Trajectories of social relationships and cognitive decline: losing and gaining in late life

Jing Liao

Thesis submitted for the degree of Doctor of Philosophy University College London

Department of Epidemiology and Public Health
University College London

September 2015

Declaration of originality

I, Jing Liao, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Abstract

Background: The extent to which social relationships influence cognitive ageing is unclear. Inconclusive evidence on the neuro-protective effect of social relationships may arise from various social relationship measures and reverse causation.

Aim: This thesis systematically investigates the longitudinal dynamic associations between social relationships from middle to early old age and cognitive ageing.

Methods and results: Analyses were based on repeat measures of functional and structural aspects of social relationships and cognition (i.e. executive function and memory) from the Whitehall II prospective cohort, providing 10-year follow-up of 6,867 participants in the age range from 45 to 80 years. A set of growth curve models was applied sequentially. Results derived from *multilevel models* showed midlife negative but not positive aspects of close relationships were associated with accelerated declines in executive function. A large friend network was associated with better concurrent executive function only. *Growth mixture models* uncovered three latent classes of social relationships with divergent longitudinal changing patterns from middle to early old age, where participants identified as consistently perceiving extremely-high levels of confiding support over years experienced the least decline in memory. Last, findings obtained from *dual change score models* revealed that a greater cognitive function at the preceding stage was related to less positive changes in confiding support and less negative changes in practical support; whereas there was no detectable influence the other way around.

Conclusions: The effect of social relationships on declines in cognition from middle to early old age is not substantial in this British civil servant cohort. On the other hand, cognitive ability appears to modify subsequent changes in support from close relationships. This study contributes to the understanding of the dynamic interplay between social relationships and cognitive decline in late life, and highlights the importance of including multiple repeat measures to better understand ageing.

Acknowledgements

I would like to thank my supervisors, Eric Brunner, Jenny Head and Graciela Muniz Terrera. I highly appreciate their professional ways of supervision. This project would not have been possible without their constant encouragement and invaluable advice.

I also would like to thank members of the Whitehall II team, particularly Meena Kumari, Steven Bell, Séverine Sabia, Martin Shipley, Aida Sanchez, David Batty, Archana Singh-Manoux and Mika Kivimaki, for their assistance and suggestion. Special thanks also go to Stephen Stansfeld who shared his expertise on social relationships. I am grateful to Anne McMunn, David Blane, Hynek Pikhart, Mai Stafford, Dorina Cadar, Shaun Scholes, Loretta Grace Platts and Owen Nicholas for their advice. Many thanks go to Angela Cooper for proofreading this thesis.

My acknowledgement and gratitude also extend to my PhD colleagues, friends and family. Their support has endowed me with the power and courage to carry on. Finally, I would like to acknowledge the support of the Guangzhou government for funding my PhD studentship.

Table of Contents

List of figures

List of tables

List of abbreviations

AIC: Akaike's information criterion

BIC: Bayesian information criterion

BLRT: bootstrap likelihood ratio test

CFI: comparative fit index

CI: confidence interval

CPQ: Close Persons Questionnaire

DCSM: dual change score model

ELSA: English Longitudinal Study of Ageing

FIML: Full information maximum likelihood

GMM: growth mixture model

ICC: intraclass correlation

LASA: Longitudinal Ageing Study of Amsterdam

LGCA: latent growth curve analysis

LMR-LRT: Lo-Mendell-Rubin adjusted likelihood ratio test

MAR: missing at random

MCAR: missing complete at random

MLM: multilevel models

MLR: maximum likelihood robust

MMSE: Mini-Mental State Examination

MNAR: missing not at random

PLCM: parallel latent curves model

RMSEA: root mean square error of approximation

SD: standard deviation

SE: standard error

TFI: Tucker-Lewis Index

Chapter 1. Introduction

Summary

This chapter sets the thesis in the context of population ageing and the growing pursuit for high quality of life in old age. In order to prevent the daunting consequences associated with cognitive decline, the hypothesized neuro-protective effect of social relationships needs to be further examined. The approach which this thesis took to assess the longitudinal dynamic association between social relationships and cognitive decline in late life is introduced, followed by the structure of the thesis.

The expanding proportion of older people ensures cognitive maintenance will continue to be one of the major public health priorities. Preceding the diagnosis of dementia up to 10-12 years (Elias *et al.*, 2000; Amieva *et al.*, 2008), age-related cognitive decline may offer a prodromal stage where interventions could be targeted before changes are irreversible. Social relationships have been proposed as cognitively protective in old age. However, current best evidence for this proposition is contradictory. This may be largely attributed to different aspects of social relationships assessed, as well as a static and unidirectional influence from social relationships to cognitive decline presumed by most previous studies. Progress in understanding the significance of social relationships for cognitive ageing requires a study design that captures the dynamic and potential bidirectional association between social relationships and cognitive decline across time. The present thesis addressed these gaps in the literature sequentially by using the Whitehall II prospective cohorts.

1.1 Background

The world is ageing at an unprecedented rate. The global population aged 60 and over is projected to triple to two billion by 2050 (United Nations Population Division, 2013). Coupled with this, falls in fertility rate have unbalanced old-age dependency ratios (Herlofson and Hagestad, 2011; Rechel *et al.*, 2013), profoundly affecting individuals (Murphy *et al.*, 2006) and society at large (Trippel *et al.*, 2011). In the endeavour to enhance quality of life in old age (Hyde *et al.*, 2003; Bowling and Dieppe, 2005), burgeoning researches have been investigating how to maximize the lifespan of effective functioning and compress the length of time with inexorable functional limitations (Fries, 1983, 2005).

Maintenance of cognitive function has been proposed as one the crucial components of successful ageing (Rowe and Kahn, 1997; Depp and Jeste, 2006; Fiocco and Yaffe, 2010).

Age-related cognitive decline is positively related with impaired daily activities (Scanlan *et al.*, 2007), chances of falls and institutionalization (Deary *et al.*, 2009; Beswick *et al.*, 2010; Gilmour, 2011), and mortality (van Gelder *et al.*, 2007; Sabia *et al.*, 2010). Furthermore, cognitive decline predicts the development of dementia (Small and Bäckman, 2007; Almkvist and Tallberg, 2009), which imposes an undue burden on healthcare systems and social resources worldwide (Brookmeyer *et al.*, 2007; Prince *et al.*, 2013a; Alzheimer's Association, 2015).

Among modifiable factors for cognitive ageing (Plassman *et al.*, 2010) and dementia (Alzheimer's Association, 2013), the potential neuro-protective effect of social relationships has been suggested. Social relationships have long been recognized as important determinants of health (Berkman *et al.*, 2000; Cohen, 2004; Uchino, 2006). Salutary effects supported by population-scale evidence include greater resistance to respiratory infections (Cohen *et al.*, 1997), better self-reported health (Heritage *et al.*, 2008; Kumar *et al.*, 2012), quality of life (Wiggins *et al.*, 2004; Shankar *et al.*, 2014), mental (Kawachi and Berkman, 2001; Stafford *et al.*, 2011; Sonnenberg *et al.*, 2013) and physical health (Lachman and Agrigoroaei, 2010), as well as lower risk of coronary heart disease (Hemingway and Marmot, 1999; De Vogli *et al.*, 2007) and mortality (Berkman *et al.*, 2004; Holt-Lunstad *et al.*, 2010; Pinquart and Duberstein, 2010; Stringhini *et al.*, 2011; Steptoe *et al.*, 2013). Notably, the effect size of social relationships on mortality in old age is comparable with many well-established mortality risk factors (Holt-Lunstad *et al.*, 2010). The importance of social relationships for health and wellbeing becomes particularly prominent as populations age, not least when older people encounter disruptions in their social networks (Rook, 2009) and gradually compromised physical and mental functioning (Broese van Groenou *et al.*, 2013).

As yet, current evidence on social relationships and cognitive ageing is mixed. Inconsistent findings depend on the characteristic of social relationships under consideration. As previous studies have measured social relationships differently and examined these measures in isolation, it remains unclear which aspects of social relationships can independently contribute to cognitive maintenance. Further, although both social relationships and cognitive function are likely to change over time with marked intra-individual variations, most studies have treated social relationships as static and only a few have investigated the longitudinal changing patterns of social relationships in relation to cognitive decline. Evidence thus is lacking about the extent to which divergent social ageing patterns may project onto different courses of cognitive decline. This gap in the literature also leads to the unestablished temporal order between changes in social relationships and changes in cognitive function. Consequently, the proposed neuro-protective effect of social relationships may be a product of reverse causation (Stoykova et al., 2011), insofar as the *social relationships* - *cognitive ageing* associations are driven more by cognitive decline than by the lack or deterioration of social relationships.

Therefore, this thesis aims to investigate the longitudinal dynamic association of social relationships and cognitive decline in late life. This work advances the understanding of the extent to which social relationships can explain the heterogeneity in age-related cognitive decline, taking into account the longitudinal changing nature of both variables as suggested by the life course perspective (Kuh *et al.*, 2012). Moreover, the potential bidirectional association of social relationships and cognitive decline is rigorously investigated, testing the possibility of both *social causation* and *health selection* processes. This work provides empirical evidence to better understand the relations between psychosocial protective factors and the development of dementia, which ultimately may contribute to policies and interventions for improving the quality of life of our ageing population.

1.2 Approach taken in this thesis

To examine the dynamics between social relationships and cognitive decline, this thesis focuses on individual's perception of social relationships. Specifically, the *structure* and the *function* of social relationships (House, 1987) are examined. These measures, assessing interpersonal relationships at individual level, differ from *social cohesion* that considers collective dimensions of the society (Kawachi and Berkman, 2000). They are also different from *social activity participation* outside one's personal network, such as volunteering, church membership etc., which is a self-selective process highly dependent upon individual's cognitive and physical competence (Gallacher *et al.*, 2005; Gow *et al.*, 2012; Small *et al.*, 2012).

As the main research interest is to study longitudinal trajectories of cognitive ageing, cognitive measures at multiple occasions rather than incident dementia are used. The Whitehall II prospective cohort is suitable for the current study, providing a large dataset with repeat measures of social relationships and cognitive function from middle to old age. Specifically, the three repeat cognitive assessments over 10 years cover a wide age range from 45 to 80 years with up to a 22-year difference in birth year (i.e. 1930 - 1952), allowing within-person age-related rate of cognitive decline and between-person birth cohort effects to be estimated simultaneously.

A set of longitudinal growth models is applied in sequence (McArdle and Grimm, 2010): *multilevel models* (MLM) are used to assess which component of social relationships at middle age affects the rate of subsequent cognitive decline; *growth mixture models* (GMM) are adopted to uncover longitudinal latent classes of social relationships, and the degree to which participants belonging to these divergent changing classes would differ in their cognitive ageing profile; *dual change score models* (DCSM) are employed to investigate the directional dynamics between social relationships and cognitive function over the late adulthood.

1.3 The structure of the thesis

Chapter 2 starts with the conceptual framework of social relationships and cognitive function, highlighting the multifaceted and dynamic nature of ageing. This chapter then systematically reviews evidence of social relationships and cognitive ageing based on recent longitudinal studies. Through critically appraising studies reviewed, gaps in literature are identified that lead to the aim and objectives of this thesis as presented in Chapter 3. Chapter 4 describes the Whitehall II dataset from which the variables used in this thesis were drawn. The next three chapters address the objectives stepwise: Chapter 5 assesses the impact of midlife social relationships on subsequent cognitive decline; Chapter 6 investigates how different longitudinal changing patterns of social relationships are associated with cognitive ageing trajectories; Chapter 7 evaluates the temporal directions of the dynamic association between functional aspects of social relationships and cognitive function. Last, Chapter 8 draws the thesis together, with a summary of the main findings, as well as a discussion of the relevance and implication of this thesis.

Chapter 2. Literature review

Summary

This chapter reviews the theoretical background of the thesis. The conceptual frameworks of social relationships and cognitive function are outlined, with an emphasis on the life course perspective of both concepts, especially in the period of late life. Two alternative theories, namely, *social causation* and *health selection,* are applied to understand the dynamics between social relationships and cognitive decline as people age. The following section scrutinizes evidence from longitudinal studies using a systematic review approach. The gaps in literature are then discussed.

2.1 Social relationships

2.1.1 Concepts

Since the link between social relationships and disease risk was proposed by Cassel (1976) and Cobb (1976), many theories have been developed to understand the nature of such health benefits (Berkman *et al.*, 2000). The wealth of literature, however, has not rendered a clear definition of social relationships (Gottlieb and Bergen, 2010). Six relevant concepts mainly addressed in the social relationship literature are summarized as the table below.

Table 2-1 Social Relationships Related Concepts and Definitions.

Concepts	Definitions
Social Network	The web of social ties surrounds an individual, featuring the structure of social relationships (Berkman *et al.*, 2000).
Social Support	Social resources that persons perceive to be available or that are actually provided to them by their social relationships (Cohen *et al.*, 2001).
Perceived Support	A person's history of receiving effective support, involving cognitive appraisal of being reliably connected to others (Barrera, 1986).
Enacted Support	The actions actually taken place when the focal person is in need (Barrera, 1986).
Social Integration	The existence of social relationships (House *et al.*, 1988b), representing the extent to which an individual embeds in informal (e.g. marital status) and formal social interactions (e.g. community involvement) (Gottlieb and Bergen, 2010), with *social isolation* pointing to its flip side (Barrera, 1986).
Social Cohesion	Collective features of society 1) the absence of social conflicts; and 2) the presence of strong social bonds. *Social capital* is a subset of social cohesion, indicating levels of trust and norms of reciprocity (Kawachi and Berkman, 2000).

In view of the multi-dimensional nature of social relationships and wide range of research contexts, it is problematic to reach consensus on a unitary definition (Barrera, 1986). Emphasis thus shifted to the elements required in constructing social relationships at both theoretical and operational levels (Undén and Orth-Gomér, 1989). By and large, two components are fundamental in defining social relationships, namely, *structure* and *function* (Orth-Gomér and Undén, 1987; House *et al.*, 1988b).

Structural aspects of social relationships

The structure of social relationships is also referred to as *social network*, representing "a specific set of linkages among defined persons" (Mitchell, 1974). An individual's social ties can be placed hierarchically into a series of concentric circles, with distance to the core reflecting relative importance and emotional closeness (Kahn and Antonucci, 1980). Evidence suggests that intimate contacts tend to provide more meaningful support than casual acquaintances (Berkman and Syme, 1979; Gottlieb and Bergen, 2010). Therefore, quantitative characteristics of network composition, size, density, durability, strength and homogeneity could imply the quality of social relationships (Stokes, 1985).

Nevertheless, structural aspects of social relationships are only moderately correlated with support provision (Cohen and Wills, 1985). Whether anticipated support will transfer into enacted supportive behaviour depends upon individual coping strategies and specific circumstances (Schaefer *et al.*, 1981). Moreover, comprised of voluntary and non-voluntary ties (Seeman and Berkman, 1988), positive associations between social network and wellbeing may only show if supportive behaviours are perceived by the individual in question (Rook, 1984; Pinquart and Sörensen, 2000; Kawachi and Berkman, 2001).

Functional aspects of social relationships

The function of social relationships indicates different types of support transacted via interpersonal networks (Gottlieb and Bergen, 2010), and directly evaluates supportive role fulfilment (Cohen *et al.*, 2001). The most cited functions were conceptualized by House (1981), containing emotional, instrumental, informational and appraisal support. *Emotional support* includes provision of trust, reassurance and empathy. *Instrumental support* involves tangible aid and helping behaviours. *Informational support* represents advice and guidance; and *appraisal support* is related to help in decision making and evaluative feedback. These four types of support can be regrouped into ‘emotional’ and ‘practical’, with informational and appraisal support allied to the emotional category (Stansfeld *et al.*, 2006; Gottlieb and Bergen, 2010).

In contrast to these positive functions, negative aspects of social relationships should also be considered (Rook, 1998; Umberson and Montez, 2010; Tun *et al.*, 2012). Well-intentioned support may elicit unpleasant encounters if the recipient finds support is ineffective, unsuitable, intrusive or over-controlling (Rook, 1984). Negative aspects of social relationships not only affect daily mood (Rook, 2001), create feelings of dependency and incompetency (Silverstein *et al.*, 1996; Gleason *et al.*, 2008), but also could adversely influence physical and mental wellbeing (Stansfeld *et al.*, 1998b; Krause and Shaw, 2002; De Vogli *et al.*, 2007), with more potent and longer-lasting effects than positive support (Rook, 1998, 2001; Newsom *et al.*, 2003; Newsom *et al.*, 2005).

2.1.2 Determinants of social relationships

Enveloped within the social fabric, individual experience of social relationships is demographically and socioeconomically patterned (House *et al.*, 1988b; Umberson and Montez, 2010). Personality influences individual competence to establish and maintain relationships (Undén and Orth-Gomér, 1989; Langford *et al.*, 1997), as well as the amount of support required and perceived (Lakey and Cassady, 1990; Stansfeld and Marmot, 1992; Gleason *et al.*, 2008). Women tend to have extensive social networks, providing and receiving support from multiple sources (Berkman and Syme, 1979; Fuhrer and Stansfeld, 2002; van Tilburg and Broese van Groenou, 2002); whereas men maintain close relations with fewer people, primarily their spouse (Fuhrer *et al.*, 1999; Fuhrer and Stansfeld, 2002), thereby drawing most support from these intimate ties (House, 1987; Gurung *et al.*, 2003). High socioeconomic positions confer greater mobility and opportunity for individuals to form diverse social ties beyond their immediate kin (Broese van Groenou and van Tilburg, 2003; Ajrouch *et al.*, 2005; Pahl and Pevalin, 2005; Stansfeld, 2006).

