *Annals of physical and rehabilitation medicine, 60*(2), 83-86.

Carriedo, A., Cecchini, J. A., Fernandez-Rio, J., & Mendez-Gimenez, A. (2020). COVID-19, Psychological Well-being and Physical Activity Levels in Older Adults During the Nationwide Lockdown in Spain. *Am J Geriatr Psychiatry, 28*(11), 1146-1155. https://doi.org/10.1016/j.jagp.2020.08.007

Carson, N., Leach, L., & Murphy, K. J. (2018). A re-examination of Montreal Cognitive Assessment (MoCA) cutoff scores. *Int J Geriatr Psychiatry, 33*(2), 379-388. https://doi.org/10.1002/gps.4756

Castillo, I., Tomas, I., & Balaguer, I. (2017). The Spanish-Version of the Subjective Vitality Scale: Psychometric Properties and Evidence of Validity. *Span J Psychol, 20*, E26. https://doi.org/10.1017/sjp.2017.22

Caughie, C., Bean, P., Tiede, P., Cobb, J., McFarland, C., & Hall, S. (2021). Dementia Worry and Neuropsychological Performance in Healthy Older Adults. *Arch Clin Neuropsychol, 36*(1), 29-36. https://doi.org/10.1093/arclin/acaa057

Cawthon, P. M., Orwoll, E. S., Ensrud, K. E., Cauley, J. A., Kritchevsky, S. B., Cummings, S. R., & Newman, A. (2020). Assessing the Impact of the COVID-19 Pandemic and Accompanying Mitigation Efforts on Older Adults. *J Gerontol A Biol Sci Med Sci, 75*(9), e123-e125. https://doi.org/10.1093/gerona/glaa099

Cech, D. J., & Martin, S. T. (2011). Nervous System Changes. In *Functional Movement Development Across the Life Span-E-Book* (pp. 174-212). Elsevier Health Sciences.

Chawla, K., Kunonga, T. P., Stow, D., Barker, R., Craig, D., & Hanratty, B. (2021). Prevalence of loneliness amongst older people in high-income countries: A systematic review and meta-analysis. *Plos One, 16*(7), e0255088.

Chen, F. T., Etnier, J. L., Chan, K. H., Chiu, P. K., Hung, T. M., & Chang, Y. K. (2020). Effects of Exercise Training Interventions on Executive Function in Older Adults: A Systematic Review and Meta-Analysis. *Sports Med, 50*(8), 1451-1467. https://doi.org/10.1007/s40279-020-01292-x

Cheng, S. T. (2016). Cognitive Reserve and the Prevention of Dementia: the Role of Physical and Cognitive Activities. *Current Psychiatry Reports, 18*(9). https://doi.org/10.1007/s11920-016-0721-2

Chua, K., Lim, W., Lin, X., Yuan, J.-M., & Koh, W.-P. (2020). Handgrip strength and timed up-and-go (TUG) test are predictors of short-term mortality among elderly in a population-based cohort in Singapore. *The journal of nutrition, health & aging*, 1-8.

Clare, L., Wu, Y. T., Teale, J. C., MacLeod, C., Matthews, F., Brayne, C., & Woods, B. (2017). Potentially modifiable lifestyle factors, cognitive reserve, and cognitive function in later life: A cross-sectional study. *PLoS Medicine, 14*(3). https://doi.org/10.1371/journal.pmed.1002259

Corbeil, R. R., & Searle, S. R. (1976). Restricted Maximum Likelihood (REML) Estimation of Variance Components in the Mixed Model. *Technometrics, 18*(1). https://doi.org/10.2307/1267913

Craig, C. L., Marshall, A. L., Sjöström, M., Bauman, A. E., Booth, M. L., Ainsworth, B. E., Pratt, M., Ekelund, U., Yngve, A., Sallis, J. F., & Oja, P. (2003). International physical activity questionnaire: 12-Country reliability and validity. *Medicine and Science in Sports and Exercise, 35*(8), 1381-1395. https://doi.org/10.1249/01.MSS.0000078924.61453.FB

Crooks, V. C., Lubben, J., Petitti, D. B., Little, D., & Chiu, V. (2008). Social network, cognitive function, and dementia incidence among elderly women. *Am J Public Health, 98*(7), 1221-1227. https://doi.org/10.2105/AJPH.2007.115923

Cruz-Jimenez, M. (2017). Normal changes in gait and mobility problems in the elderly. *Physical Medicine and Rehabilitation Clinics, 28*(4), 713-725.

Cunningham, C., O'Sullivan, R., Caserotti, P., & Tully, M. A. (2020). Consequences of physical inactivity in older adults: A systematic review of reviews and meta-analyses. *Scandinavian journal of medicine & science in sports, 30*(5), 816-827.

Cutler, S. J., & Bragaru, C. (2017). Do Worries About Cognitive Functioning and Concerns About Developing Alzheimer's Disease Affect Psychological Well-Being? *J Aging Health, 29*(8), 1271-1287. https://doi.org/10.1177/0898264316674535

Cutler, S. J., & Hodgson, L. G. (1996). Anticipatory dementia: a link between memory appraisals and concerns about developing Alzheimer's disease. *Gerontologist, 36*(5), 657-664. https://doi.org/10.1093/geront/36.5.657

Daly, M., & Robinson, E. (2021). Psychological distress associated with the second COVID-19 wave: prospective evidence from the UK Household Longitudinal Study.

Damiot, A., Pinto, A. J., Turner, J. E., & Gualano, B. (2020). Immunological Implications of Physical Inactivity among Older Adults during the COVID-19 Pandemic. *Gerontology, 66*(5), 431-438. https://doi.org/10.1159/000509216

De Pue, S., Gillebert, C., Dierckx, E., Vanderhasselt, M. A., De Raedt, R., & Van den Bussche, E. (2021). The impact of the COVID-19 pandemic on wellbeing and cognitive functioning of older adults. *Scientific Reports, 11*(1), 4636. https://doi.org/10.1038/s41598-021-84127-7

Deary, I. J., Liewald, D., & Nissan, J. (2010). A free, easy-to-use, computer-based simple and four-choice reaction time programme: the Deary-Liewald reaction time task. *Behav Res Methods, 43*(1), 258-268. https://doi.org/10.3758/s13428-010-0024-1

Department of Health and Social Care, U. G. (2020, 17 May 2021). *Making a support bubble with another household*
. Retrieved 11/11/21 from https://www.gov.uk/guidance/making-a-support-bubble-with-another-household

Deslandes, A., Moraes, H., Ferreira, C., Veiga, H., Silveira, H., Mouta, R., Pompeu, F. A., Coutinho, E. S., & Laks, J. (2009). Exercise and mental health: many reasons to move. *Neuropsychobiology, 59*(4), 191-198. https://doi.org/10.1159/000223730

Digital, N. (2019). *Statistics on Obesity, Physical Activity and Diet, England, 2019*. Retrieved 04/07/2023 from https://digital.nhs.uk/data-and-information/publications/statistical/statistics-on-obesity-physical-activity-and-diet/statistics-on-obesity-physical-activity-and-diet-england-2019/part-5-adult-physical-activity

Erickson, K. I., Hillman, C., Stillman, C. M., Ballard, R. M., Bloodgood, B., Conroy, D. E., Macko, R., Marquez, D. X., Petruzzello, S. J., Powell, K. E., & For Physical Activity Guidelines Advisory, C. (2019). Physical Activity, Cognition, and Brain Outcomes: A Review of the 2018 Physical Activity Guidelines. *Med Sci Sports Exerc, 51*(6), 1242-1251. https://doi.org/10.1249/MSS.0000000000001936

Erickson, K. I., Prakash, R. S., Voss, M. W., Chaddock, L., Heo, S., McLaren, M., Pence, B. D., Martin, S. A., Vieira, V. J., Woods, J. A., McAuley, E., & Kramer, A. F. (2010). Brain-derived neurotrophic factor is associated with age-related decline in hippocampal volume. *J Neurosci, 30*(15), 5368-5375. https://doi.org/10.1523/JNEUROSCI.6251-09.2010

Eriksen, B. A., & Eriksen, C. W. (1974). Effects of noise letters upon the identification of a target letter in a nonsearch task. *Perception & Psychophysics, 16*(1), 143-149. https://doi.org/10.3758/bf03203267

Espana-Romero, V., Ortega, F. B., Vicente-Rodriguez, G., Artero, E. G., Rey, J. P., & Ruiz, J. R. (2010). Elbow position affects handgrip strength in adolescents: validity and reliability of Jamar, DynEx, and TKK dynamometers. *J Strength Cond Res, 24*(1), 272-277. https://doi.org/10.1519/JSC.0b013e3181b296a5

Ferrucci, L., & Fabbri, E. (2018). Inflammageing: chronic inflammation in ageing, cardiovascular disease, and frailty. *Nature Reviews Cardiology, 15*(9), 505-522. https://doi.org/10.1038/s41569-018-0064-2

Fiorenzato, E., Zabberoni, S., Costa, A., & Cona, G. (2021). Cognitive and mental health changes and their vulnerability factors related to COVID-19 lockdown in Italy. *Plos One, 16*(1), e0246204. https://doi.org/10.1371/journal.pone.0246204

Fiske, A., Wetherell, J. L., & Gatz, M. (2009). Depression in older adults. *Annu Rev Clin Psychol, 5*, 363-389. https://doi.org/10.1146/annurev.clinpsy.032408.153621

Forde, C. (2018). Scoring the international physical activity questionnaire (IPAQ). *University of Dublin*.