2.1.3 Social relationship transitions from middle to old age

Social relationships change as people age (Wrzus *et al.*, 2013). The succession of social roles over the life course is accompanied by changes in social relationships, which in turn shape resources accessible (Binstock and George, 2011). In later life, social resources may signal how well older people adapt to the challenges of ageing (Rowe and Kahn, 1997). Age-specific life events such as retirement, bereavement and increasing functional limitations constrain older people's social network and may make them vulnerable to losses of social relationships (Langford *et al.*, 1997; Pahl and Pevalin, 2005; Steverink and Lindenberg, 2006; Charles and Carstensen, 2010).

Nonetheless, losses may coincide with gains. Widowhood or poor health may mobilize support and consolidate social network (Bowling and Browne, 1991; Grundy and Farquhar, 1995; van Tilburg and Broese van Groenou, 2002; Zettel and Rook, 2004; McLaughlin *et al.*, 2010). Furthermore, as fewer obligations are bonded in the Third Age (Laslett, 1991), older people can enjoy more freedom to pursue personal fulfilment (van Tilburg, 1998; Higgs *et al.*, 2003). National representative surveys reveal that social networks of older people are not necessarily constricted by age: via frequent socialization with neighbours, religious groups and volunteering, older people expand their social connectedness (Cornwell *et al.*, 2008), prosper in civil engagement and family solidarity (Kohli *et al.*, 2009), and also experience an improved quality of social relationships (Marmot *et al.*, 2003).

Several theoretical frameworks have been constructed to understand social relationships in late life (Gurung *et al.*, 2003), of which the *social convoy model* and the *socio-emotional selectivity theory* underscore life course perspectives. The *social convoy model* describes how a collection of social relationships, strengthened via exchanges of support, travels with individuals over time and adapts to changing personal and situational characteristics (Kahn and Antonucci, 1980; Antonucci *et al.*, 2011). Similarly, the *socioemotional selectivity theory* posits that, as the perception of limited future time increases, individuals orient their social goals towards attending to emotionally rewarding close relationships and proactively winnow peripheral social ties (Carstensen *et al.*, 2003; Carstensen, 2006). Together, these perspectives suggest that through careful attention to and selection of close relationships, despite inevitable network changes with age, older people with resources to optimize relationships are able to maintain or even improve the quality of their social relationships (Lang, 2001; Lang *et al.*, 2002; Gurung *et al.*, 2003). Age-related changes in social relationships hence should be viewed as the shifting of social interactions rather than a sheer loss of social connections.

A growing body of longitudinal studies corroborate these theories, showing small yet significant increases in emotional support and practical support with age (van Tilburg, 1998; Martire *et al.*, 1999; van Tilburg and Broese van Groenou, 2002; Gurung *et al.*, 2003), and relatively stable or decreased longitudinal changing patterns of negative social exchanges (Krause and Rook, 2003; Boerner *et al.*, 2004; Shaw *et al.*, 2007; Birditt *et al.*, 2009). However, selective maintenance of an inner circle of social relationships due to proactive planning (Carstensen *et al.*, 2003) or passive response to health conditions (Broese van Groenou *et al.*, 2013) may lead to deficiencies in support resources (Rook, 2009; Shouse *et al.*, 2013). Maintaining diverse and high-quality social relationships may be more beneficial for healthy ageing (Barefoot *et al.*, 2005; Layte *et al.*, 2013; Li and Zhang, 2015).

After all, theories and findings above may only apply to some but not all older people (Krause, 1999). Substantial heterogeneity in the study participants' social ageing profiles has been consistently reported (Martire *et al.*, 1999; van Tilburg and Broese van Groenou, 2002; Mavandadi *et al.*, 2007; Shaw *et al.*, 2007). Therefore, a person-centred life course approach should be considered to describe the ebbs and flows of social relationships in late life (Lang *et al.*, 2009; Antonucci *et al.*, 2013).

2.2 Cognitive function

2.2.1 Cognitive function and cognitive decline

Cognitive function refers to the faculty of information processing, comprising two major domains: *fluid* and *crystalized* cognition (Horn and Cattell, 1967). *Fluid cognition,* basic information processing ability, includes reasoning, abstracting, spatial ability, processing speed and working memory. Representing the ability to apply knowledge flexibly and adaptively, fluid cognition is best tested by novel and culture-reduced measures under time pressure. *Crystallized cognition*, the stored knowledge accumulated over time, embodies vocabulary, arithmetic and general knowledge. As a product of experience, crystallized cognition integrates society and culture; hence, it is best captured by knowledge-based tests (Deary and Batty, 2007).

Cognitive function changes over the lifespan: rapid development in childhood, relative stabilization during mid-life, followed by perceptible declines in old age (Craik and Bialystok, 2006). The absolute level of cognitive function in old age relies on both the peak level of accumulation and the rate of decline. *Cognitive decline* can be viewed as a continuum of cognitive changes (Brayne and Calloway, 1988), from within the spectrum of normal ageing to exceeding the boundary into *mild cognitive impairment* (Petersen *et al.*, 2001) and further progressing to *dementia* (DSM-5, 2013). Although people with increased age are more prone to pathological cognitive impairment (Salthouse, 1991), there is no clear indication to distinguish between normal and pathological cognitive decline (Brayne, 2007; Deary *et al.*, 2009; Plassman *et al.*, 2010). Consensus is also lacking as regards when cognitive ageing starts (Salthouse, 2009), with some evidence suggesting a decline can be detected as early as middle age (e.g. 45-49 years) (Singh-Manoux *et al.*, 2012).

Cognitive decline is characterized as *function-selective* and *individual-specific* (Salthouse, 2010b). As a function-selective process (Rabbitt, 1993), fluid cognition is more susceptible to age-related decline, whereas crystallized cognition is relatively robust (Hedden and Gabrieli, 2004; Craik and Bialystok, 2006). Evident declines in crystallized cognition may only be identified in advanced stages of dementia (Richards and Deary, 2005). Given this domain-selective vulnerability, fluid cognition is better suited to study age-related cognitive decline (Royall *et al.*, 2005; Salthouse, 2009). Of equal importance, the heterogeneity in individual rate of cognitive decline has been widely recognized (Christensen, 2001; Wilson *et al.*, 2002; Small and Bäckman, 2007; Terrera *et al.*, 2010; Hayden *et al.*, 2011). The reason why some adults can maintain sharp cognition till old age while others cannot may partially be ascribed to variations in genetics, health conditions, environmental stimulations and lifestyle behaviours (Plassman *et al.*, 2010; Daviglus *et al.*, 2011; Alzheimer's Association, 2013). APOE ε 4 and other risk genes may increase the risk of developing Alzheimer's disease, but their overall influence in the population is limited (Ballard *et al.*, 2011), let alone the complex gene-environment interaction (Dickens and Flynn, 2001; Kramer *et al.*, 2004). The following section focuses on modifiable risk factors for cognitive ageing.

2.2.2 Modifiable risk factors for cognitive decline

Before commenting on individual risk factors, it should be noted that hitherto there is no definitive conclusion that can be drawn on the association of any modifiable factors and cognitive decline (Plassman *et al.*, 2010; Daviglus *et al.*, 2011). Observational and interventional research activity in this field is developing rapidly (Institute of Medicine, 2015). Given multiple risk factors may act in combination over the life course (Richards and Deary, 2005; Whalley *et al.*, 2006; Richards and Hatch, 2011), current opinion favours that a physically and mentally active, healthy lifestyle may be cognitively beneficial and potentially delay the onset of dementia (Pope *et al.*, 2003; Barnes and Yaffe, 2011).

Health status can directly influence cognition, or accelerate the cognitive ageing process (Salthouse, 1991; Piccinin *et al.*, 2011). Cardiovascular disease (Singh-Manoux *et al.*, 2008; Savva and Stephan, 2010) and its risk factors (Knopman *et al.*, 2001; Kaffashian *et al.*, 2011; Dregan *et al.*, 2012) have been associated with faster declines in cognition. In particular, diabetes mellitus (Yaffe *et al.*, 2004a; Kumari and Marmot, 2005; Tuligenga *et al.*, 2014), hypertension (Qiu *et al.*, 2005; Singh-Manoux and Marmot, 2005; Knecht *et al.*, 2008) and metabolic syndrome (Yaffe *et al.*, 2004b; Singh-Manoux *et al.*, 2014) may erode cognitive function as early as middle age (Knopman *et al.*, 2001; Debette *et al.*, 2011; Dregan *et al.*, 2012). Depression has been related to increased risk of cognitive decline (Plassman *et al.*, 2010) and dementia (Jorm, 2001; Ownby *et al.*, 2006). Yet current evidence cannot preclude depression as an early prodromal symptom of dementia (Mirza *et al.*, 2014). Further, depression may also bring forward clinical manifestations of dementia (Jorm, 2001; Middleton and Yaffe, 2009).

Socioeconomic circumstances, such as education and occupation, may contribute to cognitive reserve (Stern, 2003; Kramer *et al.*, 2004; Valenzuela and Sachdev, 2006; Fratiglioni and Wang, 2007), which is defined as the capacity to compensate effectively for brain pathology and maximize normal cognitive performance (Stern, 2009). Educational attainment has been revealed to be a modest antecedent of midlife (Richards and Sacker, 2003) and later-life cognition (Ritchie *et al.*, 2012), independent of childhood intelligence, parental and midlife occupation. Occupation (Karp *et al.*, 2004) and work complexity (Fratiglioni and Wang, 2007) that involve high intellectual functioning have been related to lower risks of dementia. In the Whitehall II occupational cohort, the occupation hierarchy showed a larger-than-age impact on cognition (Zhao *et al.*, 2005), explaining up to 43% of the variance in middle-age cognitive performance (Singh‐Manoux *et al.*, 2011). However, existing studies mainly observed the effects of socioeconomic circumstances on cognitive capabilities, particularly these reflect preservation of learning, rather than altering the rate of cognitive decline (Rabbitt *et al.*, 2004; Karlamangla *et al.*, 2009; Muniz-Terrera *et al.*, 2009; Wilson *et al.*, 2009; Singh‐Manoux *et al.*, 2011; Lenehan *et al.*, 2015).

Healthy lifestyles have been associated with better cognitive maintenance (Pope *et al.*, 2003; Lee *et al.*, 2010). Evidence from systematic reviews indicates that being physically active (Hamer and Chida, 2009), abstaining from smoking (Anstey *et al.*, 2007), consuming a moderate amount of alcohol (Anstey *et al.*, 2009) and having a healthy diet (Gillette-Guyonnet *et al.*, 2007) may confer some protections against cognitive decline (Lee *et al.*, 2010). Among these health behaviours, physical activity demonstrates the most consistent protective effect (Lee *et al.*, 2010; Ballard *et al.*, 2011; Elwood *et al.*, 2013), which still may be contingent upon the type and duration of physical activity (Colcombe and Kramer, 2003). A synergized benefit from a combination of multiple health behaviours has also been proposed (Lee *et al.*, 2009; Sabia *et al.*, 2009; Barnes and Yaffe, 2011; Elwood *et al.*, 2013) with a life course perspective (Pope *et al.*, 2003; Whalley *et al.*, 2006; Lee *et al.*, 2010).

2.2.3 Repeated measures of cognitive function

Longitudinal data, with repeat cognitive tests, are preferred in cognitive ageing studies to provide information on the individual trajectory of cognitive decline (Hofer and Sliwinski, 2001) and distinguish age-related endogenous changes from exogenous differences due to birth year (Hofer and Sliwinski, 2006; Ferrer and Ghisletta, 2011). Longitudinal data permit simultaneous estimation of within-person change in the context of between-person difference, as well as the interaction between these two sources of variability (Hofer and Sliwinski, 2006). Although many test batteries have been validated as sensitive and specific measures for cognitive function, their sensitivity to detect subtle change over relatively short periods of time is still questionable (Wilson *et al.*, 2006; Cosentino *et al.*, 2011). Moreover, repeat measures of cognitive function at multiple occasions have inherent limitations of *practice effects* and *participant attrition*.

Practice effects refer to improvement in cognitive scores owing to repetition of testing materials, and familiarity with test procedures and environment. Performance gains because of practice artificially reduce the observed cognitive decline (Salthouse, 2010b). Several methodological approaches (Salthouse, 2010a) have been used to decompose observed cognitive change into ageing and practice effects, such as comparisons between participants taking a cognitive test once with those taking it twice (Thorvaldsson *et al.*, 2006), between changes generated from longitudinal setting with those from short-term retest intervals (Salthouse, 2009), and successive assessments with diverse test-retest intervals (Salthouse *et al.*, 2004). As practice effects can last up to 7-8 years (Salthouse *et al.*, 2004; Wilson *et al.*, 2006; Rabbitt *et al.*, 2009), widely-spaced measurement occasions may not be sufficient for practice effects to dissipate. To explicitly index practice effects as a function of the number of exposures, some patterns have been adopted (Hoffman *et al.*, 2011), which are, continuous improvement (i.e. linear 0-1-2-3 or quadratic 0-1-4-9), a single boost improvement (i.e. 0-1-1-1), or distinct improvement (i.e. dummy codes for each occasion). However, the pattern of practice effects is rather unpredictable, which can be test-specific and contingent upon individual characteristics (Ferrer *et al.*, 2004; Wilson *et al.*, 2006; Rabbitt *et al.*, 2009; Salthouse, 2010a).

Participant attrition indicates reduction in the study sample due to non-responses to follow-up. Three missing mechanisms are commonly addressed (Little and Rubin, 2002), namely, missing completely at random (MCAR), missing at random (MAR) and missing not at random (MNAR). Theoretically, key disparities between these mechanisms are, whether or not there is a systematic difference between missing values and the observed values, and if not, MCAR; whether or not this systematic difference can be explained by differences in the observed data, and if yes, MAR. However, in practice, it is impossible to distinguish between MAR and MNAR in observed dataset (Sterne *et al.*, 2009). MNAR, in the context of cognitive ageing, describes the fact that participants who drop out are more likely to have cognitive impairment and be unhealthier in general (Rabbitt *et al.*, 2004). Those remaining thus are a selected group of greater cognitive functioning and may be more resilient to cognitive decline (Rabbitt *et al.*, 2001), such that the longitudinal sample is positively biased (Salthouse *et al.*, 2004). Bias due to MNAR is most apparent when risk factors for cognitive decline are also strongly related to mortality or drop-out, such as smoking (Sabia *et al.*, 2012; Weuve *et al.*, 2012).

2.3 Social causation and health selection

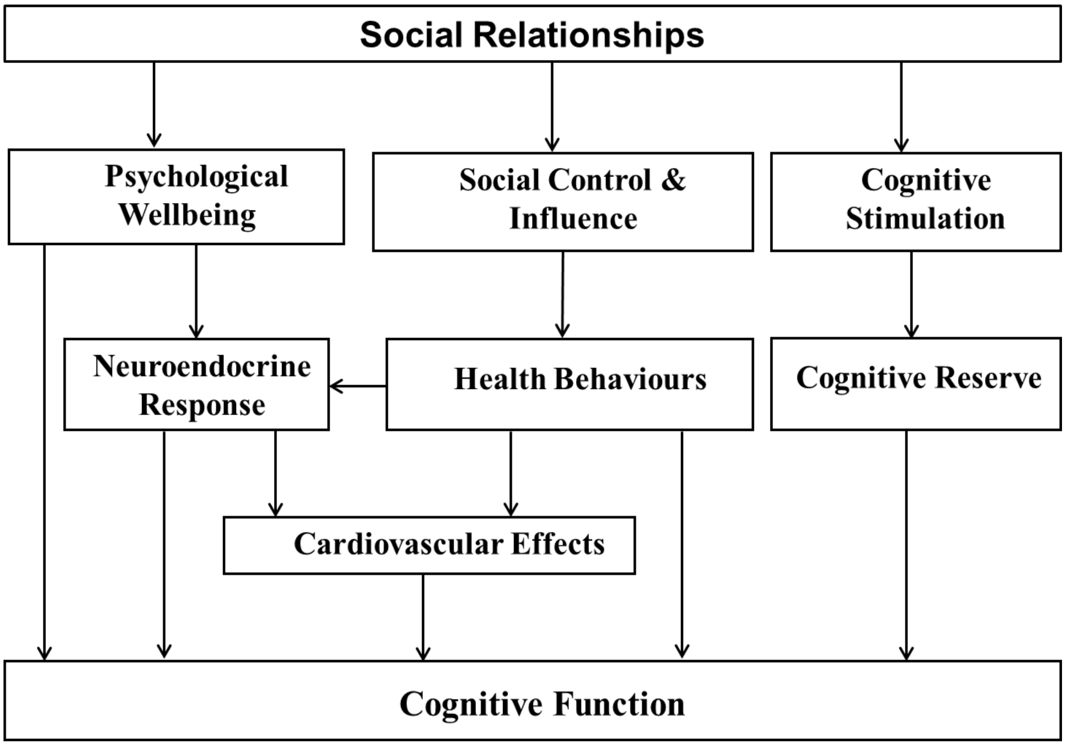
To fully investigate the association between social relationships and cognitive decline in late life, the potential influence from both directions should be considered (Hertzog *et al.*, 2008). *Social causation* and *health selection* are two major hypotheses widely used to explain social inequality in health (Black *et al.*, 1980). Social causation suggests that lower socioeconomic position and its associated environmental and material disadvantages contribute to the onset of illness, whereas health selection hypothesizes that poor health conditions lead to a slide in status or fail to improve social position (Black *et al.*, 1980; Johnson *et al.*, 1999). So far, theoretical and empirical work has been dominated by the social causation framework, but evidence on the competing health selection process has also been accumulated. The debate on the social causation vs. health selection processes is highly contested (Blane *et al.*, 1993; Chandola *et al.*, 2003; Ki *et al.*, 2011), which, after all, may be bound in a cycle emerging at a different stage of the life event (Kaniasty and Norris, 2008) and reinforcing over the life course (Blane *et al.*, 1993; Elovainio *et al.*, 2011). In addition, the relative importance of these alternative hypotheses may depend on the indicators of socioeconomic factors and health outcomes chosen (Johnson *et al.*, 1999; Warren, 2009). The following section applies the concept of social causation and health selection to address the potential reciprocal association between social relationships and cognitive decline.

2.3.1 Social causation

In light of the social causation hypothesis, most previous studies used social relationships as explanatory factors for variations in health and wellbeing (House *et al.*, 1988a; Cohen *et al.*, 2001). As reviewed by Berkman and colleagues (2000), the origin of such an investigation can be traced back to Durkheim’s classic study that established the link between social integration and rates of suicide. Social integration at the individual’s level then was characterized as attachments to social relationships, which provide a sense of purpose and shape resources available. Thereby, social relationships may directly benefit health by bolstering self-esteem, encouraging health promoting behaviours and enhancing the flow of health-related information (Berkman *et al.*, 2000). Meanwhile, social relationships may also modify stressful experiences (Thoits, 1982; Cohen and Wills, 1985), through reducing the likelihood of life event occurrence, intervening stress appraisal and alleviating the impact of stress response (Cohen *et al.*, 2001).

In the context of social relationships – cognitive function association, social causation emphasizes the leading role of supportive social relationships in maintaining cognitive function. Fratiglioni and colleagues (2004) have proposed three interrelated biological pathways, including psychological wellbeing & stress-buffering, cognitive stimulation & cognitive reserve, and health behaviours & cardiovascular hypothesis (Figure 2-1).

Figure 2-1 Biological Pathways between Social Relationships and Cognitive Function, Adapted from Cohen *et al.* (2001).



Psychological wellbeing & stress-buffering

Social relationships influence emotional state and psychological wellbeing. Through promoting positive affects (Cohen and Wills, 1985; Thoits, 2011), supportive relationships prevent self-neglect (Glass *et al.*, 1997) and alleviate depression (Stansfeld *et al.*, 1998a; Golden *et al.*, 2009; Stafford *et al.*, 2011; Byers *et al.*, 2012). Perceived social support and endorsement from significant others (Berscheid and Ammazzalorso, 2004) are important sources of self-identification and meaning in life (Settersten and Richard 2002; Reis *et al.*, 2004). Hence, by providing a sense of belonging and protection (Baumeister and Leary, 1995; Ross and Mirowsky, 2002), social relationships, particularly their functional component such as confiding and emotional support, can buffer stress response and maintain homeostasis (Thoits, 1982; Cohen and Wills, 1985). The absence of social relationships, in contrast, can trigger a stress reaction that accelerates functional decline (Berkman *et al.*, 2000). Animal experiments indicate that aged rats that were not handled during the post-natal period showed marked cognitive impairment and hippocampal cell loss in comparison with their handled counterparts (Meaney *et al.*, 1988; Meaney *et al.*, 1991). In humans, maladaptive reaction to stress has also been associated with hippocampal damage that causes memory and learning deficits, and doubled the risk of developing Alzheimer's disease (Wilson *et al.*, 2003). Elevated diurnal cortisol levels due to hypothalamic-pituitary-adrenal (HPA) stress response has been related to poor cognitive performance in a community based elderly sample (Beluche *et al.*, 2010). The dysregulation of the immune system, marked by raised levels of peripheral inflammatory proteins, may predict faster cognitive declines (Yaffe *et al.*, 2004b; Singh-Manoux *et al.*, 2014) and the onset of dementia (Schmidt *et al.*, 2002; Engelhart *et al.*, 2004).

Cognitive stimulation & cognitive reserve

Social interactions offer cognitive stimulation (Ybarra *et al.*, 2008; Cacioppo and Hawkley, 2009). Based on the 'use it or lose it' theory (Hultsch *et al.*, 1999), frequent social contacts and support exchanges among social partners can mobilize cognitive ability via social cue navigation, social role fulfilment and social issue settlement. As a proxy for environmental complexity, the structure aspects of social relationships (e.g. network size and diversity) have shown positive correlations with amygdala volume, which regulates emotional learning and memory consolidation (Bickart *et al.*, 2010). Complex social relationships, owing to their cognitively challenging feature (Ybarra *et al.*, 2008), may optimize neuronal structure and brain function (Bielak, 2010; Valenzuela *et al.*, 2012); and further contribute to cognitive reserve (Stern, 2002) by efficiently compensating for brain pathology. Having an extensive social network, more importantly, with adequate and satisfying social support, has been found to protect against dementia (Fratiglioni *et al.*, 2000; Amieva *et al.*, 2010). Studies have also shown that large social networks modified the clinical symptoms of Alzheimer's disease (Bennett *et al.*, 2006; Bennett *et al.*, 2014), and high levels of emotional support significantly facilitated cognitive recovery after a stroke event (Glymour *et al.*, 2008).

Health behaviours & cardiovascular hypothesis

Through social control and influence (e.g. social norms and social comparisons), social relationships may reinforce health-promoting behaviours and alter health-damaging behaviours (Cohen and Janicki-Deverts, 2009). Evidence suggests that large social networks and positive social support are associated with being physically active (Kouvonen *et al.*, 2012), limited alcohol intake, smoking cessation, healthy dietary patterns (Sorensen *et al.*, 2007), and treatment adherence (Berkman *et al.*, 2000; Umberson *et al.*, 2010; Harvey and Alexander, 2012). The majority of these health behaviours have been found to prevent cognitive decline (see Section 2.2.2 for details). Thus social relationships may generate cognitive benefits attributable to a healthy life style. Given health behaviours are also important risk factors for cardiovascular diseases, the cardiovascular hypothesis proposes that social relationships, by promoting health behaviours and regulating neuroendocrine response (Grant *et al.*, 2009; Kiecolt-Glaser *et al.*, 2010), result in decreased risks of cardiovascular events (Hemingway and Marmot, 1999; Barefoot *et al.*, 2005), which are involved in the pathogenesis and progression of dementia (Fratiglioni *et al.*, 2004; Deary *et al.*, 2009).

2.3.2 Health selection

In the domain of social relationships, health selection operates where healthy individuals are more likely to be selected into prosperous social relationships. Conversely, individuals may downwardly drift into deteriorated social relationships due to their existing illness (Kaniasty and Norris, 2008). The underlying mechanism of health selection process may be contingent on the specific health condition of interest. With respect to the importance of cognitive function for social relationships, cognitive competence may be a prerequisite for sustaining social functioning and social reciprocity.

Social interactions involve intellectual resources on all levels of cognitive processing (Lieberman, 2007; Ybarra *et al.*, 2008; Beauchamp and Anderson, 2010). The grey matter density especially in the frontal lobe, may reflect the ability to handle social complexity (Lewis *et al.*, 2011). As implied by the social brain hypothesis (Dunbar, 1998), individuals' cognitive competences indicated largely by the neocortex volume, positively correlate with the number of social relationships one can operate simultaneously. Although the direction of this correlation is still debatable (Roth and Dicke, 2005) and human's capacity to form relationships may go well beyond such biological constraints in contemporary sociocultural and technological contexts (De Ruiter *et al.*, 2011), it is clear well-adapted brain is crucial to complex social behaviours (Adolphs, 2009; De Ruiter *et al.*, 2011; Lewis *et al.*, 2011). There is basic cognition required to develop and maintain any social relationships (Washburn *et al.*, 2003; Lieberman, 2007; Bailey *et al.*, 2008), for instance, the ability to take the role of others and infer their mental states (e.g. beliefs, desires and intentions etc.) (Frith and Frith, 2003), understanding and controlling oneself, as well as interpersonal problem solving skills (Marsiske and Margrett, 2006). Cognitive ability, like being pragmatic, observant and reflective, may explain individual differences in social functioning (Beauchamp and Anderson, 2010; Ardelt, 2011). A study shows that cognitive training can enhance participants' social network and improve the quality of social relationships (Winningham and Pike, 2007). In contrast, cognitive impairment and associated illness behaviours and mental symptoms like depression, may undermine sufferers' ability to fulfil their social roles, such that they may become forgetful and struggle to sustain a conversation, lose interest in social activities or interacting with other people, and eventually withdraw from their social networks.

Further, cognitive impairment may disrupt the collectively negotiated social reciprocity presumed in many social relationships. According to the exchange theory (Gouldner, 1960; Lang *et al.*, 2009), individuals differentiate their support exchange based on the expectation of costs and benefits. While a balance between support giving and receiving is preferred, unbalanced support exchanges with social network members may make social interactions strenuous (Lang, 2001; Sims *et al.*, 2014). Support recipients may feel indebted as a result of being unable to return the favour; whereas increasing demand and dependence on their social partners may overburden those close to them, to the extent that social relationships may eventually impoverish or even terminate (Shouse *et al.*, 2013). This especially applies to social ties with non-kin relationships, whereby strong reciprocity is required (Lang *et al.*, 2009).

2.4 Systematic review on the association of social relationships and cognitive decline

2.4.1 Methods of systematic review

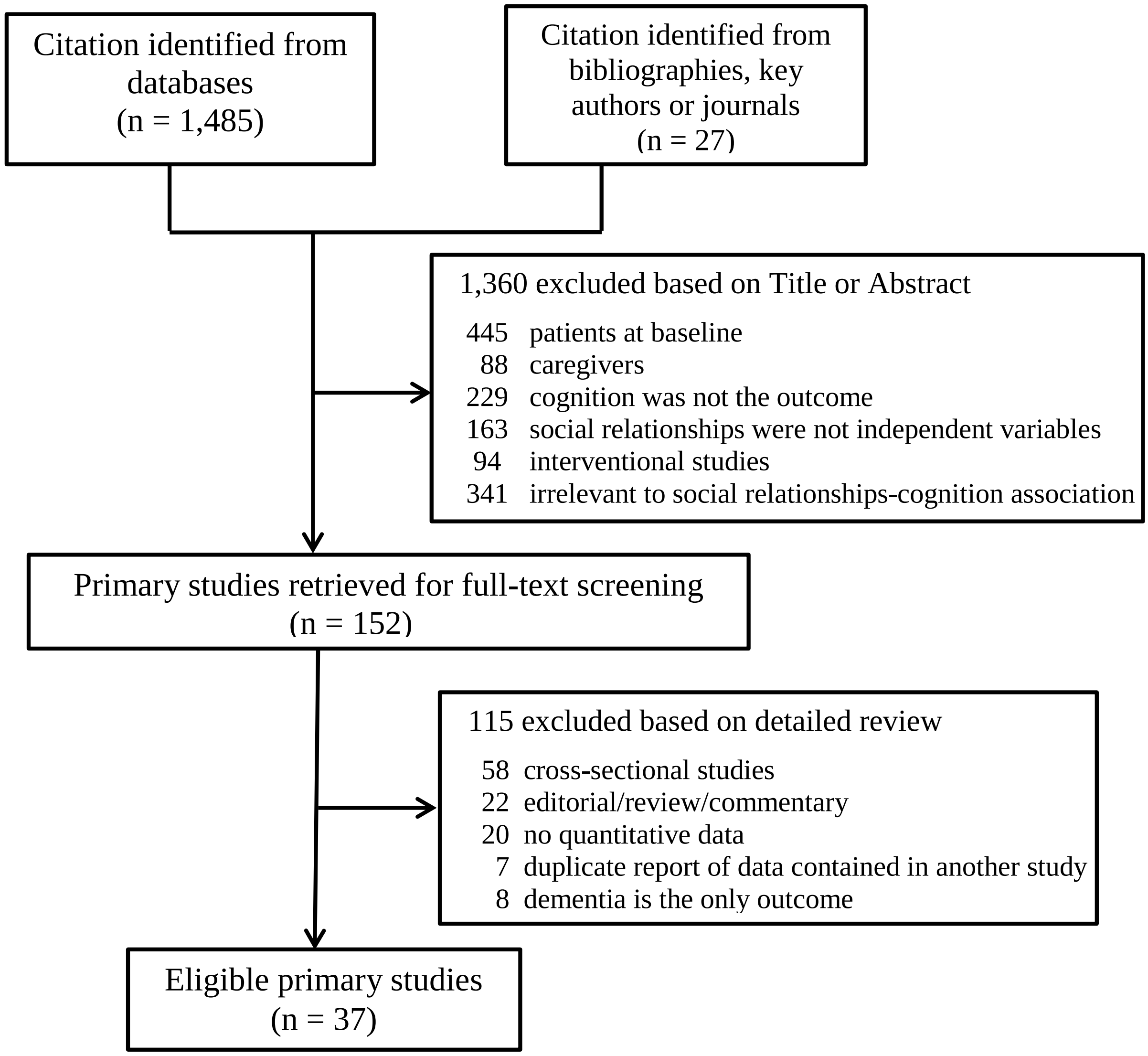
The **aim** of this systematic review is to synthesize existing evidence from longitudinal studies on social relationships and age-related cognitive decline in late adulthood. Thesaurus and text-word searching techniques were conducted in the following databases: *Medline (1946 to present), Embase (1980 to present), PsycINFO (1806) / PsycEXTRA (1908), IBSS, CINAHL plus, Web of Science* and *Scopus*. Multiple search terms were used for both social relationships and cognitive decline, including *social support, social network, isolation, social integration, social engagement, social relations, social relationships* and *cognitive aging/ageing, cognitive decline, cognition, cognitive change, memory, executive function or performance.* A manual search of key authors and journals was also carried out to locate relevant articles that had not been identified in the database searching.

Studies included were observational prospective cohort studies of middle to old aged participants drawn from general populations, providing quantitative data on social relationships in relation to age-related cognitive decline. The direction of this association was not specified given the potential bidirectional association between social relationships and cognitive function. Studies using social relationships as interventions, social support provided to others only (e.g. caregivers), or non-human sources of social relationships (e.g. pet) were excluded. As the main focus is on cognitive decline as a function of age, studies only reporting dementia cases were also excluded.

2.4.2 Main characteristics of studies identified

Overall, 1,512 articles were retrieved from databases and bibliographies. Out of the 152 studies evaluated by full-text review, 37 primary longitudinal studies met the eligibility criteria (Figure 2-2). Detailed characteristics of these studies are presented in Appendix 1.

Figure 2-2 Flow Chart of Literature Selection



Studies identified represented a range of regions and cultures: North America, Europe, Oceania and Asia, showing evidence from well-known ageing cohorts, such as, the MacArthur Studies of Ageing, the Health, Aging and Body composition study (Health ABC), the Health and Retirement Study (HRS), the Longitudinal Ageing Study Amsterdam (LASA), and the English Longitudinal Study of Ageing (ELSA). Among these, 12 had more than 10 years' follow-up and 17 had three or more repeat cognitive assessments.

Study sample size varied from 89 (Bennett *et al.*, 2006) to 16,638 (Ertel *et al.*, 2008), with 23 studies having over one thousand participants. There are two studies that recruited only male (van Gelder *et al.*, 2006) and only female participants (Barnes *et al.*, 2007). Included studies primarily focused on older people (mean age range at baseline: 60~85 years), except for four studies following the participants since their middle age (mean age 51 years) (Green *et al.*, 2008; Håkansson *et al.*, 2009; Seeman *et al.*, 2011; Fiori and Jager, 2012).

The definition of social relationships varied conceptually and operationally (Table 2-2). Furthermore, only few studies considered changes in social relationships over time (Béland *et al.*, 2005; Håkansson *et al.*, 2009; Seeman *et al.*, 2011; Thomas, 2011b; Ellwardt *et al.*, 2013; Li and Zhang, 2015).

Table 2-2 Assessments of Social Relationships in Studies Reviewed

Type of Measures	Description	Selected Examples
Functional		
Perceived Social Support	Perception of availability of support if needed	Eisele *et al*., 2012
Specific Function	Emotional, practical and negative aspects of support	Ellwardt *et al*., 2013
Structural		
Social Network	Types of ties, frequency of contacts and complexity of social roles	Barnes *et al*., 2004 Ellward *et al*., 2015 Fiori and Jager, 2012
Marital Status	Married/cohabiting, widow, divorced or single	Håkansson *et al*., 2009
Social Integration	Community, family or friends engagement, involving in a broad range of social interactions.	Béland *et al*., 2005 Thomas, 2011 a,b
Social Isolation	Lack of social contacts, no membership in any association and being single	Shankar *et al*., 2013
Combined		
Multifaceted Measures	Multiple measures assess more than one of the concepts above	Hughes *et al*., 2008 Seeman *et al*., 2011
A Composite Index	A single score assesses multiple components of social relationships	Andrew & Rockwood 2010 Stoykova 2011

The cognitive measures also took a variety of forms. Some studies tested global cognition (Bassuk *et al.*, 1999) or specific cognition, like memory (Ertel *et al.*, 2008); others used cognitive batteries evaluating multiple cognitive domains (Seeman *et al.*, 2011), or measures of neuropathology (Eisele *et al.*, 2012). The Mini-Mental State Examination

(MMSE) and its modified version (3MS) were most used, yet with different scales (Barnes *et al.*, 2007; Yaffe *et al.*, 2009).