Fox, K. R. (1999). The influence of physical activity on mental well-being. *Public Health Nutr, 2*(3A), 411-418. https://doi.org/10.1017/s1368980099000567

Franceschi, C., Capri, M., Monti, D., Giunta, S., Olivieri, F., Sevini, F., Panourgia, M. P., Invidia, L., Celani, L., Scurti, M., Cevenini, E., Castellani, G. C., & Salvioli, S. (2007). Inflammaging and anti-inflammaging: A systemic perspective on aging and longevity emerged from studies in humans. *Mechanisms of Ageing and Development, 128*(1), 92-105. https://doi.org/10.1016/j.mad.2006.11.016

Gabay, C. (2006). Interleukin-6 and chronic inflammation. *Arthritis Research and Therapy, 8*(SUPPL. 2). https://doi.org/10.1186/ar1917

Ganguli, M. (2009). Depression, cognitive impairment and dementia: Why should clinicians care about the web of causation? *Indian journal of psychiatry, 51*(Suppl1), S29.

Garcia-Portilla, P., de la Fuente Tomas, L., Bobes-Bascaran, T., Jimenez Trevino, L., Zurron Madera, P., Suarez Alvarez, M., Menendez Miranda, I., Garcia Alvarez, L., Saiz Martinez, P. A., & Bobes, J. (2020). Are older adults also at higher psychological risk from COVID-19? *Aging Ment Health*, 1-8. https://doi.org/10.1080/13607863.2020.1805723

Garmany, A., Yamada, S., & Terzic, A. (2021). Longevity leap: mind the healthspan gap. *NPJ Regen Med, 6*(1), 57. https://doi.org/10.1038/s41536-021-00169-5

Gilbody, S., Richards, D., Brealey, S., & Hewitt, C. (2007). Screening for depression in medical settings with the Patient Health Questionnaire (PHQ): a diagnostic meta-analysis. *J Gen Intern Med, 22*(11), 1596-1602. https://doi.org/10.1007/s11606-007-0333-y

Glisky, E. L. (2007). Changes in cognitive function in human aging. *Brain aging*, 3-20.

Gollan, T. H., & Brown, A. S. (2006). From tip-of-the-tongue (TOT) data to theoretical implications in two steps: when more TOTs means better retrieval. *J Exp Psychol Gen, 135*(3), 462-483. https://doi.org/10.1037/0096-3445.135.3.462

Gonzalez-Sanguino, C., Ausin, B., Castellanos, M. A., Saiz, J., Lopez-Gomez, A., Ugidos, C., & Munoz, M. (2020). Mental health consequences during the initial stage of the 2020 Coronavirus pandemic (COVID-19) in Spain. *Brain Behav Immun, 87*, 172-176. https://doi.org/10.1016/j.bbi.2020.05.040

Goodpaster, B. H., Park, S. W., Harris, T. B., Kritchevsky, S. B., Nevitt, M., Schwartz, A. V., Simonsick, E. M., Tylavsky, F. A., Visser, M., & Newman, A. B. (2006). The loss of skeletal muscle strength, mass, and quality in older adults: the health, aging and body composition study. *J Gerontol A Biol Sci Med Sci, 61*(10), 1059-1064. https://doi.org/10.1093/gerona/61.10.1059

Gosche, K. M., Mortimer, J. A., Smith, C. D., Markesbery, W. R., & Snowdon, D. A. (2002). Hippocampal volume as an index of Alzheimer neuropathology: findings from the Nun Study. *Neurology, 58*(10), 1476-1482. https://doi.org/10.1212/wnl.58.10.1476

Green, C. S., & Bavelier, D. (2008). Exercising Your Brain: A Review of Human Brain Plasticity and Training-Induced Learning. *Psychology and Aging, 23*(4), 692-701. https://doi.org/10.1037/a0014345

Green, C. S., & Bavelier, D. (2012). Learning, attentional control, and action video games. *Curr Biol, 22*(6), R197-206. https://doi.org/10.1016/j.cub.2012.02.012

Green, C. S., Strobach, T., & Schubert, T. (2014). On methodological standards in training and transfer experiments. *Psychological Research, 78*(6), 756-772. https://doi.org/10.1007/s00426-013-0535-3

Grégoire, J., & Van der Linden, M. (1997). Effect of age on forward and backward digit spans. *Aging, Neuropsychology, and Cognition, 4*(2), 140-149.

Groarke, J. M., Berry, E., Graham-Wisener, L., McKenna-Plumley, P. E., McGlinchey, E., & Armour, C. (2020). Loneliness in the UK during the COVID-19 pandemic: Cross-sectional results from the COVID-19 Psychological Wellbeing Study. *Plos One, 15*(9), e0239698. https://doi.org/10.1371/journal.pone.0239698

Grossman, E. S., Hoffman, Y. S. G., Palgi, Y., & Shrira, A. (2021). COVID-19 related loneliness and sleep problems in older adults: Worries and resilience as potential moderators. *Pers Individ Dif, 168*, 110371. https://doi.org/10.1016/j.paid.2020.110371

Gunstad, J., Benitez, A., Smith, J., Glickman, E., Spitznagel, M. B., Alexander, T., Juvancic-Heltzel, J., & Murray, L. (2008). Serum brain-derived neurotrophic factor is associated with cognitive function in healthy older adults. *J Geriatr Psychiatry Neurol, 21*(3), 166-170. https://doi.org/10.1177/0891988708316860

Guye, S., & von Bastian, C. C. (2017). Working memory training in older adults: Bayesian evidence supporting the absence of transfer. *Psychology and Aging, 32*(8). https://doi.org/10.1037/pag0000206

Hamer, M., Lavoie, K. L., & Bacon, S. L. (2014). Taking up physical activity in later life and healthy ageing: the English longitudinal study of ageing. *Br J Sports Med, 48*, 239-243. http:// https://bjsm.bmj.com/content/bjsports/48/3/239.full.pdf

Hantke, N. C., & Gould, C. (2020). Examining Older Adult Cognitive Status in the Time of COVID-19. *J Am Geriatr Soc, 68*(7), 1387-1389. https://doi.org/10.1111/jgs.16514

Hardy, J. L., Nelson, R. A., Thomason, M. E., Sternberg, D. A., Katovich, K., Farzin, F., & Scanlon, M. (2015). Enhancing Cognitive Abilities with Comprehensive Training: A Large, Online, Randomized, Active-Controlled Trial. *Plos One, 10*(9), e0134467. https://doi.org/10.1371/journal.pone.0134467

Harvey, L. O. (1992). The critical operating characteristic and the evaluation of expert judgment. *Organizational Behavior and Human Decision Processes, 53*(2), 229-251. https://doi.org/10.1016/0749-5978(92)90063-d

Harvey, P. D., Balzer, A. M., & Kotwicki, R. J. (2020). Training engagement, baseline cognitive functioning, and cognitive gains with computerized cognitive training: A cross-diagnostic study. *Schizophr Res Cogn, 19*, 100150. https://doi.org/10.1016/j.scog.2019.100150

Hausdorff, J. M., Rios, D. A., & Edelberg, H. K. (2001). Gait variability and fall risk in community-living older adults: A 1-year prospective study. *Archives of Physical Medicine and Rehabilitation, 82*(8), 1050-1056. https://doi.org/10.1053/apmr.2001.24893

Heinzel, S., Lorenz, R. C., Pelz, P., Heinz, A., Walter, H., Kathmann, N., Rapp, M. A., & Stelzel, C. (2016). Neural correlates of training and transfer effects in working memory in older adults. *Neuroimage, 134*, 236-249. https://doi.org/10.1016/j.neuroimage.2016.03.068

Hill, N. T., Mowszowski, L., Naismith, S. L., Chadwick, V. L., Valenzuela, M., & Lampit, A. (2017). Computerized Cognitive Training in Older Adults With Mild Cognitive Impairment or Dementia: A Systematic Review and Meta-Analysis. *Am J Psychiatry, 174*(4), 329-340. https://doi.org/10.1176/appi.ajp.2016.16030360

Hirvensalo, M., Rantanen, T., & Heikkinen, E. (2000). Mobility difficulties and physical activity as predictors of mortality and loss of independence in the community-living older population. *Journal of the American Geriatrics Society, 48*(5), 493-498.

Howard, M. C., & Hoffman, M. E. (2017). Variable-Centered, Person-Centered, and Person-Specific Approaches. *Organizational Research Methods, 21*(4), 846-876. https://doi.org/10.1177/1094428117744021

Huang, T., Larsen, K. T., Ried-Larsen, M., Moller, N. C., & Andersen, L. B. (2014). The effects of physical activity and exercise on brain-derived neurotrophic factor in healthy humans: A review. *Scand J Med Sci Sports, 24*(1), 1-10. https://doi.org/10.1111/sms.12069

Huberman, M., Sredni, B., Stern, L., Kott, E., & Shalit, F. (1995). IL-2 and IL-6 secretion in dementia: correlation with type and severity of disease. *Journal of the Neurological Sciences*. https://doi.org/10.1016/0022-510X(95)00016-U

Hughes, M. E., Waite, L. J., Hawkley, L. C., & Cacioppo, J. T. (2004). A Short Scale for Measuring Loneliness in Large Surveys: Results From Two Population-Based Studies. *Res Aging, 26*(6), 655-672. https://doi.org/10.1177/0164027504268574

Hurtig-Wennlöf, A., Hagströmer, M., & Olsson, L. A. (2010). The International Physical Activity Questionnaire modified for the elderly: aspects of validity and feasibility. *Public Health Nutrition, 13*(11), 1847-1854.

Hyland, P., Shevlin, M., McBride, O., Murphy, J., Karatzias, T., Bentall, R. P., Martinez, A., & Vallieres, F. (2020). Anxiety and depression in the Republic of Ireland during the COVID-19 pandemic. *Acta Psychiatr Scand, 142*(3), 249-256. https://doi.org/10.1111/acps.13219

Iacobucci, G. (2020). Covid-19: Increased risk among ethnic minorities is largely due to poverty and social disparities, review finds. *BMJ, 371*, m4099. https://doi.org/10.1136/bmj.m4099

Jaeggi, S. M., Buschkuehl, M., Perrig, W. J., & Meier, B. (2010). The concurrent validity of the N-back task as a working memory measure. *Memory, 18*(4), 394-412. https://doi.org/10.1080/09658211003702171

Jakobsen, J. C., Gluud, C., Wetterslev, J., & Winkel, P. (2017). When and how should multiple imputation be used for handling missing data in randomised clinical trials–a practical guide with flowcharts. *BMC medical research methodology, 17*(1), 1-10.

Jennings, J. M., Dagenbach, D., Engle, C. M., & Funke, L. J. (2007). Age-related changes and the attention network task: an examination of alerting, orienting, and executive function. *Neuropsychol Dev Cogn B Aging Neuropsychol Cogn, 14*(4), 353-369. https://doi.org/10.1080/13825580600788837

Johannsen, D. L., & Ravussin, E. (2010). Obesity in the elderly: Is faulty metabolism to blame? *Aging health, 6*(2), 159-167. https://doi.org/10.2217/ahe.10.12

Johnson, S. K. (2021). Latent profile transition analyses and growth mixture models: A very non-technical guide for researchers in child and adolescent development. *New Dir Child Adolesc Dev, 2021*(175), 111-139. https://doi.org/10.1002/cad.20398

Judd, C. M., Westfall, J., & Kenny, D. A. (2012). Treating stimuli as a random factor in social psychology: a new and comprehensive solution to a pervasive but largely ignored problem. *Journal of personality and social psychology, 103*(1), 54.

Jurca, R., Jackson, A. S., LaMonte, M. J., Morrow, J. R., Blair, S. N., Wareham, N. J., Haskell, W. L., Van Mechelen, W., Church, T. S., Jakicic, J. M., & Laukkanen, R. (2005). Assessing cardiorespiratory fitness without performing exercise testing. *American Journal of Preventive Medicine, 29*(3), 185-193. https://doi.org/10.1016/j.amepre.2005.06.004

Kable, J. W., Caulfield, M. K., Falcone, M., McConnell, M., Bernardo, L., Parthasarathi, T., Cooper, N., Ashare, R., Audrain-McGovern, J., Hornik, R., Diefenbach, P., Lee, F. J., & Lerman, C. (2017). No effect of commercial cognitive training on brain activity, choice behavior, or cognitive performance. *Journal of Neuroscience, 37*(31), 7390-7402. https://doi.org/10.1523/JNEUROSCI.2832-16.2017

Kandola, A. A., Osborn, D. P., Stubbs, B., Choi, K. W., & Hayes, J. F. (2020). Individual and combined associations between cardiorespiratory fitness and grip strength with common mental disorders: a prospective cohort study in the UK Biobank. *BMC Medicine, 18*(1), 1-11.

Karbach, J., & Verhaeghen, P. (2014). Making Working Memory Work: A Meta-Analysis of Executive-Control and Working Memory Training in Older Adults. *Psychological Science, 25*(11), 2027-2037. https://doi.org/10.1177/0956797614548725

Kearney, F. C., Harwood, R. H., Gladman, J. R., Lincoln, N., & Masud, T. (2013). The relationship between executive function and falls and gait abnormalities in older adults: a systematic review. *Dementia and geriatric cognitive disorders, 36*(1-2), 20-35.

Kelly, M. E., Duff, H., Kelly, S., McHugh Power, J. E., Brennan, S., Lawlor, B. A., & Loughrey, D. G. (2017). The impact of social activities, social networks, social support and social relationships on the cognitive functioning of healthy older adults: a systematic review. *Systematic reviews, 6*(1), 1-18.

Kendall, J. M. (2003). Designing a research project: randomised controlled trials and their principles. *Emerg Med J, 20*(2), 164-168. https://doi.org/10.1136/emj.20.2.164

Kessler, E. M., Bowen, C. E., Baer, M., Froelich, L., & Wahl, H. W. (2012). Dementia worry: a psychological examination of an unexplored phenomenon. *Eur J Ageing, 9*(4), 275-284. https://doi.org/10.1007/s10433-012-0242-8

Kiely, K. M., Brady, B., & Byles, J. (2019). Gender, mental health and ageing. *Maturitas, 129*, 76-84. https://doi.org/10.1016/j.maturitas.2019.09.004

Kivimäki, M., Shipley, M. J., Batty, G. D., Hamer, M., Akbaraly, T. N., Kumari, M., Jokela, M., Virtanen, M., Lowe, G. D., Ebmeier, K. P., Brunner, E. J., & Singh-Manoux, A. (2014). Long-term inflammation increases risk of common mental disorder: A cohort study. *Molecular Psychiatry, 19*(2), 149-150. https://doi.org/10.1038/mp.2013.35

Kleitman, S., Fullerton, D. J., Zhang, L. M., Blanchard, M. D., Lee, J., Stankov, L., & Thompson, V. (2021). To comply or not comply? A latent profile analysis of behaviours and attitudes during the COVID-19 pandemic. *Plos One, 16*(7), e0255268. https://doi.org/10.1371/journal.pone.0255268

Krendl, A. C., & Perry, B. L. (2021). The Impact of Sheltering in Place During the COVID-19 Pandemic on Older Adults' Social and Mental Well-Being. *J Gerontol B Psychol Sci Soc Sci, 76*(2), e53-e58. https://doi.org/10.1093/geronb/gbaa110

Kroenke, K., Spitzer, R. L., Williams, J. B., Monahan, P. O., & Lowe, B. (2007). Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. *Ann Intern Med, 146*(5), 317-325. https://doi.org/10.7326/0003-4819-146-5-200703060-00004

Kroenke, K., Strine, T. W., Spitzer, R. L., Williams, J. B. W., Berry, J. T., & Mokdad, A. H. (2009). The PHQ-8 as a measure of current depression in the general population. *Journal of Affective Disorders, 114*(1-3), 163-173. https://doi.org/10.1016/j.jad.2008.06.026

Kueider, A. M., Parisi, J. M., Gross, A. L., & Rebok, G. W. (2012). Computerized cognitive training with older adults: a systematic review. *Plos One, 7*(7), e40588. https://doi.org/10.1371/journal.pone.0040588

Kuiper, J. S., Zuidersma, M., Oude Voshaar, R. C., Zuidema, S. U., van den Heuvel, E. R., Stolk, R. P., & Smidt, N. (2015). Social relationships and risk of dementia: A systematic review and

meta-analysis of longitudinal cohort studies. *Ageing Res Rev, 22*, 39-57. https://doi.org/10.1016/j.arr.2015.04.006

La Grow, S., Yeung, P., Towers, A., Alpass, F., & Stephens, C. (2013). The impact of mobility on quality of life among older persons. *Journal of Aging and Health, 25*(5), 723-736.