2.4.3 Methodology of studies reviewed

All reviewed studies were controlled for demographic characteristics and education, with a few (24%) including other indicators of socioeconomic circumstances, for instance, income and employment status. Some were controlled for chronic disease (29%), depression (35%) and personality (8%). Several studies (23%) were conditional on baseline cognition, which may possibly incur spurious estimations biased by measurement error or changes in cognition preceding baseline assessment (Glymour *et al.*, 2005). Although repeat cognitive measures were used in the majority of these studies, only one study (Karlamangla *et al.*, 2009) explicitly modelled practice effects.

Different analytical strategies were applied to quantify cognitive decline (Table 2-3). Growth curve models prevail in recent literature as compelling methods to depict individual cognitive trajectories as a function of age or time since baseline. Several studies used multilevel models (MLM) to investigate the extent to which trajectories of cognitive decline were influenced by baseline (Ertel *et al.*, 2008; Stoykova *et al.*, 2011; Giles *et al.*, 2012) or concurrent (Béland *et al.*, 2005) levels of social relationships. Growth mixture model (GMM) was employed to examine how different changing patterns of social engagement over time were related to the development of cognitive limitations simultaneously (Thomas, 2011b). Latent growth mediation models were adopted to evaluate the direct and indirect effect of social relationships on cognitive ageing trajectories (Ellwardt *et al.*, 2013).

To clarify the direction of these *social relationships-cognitive ageing* associations, some studies excluded participants with lower baseline cognitive scores (Barnes *et al.*, 2004) or incident dementia during follow-up (Stoykova *et al.*, 2011), such that the effect of cognitive impairment may be minimized. Other studies used cognitive ability to evaluate subsequent social integration level (Ertel *et al.*, 2008) or changes in social relationships (Ellwardt *et al.*, 2013). Structure equation modelling, such as cross-lagged models (Thomas, 2011a; Li and Zhang, 2015), were also employed to address temporality.

Table 2-3 Statistical Methods Used in the Reviewed Studies to Quantify Cognitive Decline

Statistical Methods	**Comments**	**Selected Examples**
Change of Cognitive Scores	Use when only two time-point cognitive scores are available. Can be severely biased by practice effects, measurement error and regression to the mean; inaccurate to distinguish pathological changes from random variation.	Seeman *et al.*, 2001, Green *et al.*, 2008, Dickinson *et al.*, 2011, Eisele *et al.*, 2012
Statistical Criteria Based Methods	To define a statistically meaningful cognitive decline. The decision on cut-off points is arbitrary and varies across studies.	Bassuk *et al.*, 1999
Growth Curve Models	Handle dependency among repeat measures, allow for time-varying covariates and accommodate unbalanced designs (e.g. different length of follow-up). Simultaneously estimate inter-individual difference and intra-individual change. Combines the features of multivariable regression, factor analysis and path analysis, and enables hypotheses about latent variables and mediation to be tested.	Béland *et al.*, 2005, Thomas, 2011b, Ellwardt *et, al*. 2013

2.4.4 Findings from studies reviewed

In view of substantial heterogeneities apparent in the longitudinal studies identified, a narrative review was conducted. Findings were synthesized broadly under the two alternative theories: studies examining *social causation* via evaluating 1) specific characteristics of social relationships in relation to subsequent cognitive decline, 2) multiple repeat measures of social relationships as indicators of cognitive ageing; as well as evidence suggesting 3) the *health selection* process on social relationships as a consequence of cognitive decline.

Specific components of social relationships and cognitive decline

Functional aspects of social relationships have been reported as cognitively beneficial by some but not all studies reviewed. Specifically, a cross-sectional association between *emotional support* and better cognition was revealed by several studies (Seeman *et al.*, 2001; Green *et al.*, 2008; Eisele *et al.*, 2012), yet only one study demonstrated this positive association longitudinally (Seeman *et al.*, 2001). Likewise, the effect of *practical support* remained unclear, with either beneficial (Dickinson *et al.*, 2011), adverse (Ellwardt *et al.*, 2013) or non-significant (Seeman *et al.*, 2001; Hughes *et al.*, 2008) impacts on cognitive ageing. As for *negative aspects of social relationships*, Seeman and colleagues (2011) showed cumulative social conflicts predicted poor executive function measured 10 years after the baseline. In contrast, two studies found negative support was associated with better concurrent cognition, with no evidence of longitudinal associations (Seeman *et al.*, 2001; Hughes *et al.*, 2008). Few studies have examined positive and negative aspects of social relationships simultaneously (Seeman *et al.*, 2001; Hughes *et al.*, 2008; Seeman *et al.*, 2011). Given social relationships are likely to involve both positive and negative exchanges (Fingerman *et al.*, 2004), it may be more informative to study how they work in tandem (Walen and Lachman, 2000).

Structural aspects of social relationships have also shown equivocal findings in relation to cognitive decline (Barnes *et al.*, 2004; Holtzman *et al.*, 2004; Glei *et al.*, 2005; Barnes *et al.*, 2007; Green *et al.*, 2008; Yaffe *et al.*, 2009; Shankar *et al.*, 2013), indicating the mere existence of a social network may be insufficient to represent support available or the quality of social relationships (Pinquart and Sörensen, 2000; Eisele *et al.*, 2012; Gow *et al.*, 2013). Furthermore, distinct effects of a *friend network* and a *relative network* have been documented. As such, friends-oriented networks were more cognitively stimulating than family-focused networks (Fiori and Jager, 2012), to the extent that friend networks may profoundly protect against cognitive decline (Giles *et al.*, 2012), which seems to be particularly evident among women (Zunzunegui *et al.*, 2003; Béland *et al.*, 2005; Giles *et al.*, 2012). Nevertheless, studies also revealed engagement with relatives (Béland *et al.*, 2005), such as frequent visual contacts (Zunzunegui *et al.*, 2003), reduced the probability of cognitive decline. Also, older people who lost their spouse showed greater cognitive declines (Aartsen *et al.*, 2005; van Gelder *et al.*, 2006) and higher risks of cognitive impairment (Håkansson *et al.*, 2009) than their counterparties who remained married.

Repeat social relationships measures and cognitive decline

Few studies have considered the changing nature of social relationships in late adulthood. Evidence suggests that persistent social disengagement history (Bassuk *et al.*, 1999), shrinking social network (Holtzman *et al.*, 2004; Seeman *et al.*, 2011), decreased social interaction (Dickinson *et al.*, 2011) and being consistently without a partner (van Gelder *et al.*, 2006; Håkansson *et al.*, 2009) predicted greater cognitive decline. Only four studies estimated the conjoint trajectories of social relationships and cognitive ageing. Findings showed that participants who experienced high and improving social relationships with age (Thomas, 2011b), particularly engaging with relatives and friends (Béland *et al.*, 2005), playing multiple social roles (Ellwardt *et al.*, 2015), and perceiving more emotional support but not practical support (Ellwardt *et al.*, 2013), had slow cognitive declines and few cognitive limitations over time.

Health selection on social relationships due to cognitive decline

The aforementioned studies suggest *social causation* operates. Conversely, there is also evidence pointing to *health selection* (Green *et al.*, 2008; Stoykova *et al.*, 2011). Better cognitive maintenance was associated with increased social network size with age (van Tilburg and Broese van Groenou, 2002), facilitating the continuation of longstanding relationships and development of new relationships (Broese van Groenou *et al.*, 2013). Cognitive decline instead was related to losses of potential supporters (Aartsen *et al.*, 2004), as older people withdrew from a more diversified social network to restricted network types (Li and Zhang, 2015). Cognitively impaired individuals also reported more negative social interactions (Gurung *et al.*, 2003). As a result, cognitive decline may not only jeopardize the structure of social relationships but also affect their quality. It is also worth noting that an individual's capability to recruit and maintain social relationships may be traced back to cognitive ability in early life (Bourne *et al.*, 2007). To the degree that, memory performance at middle life explained less than 1% of the variation in subsequent social integration (Ertel *et al.*, 2008), whereas age-11 intelligence quotient attenuated the social relationships-cognition association at age-70 by 40-60% (Gow *et al.*, 2013). Regulated by the principle of reciprocity (Gouldner, 1960; Lang *et al.*, 2009), mobilizing social relationships in times of need may rely upon the support bank built up over the entire life course (van Tilburg and Broese van Groenou, 2002; Antonucci *et al.*, 2010).

2.5 Summary of literature review and gaps in knowledge

This systematic review identified 37 longitudinal studies on the association between social relationships and cognitive decline in old age. Researches have been primarily conducted in North America and Europe, using large population-based (average sample size n = 2,530) ageing cohorts with a median 7.5-year follow-up. The reviewed literature reveals inconclusive evidence on the effect of social relationships on cognitive ageing. The wide variation in the definition and measurement of social relationships and cognition impede the attempt to synthesize the evidence quantitatively. Although studies with three or more repeat measures most applied growth curve modelling to quantify cognitive decline, differences in analytical methods, such as alternative time metrics adopted (Hoffman, 2012), lead to discrepant results.

Inconsistent findings to date leave several main questions to be answered. First, *which aspect of social relationships is cognitively beneficial?* Lack of detail in the assessments of functional and structural aspects of social relationships obscures the identification of cognitively beneficial components. The functional aspect of social relationships (e.g. emotional and practical support) may protect against cognitive ageing via the psychological wellbeing & stress-buffering pathway. Yet, given the detrimental effect of negative support, it is unclear how positive and negative aspects of social relationships work together to influence cognitive decline (Seeman *et al.,* 2011). Also, different types of social networks may not be equally cognitively enriching. As friendships are normally formed on the basis of shared interests and needs of pleasure, friend networks may be more diverse and cognitively stimulating compared with relative networks that may mainly involve routine tasks (Keller-Cohen *et al.*, 2006; Fiori and Jager, 2012). More research hence is needed to assess the distinct cognitive effect friend networks and relative networks may engender. The relative importance of functional and structural aspects of social relationships to cognitive ageing also requires clarification (Amieva *et al.*, 2010). Understanding the extent to which specific components of social relationships make independent contributions to cognitive ageing would facilitate well-targeted intervention.

Second, *how social relationships and cognitive function coevolve with age?* The longitudinal associations between social relationship transitions and cognitive ageing remain largely unexplored. Most studies used baseline measures of social relationships only, with little attention to the changes in social relationships during late adulthood (Dodge *et al.*, 2014). Social relationships are not static but rather fluctuate across the life course marked by substantial intra-individual heterogeneity (Section 2.1.3 Chapter 2). Such change may lead to complex dynamics between social relationships and cognitive ageing across time, which a cross-sectional snapshot of social relationships cannot represent. Moreover, where both social relationships and cognitive function are changing with age, social aspects of ageing may not necessarily be in the same direction as functional deteriorations (Carstensen *et al.*, 2006). Adequate psychosocial resources may compensate for inevitable functional declines such that differentiating those who age well from those who do not (Saczynski *et al.*, 2006; Young *et al.*, 2009). Therefore, examining the association between divergent changing patterns of social relationships and cognitive decline can provide important leverage to understand the implication of person-specific social ageing trajectories for the unfolding course of cognitive decline.

Third, *what is the temporal order of the association between social relationships and cognitive decline?* The direction of social relationships-cognitive function associations is open for investigation. A major caveat of observational studies is unclear temporal order, confounding the true cognitively protective effects (Berkman *et al.*, 2011). Owing to the long prodromal phase of dementia, impoverished social relationships may result from cognitive deterioration (Stoykova *et al.*, 2011). Current evidence suggests the possibility of both *social causation* and *health selection* processes, however, studies evaluating both pathways simultaneously are lacking. Progress in understanding the dynamics between social relationships and cognitive decline requires a study design systematically investigating the directionality of these associations in late life.

Chapter 3. Aim, objectives and hypotheses

The proposed neuro-protective effect of social relationships is of substantial public health relevance, particularly because social relationships may act as modifiable risk factors for dementia. Review of the literature indicates that more evidence is required to identify the cognitively beneficial components of social relationships, to assess the social relationships-cognitive ageing associations from a longitudinal perspective, and to investigate the temporal order of these dynamic associations.

Accordingly, the **aim** of this PhD project is to examine the longitudinal dynamic associations between *social relationships* from middle to old age and *cognitive ageing*. In order to investigate these associations, this thesis uses *functional* and *structural* aspects of social relationships, which were measured on multiple occasions from middle to early old age, and age-related cognitive decline, quantified as the slope of cognitive trajectories derived from three repeat cognitive tests over 10 years of follow-up in the age range of 45 to 80 years. Two cognitive domains are assessed, that is, *executive function* and *memory*.

Three **objectives** are developed in sequence to achieve this aim.

Objective one: *Mid-life social relationships as risk factors of cognitive ageing.* To assess independent associations between multiple facets of social relationships and age-related cognitive decline, objective one employs repeat functional and structural measures of social relationships over middle life and examines their impact on subsequent decline in cognition simultaneously. The intention is to investigate effective components of social relationships in relation to cognitive ageing.

Objective two**:** *Longitudinal association between social relationship transitions from middle to old age and cognitive ageing*. To examine how longitudinal changing patterns of social relationships are associated with cognitive decline, objective two traces trajectories of social relationships and cognitive decline over time. The time-varying and person-specific characters of social relationships are captured through identifying longitudinal latent classes. The extent to which these divergent changing patterns of social relationships are associated with concurrent cognitive ageing trajectories is then evaluated.

Objective three: *Reciprocity between social relationships and cognitive function from middle to early old age.* To simultaneously investigate social causation and health selection processes, objective three tests the bidirectional association between changes in social relationships and changes in cognitive function. Three parallel assessments of social relationships and cognitive function allow the investigation of the temporal direction.

The corresponding **hypotheses** are,

Objective one: It is hypothesized that both functional and structural aspects of social relationships have beneficial effects on cognitive ageing. Specifically, high-quality social relationships and large social networks especially with friends are positively associated with cognitive function maintenance. Function in comparison with structure of social relationships is more protective for cognitive ageing.

Objective two: It is hypothesized that from middle to old age, the size of social networks decreases whereas the quality of social relationships improves. Moreover, these age-related changes in social relationships vary across individuals. In relation to cognitive ageing, participants having enhanced social relationships as they age experience decelerated cognitive decline, compared with their counterparts with unsatisfying social relationships.

Objective three: It is hypothesized that there is a bidirectional association between social relationships and cognitive ageing. High-quality and supportive social relationships protect against cognitive decline; on the other hand, low cognitive function impoverishes existing social relationships. There is no specific hypothesis regarding the relative strength of these bidirectional effects.

Chapter 4. Methodology

Summary

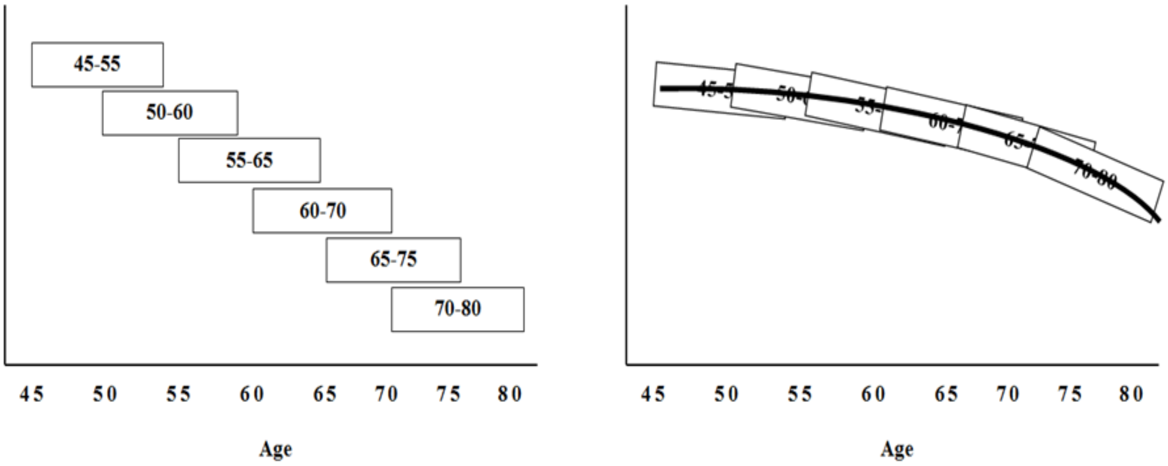
This chapter introduces the Whitehall II prospective cohort used in this thesis. The multiple repeat measures of social relationships and cognitive function are described, along with other covariates included in the analyses. Data attrition and characteristics of the study sample are then presented. An overview of the statistical analyses adopted to investigate each objective is provided; while more detailed explanation of these statistical methods are amplified in the corresponding chapters.

4.1 The Whitehall II study design

The Whitehall II prospective cohort recruited 10,308 participants (66% male, aged 35-55 y) from 20 London based civil service departments in 1985-1988. At study baseline, all participants underwent clinical health check-ups and completed self-administered questionnaires. Subsequent data collection was administered approximately every two years, alternating between postal questionnaires alone and postal questionnaires accompanied by clinical check-ups (Marmot and Brunner, 2005). Eleven phases of data collection have been completed, with Phase 12 (2015-2016) currently in progress. Ethical approval was obtained from the University College London Medical School Committees on the Ethics of Human Research. All participants are asked to give written informed consent at each phase.

The Whitehall II study has been collecting data from individuals of sequential birth years from 1930 to 1952 since the study baseline 1985-1988. A feature of this *accelerated longitudinal design* (Sliwinski *et al.*, 2010) is that overlapping age cohorts allow estimation of a general trajectory across the entire range of the observed age, which presents a longer time span than what is directly observed from the longitudinal study follow-up period (Figure 4-1). Herein *age* embodies a mixture effect of longitudinal within-person changes (i.e. getting older) and cross-sectional between-person differences (i.e. being older). The assumption underlying age-based models is *age convergence*, positing that individuals of different birth cohorts all converge onto the same trajectory. It assumes one's functional ability only depends on individual's age, regardless of the time when the person reaches that age. *Age convergence* may not hold when the initial age range is wide, which is susceptible to birth cohort effect, non-random selection and attrition (Hofer and Hoffman, 2007). This assumption should be verified by introducing time-invariant variables (e.g. year of birth) to take into account contextual effects (Sliwinski *et al.*, 2010).