Lampinen, P., & Heikkinen, E. (2003). Reduced mobility and physical activity as predictors of depressive symptoms among community-dwelling older adults: an eight-year follow-up study. *Aging Clin Exp Res, 15*(3), 205-211. https://doi.org/10.1007/BF03324501

Lampit, A., Hallock, H., & Valenzuela, M. (2014). Computerized Cognitive Training in Cognitively Healthy Older Adults: A Systematic Review and Meta-Analysis of Effect Modifiers. *PLoS Medicine, 11*(11). https://doi.org/10.1371/journal.pmed.1001756

Lara, E., Caballero, F. F., Rico-Uribe, L. A., Olaya, B., Haro, J. M., Ayuso-Mateos, J. L., & Miret, M. (2019). Are loneliness and social isolation associated with cognitive decline? *Int J Geriatr Psychiatry, 34*(11), 1613-1622. https://doi.org/10.1002/gps.5174

Lautenschlager, N. T., & Almeida, O. P. (2006). Physical activity and cognition in old age. *Current opinion in Psychiatry, 19*(2), 190-193.

Law, C. K., Lam, F. M., Chung, R. C., & Pang, M. Y. (2020). Physical exercise attenuates cognitive decline and reduces behavioural problems in people with mild cognitive impairment and dementia: a systematic review. *J Physiother, 66*(1), 9-18. https://doi.org/10.1016/j.jphys.2019.11.014

Ledreux, A., Hakansson, K., Carlsson, R., Kidane, M., Columbo, L., Terjestam, Y., Ryan, E., Tusch, E., Winblad, B., Daffner, K., Granholm, A. C., & Mohammed, A. K. H. (2019). Differential Effects of Physical Exercise, Cognitive Training, and Mindfulness Practice on Serum BDNF Levels in Healthy Older Adults: A Randomized Controlled Intervention Study. *J Alzheimers Dis, 71*(4), 1245-1261. https://doi.org/10.3233/JAD-190756

Lee, E.-K. O., & Lee, J. (2011). Gender differences in predictors of mental health among older adults in South Korea. *The International Journal of Aging and Human Development, 72*(3), 207-223.

Lee, G. J., Do, C., & Suhr, J. A. (2020). Effects of personal dementia exposure on subjective memory concerns and dementia worry. *Neuropsychol Dev Cogn B Aging Neuropsychol Cogn*, 1-16. https://doi.org/10.1080/13825585.2020.1836119

Lee, H. K., Kent, J. D., Wendel, C., Wolinsky, F. D., Foster, E. D., Merzenich, M. M., & Voss, M. W. (2020). Home-Based, Adaptive Cognitive Training for Cognitively Normal Older adults: Initial Efficacy Trial. *J Gerontol B Psychol Sci Soc Sci, 75*(6), 1144-1154. https://doi.org/10.1093/geronb/gbz073

Lowe, B., Decker, O., Muller, S., Brahler, E., Schellberg, D., Herzog, W., & Herzberg, P. Y. (2008). Validation and standardization of the Generalized Anxiety Disorder Screener (GAD-7) in the general population. *Med Care, 46*(3), 266-274. https://doi.org/10.1097/MLR.0b013e318160d093

Lubben, J., Blozik, E., Gillmann, G., Iliffe, S., von Renteln Kruse, W., Beck, J. C., & Stuck, A. E. (2006). Performance of an abbreviated version of the Lubben Social Network Scale among three European community-dwelling older adult populations. *Gerontologist, 46*(4), 503-513. https://doi.org/10.1093/geront/46.4.503

Lumosity. (2023). Retrieved 21/02/23 from https://www.lumosity.com/en/

Macmillan, N. A., & Creelman, C. D. (2004). *Detection Theory: A User's Guide*. Taylor & Francis Group.

Mailey, E. L., White, S. M., Wójcicki, T. R., Szabo, A. N., Kramer, A. F., & McAuley, E. (2010). Construct validation of a non-exercise measure of cardiorespiratory fitness in older adults. *BMC Public Health, 10*(1), 59-undefined. http://www.biomedcentral.com/1471-2458/10/59

Makowski, D., Lüdecke, D., Patil, I., Thériault, R., Ben-Shachar, M. S., & Wiernik, B. M. (2023). *Automated Results Reporting as a Practical Tool to Improve Reproducibility and Methodological Best Practices Adoption. CRAN.* https://easystats.github.io/report/

Marsh, H. W., Lüdtke, O., Trautwein, U., & Morin, A. J. (2009). Classical latent profile analysis of academic self-concept dimensions: Synergy of person-and variable-centered approaches to theoretical models of self-concept. *Structural Equation Modeling: A Multidisciplinary Journal, 16*(2), 191-225.

Martin, A., Rief, W., Klaiberg, A., & Braehler, E. (2006). Validity of the Brief Patient Health Questionnaire Mood Scale (PHQ-9) in the general population. *Gen Hosp Psychiatry, 28*(1), 71-77. https://doi.org/10.1016/j.genhosppsych.2005.07.003

Masurovsky, A. (2020). Controlling for Placebo Effects in Computerized Cognitive Training Studies With Healthy Older Adults From 2016-2018: Systematic Review. *JMIR Serious Games, 8*(2), e14030. https://doi.org/10.2196/14030

Matsui, T., Mitsuma, S., Nagata, A., Matsushita, S., & Asahi, T. (2023). Accelerated cognitive decline after the COVID-19 pandemic in a community population of older persons with cognitive impairment: A 4-year time series analysis in the Tokyo Metropolis area. *Geriatr Gerontol Int, 23*(3), 200-204. https://doi.org/10.1111/ggi.14543

Maxfield, M., & Pituch, K. A. (2022). Profiles in Dementia-Related Anxiety: A Latent Profile Analysis. *J Gerontol B Psychol Sci Soc Sci, 77*(12), 2182-2191. https://doi.org/10.1093/geronb/gbac082

Maylor, E. A. (1990). Age, blocking and the tip of the tongue state. *British journal of psychology, 81*(2), 123-134.

McDougall, S., & House, B. (2012). Brain training in older adults: evidence of transfer to memory span performance and pseudo-Matthew effects. *Neuropsychol Dev Cogn B Aging Neuropsychol Cogn, 19*(1-2), 195-221. https://doi.org/10.1080/13825585.2011.640656

McGeer, P. L., Schulzer, M., & McGeer, E. G. (1996). Arthritis and anti-inflammatory agents as possible protective factors for Alzheimer's disease: a review of 17 epidemiologic studies. *Neurology, 47*(2), 425-432. https://doi.org/10.1212/wnl.47.2.425

Mekari, S., Neyedli, H. F., Fraser, S., O'Brien, M. W., Martins, R., Evans, K., Earle, M., Aucoin, R., Chiekwe, J., Hollohan, Q., Kimmerly, D. S., & Dupuy, O. (2020). High-Intensity Interval Training Improves Cognitive Flexibility in Older Adults. *Brain Sci, 10*(11). https://doi.org/10.3390/brainsci10110796

Melby-Lervåg, M., Redick, T. S., & Hulme, C. (2016). Working Memory Training Does Not Improve Performance on Measures of Intelligence or Other Measures of "Far Transfer": Evidence From a Meta-Analytic Review. *Perspectives on Psychological Science, 11*(4), 512-534. https://doi.org/10.1177/1745691616635612

Meltzer, J. A., Kates Rose, M., Le, A. Y., Spencer, K. A., Goldstein, L., Gubanova, A., Lai, A. C., Yossofzai, M., Armstrong, S. E. M., & Bialystok, E. (2023). Improvement in executive function for older adults through smartphone apps: a randomized clinical trial comparing language learning and brain training. *Neuropsychol Dev Cogn B Aging Neuropsychol Cogn, 30*(2), 150-171. https://doi.org/10.1080/13825585.2021.1991262

Miranda, M., Morici, J. F., Zanoni, M. B., & Bekinschtein, P. (2019). Brain-Derived Neurotrophic Factor: A Key Molecule for Memory in the Healthy and the Pathological Brain. *Front Cell Neurosci, 13*, 363. https://doi.org/10.3389/fncel.2019.00363

Montori, V. M., & Guyatt, G. H. (2001). Intention-to-treat principle. *Cmaj, 165*(10), 1339-1341.

Morrison, J. H., & Baxter, M. G. (2012). The ageing cortical synapse: Hallmarks and implications for cognitive decline. *Nature Reviews Neuroscience, 13*(4), 240-250. https://doi.org/10.1038/nrn3200

Motter, J. N., Grinberg, A., Lieberman, D. H., Iqnaibi, W. B., & Sneed, J. R. (2019). Computerized cognitive training in young adults with depressive symptoms: Effects on mood, cognition, and everyday functioning. *Journal of Affective Disorders, 245*, 28-37. https://doi.org/10.1016/j.jad.2018.10.109

Murman, D. L. (2015). The Impact of Age on Cognition. *Seminars in Hearing, 36*(3), 111-121. https://doi.org/10.1055/s-0035-1555115

Narazaki, M., & Kishimoto, T. (2018). The Two-Faced Cytokine IL-6 in Host Defense and Diseases. *Int J Mol Sci, 19*(11). https://doi.org/10.3390/ijms19113528

Nasreddine, Z. S., Phillips, N. A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., Cummings, J. L., & Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA: A Brief Screening Tool For Mild Cognitive Impairment. *Journal of the American Geriatrics Society, 53*(4), 695-699. www.mocatest.
https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1532-5415.2005.53221.x

National Academies of Sciences, E., & Medicine. (2020). *Social isolation and loneliness in older adults: Opportunities for the health care system*. National Academies Press.

National Institute for Health and Care Excellence, N. (2013). *Falls in older people: assessing risk and prevention*. NICE.

Nguyen, L., Murphy, K., & Andrews, G. (2022). A Game a Day Keeps Cognitive Decline Away? A Systematic Review and Meta-Analysis of Commercially-Available Brain Training Programs in Healthy and Cognitively Impaired Older Adults. *Neuropsychol Rev, 32*(3), 601-630. https://doi.org/10.1007/s11065-021-09515-2

Noack, H., Lövdén, M., & Schmiedek, F. (2014). On the validity and generality of transfer effects in cognitive training research. *Psychological Research, 78*(6), 773-789. https://doi.org/10.1007/s00426-014-0564-6

Noguchi, T., Kubo, Y., Hayashi, T., Tomiyama, N., Ochi, A., & Hayashi, H. (2021). Social isolation and self-reported cognitive decline among older adults in Japan: A longitudinal study in the COVID-19 pandemic. *Journal of the American Medical Directors Association*. https://doi.org/10.1016/j.jamda.2021.05.015

Northey, J. M., Cherbuin, N., Pumpa, K. L., Smee, D. J., & Rattray, B. (2018). Exercise interventions for cognitive function in adults older than 50: a systematic review with meta-analysis. *Br J Sports Med, 52*(3), 154-160. https://doi.org/10.1136/bjsports-2016-096587

Oliveira, M. R., Sudati, I. P., Konzen, V. M., de Campos, A. C., Wibelinger, L. M., Correa, C., Miguel, F. M., Silva, R. N., & Borghi-Silva, A. (2022). Covid-19 and the impact on the physical activity level of elderly people: A systematic review. *Exp Gerontol, 159*, 111675. https://doi.org/10.1016/j.exger.2021.111675

ONS. (2020a). *Coronavirus and depression in adults, Great Britain: June 2020*. Retrieved 17/1/2022 from https://www.ons.gov.uk/peoplepopulationandcommunity/wellbeing/articles/coronavirusanddepressioninadultsgreatbritain/june2020#introduction

ONS. (2020b). *Deaths involving COVID-19, England and Wales: deaths occurring in June 2020*. Retrieved 13/7/21 from https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsinvolvingcovid19englandandwales/deathsoccurringinjune2020

Owen, A. M., Hampshire, A., Grahn, J. A., Stenton, R., Dajani, S., Burns, A. S., Howard, R. J., & Ballard, C. G. (2010). Putting brain training to the test. *Nature, 465*(7299), 775-778. https://doi.org/10.1038/nature09042

Park, D. C., Lautenschlager, G., Hedden, T., Davidson, N. S., Smith, A. D., & Smith, P. K. (2002). Models of visuospatial and verbal memory across the adult life span. *Psychology and Aging, 17*(2), 299-320. https://doi.org/10.1037/0882-7974.17.2.299

Park, S., Castaneda-Gameros, D., & Oh, I. H. (2019). Latent profile analysis of walking, sitting, grip strength, and perceived body shape and their association with mental health in older Korean adults with hypertension: A national observational study. *Medicine (Baltimore), 98*(39), e17287. https://doi.org/10.1097/MD.0000000000017287

Park, S., Thøgersen-Ntoumani, C., Ntoumanis, N., Stenling, A., Fenton, S. A., & Veldhuijzen van Zanten, J. J. (2017). Profiles of physical function, physical activity, and sedentary behavior and their associations with mental health in residents of assisted living facilities. *Applied Psychology: Health and Well-Being, 9*(1), 60-80.

Peak. (2023). Retrieved 21/02/23 from https://peak.net

Pearson, M. R., Lawless, A. K., Brown, D. B., & Bravo, A. J. (2015). Mindfulness and emotional outcomes: Identifying subgroups of college students using latent profile analysis. *Personality and Individual Differences, 76*, 33-38.

Peirce, J., Gray, J. R., Simpson, S., MacAskill, M., Hochenberger, R., Sogo, H., Kastman, E., & Lindelov, J. K. (2019). PsychoPy2: Experiments in behavior made easy. *Behav Res Methods, 51*(1), 195-203. https://doi.org/10.3758/s13428-018-01193-y

Penner, I. K., Vogt, A., Stocklin, M., Gschwind, L., Opwis, K., & Calabrese, P. (2012). Computerised working memory training in healthy adults: a comparison of two different training schedules. *Neuropsychol Rehabil, 22*(5), 716-733. https://doi.org/10.1080/09602011.2012.686883

Pentikainen, H., Savonen, K., Ngandu, T., Solomon, A., Komulainen, P., Paajanen, T., Antikainen, R., Kivipelto, M., Soininen, H., & Rauramaa, R. (2019). Cardiorespiratory Fitness and Cognition: Longitudinal Associations in the FINGER Study. *J Alzheimers Dis, 68*(3), 961-968. https://doi.org/10.3233/JAD-180897

Perez-Arce, F., Angrisani, M., Bennett, D., Darling, J., Kapteyn, A., & Thomas, K. (2021). COVID-19 vaccines and mental distress. *Plos One, 16*(9), e0256406. https://doi.org/10.1371/journal.pone.0256406

Posner, M. I., & Cohen, Y. (1984). Components of visual orienting. *Attention and performance X: Control of language processes, 32*, 531-556.

Proto, E., & Quintana-Domeque, C. (2021). COVID-19 and mental health deterioration by ethnicity and gender in the UK. *Plos One, 16*(1), e0244419. https://doi.org/10.1371/journal.pone.0244419

Quattropani, M. C., Sardella, A., Morgante, F., Ricciardi, L., Alibrandi, A., Lenzo, V., Catalano, A., Squadrito, G., & Basile, G. (2021). Impact of Cognitive Reserve and Premorbid IQ on Cognitive and Functional Status in Older Outpatients. *Brain Sci, 11*(7). https://doi.org/10.3390/brainsci11070824

Rabipour, S., & Davidson, P. S. R. (2015). Do you believe in brain training? A questionnaire about expectations of computerised cognitive training. *Behav Brain Res, 295*, 64-70. https://doi.org/10.1016/j.bbr.2015.01.002

Rajkumar, R. P. (2020). COVID-19 and mental health: A review of the existing literature. *Asian J Psychiatr, 52*, 102066. https://doi.org/10.1016/j.ajp.2020.102066

Randall, M. (2017). *Overview of the UK population: July 2017*.

Rantakokko, M., Manty, M., & Rantanen, T. (2013). Mobility decline in old age. *Exerc Sport Sci Rev, 41*(1), 19-25. https://doi.org/10.1097/JES.0b013e3182556f1e

Reeh, H., Rudolph, N., Billing, U., Christen, H., Streif, S., Bullinger, E., Schliemann-Bullinger, M., Findeisen, R., Schaper, F., Huber, H. J., & Dittrich, A. (2019). Response to IL-6 trans- and IL-6 classic signalling is determined by the ratio of the IL-6 receptor α to gp130 expression: Fusing experimental insights and dynamic modelling. *Cell Communication and Signaling, 17*(1). https://doi.org/10.1186/s12964-019-0356-0

Reuter-Lorenz, P. A., & Cappell, K. A. (2008). Neurocognitive Aging and the Compensation Hypothesis. *Current Directions in Psychological Science, 17*(3), 177-182. https://doi.org/10.1111/j.1467-8721.2008.00570.x

Reuter-Lorenz, P. A., Festini, S. B., & Jantz, T. K. (2021). Executive functions and neurocognitive aging. In *Handbook of the psychology of aging* (pp. 67-81). Elsevier.