Figure 4-1The Age Accelerated Longitudinal Design, Based on Data of the Whitehall II Cohort from Phase 5 (1997-1999) to Phase 7 (2007-2009), Adapted from Hoffman (2012).

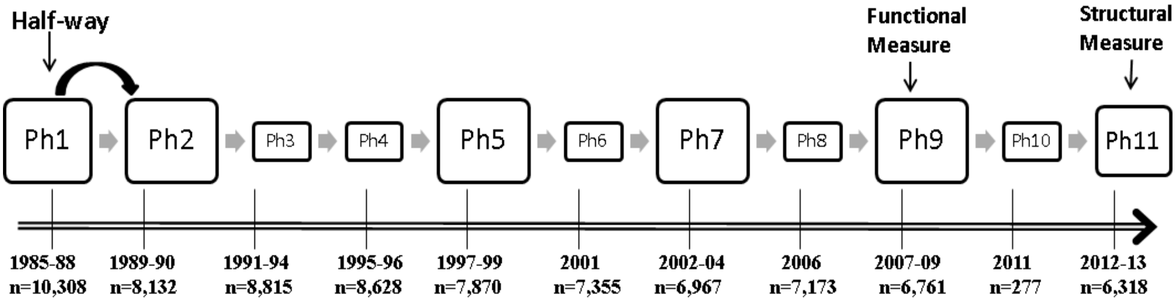


4.2 Variables of interest

4.2.1 Social relationships

The Close Persons Questionnaire (CPQ) was developed in the Whitehall II cohort to measure both functional and structural aspects of social relationships (Stansfeld and Marmot, 1992). Good test-retest reliability over 4-week intervals and the validity of this questionnaire have been documented (Stansfeld and Marmot, 1992). A full CPQ is included as Appendix 2.

Figure 4-2 Repeat Measures of Social Relationships in the Whitehall II Cohort (Ph: Phase).



Introduced halfway through Phase 1, functional and structural measures of social relationships were available at Phase 2, 5 and 7, with only functional measures at Phase 9 and structural measures at Phase 11 (Figure 4-2). This thesis used data on social relationships from Phase 2 to Phase 9. Missing values in Phase 2 were replaced by Phase 1 data, as there were fairly high corrections between Phase 1 and 2 measures (range 0.55-0.63).

On each occasion, respondents were invited to give a total number of people they feel very close to and nominate the close persons in the last 12 months. At Phase 1 and 2, up to four close persons were nominated. From Phase 5 onwards, only the closest person was identified, where the highest reliability of the CPQ lies. The identity of the closest person varied but can be broadly categorized into four types, which are *spouse or partner* (71% ~73% over phases), *relatives* (13%~16%), *friends* (12%~14%) and *others* (< 1%). The last category contains heterogeneous nominations, such as God, pets and social workers etc. Nearly all married men (93%) in contrast to 85% of married women nominated their spouse as the closest person.

Functional measures of social relationships

Derived from Schaefer *et al*., (1981) and Power *et al.*, (1988), 15 items of the Close Persons Questionnaire assess functional aspects of social relationships. Three subscales were identified by factor analysis (Stansfeld and Marmot, 1992): confiding/emotional support, practical support and negative aspects of close relationships (Note: The item on 'reliance' was dropped from emotional support scale due to low factor loading. Confirmation factor analysis was applied to measures in later phases to verify the same composite variables held regardless of age, see Appendix 3).

Confiding/emotional support (7 items, *Cronbach's α* ranges from 0.85~0.86 over phases) included being given information and guidance, wanting to confide, sharing interests, boosting self-esteem and reciprocity. *Practical support* (3 items, *Cronbach's α* 0.78~0.82) indicated the perceived receipt of tangible support, such as financial assistance or aid in daily chores. *Negative aspects of close relationships* (4 items, *Cronbach's α* 0.63~0.65) captured adverse interactions (e.g. making things worse, causing worries, problems and stress) and inadequacy of support (e.g. need more help) (Note: This thesis also refers to the *negative aspects of social relationships* as *negative support* for simplicity).

Each item was rated on a four-point Likert scale, with higher scores indicating higher support or greater negative aspects of close relationships. The Likert-scaled responses were summed for each subscale of functional social relationships.

Structural measures of social relationships

Structural social relationships were measured: marital status, friend network and relative network (Berkman and Syme, 1979). The friend network (2 items, *Cronbach's α* 0.62~0.65) and relative network (2 items, *Cronbach's α* 0.67~0.73) were derived from questions on 1) *frequency of contacts* with friends or relatives 2) *total number* of friends or relatives seen once a month or more. The five-point Likert scaled responses were summed. Marital status was coded as married/cohabiting, single, divorced and widowed. Repeat measures of social relationship variables were summarized as table below.

Table 4-1 Social Relationship Variables from Phase 2 to Phase 9 (Maximum Cases)

Variable	No.	Mean	SD	Min	Max
Confiding Support					
Phase 2	7,952	14.8	4.3	0	21
Phase 5	6,954	13.3	4.2	0	21
Phase 7	6,631	13.5	4.2	0	21
Phase 9	6,475	13.7	4.2	0	21
Practical Support					
Phase 2	7,966	5.3	2.8	0	9
Phase 5	6,979	4.5	2.5	0	9
Phase 7	6,633	4.4	2.4	0	9
Phase 9	6,472	4.2	2.4	0	9
Negative Support					
Phase 2	7,949	2.8	2.4	0	12
Phase 5	6,964	2.4	2.0	0	12
Phase 7	6,624	2.2	1.9	0	12
Phase 9	6,478	2.1	1.9	0	12
Friend Network					
Phase 2	8,089	3.8	1.9	0	8
Phase 5	6,599	4.1	2.0	0	8
Phase 7	6,710	4.4	2.0	0	8
Relative Network					
Phase 2	8,106	3.0	1.8	0	8
Phase 5	6,679	3.2	1.9	0	8
Phase 7	6,542	3.2	2.0	0	8

(continued)

Table 4-1 Continued

	No.	Percent %
Marital Status		
Phase 5		
Married/Cohabiting	5,425	78.4
Single	818	11.8
Divorced	465	6.7
Widowed	213	3.1
Phase 7		
Married/Cohabiting	5,216	75.4
Single	875	12.7
Divorced	516	7.5
Widowed	310	4.5
Phase 9		
Married/Cohabiting	4,999	75.2
Single	751	11.3
Divorced	475	7.2
Widowed	421	6.3

SD: standard deviation

Correlations between functional and structural measures of social relationships

Functional measures of social relationships were only weakly related to structural measures (Table 4-2). Negative aspects of close relationships were correlated adversely with confiding support but positively with practical support. These weak correlations between negative aspects of close relationships and confiding or practical support were found in other studies (Rook, 1994; Mavandadi *et al.*, 2007). Larger friend and relative networks were associated with less negative aspects of close relationships, and more confiding and practical support.

Table 4-2 Spearman Correlation between Functional and Structural Social Relationships of the Whitehall II at Phase 5, All Significant at P = 0.05 Level

	Confiding Support	Practical Support	Negative Support	Friend Network	Relative Network
Confiding Support	1				
Practical Support	0.50	1			
Negative Support	-0.15	0.05	1		
Friend Network	0.11	0.06	-0.07	1	
Relative Network	0.11	0.12	-0.06	0.20	1

Correlations between repeat social relationships measures

Table 4-3 presents the correlations within a month and over different periods' follow-up. Correlations became smaller as test-retest time intervals became longer, with comparable correlations over the same length of time-lag. These differences suggest that change over years was greater than it might be expected from short-term fluctuation.

Table 4-3 Spearman Correlations between Repeat Measures of Social Relationships

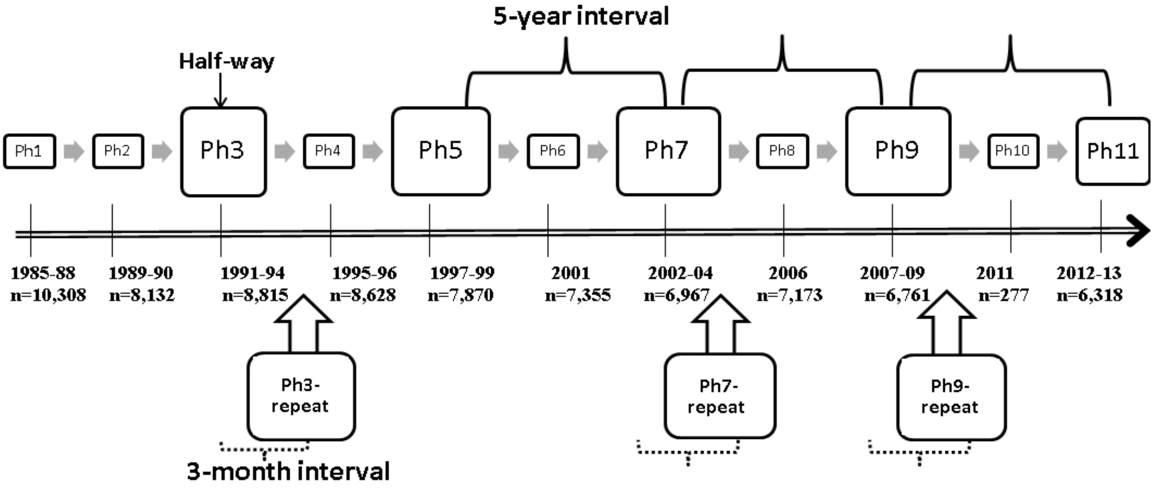
	4-week repeat [a]	5-year repeat		8-year repeat	10-year repeat	13-year repeat	18-year repeat
	Phase1	Phase 5 vs Phase 7	Phase 7 vs Phase 9	Phase 2 vs Phase 5	Phase 5 vs Phase 9	Phase 2 vs Phase 7	Phase 2 vs Phase 9
	n=153	n=5,918	n=5,848	n=6,039	n=5,665	n=5,730	n=5,573
Confiding Support	0.88	0.63	0.65	0.53	0.56	0.48	0.45
Practical Support	0.67	0.55	0.57	0.45	0.48	0.39	0.36
Negative Support	0.71	0.49	0.50	0.42	0.44	0.35	0.35
Friend Network	0.68	0.58	/	0.51	/	0.43	/
Relative Network	0.57	0.62	/	0.48	/	0.41	/

[a] Data obtained from Stansfeld and Marmot (1992)

4.2.2 Cognitive function

A cognitive test battery was initiated halfway through Phase 3 (40% of Phase 3 participants). Repeated examinations were administered in the entire cohort at Phase 5, 7 , 9 and 11 with 5-year intervals, alongside subsamples collected three months after Phase 3, 7 and 9 (Figure 4-3). Amongst the initial 10,308 participants, 269 (3%) took repeat cognitive tests up to five times by Phase 9. The most common pattern was taking cognitive tests at Phase 5, 7 and 9 (24%), followed by not taking any (22%) and taking cognitive tests at Phase 3, 5, 7 and 9 (17%). Cognitive data from Phase 5, 7 and 9 over 10-year follow-up were used in the main analyses of this thesis.

Figure 4-3 Repeat Cognitive Measures in the Whitehall II Cohort (Ph: Phase).



In this cognitive test battery, four standard tasks, described below, assessed fluid cognitive function.

The *short-term verbal memory test* was assessed by a 20-word audiotaped list of single or double syllable words (Marzano, 2005) at 2-second intervals, which participants were required to recall in writing within 2 minutes.

The *Alice Heim 4-I (AH 4-I) test*, an inductive reasoning test, consists of 65 verbal and numeric items to be completed within 10 minutes. This test measures one's ability to identify patterns and infer principles.

Two measures of verbal fluency were used, which are *phonemic* and *semantic fluency*. Participants were instructed to recall in writing as many words beginning with "S" (*phonemic fluency*) and as many animal names (*semantic fluency*) as possible in 1 minute.

These four tests included in the main analysis had high test-retest reliability, ranging from 0.60-0.89, estimated using the 556 participants who took Phase 7 and Phase 7 repeat 3 months apart (second column of Table 4-4). For all measures of cognitive function, correlations decreased as time-intervals lengthened, indicating the changes over time were greater than short-term fluctuation.

Table 4-4 Pearson's Correlations between Repeat Cognitive Measures

	3-month repeat [a]		**5-year repeat**		**10-year repeat**
	Phase7 & Phase7 repeat n=554	**Phase9 & Phase9 repeat n=210**	**Phase 5 vs Phase 7 n=5,192**	**Phase 7 vs Phase 9 n=5,540**	**Phase 5 vs Phase 9 n=4,877**
Memory	0.60	0.60	0.46	0.48	0.46
AH4-I	0.89	0.93	0.88	0.89	0.86
Semantic Fluency	0.73	0.72	0.70	0.69	0.66
Phonemic Fluency	0.69	0.67	0.67	0.70	0.65

[a] Correlations of short-term repeat measures indicate test-retest reliability.

A composite *executive function* score was derived from reasoning (AH4-I), phonemic and semantic fluency by first standardizing the raw scores of each test to z-scores (mean = 0; standard deviation (SD) = 1) based on Phase 5 mean and SD for each test in the entire cohort; then these z-scores were averaged to yield executive function score. Average z-scores constructed in this manner seem to minimize measurement errors (Wilson *et al.*, 2010). Memory score was also standardized to allow comparability with the executive function score. Table 4-5 summarizes these two sets of standardized scores over phases.

Table 4-5 Standardized Cognitive Scores from Phase 5 to Phase 9 (Maximum Cases)

Variable	No.	Mean	SD	Min	Max
Standardized Executive Function Scores					
Phase 5	5,970	0.00	1.00	-4.19	3.65
Phase7	6,324	-0.28	0.96	-4.05	2.72
Phase 9	6,045	-0.36	0.94	-3.98	3.27
Standardized Memory Scores					
Phase 5	6,017	0.00	1.00	-2.80	4.55
Phase7	6,349	-0.03	0.99	-2.39	4.55
Phase 9	6,060	-0.26	0.94	-2.39	5.36

SD: standard deviation

Besides the aforementioned tests, the Mini-Mental State Examination (MMSE) (Folstein *et al.*, 1975) was also included in the cognitive test battery. Given the substantial ceiling effects showed in MMSE of the Whitehall II study, it was only used to exclude potential dementia cases (MMSE scores < 23) at study baseline and during follow-up in the sensitivity analysis.

Practice effects

To quantify the magnitude of practice effects, the difference between the 3-month test-retest memory scores at Phase 7 (i.e. Phase 7 repeat – Phase 7) was computed, as changes in cognitive performance within a short time largely reflects practice effects (Salthouse, 2009). The positive difference (1.52, 95% Confidence Interval (CI): 1.33-1.71) denoted a significant improvement in memory test (P-value of paired t-test < 0.0001). The correlation between Phase 7 memory test scores and practice effects was -0.35, showing higher initial memory scores were correlated with less improvement between Phase 7 and Phase 7 repeat memory tests. Conversely, a positive correlation estimated as 0.54 between practice effects and repeat Phase 7 memory score suggested stronger practice effects were related to better retest score.

To estimate the impact of practice effects on the subsequent cognitive test, standardized regression-based formulae were used, which allow using baseline test performances and other demographic variables to predict follow-up test performance in multiple regression algorithms (Duff *et al.*, 2010). Accordingly, Phase 7 memory score and practice effects were used to predict Phase 9 memory score.

Table 4-6 Practice Effects on Phase 9 Memory Score in the Whitehall II (N = 519) [a.]

	Model 1		Model 2	
	Beta (SE)	**P-value**	**Beta (SE)**	**P-value**
Phase 7 Memory Score	0.61 (0.04)	<0.001	0.57 (0.04)	<0.001
Practice Effects	0.33 (0.04)	<0.001	0.30 (0.04)	<0.001
Female			0.24 (0.25)	0.34
Age at Phase 9			-0.06 (0.02)	<0.001
Education			-0.12 (0.15)	0.41

[a] Practice effects were computed as the changes in memory scores between Phase 7 and Phase-7 repeat. SE: standard error.

As shown in Table 4-6, practice effects were significantly related to Phase 9 memory score, explaining 0.09 of the variation as indicated by the adjusted R^2. No statistically significant interaction between Phase 7 memory score and practice effects (P = 0.12) was detected in this regression model. Meanwhile, non-significant interaction was found between practice effects and demographic variables included. Thus there was no sufficient evidence to support that practice effects differ by previous memory performance, sex, age or education in this subsample of Whitehall II cohort.

Analyses above were based on short-term practice effects among participants who had cognitive measures at Phase 7, Phase-7 repeat and Phase 9, without accounting for prior tests since Phase 3. Albeit based on a selected subsample, results indicate practice effects do exist in this cohort and persist for at least 5 years. It is plausible the magnitude of practice effect depends on both the number of prior tests and test-retest intervals (Salthouse, 2009; Duff *et al.*, 2010). However, incorporating a test-retest interval into the model would result in adding another “time” metric, and parallels the intractable problem of decomposing age, birth cohort and period effects (Hall *et al.*, 2007).

Therefore, this thesis models the practice effects as the number of tests taken up to Phase 9 (Landy, 2012). It is assumed the effect of practice depends solely on the number of exposures to cognitive tests, that is, the second test would be influenced to a similar extent by previous tests irrelevant to the time interval between repeat cognitive tests (Hoffman *et al.*, 2011). Several models were chosen to estimate practice effects in the supplementary analysis, including linear, quadratic and categorical patterns (i.e. distinct improvement indicated by dummy variables for each phase).

4.2.3 Other covariates

Several covariates were considered as confounders on the basis of being associated with both social relationships (Section 2.1.2 Chapter 2) and cognitive decline (Section 2.2.2 Chapter 2), but not on the hypothesized causal pathways (Section 2.3 Chapter 2). For example, health behaviours were not included as they may potentially mediate the association under investigation.

Demographic variables included were age, year of birth (1930-1952, centred at 1940), sex (male = 0, female = 1) and ethnicity (white = 0, non-white = 1). Year of birth, as an indicator of the cohort effect, was included to take into account age non-convergence if cognitive decline was modelled as a function of age (Hoffman, 2012). Individuals from latter birth cohorts may have substantially higher cognitive test scores than their counterparts born earlier, known as the Flynn effect (Flynn, 1987). Thus, cognitive trajectories of different birth cohorts may not converge onto a single age-related trajectory (i.e. age non-convergence). Also, given cohort differences in developing and maintaining personal relationships (Allan, 2001; Stevens and van Tilburg, 2010; van Tilburg and Thomése, 2010), the social relationships-cognition association may be confounded by birth cohorts. For example, those from younger cohorts may have a relatively large number of friends and better cognition; as such the cohort effect could lead to a spurious association between large friend networks and higher cognitive function.

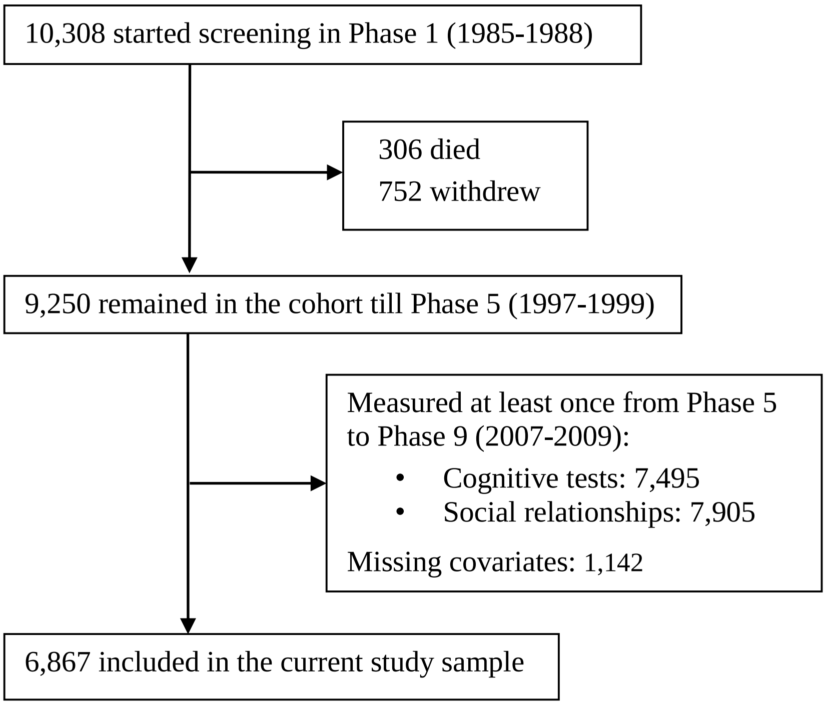
Two indicators of *socioeconomic circumstances* were used, which were educational attainment and employment grade. Educational attainment, measured as the highest qualification on leaving full-time education, was categorized into no formal education [low], up to secondary education [medium] and university or higher degree [high]. Employment grades, namely, clerical or support grades [low], professional or executive grades [medium] or executive and administrative grades [high], were based on the current British civil service grades if the participant was still working in the civil service or the last job grade if the participant had left the civil service or retired.

Health status was assessed by self-reported longstanding illness, depressive symptoms and prevalent chronic diseases. Longstanding illness was defined as any disease or medical condition that troubled participants over the last 12 months and was likely to continually affect them. Depressive symptoms were defined as General Health Questionnaire score ≥ 4 or use of anti-depressant medicine (Watson *et al.*, 2008). Prevalent chronic diseases were diagnosed coronary heart disease, stroke, diabetes or cancer. Coronary heart disease prevalence was ascertained according to clinically verified events, including myocardial infarction and definite angina (Ferrie *et al.*, 2006). Stroke cases were confirmed from participants' general practitioners, information extracted from hospital medical records or data from the National Health Hospital Episode Statistics databases (Britton *et al.*, 2012). Diabetes was assessed based on the WHO diagnostic criteria: having fasting glucose $\geq$7.0 (126mg/dl) or 2-hour plasma glucose $\geq$ 11.1mmol/l (200mg/dl), reported physician-diagnosed diabetes or use of diabetes medication (WHO, 2006). Physician-diagnosed cancer was identified via Cancer Registry and National Health Service-Wide Clearing Service notifications (Marmot and Brunner, 2005).

4.3 Data attrition and the analytic sample

Of the 10,308 participants at Whitehall II cohort inception, 306 had died and 752 had withdrawn before the start of cognitive data collection at Phase 5. Among the 9,250 participants remaining in the cohort, 7,495 completed at least one of the three cognitive tests, and 7,905 provided any measure of social relationships over the 10-year follow-up. This thesis' analyses were based on 6,867 participants who completed one or more cognitive tests and had data on social relationships and other covariates (Figure 4-4).

Figure 4-4 Flow Chart Mapping the Study Sample Selection



Compared with those remaining in the cohort but missing key variables for the current analysis, the included participants tended to be younger, more likely to be male, white, better educated and have a higher employment grade (Table 4-7). The study sample had a mean age of 55.8 at the analysis baseline (Phase 5). The predominant participants were white males, and nearly half of them had a university qualification and were in a high employment grade. As regards health status, 50.2% reported at least one longstanding illness, 13.1% had depressive symptoms and 13.9% had been diagnosed with at least one chronic disease at Phase 5 (data not shown).

Table 4-7 Comparison of the Remaining Participants till Phase 5 by whether or not Included in the Analytic Sample

Characteristics at Phase 5	**Participants not included (n =2,383)**	**Participants included (n = 6,867)**	P-value [a]
Age Mean (SD)	56.6 (6.1)	55.8 (6.0)	0.0003
Male (%)	59.6	70.8	<0.0001
White (%)	82.6	92.3	<0.0001
University Degree (%)	24.0	41.1	<0.0001
Highest employment grade (%)	31.1	42.8	<0.0001

[a] P-value for difference using ANOVA or Chi-Square.
SD: standard deviation

Of these 6,867 eligible participants, 68% had complete data for all three repeat measures of cognition, 20% had two repeat measures and 12% had only one cognitive measure over Phase 5 to Phase 9. Taking into account Phase 3, Phase 3-repeat and Phase 7-repeat, 71% of the analytic sample had taken cognitive tests three times or more (Table 4-8).

Table 4-8 Number of Cognitive Tests Taken by Phase 9 of the Analytic Sample (n = 6,867).[a]

Number of Times Taking Cognitive Tests	**Frequency**	**Percentage %**
1	853	12.4
2	1,161	16.9
3	2,755	40.1
4	1,840	26.8
5	258	3.8
Total	6,867	100

[a] Computed using all available cognitive data from main phases and subsample tests since Phase 3.

As shown in Table 4-9, measures of social relationships did not differ between participants successively taking cognitive assessments in the main three phases (Phase 5-9) and those with one or two cognitive tests missing, except for marital status (P = 0.002). Participants took all cognitive tests from Phase 5 to 9 had higher cognitive scores at Phase 5 than those missed subsequent tests (P < 0.001).

Table 4-9 Social Relationships and Cognitive Scores at Phase 5 by Number of Cognitive Tests between Phase 5 and Phase 9

	Participants with complete cognitive tests for three phases (n = 4,670)		**Participants with 1 or two cognitive tests missing (n = 2,197)**		P-value [a]
Characteristics at Phase 5	**Mean**	**SD**	**Mean**	**SD**	
Confiding Support	13.3	4.1	13.3	4.3	0.94
Practical Support	4.5	2.4	4.5	2.5	0.85
Negative Support	2.4	1.9	2.4	2.0	0.77
Friend Network	4.1	2.0	4.1	2.0	0.28
Relative Network	3.2	1.8	3.2	1.9	0.48
Married/Cohabiting (%)	80.2		76.4		0.002
Standardized Cognitive Scores [b]					
Executive Function	0.08	0.9	-0.28	1.1	<0.001
Memory	0.05	1.0	-0.16	1.0	<0.001

[a] P-value for difference
[b] Age-adjusted cognitive function scores
SD: standard deviation

During the 10-year follow-up between Phase 5 (1997-1999) to Phase 9 (2007-2009), 368 (5.4%) had died and 680 (9.9%) did not respond or had withdrawn from the study sample by Phase 9. As presented in Table 4-10, participants lost to follow-up were more likely to be older, female, ethnic minority, had relatively lower socioeconomic positions, reported more longstanding illnesses, and had higher prevalence of depressive symptoms and chronic diseases at analysis baseline (Phase 5). Most of the social relationship measures did not vary by participation status, but those participating at Phase 9 appeared to have a slightly larger friend network (P = 0.06) and were more likely to be married or cohabiting (P < 0.001) at Phase 5 than their dropped-out counterparts. It was also evident that those who dropped out in the later phases were more likely to have lower baseline cognitive scores (P < 0.001).

Table 4-10 Descriptive Statistics for Variables Used in Analysis by Participation Status at Phase 9 (n = 6,867)

Characteristics at Phase 5	**Participated at Phase 9 (n=5,819)**		**Not Participated at Phase 9 (n=1,048)**		P-value [a]
	Mean	SD	Mean	SD	
Demographic Variables					
Age, years	55.5	6.0	57.6	6.1	<0.0001
Male (%)	71.6		66.4		0.001
White (%)	93.0		88.2		<0.001
Socioeconomic Circumstance (%)					
University degree	42.0		35.5		<0.001
Highest employment grade	44.6		32.5		<0.001
Health Status (%)					
Had longstanding illness	48.7		55.7		<0.001
Depressed	12.4		16.8		<0.001
Had chronic disease [b]	12.5		21.7		<0.001
Social Relationships					
Confiding Support (range:0-21)	13.3	4.1	13.4	4.4	0.53
Practical Support (range: 0-9)	4.5	2.4	4.6	2.6	0.21
Negative Support (range: 0-12)	2.4	1.9	2.4	2.0	0.91
Friend Network (range: 0-8)	4.1	2.0	4.0	2.0	0.06
Relative Network (range: 0-8)	3.2	1.9	3.2	1.9	0.90
Married/Cohabiting (%)	79.5		73.4		<0.001
Standardized Cognitive Scores [c]					
Executive Function	0.06	0.9	-0.26	1.1	<0.001
Memory	0.03	1.0	-0.17	1.0	<0.001

[a] P-value for difference
[b] Prevalent chronic disease was diagnosed coronary heart disease, stroke, diabetes or cancer.
[c] Age-adjusted cognitive function scores
SD: standard deviation

4.4 Overview of the statistical approaches

The testing of hypotheses for the three objectives utilised different statistical methods as follows:

Objective one**:** The impact of middle-life social relationships on subsequent age-related rate of cognitive decline was addressed by *multilevel modelling* (MLM). The relative importance of functional and structural aspects of social relationships was examined by simultaneously entering both components into the fully adjusted model.

Objective two**:** *Growth mixture modelling* (GMM) was utilized to uncover the longitudinal patterns of social relationship transitions in relation to cognitive ageing. Two sub-steps were involved. First, the optimal number of classes and shapes of latent growth trajectories that best characterize social relationship transitions were identified. Then, these derived longitudinal latent classes of social relationships were used as dummy indicators to examine differences in the trajectories of cognitive ageing by MLM.

Objective three: The temporal direction between changes in social relationships and changes in cognitive function was investigated by using the *dual change score model* (DCSM). The dynamic hypotheses on social causation and health selection were statistically evaluated by comparing the lead-lag estimates of four alternative DCSMs.

The following three chapters introduce these three main statistical models in detail. Their applications to the Whitehall II analytic sample and the corresponding results are also presented sequentially.

Chapter 5. Objective one: the effect of mid-life social relationships on cognitive ageing

Summary

This chapter examines which components of social relationships at mid-life are associated with cognitive ageing. Functional and structural measures of social relationships, which were assessed twice during the 8 years preceding cognitive assessment, were used to predict the annual rate of decline in executive function and memory over the subsequent 10-year follow-up. Multilevel modelling (MLM) was used to depict the trajectory of cognitive decline as a function of age, separating ageing effect from birth cohort effect. The potential influence of practice effects was also explored.

5.1 Introduction

As discussed in literature review chapter (Page 38), lack of detail in assessments of social relationships blurs the investigation of cognitively beneficial components. This chapter hence assessed the association between middle-life functional and structural aspects of social relationships and age-related decline in cognitive ageing over the subsequent 10 years from middle age to early old age. Multilevel modelling (MLM) was used to make full use of repeat cognitive tests allowing for individual variations.

Introduction to MLM

A distinctive feature of MLM is to handle hierarchical data (Singer and Willett, 2003). In longitudinal studies, repeated measures obtained over time from the same individual are dependent. Multilevel modelling addresses this dependency by distributing the residual variance into a hierarchical structure, that is, between-person (level-2) and within-person (level-1) variances. Between-person variation represents time-invariant inter-individual differences, while within-person variation denotes time-varying intra-individual differences. Both types of variation along with their interaction can be estimated simultaneously by MLM. In addition, MLM can accommodate unbalanced designs due to missing repeat measures (assuming MCAR or MAR), unequal numbers of follow-up and different observational intervals.

Empty Model (Random Intercept)

$$Level\ 1: \quad y_{ti} = \beta_{0i} + e_{ti}$$

$$Level\ 2: \quad \beta_{0i} = \beta_0 + U_{0i}$$

The equation above presents the *empty model* without any predictor, in which y_{ti} is the outcome at phase ***t*** (level-1) for individual ***i*** (level-2). β_0 is the fixed grand mean of the outcome (constant). U_{0i} is the level-2 random effect, allowing each individual to deviate randomly from the grand mean; thus $\beta_0 + U_{0i}$ represents the mean of the outcome for individual ***i*** over all phases (random intercept). e_{ti} is the level-1 residual, indicating differences between the observed outcome (y_{ti}) at ***t*** th occasion and the overall individual mean, i.e. $e_{ti} = y_{ti} - (\beta_0 + U_{0i})$. This model assumes that both U_{0i} and e_{ti} are normally distributed.

To indicate the dependency of repeat measures, intraclass correlation (ICC) can be calculated from this empty model. ICC is the proportion of total variance that is due to between-person variations. ICC shows the average correlation among occasions, with larger ICC suggesting higher correlation.

Intraclass correlation (ICC)

$$\text{ICC} = \frac{\text{BP}}{\text{BP} + \text{WP}} = \frac{\text{Intercept Variance}}{\text{Intercept Variance} + \text{Residual Variance}}$$

$$= \frac{\text{BP Variance in Mean Outcome}}{\text{Total Outcome Variance}} = \frac{\sigma_u^2}{\sigma_u^2 + \sigma_e^2}$$

BP: between-person difference; WP: within-person difference.

Random Slope Model (Random Linear Age)

$$Level\ 1: \quad y_{ti} = \beta_{0i} + \beta_{1i}(age_{ti}) + e_{ti}$$

$$Level\ 2: \quad \beta_{0i} = \beta_0 + U_{0i}$$

$$\beta_{1i} = \beta_1 + U_{1i}$$

The equation above supposes the outcome y_{ti} is a linear function of age (slope). The random slope model allows both intercept and slope to vary randomly across individuals. Compared with the *empty model*, a new term $\beta_{1i}(age_{ti})$ has been introduced into this model. The random slope $\beta_{1i} = \beta_1 + U_{1i}$, where β_1 is the fixed slope of average regression, signifying the effect of one unit increase in age on the outcome across all individuals; U_{1i} indicates individual-specific deviation from the fixed linear slope. U_{1i} is also assumed to be normally distributed. A covariance of random intercepts and random slopes was estimated by this model, indicating how between-person variation changes with age. Here, age is fitted in the model as a time-varying variable, with both fixed and random effect. Time-invariant predictors can be added into a multilevel model with fixed effect only, to explain the variance of intercept and slope (interaction with age).

5.2 Methods

MLM was applied to cognitive data from three phases (1997-1999, 2002-2004 and 2007-2009) to determine the core terms, *fixed effects*: age (centred at 60 years), age squared, year of birth (centred at 1940), sex, ethnicity, social relationships, educational attainment, employment grade, health status measured at Phase 5 and their interactions with age; *random effect* for intercept and slope (age) to allow individual variation on intercept and rate of cognitive decline. The proportions of within- and between- person variation were calculated via ICC. The within-person variation was further explored using the indices suggested by Salthouse (2007).

The analytic strategy for the longitudinal analysis was developed, for each cognitive domain, by adding variables in following three blocks (Table 5-1). **Block One** obtained the base growth-curve model to estimate cognitive decline as a function of age. The age convergence assumption was tested via introducing between-person cohort effect (year of birth). Sex and ethnicity were controlled for to examine whether the rate of cognitive decline varies across demographic characteristics.