Rikli, R. E., & Jones, C. J. (1999). Development and Validation of a Functional Fitness Test for Community-Residing Older Adults. *Journal of Aging and Physical Activity, 7*(2), 129-161. https://doi.org/10.1123/japa.7.2.129

Riley, S., Wang, H., Eales, O., Haw, D., Walters, C. E., Ainslie, K. E. C., Atchison, C., Fronterre, C., Diggle, P. J., Ashby, D., Donnelly, C. A., Cooke, G., Barclay, W., Ward, H., Darzi, A., & Elliott, P. (2021). REACT-1 round 9 final report: Continued but slowing decline of prevalence of SARS-CoV-2 during national lockdown in England in February 2021. *MedRxiv*. https://doi.org/10.1101/2021.03.03.21252856

Ripp, I., Emch, M., Wu, Q., Lizarraga, A., Udale, R., von Bastian, C. C., Koch, K., & Yakushev, I. (2022). Adaptive working memory training does not produce transfer effects in cognition and neuroimaging. *Transl Psychiatry, 12*(1), 512. https://doi.org/10.1038/s41398-022-02272-7

Robb, C. E., de Jager, C. A., Ahmadi-Abhari, S., Giannakopoulou, P., Udeh-Momoh, C., McKeand, J., Price, G., Car, J., Majeed, A., Ward, H., & Middleton, L. (2020). Associations of Social Isolation with Anxiety and Depression During the Early COVID-19 Pandemic: A Survey of Older Adults in London, UK. *Front Psychiatry, 11*, 591120. https://doi.org/10.3389/fpsyt.2020.591120

Robineau, D. (2016). Ageing Britain: two-fifths of NHS budget is spent on over-65s. *The Guardian*. https://www.theguardian.com/society/2016/feb/01/ageing-britain-two-fifths-nhs-budget-spent-over-65s

Rogers, J., Kirby, L. C., Hempelman, S. R., Berry, D. L., McGeer, P. L., Kaszniak, A. W., Zalinski, J., Cofield, M., Mansukhani, L., Willson, P., & Kogan, F. (1993). Clinical trial of indomethacin in Alzheimer's disease. *Neurology, 43*(8). https://doi.org/10.1212/WNL.43.8.1609

Roheger, M., Meyer, J., Kessler, J., & Kalbe, E. (2020). Predicting short- and long-term cognitive training success in healthy older adults: who benefits? *Neuropsychol Dev Cogn B Aging Neuropsychol Cogn, 27*(3), 351-369. https://doi.org/10.1080/13825585.2019.1617396

Rolenz, E., & Reneker, J. C. (2016). Validity of the 8-Foot Up and Go, Timed Up and Go, and Activities-Specific Balance Confidence Scale in older adults with and without cognitive impairment. *J Rehabil Res Dev, 53*(4), 511-518. https://doi.org/10.1682/JRRD.2015.03.0042

Rose, D. J., Jones, C. J., & Lucchese, N. (2002). Predicting the Probability of Falls in Community-Residing Older Adults Using the 8-Foot Up-and-Go: A New Measure of Functional Mobility. *Journal of Aging and Physical Activity, 10*(4), 466-475. https://doi.org/10.1123/japa.10.4.466

Rosenberg, J., Beymer, P., Anderson, D., van Lissa, C. j., & Schmidt, J. (2018). tidyLPA: An R Package to Easily Carry Out Latent Profile Analysis (LPA) Using Open-Source or Commercial Software. *Journal of Open Source Software, 3*(30). https://doi.org/10.21105/joss.00978

Roser, M., Ortiz-Ospina, E., & Ritchie, H. (2013). *Life Expectancy*. Retrieved 19th February 2021 from 'https://ourworldindata.org/life-expectancy [Online Resource]

Rosso, A. L., Taylor, J. A., Tabb, L. P., & Michael, Y. L. (2013). Mobility, disability, and social engagement in older adults. *Journal of Aging and Health, 25*(4), 617-637.

Roth, P. L., & Switzer III, F. S. (1995). A Monte Carlo analysis of missing data techniques in a HRM setting. *Journal of Management, 21*(5), 1003-1023.

RStudio Team, R. (2020). *RStudio: Integrated Development for R.* In RStudio, PBC, Boston, MA. http://www.rstudio.com/

Rubio Castañeda, F., & Aznar, T. (2017). Validity, reliability and associated factors of the international physical activity questionnaire adapted to elderly (IPAQ-E). *Revista espanola de salud publica, 91*.

Russell, D. W. (1996). UCLA Loneliness Scale (Version 3): reliability, validity, and factor structure. *J Pers Assess, 66*(1), 20-40. https://doi.org/10.1207/s15327752jpa6601_2

Ryan, R. M., & Frederick, C. (1997). On energy, personality, and health: Subjective vitality as a dynamic reflection of well-being. *Journal of personality, 65*(3), 529-565.

Sala, G., Aksayli, N. D., Tatlidil, K. S., Tatsumi, T., Gondo, Y., Gobet, F., Zwaan, R., & Verkoeijen, P. (2019). Near and Far Transfer in Cognitive Training: A Second-Order Meta-Analysis. *Collabra: Psychology, 5*(1). https://doi.org/10.1525/collabra.203

Salthouse, T. A. (2010). Selective review of cognitive aging. *Journal of the International Neuropsychological Society, 16*(5), 754-760. https://doi.org/10.1017/S1355617710000706

Salthouse, T. A., & Babcock, R. L. (1991). Decomposing adult age differences in working memory. *Developmental Psychology, 27*(5), 763-776. https://doi.org/10.1037/0012-1649.27.5.763

Sandberg, P., Rönnlund, M., Nyberg, L., & Stigsdotter Neely, A. (2014). Executive process training in young and old adults. *Aging, Neuropsychology, and Cognition, 21*(5), 577-605. https://doi.org/10.1080/13825585.2013.839777

Savulich, G., Thorp, E., Piercy, T., Peterson, K. A., Pickard, J. D., & Sahakian, B. J. (2019). Improvements in attention following cognitive training with the novel "decoder" game on an ipad. *Frontiers in Behavioral Neuroscience, 13*. https://doi.org/10.3389/fnbeh.2019.00002

Schafer, J. L. (1999). Multiple imputation: a primer. *Statistical methods in medical research, 8*(1), 3-15.

Scharf, S., Mander, A., Ugoni, A., Vajda, F., & Christophidis, N. (1999). A double-blind, placebo-controlled trial of diclofenac/misoprostol in Alzheimer's disease. *Neurology, 53*(1). https://doi.org/10.1212/WNL.53.1.197

Scharfen, J., Peters, J. M., & Holling, H. (2018). Retest effects in cognitive ability tests: A meta-analysis. *Intelligence, 67*, 44-66. https://doi.org/10.1016/j.intell.2018.01.003

Schwartz, E., & Litwin, H. (2019). The Reciprocal Relationship Between Social Connectedness and Mental Health Among Older European Adults: A SHARE-Based Analysis. *J Gerontol B Psychol Sci Soc Sci, 74*(4), 694-702. https://doi.org/10.1093/geronb/gbx131

Scrucca, L., Fop, M., Murphy, T. B., & Raftery, A. E. (2016). mclust 5: Clustering, Classification and Density Estimation Using Gaussian Finite Mixture Models. *R J, 8*(1), 289-317. https://www.ncbi.nlm.nih.gov/pubmed/27818791

Seeman, T. E., Lusignolo, T. M., Albert, M., & Berkman, L. (2001). Social relationships, social support, and patterns of cognitive aging in healthy, high-functioning older adults: MacArthur studies of successful aging. *Health Psychol, 20*(4), 243-255. https://doi.org/10.1037//0278-6133.20.4.243

Segaert, K., Lucas, S. J. E., Burley, C. V., Segaert, P., Milner, A. E., Ryan, M., & Wheeldon, L. (2018). Higher physical fitness levels are associated with less language decline in healthy ageing. *Scientific Reports, 8*(1). https://doi.org/10.1038/s41598-018-24972-1

Shah, S. G. S., Nogueras, D., van Woerden, H. C., & Kiparoglou, V. (2020). The COVID-19 Pandemic: A Pandemic of Lockdown Loneliness and the Role of Digital Technology. *J Med Internet Res, 22*(11), e22287. https://doi.org/10.2196/22287

Shaw, F. E., Bond, J., Richardson, D. A., Dawson, P., Steen, N., McKeith, I. G., & Kenny, R. A. (2003). Multifactorial intervention after a fall in older people with cognitive impairment and dementia presenting to the accident and emergency department: randomised controlled trial. *BMJ, 326*(73).

Shevlin, M., McBride, O., Murphy, J., Miller, J. G., Hartman, T. K., Levita, L., Mason, L., Martinez, A. P., McKay, R., Stocks, T. V. A., Bennett, K. M., Hyland, P., Karatzias, T., & Bentall, R. P. (2020). Anxiety, depression, traumatic stress and COVID-19-related anxiety in the UK general population during the COVID-19 pandemic. *BJPsych Open, 6*(6), e125. https://doi.org/10.1192/bjo.2020.109

Shimada, H., Makizako, H., Doi, T., Park, H., Tsutsumimoto, K., Verghese, J., & Suzuki, T. (2018). Effects of Combined Physical and Cognitive Exercises on Cognition and Mobility in Patients With Mild Cognitive Impairment: A Randomized Clinical Trial. *Journal of the American Medical Directors Association, 19*(7), 584-591. https://doi.org/10.1016/j.jamda.2017.09.019

Shimada, H., Makizako, H., Doi, T., Yoshida, D., Tsutsumimoto, K., Anan, Y., Uemura, K., Lee, S., Park, H., & Suzuki, T. (2014). A large, cross-sectional observational study of serum BDNF, cognitive function, and mild cognitive impairment in the elderly. *Front Aging Neurosci, 6*, 69. https://doi.org/10.3389/fnagi.2014.00069

Shimada, H., Park, H., Makizako, H., Doi, T., Lee, S., & Suzuki, T. (2014). Depressive symptoms and cognitive performance in older adults. *J Psychiatr Res, 57*, 149-156. https://doi.org/10.1016/j.jpsychires.2014.06.004

Simons, D. J., Boot, W. R., Charness, N., Gathercole, S. E., Chabris, C. F., Hambrick, D. Z., & Stine-Morrow, E. A. (2016). Do "Brain-Training" Programs Work? *Psychol Sci Public Interest, 17*(3), 103-186. https://doi.org/10.1177/1529100616661983

Singh-Manoux, A., Dugravot, A., Brunner, E., Kumari, M., Shipley, M., Elbaz, A., & Kivimaki, M. (2014). Interleukin-6 and C-reactive protein as predictors of cognitive decline in late midlife. *Neurology*. https://doi.org/10.1212/WNL.0000000000000665

Smets, E. M. A., Garssen, B., Bonke, B., & De Haes, J. C. J. M. (1995). The multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. *Journal of Psychosomatic Research, 39*(3), 315-325. https://doi.org/10.1016/0022-3999(94)00125-o

Smith, K. J., Gavey, S., NE, R. I., Kontari, P., & Victor, C. (2020). The association between loneliness, social isolation and inflammation: A systematic review and meta-analysis. *Neurosci Biobehav Rev, 112*, 519-541. https://doi.org/10.1016/j.neubiorev.2020.02.002

Smith, M. L., Steinman, L. E., & Casey, E. A. (2020). Combatting Social Isolation Among Older Adults in a Time of Physical Distancing: The COVID-19 Social Connectivity Paradox. *Front Public Health, 8*, 403. https://doi.org/10.3389/fpubh.2020.00403

Smith-Ray, R. L., Hughes, S. L., Prohaska, T. R., Little, D. M., Jurivich, D. A., & Hedeker, D. (2015). Impact of Cognitive Training on Balance and Gait in Older Adults. *Journals of Gerontology - Series B Psychological Sciences and Social Sciences, 70*(3), 357-366. https://doi.org/10.1093/geronb/gbt097

[Record #997 is using a reference type undefined in this output style.]

Spitzer, R. L., Kroenke, K., Williams, J. B. W., & Löwe, B. (2006). A Brief Measure for Assessing Generalized Anxiety Disorder The GAD-7. *Archives of internal medicine, 166*, 1092-1097. https://jamanetwork.com/
https://jamanetwork.com/journals/jamainternalmedicine/articlepdf/410326/ioi60000.pdf

Spurk, D., Hirschi, A., Wang, M., Valero, D., & Kauffeld, S. (2020). Latent profile analysis: A review and "how to" guide of its application within vocational behavior research. *Journal of vocational behavior, 120*, 103445.

Steptoe, A., Shankar, A., Demakakos, P., & Wardle, J. (2013). Social isolation, loneliness, and all-cause mortality in older men and women. *Proc Natl Acad Sci U S A, 110*(15), 5797-5801. https://doi.org/10.1073/pnas.1219686110

Stern, Y., Gurland, B., Tatemichi, T. K., Tang, M. X., Wilder, D., & Mayeux, R. (1994). Influence of Education and Occupation on the Incidence of Alzheimer's Disease. *JAMA, 271*(13), 1004-1010. https://jamanetwork.com/journals/jama/article-abstract/368856

Sternang, O., Reynolds, C. A., Finkel, D., Ernsth-Bravell, M., Pedersen, N. L., & Dahl Aslan, A. K. (2016). Grip Strength and Cognitive Abilities: Associations in Old Age. *J Gerontol B Psychol Sci Soc Sci, 71*(5), 841-848. https://doi.org/10.1093/geronb/gbv017

Stojanoski, B., Lyons, K. M., Pearce, A. A. A., & Owen, A. M. (2018). Targeted training: Converging evidence against the transferable benefits of online brain training on cognitive function. *Neuropsychologia, 117*, 541-550. https://doi.org/10.1016/j.neuropsychologia.2018.07.013

Sui, X., LaMonte, M. J., Laditka, J. N., Hardin, J. W., Chase, N., Hooker, S. P., & Blair, S. N. (2007). Cardiorespiratory fitness and adiposity as mortality predictors in older adults. *JAMA, 298*(21), 2507-2516. https://doi.org/10.1001/jama.298.21.2507

Sutin, A. R., Terracciano, A., Milaneschi, Y., An, Y., Ferrucci, L., & Zonderman, A. B. (2013). The trajectory of depressive symptoms across the adult life span. *JAMA psychiatry, 70*(8), 803-811.

Sutton, E., Catling, J., Segaert, K., & Veldhuijzen van Zanten, J. (2022). Cognitive Health Worries, Reduced Physical Activity and Fewer Social Interactions Negatively Impact Psychological Wellbeing in Older Adults During the COVID-19 Pandemic. *Front Psychol, 13*, 823089. https://doi.org/10.3389/fpsyg.2022.823089

Svennerholm, L., Bostrom, K., & Jungbjer, B. (1997). Changes in weight and compositions of major membrane components of human brain during the span of adult human life of Swedes. *Acta Neuropathol, 94*(4), 345-352. https://doi.org/10.1007/s004010050717

Syddall, H., Cooper, C., Martin, F., Briggs, R., & Aihie Sayer, A. (2003). Is grip strength a useful single marker of frailty? *Age Ageing, 32*(6), 650-656. https://doi.org/10.1093/ageing/afg111

Szekely, C. A., Breitner, J. C. S., Fitzpatrick, A. L., Rea, T. D., Psaty, B. M., Kuller, L. H., & Zandi, P. P. (2008). NSAID use and dementia risk in the Cardiovascular Health Study: Role of APOE and NSAID type. *Neurology, 70*(1), 17-24. https://doi.org/10.1212/01.wnl.0000284596.95156.48

Tein, J. Y., Coxe, S., & Cham, H. (2013). Statistical Power to Detect the Correct Number of Classes in Latent Profile Analysis. *Struct Equ Modeling, 20*(4), 640-657. https://doi.org/10.1080/10705511.2013.824781

Terhune, D. B. (2015). Discrete response patterns in the upper range of hypnotic suggestibility: A latent profile analysis. *Conscious Cogn, 33*, 334-341. https://doi.org/10.1016/j.concog.2015.01.018

Thomeer, M. B., Moody, M. D., & Yahirun, J. (2023). Racial and Ethnic Disparities in Mental Health and Mental Health Care During The COVID-19 Pandemic. *J Racial Ethn Health Disparities, 10*(2), 961-976. https://doi.org/10.1007/s40615-022-01284-9

Tinetti, M. E., Franklin Williams, T., Mayewski, R., & York, N. (1986). Fall Risk Index for Elderly Patients Based on Number of Chronic Disabilities. *The American Journal of Medicine, 80*(3), 429-434. https://www.amjmed.com/article/0002-9343(86)90717-5/pdf

Trabelsi, K., Ammar, A., Masmoudi, L., Boukhris, O., Chtourou, H., Bouaziz, B., Brach, M., Bentlage, E., How, D., Ahmed, M., Mueller, P., Mueller, N., Hsouna, H., Elghoul, Y., Romdhani, M., Hammouda, O., Paineiras-Domingos, L. L., Braakman-Jansen, A., Wrede, C., Bastoni, S., Pernambuco, C. S., Mataruna-Dos-Santos, L. J., Taheri, M., Irandoust, K., Bragazzi, N. L., Strahler, J., Washif, J. A., Andreeva, A., Bailey, S. J., Acton, J., Mitchell, E., Bott, N. T., Gargouri, F., Chaari, L., Batatia, H., Khoshnami, S. C., Samara, E., Zisi, V., Sankar, P., Ahmed, W. N., Ali, G. M., Abdelkarim, O., Jarraya, M., Abed, K. E., Moalla, W., Souissi, N., Aloui, A., Souissi, N., Gemert-Pijnen, L. V., Riemann, B. L., Riemann, L., Delhey, J., Gomez-Raja, J., Epstein, M., Sanderman, R., Schulz, S., Jerg, A., Al-Horani, R., Mansi, T., Dergaa, I., Jmail, M., Barbosa, F., Ferreira-Santos, F., Simunic, B., Pisot, R., Pisot, S., Gaggioli, A., Steinacker, J., Zmijewski, P., Apfelbacher, C., Glenn, J. M., Khacharem, A., Clark, C. C. T., Saad, H. B., Chamari, K., Driss, T., Hoekelmann, A., & On Behalf Of The Eclb-Covid, C. (2021). Sleep Quality and Physical Activity as Predictors of Mental Wellbeing Variance in Older Adults during COVID-19 Lockdown: ECLB COVID-19 International Online Survey. *Int J Environ Res Public Health, 18*(8). https://doi.org/10.3390/ijerph18084329

Ullrich-French, S., & Cox, A. E. (2020). The use of latent profiles to explore the multi-dimensionality of self-compassion. *Mindfulness, 11*, 1483-1499.