Block Two tested the key effect of social relationships on cognitive function and rate of cognitive decline. To summarise the history of social relationships in middle age, a cumulative score of social relationships was calculated by averaging Phase 2 and Phase 5 scores for each social relationships subscale (except for marital status where only Phase 5 categories were used). If either phase value was missing, the score from the available phase was imputed as the cumulative score. These average scores were then divided into three groups based on Phase 2 tertile cut-points. Three-way interaction terms between social relationships, age and sex with all lower order interaction terms were used to assess sex differences in the effects of social relationships on cognitive decline. Models were further adjusted for socioeconomic and health status. **Block Three** compared the relative importance of functional and structural measures of social relationships in relation to cognitive ageing, by fitting all components of social relationships simultaneously into the fully-adjusted model.

Table 5-1 Fixed and Random Effect Terms in Primary Multilevel Models [a]

Model	Fixed Effect Terms	Random Effect Terms
Block One:		
Age Effect		
Model 1:	Age	
Model 2:	Age	Age
Model 3:	Age + Age^2	Age
Model 4:	Age + Age^2	Age , Age^2
Age Convergence (Cohort Effect)		
Model 5:	Model 3 + Cohort (year of birth)	Age
Model 6:	Model 5 + Cohort*Age	Age
Model 7:	Model 6 + Sex	Age
Model 8:	Model 7 + Sex*Age	Age
Model 9:	Model 7 + Ethnicity	Age
Model 10:	Model 9 + Ethnicity*Age	Age
Block Two:		
Effect of Social Relationships		
Model 11:	Model 10 + Social relationships (one component)	Age
Model 12:	Model 11 + Social relationships*Age	Age
Sex - Social Relationships Interaction		
Model 13:	Model 12 + Social relationships*Sex	Age
Model 14:	Model 13 + Social relationships*Age*Sex	Age
Socioeconomic Circumstance [b]		
Model 15:	Model 12 + Socioeconomic Circumstance	Age
Model 16:	Model 15 + Socioeconomic Circumstance * Age	Age
Health Status [c]		
Model 17:	Model 16 + Health	Age
Model 18:	Model 17 + Health*Age	Age
Block Three:		
Relative importance of functional and structural measures of social relationships		
Model 19:	Model 18 + Functional social relationships (all)	Age
Model 20:	Model 19 + Structural social relationships	Age

[a] Standard errors could not be computed for the random effect of age squared. For all models interactions with quadratic age slope were tested. As these interactions were non-significant (or borderline significant with larger BIC), models were simplified with interaction with linear age slope only.
[b] Socioeconomic circumstance was indicated by educational attainment and employment grade.
[c] Health status was assessed by self-reported longstanding illness, depressive symptoms and prevalent chronic diseases.

Supplementary analyses were conducted to examine practice effects by controlling for the number of times taking the repeat cognitive tests. Practice effects were entered as time-varying variables and modelled by linear, quadratic and categorical terms. Considering potential reverse causation, possible dementia cases (MMSE less than 23 over the follow-up) were excluded; further, Phase 5 cognitive scores (entered as continuous variables) were used to examine the association with the trajectories of functional social relationships from Phase 5 to Phase 9. Last, the growth curves of cognitive function were modelled as a function of time-in-study rather than age, to verify whether findings of main analyses would be confounded by a mixed effect of between-person age difference and within-person age change.

Maximum likelihood was used in estimating all model parameters. The model fit was tested using Akaike information criterion (AIC), Bayesian Information Criteria (BIC) and likelihood ratio tests. All analyses were performed with STATA SE version 13.1 (StataCrop LP, College Station, Texas).

5.3 Results

Before modelling cognitive decline as a function of age, several checks were conducted to assess within-person (WP) and between-person (BP) variations of the three repeat cognitive measures and their associations with age (Salthouse, 2007). As shown in Table 5-2 , ICC was 0.83 for executive function and 0.45 for memory, indicating BP variance accounted for four fifths of the total variance for executive function, while less than half for memory. The average correlation of memory scores thus is lower compared with that of executive function. Greater WP variability is expected for memory scores; such that the mean WP variability (M_{WP}) was equivalent to 36% of the variability in BP difference (SD_{BP}) for executive function, whereas the corresponding ratio is 71% for memory (column 7 of Table 5-2). The positive correlations of BP difference and WP change suggest WP variability was larger for participants who had higher mean cognitive scores. The mean BP cognitive scores were negatively related to age, implying lower average cognitive function for older participants. On the other hand, the relatively small correlations between WP variability and age (non-significant for WP variability in memory and age) suggest little systematic change in WP variability with age (Allerhand *et al.*, 2014).

Table 5-2 Intraclass Correlation and Indices of Within-Person Variability

	ICC	**Mean**		**SD**		**M (SD)/ SD(M)**	**Correlation M.SD**	**M.Age**	**SD.Age**
		M_{BP}	SD_{BP}	M_{WP}	SD_{WP}				
Executive Function	0.83	-0.28	0.96	0.35	0.23	0.36	0.06	-0.32	0.07
Memory	0.45	-0.13	0.84	0.60	0.43	0.71	0.20	-0.30	0.00

ICC = intraclass correlation;
Mean (M): the mean of the three repeat cognitive measures, indicating between-person (BP) difference quantified by an overall mean M_{BP} and standard deviation SD_{BP};
SD: the standard deviation of the three repeat cognitive measures, indicating within-person (WP) change quantified by the overall mean M_{WP} and standard deviations SD_{WP};
M (SD)/SD(M) = the ratio of the average within-person change M_{wp} over the standard deviation of between-person difference SD_{BP};
Correlation M.SD = the correlation between between-person mean M_{BP} and within-person change M_{wp};
M.Age = correlation of between-person mean M_{BP} and age;
SD.Age = correlation of within-person change M_{wp} and age.

5.3.1 Block one

Table 5-3 and Table 5-4 present a series of MLMs used to obtain the conditional base growth curve models of executive function and memory.

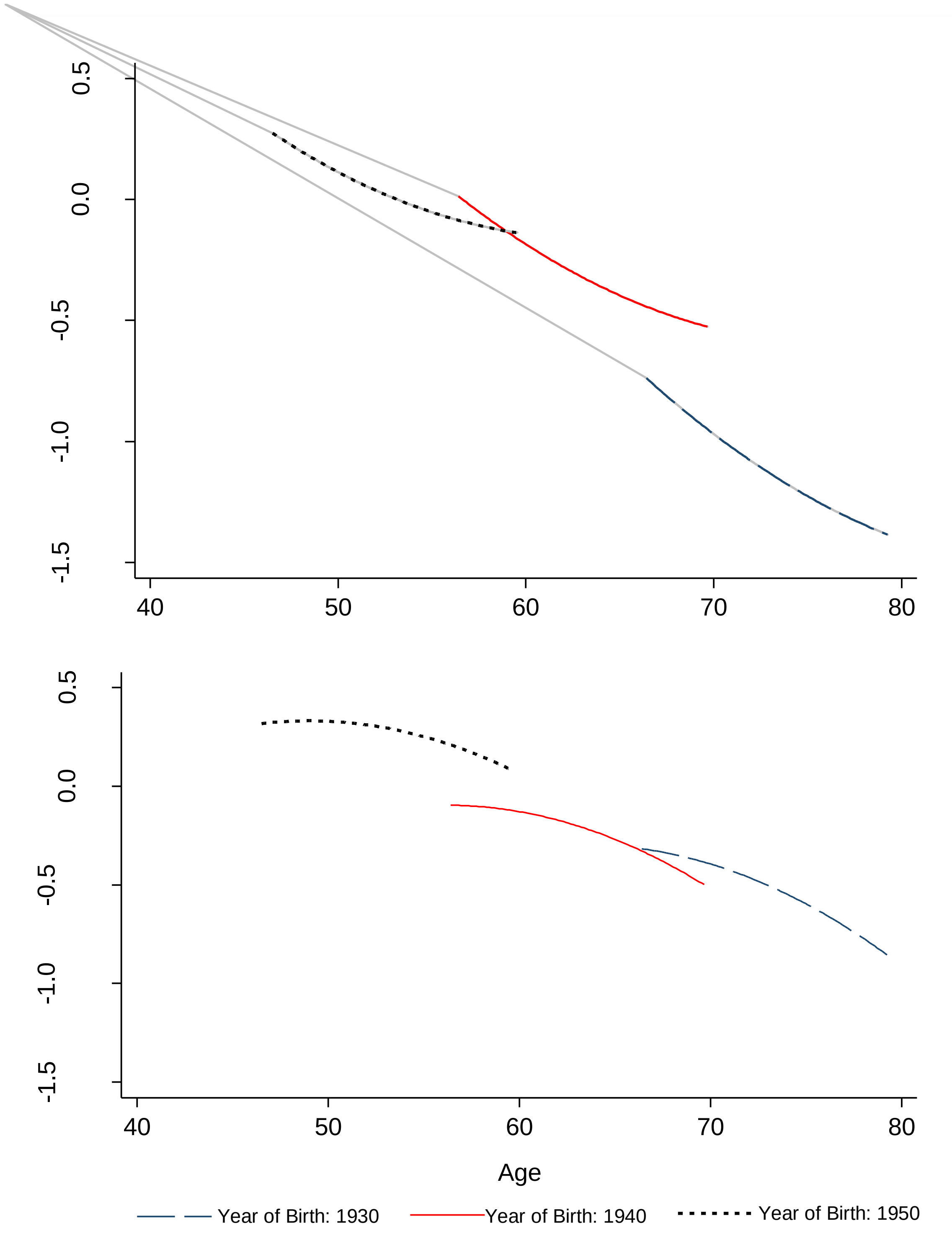
Age effect

The model fit was significantly improved by inclusion of a random effect for linear age (Model 2) and further improved by inclusion of a quadratic term for age (Model 3). However, standard errors could not be computed when adding the random effect of age-squared, suggesting the model was too complex for the data. Thus only the linear-age slope was allowed to be random (Model 3). The annual rate of cognitive decline was estimated -0.04 of baseline SD for executive function and -0.03 of baseline SD for memory at age 60, accelerating with age (negative quadratic age slope).

Cohort Effect

Incremental effects of birth cohort were found on the intercept (Model 5) and linear age slope (Model 6) signifying age non-convergence. Participants born more recently had higher initial executive function combined with slower rates of decline. As for memory, those born more recently showed higher initial scores and similar rate of decline as their earlier born counterparts (Figure 5-1). The interactions between cohort and quadratic age slopes were not significant. Therefore, Model 6, cohort interacted with linear age slope only, was retained.

Figure 5-1 Predicted Executive Function and Memory Trajectories by Year of Birth, Estimates Derived from Model 6



Next, demographic variations in the base growth-curve were checked (Model 7-10). Baseline cognitive function differed by sex and ethnicity, whereas the rate of cognitive decline was only affected by ethnicity. Hence, sex, ethnicity and interaction between ethnicity and linear age were retained in Model 10 as the basis for Block Two.

Table 5-3 Block One: Model Development for Base Growth Curve Model of Executive Function [a]

Executive Function	Model1 Beta (SE)	Model 2 Beta (SE)	Model 3 Beta (SE)	Model 5 Beta (SE)	Model 6 Beta (SE)	Model 7 Beta (SE)	Model 10 Beta (SE)
Fixed Effects:							
Intercept	-0.24 (0.01)	-0.23 (0.01)	-0.22 (0.01)	-0.24 (0.01)	-0.19 (0.01)	-0.07 (0.01)	1.22 (0.04)
Year of Birth (centred at 1940)				0.01 (0.002)	0.004 (0.002)	0.003(0.002)	-0.001 (0.002)
Female						-0.38 (0.02)	-0.30 (0.02)
Non-white							-1.20 (0.03)
Age (centred at 60)	-0.04 (0.001)	-0.04 (0.001)	-0.04 (0.001)	-0.04 (0.001)	-0.05 (0.001)	-0.05 (0.001)	-0.05 (0.001)
Age squared (centred at 60)			-0.0004 (0.0001)	-0.0003 (0.0001)	0.002 (0.0002)	0.001 (0.0002)	0.002 (0.0002)
Year of birth* Age					0.004 (0.0003)	0.004 (0.0003)	0.004 (0.0002)
Age * Female							NS
Age*Non-white							0.01 (0.003)
Random effect:							
Variance Components							
Intercept Variance	0.76 (0.01)	0.77 (0.01)	0.77 (0.01)	0.76 (0.01)	0.77 (0.01)	0.74 (0.01)	0.63 (0.01)
Linear Variance		0.001 (0.00)	0.001 (0.00)	0.001 (0.00)	0.001 (0.00)	0.001 (0.00)	0.001 (0.00)
Intercept-Linear Covariance		-0.003 (0.001)	-0.003 (0.001)	-0.003 (0.001)	-0.003 (0.001)	-0.004 (0.001)	-0.003 (0.001)
Residual Variance	0.13 (0.002)	0.12 (0.002)	0.12 (0.002)	0.12 (0.002)	0.11 (0.002)	0.11 (0.002)	0.11 (0.002)
Goodness of fit							
-Log likelihood	17406	17362	17339	17321	17253	17112	16556
Number of parameters	4	6	7	8	9	10	12
AIC	34819	34735	34692	34659	34525	34245	33136
BIC	34847	34777	34741	34714	34587	34313	33219
LR test		<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

[a] Model 4, 8 and 9 were not shown due to non-significant parameters.
SE: standard error; LR test: likelihood ratio test in reference to previous model; NS: non-significant.

Table 5-4 Block One: Model Development for Base Growth Curve Model of Memory [a]

Memory	Model1 Beta (SE)	Model 2 Beta (SE)	Model 3 Beta (SE)	Model 5 Beta (SE)	Model 6 Beta (SE)	Model 7 Beta (SE)	Model 10 Beta (SE)
Fixed Effects:							
Intercept	-0.09 (0.01)	-0.09 (0.01)	-0.06 (0.01)	-0.09 (0.01)	-0.13 (0.01)	-0.14 (0.01)	0.45 (0.04)
Year of Birth (centred at 1940)				0.01 (0.002)	0.02 (0.002)	0.02 (0.002)	0.02(0.002)
Female						0.05 (0.02)	0.09 (0.02)
Non-white							-0.55 (0.03)
Age (centred at 60)	-0.03 (0.001)	-0.03 (0.001)	-0.03 (0.001)	-0.03 (0.001)	-0.02 (0.002)	-0.02 (0.002)	-0.02 (0.002)
Age squared (centred at 60)			-0.0006 (0.0001)	-0.001 (0.0001)	-0.002 (0.0003)	-0.002 (0.0003)	-0.002 (0.0003)
Year of birth* Age					-0.003 (0.0005)	-0.003 (0.0005)	-0.003 (0.0005)
Age * Female							NS
Age*Non-white							0.01 (0.004)
Random effect:							
Variance Components							
Intercept Variance	0.40 (0.01)	0.39 (0.01)	0.39 (0.01)	0.39 (0.01)	0.39 (0.01)	0.39 (0.01)	0.37 (0.01)
Linear Variance		0.0001 (0.00)	0.0002 (0.00)	0.0002 (0.00)	0.0002 (0.00)	0.0002 (0.00)	0.0002 (0.00)
Intercept-Linear Covariance		-0.003 (0.001)	-0.003 (0.001)	-0.003 (0.001)	-0.003 (0.001)	-0.003 (0.001)	-0.003 (0.001)
Residual Variance	0.51 (0.01)	0.51 (0.01)	0.51 (0.01)	0.51 (0.01)	0.50 (0.01)	0.50 (0.01)	0.50 (0.01)
Goodness of fit							
-Log likelihood	23870	23860	23849	23814	23790	23787	23650
Number of parameters	4	6	7	8	9	10	12
AIC	47748	47732	47694	47644	47597	47594	47324
BIC	47775	47774	47742	47699	47660	47663	47407
LR test		<0.0001	<0.0001	<0.0001	<0.0001	0.02	<0.0001

[a] Model 4, 8 and 9 were not shown due to non-significant parameters.
SE: standard error; LR test: likelihood ratio test in reference to previous model; NS: non-significant.

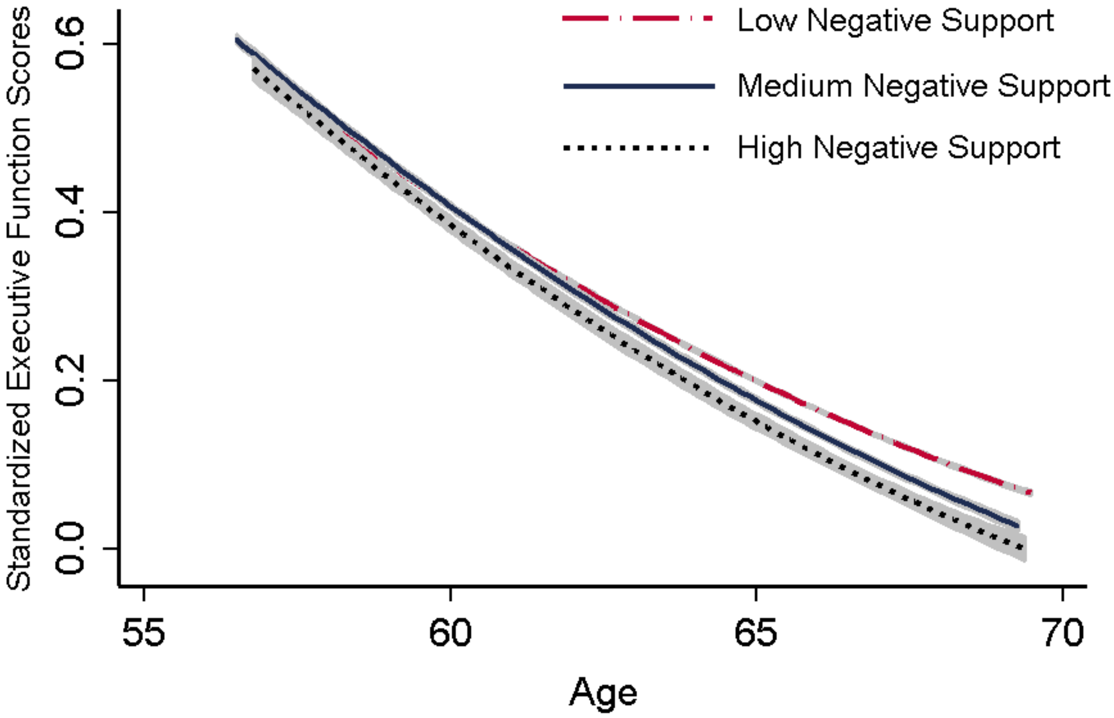
5.3.2 Block two

Block Two assessed the effect of midlife social relationships on annual rate of cognitive decline. One at a time, each component of social relationships was added as an independent variable. The key interaction term between each measure of social relationships and age tested whether social relationships were related to the rate of cognitive decline. This interaction test was based on the null hypothesis that there were no differences in cognitive decline between high, medium and low social relationship groups.