Urtasun, M., Daray, F. M., Teti, G. L., Coppolillo, F., Herlax, G., Saba, G., Rubinstein, A., Araya, R., & Irazola, V. (2019). Validation and calibration of the patient health questionnaire (PHQ-9) in Argentina. *BMC Psychiatry, 19*(1), 291. https://doi.org/10.1186/s12888-019-2262-9

Valenzuela, M. J., & Sachdev, P. (2006). Brain reserve and dementia: a systematic review. *Psychol Med, 36*(4), 441-454. https://doi.org/10.1017/S0033291705006264

van Muijden, J., Band, G. P. H., & Hommel, B. (2012). Online Games Training Aging Brains: Limited transfer to cognitive control functions. *Frontiers in Human Neuroscience*(JULY). https://doi.org/10.3389/fnhum.2012.00221

Vink, D., Aartsen, M. J., & Schoevers, R. A. (2008). Risk factors for anxiety and depression in the elderly: A review. *Journal of Affective Disorders, 106*(1-2), 29-44. https://doi.org/10.1016/j.jad.2007.06.005

Visser, M., Pluijm, S. M., Stel, V. S., Bosscher, R. J., & Deeg, D. J. (2002). Physical activity as a determinant of change in mobility performance: the Longitudinal Aging Study Amsterdam. *Journal of the American Geriatrics Society, 50*(11), 1774-1781.

von Bastian, C. C., & Oberauer, K. (2014). Effects and mechanisms of working memory training: a review. *Psychological Research, 78*(6), 803-820. https://doi.org/10.1007/s00426-013-0524-6

Walsh, E. I., Smith, L., Northey, J., Rattray, B., & Cherbuin, N. (2020). Towards an understanding of the physical activity-BDNF-cognition triumvirate: A review of associations and dosage. *Ageing Res Rev, 60*, 101044. https://doi.org/10.1016/j.arr.2020.101044

Wannheden, C., Roczniewska, M., Hasson, H., Karlgren, K., & von Thiele Schwarz, U. (2022). Better self-care through co-care? A latent profile analysis of primary care patients' experiences of e-health–supported chronic care management. *Frontiers in Public Health*, 3310.

Wei, J., Xu, H., Davies, J. L., & Hemmings, G. P. (1992). Increase of plasma IL-6 concentration with age in healthy subjects. *Life Sci, 51*(25), 1953-1956. https://doi.org/10.1016/0024-3205(92)90112-3

Weller, B. E., Bowen, N. K., & Faubert, S. J. (2020). Latent Class Analysis: A Guide to Best Practice. *Journal of Black Psychology, 46*(4), 287-311. https://doi.org/10.1177/0095798420930932

WHO. (2012). *The World Health Organization Quality of Life (WHOQOL)*. https://www.who.int/publications/i/item/WHO-HIS-HSI-Rev.2012.03

Wickham, H., François, R., Henry, L., Müller, K., & Vaughan, D. (2023). *dplyr: A Grammar of Data Manipulation.* https://dplyr.tidyverse.org, https://github.com/tidyverse/dplyr

Willis, S. L., Tennstedt, S. L., Marsiske, M., Ball, K., Elias, J., Mann Koepke, K., Morris, J. N., Rebok, G. W., Unverzagt, F. W., Stoddard, A. M., & Wright, E. (2006). Long-term Effects of Cognitive Training on Everyday Functional Outcomes in Older Adults. *JAMA, 296*(23), 2805-2814. https://jamanetwork.com/ https://jamanetwork.com/journals/jama/articlepdf/204643/joc60167_2805_2814.pdf

Wilson, R. S., Barnes, L. L., Aggarwal, N. T., Boyle, P. A., Hebert, L. E., Mendes De Leon, C. F., & Evans, D. A. (2010). *Cognitive activity and the cognitive morbidity of Alzheimer disease*. www.neurology.org

Wilson, R. S., Krueger, K. R., Arnold, S. E., Schneider, J. A., Kelly, J. F., Barnes, L. L., Tang, Y., & Bennett, D. A. (2007). Loneliness and risk of Alzheimer disease. *Arch Gen Psychiatry, 64*(2), 234-240. https://doi.org/10.1001/archpsyc.64.2.234

Wilson, R. S., Scherr, P. A., Schneider, J. A., Tang, Y., & Bennett, D. A. (2007). Relation of cognitive activity to risk of developing Alzheimer disease. *Neurology, 69*(20), 1911-1920. https://doi.org/10.1212/01.wnl.0000271087.67782.cb

Wittenberg, R., Hu, B., Barraza-Araiza, L., & Rehill, A. (2019). Projections of older people with dementia and costs of dementia care in the United Kingdom, 2019–2040. *Care Policy and Evaluation Centre, London School of Economics and Political Sciences (https://www. alzheimers. org. uk/sites/default/files/2019-11/cpec_report_november_2019. pdf)*.

Woods, J. A., Wilund, K. R., Martin, S. A., & Kistler, B. M. (2012). Exercise, Inflammation and Aging. *Aging and disease, 3*(1), 130-140. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3320801/pdf/ad-3-1-130.pdf

Wright, L. J., Williams, S. E., & Veldhuijzen van Zanten, J. (2021). Physical Activity Protects Against the Negative Impact of Coronavirus Fear on Adolescent Mental Health and Well-Being During the COVID-19 Pandemic. *Front Psychol, 12*, 580511. https://doi.org/10.3389/fpsyg.2021.580511

Yaffe, K., Lindquist, K., Penninx, Simonsick, E. M., Pahor, M., Kritchevsky, S., Launer, L., Kuller, L., Rubin, S., & Harris, T. (2003). Inflammatory markers and cognition in well-functioning African-American and white elders. *Neurology*. https://doi.org/10.1212/01.WNL.0000073620.42047.D7

Yu, B., Steptoe, A., Chen, Y., & Jia, X. (2021). Social isolation, rather than loneliness, is associated with cognitive decline in older adults: the China Health and Retirement Longitudinal Study. *Psychol Med*, 1-8. https://doi.org/10.1017/S0033291720001026

Zaninotto, P., Iob, E., Demakakos, P., & Steptoe, A. (2022). Immediate and longer-term changes in the mental health and well-being of older adults in England during the COVID-19 pandemic. *JAMA psychiatry, 79*(2), 151-159.

APPENDICES

Appendix 1. Variance and Covariance matrix for LPA models 1, 2, 3, and 6, with corresponding Mclust model name.

	Variances	**Covariances**	**Mclust model**
Model 1	Equal	Zero	EEI
Model 2	Varying	Zero	VVI
Model 3	Equal	Equal	EEE
Model 6	Varying	Varying	VVV

Appendix 2. Full fit indices for models 1, 2, 3, and 6. Note that models 2 and 6 failed to converge so values for 2-4 profiles are not included

Model	No. of profiles	AIC	BIC	SABIC	Entropy	prob_min	prob_max	n_min	BLRT_p
1	1	2810.92	2859.36	2802.48	1.00	1.00	1.00	1.00	-
1	2	2763.89	2839.25	2750.77	0.72	0.88	0.95	0.40	0.01
1	**3**	**2709.79**	**2812.06**	**2691.99**	**0.81**	**0.85**	**0.97**	**0.20**	**0.01**
1	4	2715.23	2844.41	2692.74	0.82	0.85	0.95	0.12	0.57
2	1	2810.92	2859.36	2802.48	1.00	1.00	1.00	1.00	-
2	2								
2	3								
2	4								
3	1	2717.21	2862.55	2691.91	1.00	1.00	1.00	1.00	-
3	2	2706.91	2879.16	2676.93	0.89	0.97	0.97	0.25	0.01
3	3	2652.54	2851.70	2617.87	0.94	0.94	0.98	0.18	0.01
3	4	2650.15	2876.22	2610.79	0.93	0.93	0.99	0.05	0.13
6	1	2717.21	2862.55	2691.91	1.00	1.00	1.00	1.00	-
6	2								
6	3								
6	4								