To examine the sex-specific effect of social relationships on cognitive decline, an interaction term between sex, age and social relationships plus all lower order interaction terms were added in Model 14. Statistically non-significant P-value for the three-way interaction suggested the association between social relationships and cognitive ageing was similar in men and women (P-value range: 0.27~0.94). Thus analyses were conducted with men and women combined.

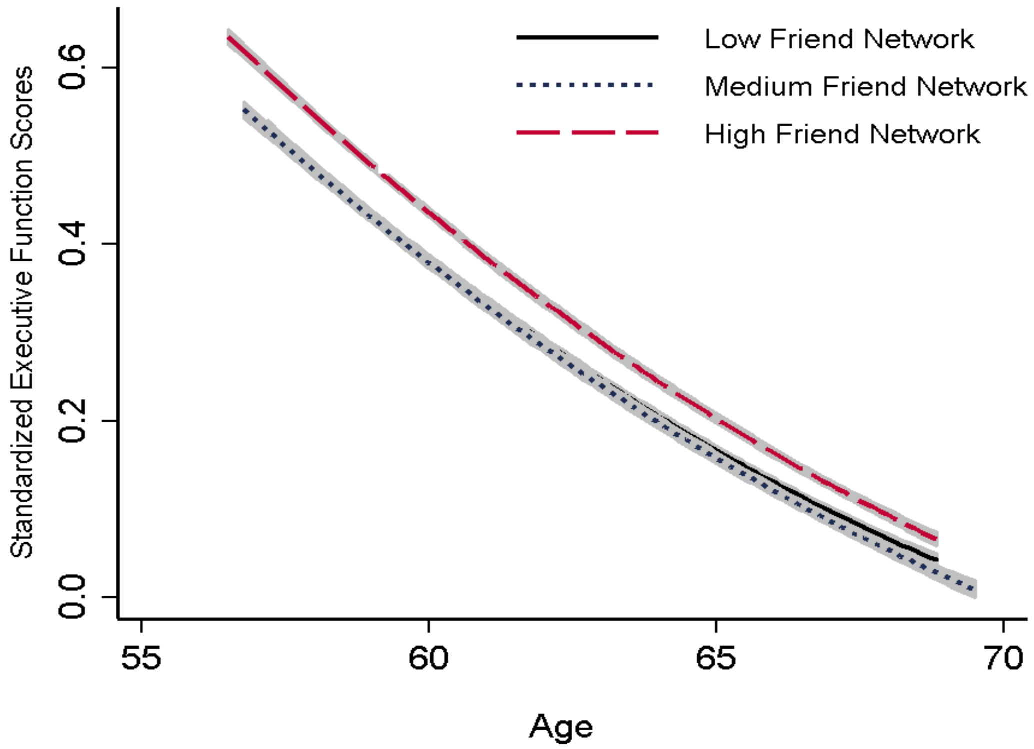
Table 5-5 shows the effect of mid-life social relationships on the intercept (centred at age 60) and annual rate of decline in executive function (Model 12), stepwise adjusted for socioeconomic circumstance (Model 16) and health status (Model 18). As regards functional measures of social relationships (upper panels of Table 5-5), the positive association between higher practical support and better executive function at age 60 was not statistically significant after adjustment for socioeconomic status. The rate of decline in executive function did not differ by positive aspects of social relationships in either the confiding support or practical support groups. In contrast, participants reporting a higher level of negative support showed faster decline in executive function (Figure 5-2), with an annual change accelerated by -0.005 SD (95%CI: -0.009,-0.001) compared with those who perceived low negative support at middle age (P-value for *negative support*age* = 0.009). This association remained after adjustment for all covariates included. Thus the -0.05 difference in 10-year decline in executive function between highest and lowest third of negative support corresponds to one extra year of decline in executive function for participants aged 60 years (annual rate of decline estimated at -0.05 standard error (SE): 0.001, Table 5-3).

Figure 5-2 Predicted Age-Based Trajectories of Executive Function by Cumulative Negative Support Categories (Prediction for White Male Participants of Whitehall II Cohort Born in 1940, in the Highest Employment Grade and Having a University Qualification, and No Longstanding Illness, Depressive Symptoms or Prevalent Chronic Diseases at Phase 5; Grey Area around the Trajectories Indicate 95% Confidence Interval).



As for structural measures of social relationships (lower panels Table 5-5), participants reporting high friend networks showed better executive function at age 60 in comparison with those reporting low friend networks. Socioeconomic and health variations together attenuated this effect by 61%, yet statistically significant difference still remained (0.06, 95% CI: 0.01, 0.11). Having more relatives or being non-married was related to lower executive function at age 60, but these negative associations were due to variations in socioeconomic circumstances and health status. On the other hand, the rate of decline in executive function did not differ significantly across either measure of structural social relationships. Figure 5-3 illustrates the age-based trajectories of executive function by friend network categories, with participants reporting low and high friend network differentiated by their initial cognitive scores but not the rate of decline.

Figure 5-3 Predicted Age-Based Trajectories of Executive Function by Cumulative Friend Network Categories (Prediction for White Male Participants of Whitehall II Cohort Born in 1940, in the Highest Employment Grade and Having a University Qualification, and No Longstanding Illness, Depressive Symptoms or Prevalent Chronic Diseases at Phase 5; Grey Area around the Trajectories Indicate 95% Confidence Interval).



The corresponding associations between social relationships and age-based trajectories of memory are presented in Table 5-6. Neither confiding support nor practical support was associated with the rate of decline in memory. Negative support was related to lower memory scores at age 60 (high vs low = -0.07, 95% CI: -0.13,-0.02), but the effect was absent longitudinally (P-value for *negative support*age* = 0.19). The positive association between friend network and memory score was not statistically significant once controlled for socioeconomic and health variations. The rate of decline in memory was not different by structural measures of social relationships either.

Table 5-5 Association between Mid-life Social Relationships and Age-Based Trajectories of Executive Function [a]

	Model 12		Model 16		Model 18	
	Intercept Beta [95% CI]	**Slope (per year)** Beta [95% CI]	**Intercept** Beta [95% CI]	**Slope (per year)** Beta [95% CI]	**Intercept** Beta [95% CI]	**Slope (per year)** Beta [95% CI]
Confiding Support						
Low	ref.		ref.		ref.	
Medium	0.037 [-0.005,0.080]	-0.003 [-0.006,0.000]	0.010 [-0.027,0.047]	-0.003 [-0.006,0.000]	0.010 [-0.027,0.046]	-0.003 [-0.006,0.000]
High	0.034 [-0.035,0.102]	-0.002 [-0.006,0.003]	-0.043 [-0.102,0.016]	-0.001 [-0.005,0.004]	-0.046 [-0.105,0.013]	-0.001 [-0.005,0.004]
Practical Support						
Low	ref.		ref.		ref.	
Medium	0.045* [0.001,0.089]	-0.003 [-0.006,0.000]	0.006 [-0.032,0.044]	-0.002 [-0.005,0.001]	0.005 [-0.033,0.043]	-0.002 [-0.005,0.001]
High	0.070* [0.011,0.129]	-0.004 [-0.008,0.000]	-0.001 [-0.051,0.050]	-0.003 [-0.007,0.001]	-0.001 [-0.052,0.049]	-0.003 [-0.007,0.001]
Negative Support						
Low	ref.		ref.		ref.	
Medium	0.038 [-0.011,0.087]	-0.005** [-0.008,-0.002]	0.002 [-0.039,0.044]	-0.004** [-0.008,-0.001]	0.004 [-0.038,0.046]	-0.005** [-0.008,-0.001]
High	0.011 [-0.046,0.068]	-0.006** [-0.009,-0.002]	-0.016 [-0.065,0.033]	-0.005* [-0.008,-0.001]	-0.009 [-0.058,0.041]	-0.005* [-0.009,-0.001]
Friend Network						
Low	ref.		ref.		ref.	
Medium	0.048 [-0.004,0.099]	-0.001 [-0.005,0.002]	0.003 [-0.041,0.048]	-0.001 [-0.005,0.002]	0.000 [-0.044,0.045]	-0.001 [-0.005,0.002]
High	0.140*** [0.087,0.193]	-0.003 [-0.007,0.000]	0.060* [0.014,0.106]	-0.003 [-0.007,0.000]	0.055* [0.009,0.101]	-0.003 [-0.007,0.000]
Relative Network						
Low	ref.		ref.		ref.	
Medium	0.017 [-0.035,0.069]	0.000 [0.000,0.000]	0.020 [-0.025,0.064]	0.000 [0.000,0.000]	0.019 [-0.026,0.064]	0.000 [0.000,0.000]
High	-0.088** [-0.140,-0.035]	0.000 [-0.003,0.004]	0.012 [-0.034,0.058]	0.000 [-0.003,0.004]	0.011 [-0.034,0.057]	0.000 [-0.003,0.004]
Marital Status						
Married/Cohabiting	ref.		ref.		ref.	
Single	-0.158*** [-0.222,-0.094]	0.004 [-0.001,0.008]	-0.056* [-0.112,-0.001]	0.003 [-0.002,0.007]	-0.054 [-0.110,0.002]	0.002 [-0.002,0.007]
Divorced	-0.127** [-0.211,-0.043]	0.000 [-0.006,0.006]	-0.039 [-0.112,0.034]	-0.001 [-0.006,0.005]	-0.035 [-0.108,0.037]	-0.001 [-0.006,0.005]
Widowed	-0.139* [-0.268,-0.009]	-0.006 [-0.014,0.003]	-0.001 [-0.114,0.112]	-0.005 [-0.014,0.003]	0.001 [-0.112,0.114]	-0.005 [-0.014,0.003]

[a] Cumulative scores of mid-life social relationships were calculated by averaging Phase 2 & 5 measures, which were then divided into three groups. Marital status at Phase 5 was used.
Model 12: adjusted for birth cohort, sex and ethnicity; Model 16: Model 12 + education + employment grade; Model 18: Model 16 + longstanding illness + depressive symptoms + chronic diseases
* P < 0.05, ** P < 0.01, *** P < 0.001; CI: confidence interval

Table 5-6 Association between Mid-life Social Relationships and Age-Based Trajectories of Memory [a]

	Model 12		**Model 16**		**Model 18**	
	Intercept Beta [95% CI]	**Slope (per year)** Beta [95% CI]	**Intercept** Beta [95% CI]	**Slope (per year)** Beta [95% CI]	**Intercept** Beta [95% CI]	**Slope (per year)** Beta [95% CI]
Confiding Support						
Low	ref.		ref.		ref.	
Medium	0.024 [-0.015,0.064]	-0.003 [-0.007,0.001]	0.010 [-0.028,0.048]	-0.003 [-0.007,0.002]	0.008 [-0.030,0.047]	-0.003 [-0.007,0.001]
High	0.023 [-0.041,0.087]	0.003 [-0.004,0.009]	-0.011 [-0.073,0.051]	0.003 [-0.004,0.010]	-0.015 [-0.076,0.047]	0.003 [-0.004,0.010]
Practical Support						
Low	ref.		ref.		ref.	
Medium	0.019 [-0.022,0.060]	-0.003 [-0.007,0.002]	0.000 [-0.040,0.040]	-0.002 [-0.007,0.002]	-0.001 [-0.041,0.039]	-0.002 [-0.007,0.002]
High	0.063* [0.008,0.117]	-0.003 [-0.009,0.003]	0.029 [-0.024,0.082]	-0.001 [-0.007,0.005]	0.029 [-0.024,0.081]	-0.002 [-0.007,0.004]
Negative Support						
Low	ref.		ref.		ref.	
Medium	-0.010 [-0.056,0.035]	-0.004 [-0.009,0.001]	-0.026 [-0.070,0.018]	-0.004 [-0.009,0.001]	-0.023 [-0.067,0.022]	-0.004 [-0.009,0.001]
High	-0.071** [-0.124,-0.018]	-0.002 [-0.008,0.004]	-0.085** [-0.136,-0.033]	-0.001 [-0.006,0.005]	-0.074** [-0.126,-0.021]	-0.000 [-0.006,0.005]
Friend Network						
Low	ref.		ref.		ref.	
Medium	0.052* [0.004,0.100]	0.001 [-0.005,0.006]	0.032 [-0.015,0.078]	0.001 [-0.004,0.006]	0.027 [-0.019,0.074]	0.000 [-0.005,0.006]
High	0.088*** [0.038,0.137]	0.002 [-0.003,0.007]	0.052* [0.004,0.100]	0.002 [-0.004,0.007]	0.046 [-0.002,0.094]	0.001 [-0.004,0.006]
Relative Network						
Low	ref.		ref.		ref.	
Medium	0.043 [-0.005,0.091]	-0.002 [-0.007,0.004]	0.043 [-0.003,0.090]	-0.002 [-0.007,0.003]	0.042 [-0.005,0.089]	-0.002 [-0.007,0.003]
High	-0.031 [-0.080,0.018]	0.003 [-0.003,0.008]	0.013 [-0.034,0.061]	0.001 [-0.004,0.006]	0.011 [-0.036,0.059]	0.001 [-0.005,0.006]
Marital Status						
Married/Cohabiting	ref.		ref.		ref.	
Single	-0.057 [-0.117,0.003]	-0.000 [-0.006,0.006]	-0.010 [-0.069,0.048]	-0.001 [-0.007,0.005]	-0.006 [-0.065,0.052]	-0.000 [-0.007,0.006]
Divorced	0.027 [-0.052,0.106]	-0.007 [-0.015,0.002]	0.066 [-0.011,0.143]	-0.007 [-0.015,0.002]	0.070 [-0.007,0.147]	-0.007 [-0.015,0.002]
Widowed	-0.055 [-0.184,0.074]	0.001 [-0.012,0.014]	0.001 [-0.125,0.127]	0.002 [-0.011,0.015]	0.002 [-0.123,0.128]	0.002 [-0.011,0.015]

[a] Cumulative scores of mid-life social relationships were calculated by averaging Phase 2 & 5 measures, which were then divided into three groups. Marital status at Phase 5 was used.
Model 12: adjusted for birth cohort, sex and ethnicity; Model 16: Model 12 + education + employment grade; Model 18: Model 16 + longstanding illness + depressive symptoms + chronic diseases
* P < 0.05, ** P < 0.01, *** P < 0.001; CI: confidence interval

5.3.3 Block three

Block three compared the relative importance of functional and structural measures of social relationships in relation to trajectories of cognitive ageing (Table 5-7). Of the three functional measures of social relationships, negative support showed an independent effect on memory at age 60 years (P-value = 0.01) and the annual rate of decline in executive function (*negative support *age* P-value = 0.01) irrespective of confiding support and practical support. As regards structural measures of social relationships, friend network was positively associated with better executive function at age-60 (P-value = 0.008), but marginally significantly related to a faster decline in executive function (*friend network *age* P-value = 0.05). The functional and structural measures of social relationships appeared to work independently, as the effects of significant components remained after mutual adjustment (Model 20).

Table 5-7 Comparisons between Function and Structural Social Relationships and Age-Based Trajectories of Cognitive Decline [a]

	Executive Function						**Memory**					
	Functional		**Structural**		**Functional & Structural** [b]		**Functional**		**Structural**		**Functional & Structural** [b]	
	Intercept	**Slope**	**Intercept**	**Slope**	**Intercept**	**Slope**	**Intercept**	**Slope**	**Intercept**	**Slope**	**Intercept**	**Slope**
	Beta (SE)	Beta (SE)	Beta (SE)	Beta (SE)	Beta (SE)	Beta (SE)	Beta (SE)	Beta (SE)	Beta (SE)	Beta (SE)	Beta (SE)	Beta (SE)
Confiding Support												
Low	ref.						ref.					
Medium	0.00(0.02)	-0.002 (0.002)					-0.01(0.02)	-0.002 (0.002)				
High	-0.05(0.03)	-0.001 (0.003)					-0.05(0.04)	0.004 (0.004)				
Practical Support												
Low	ref.						ref.					
Medium	0.01(0.02)	-0.002 (0.002)					0.01(0.02)	-0.002 (0.002)				
High	0.01(0.03)	-0.002 (0.002)					0.04(0.03)	-0.002 (0.003)				
Negative Support												
Low	ref.				ref.		ref.				ref.	
Medium	-0.00(0.02)	*-0.005 (0.002)*			0.00(0.02)	*-0.005 (0.002)*	-0.03(0.02)	-0.003 (0.002)			-0.02(0.02)	-0.005 (0.003)
High	-0.02(0.03)	*-0.005 (0.002)*			-0.01(0.03)	*-0.005 (0.002)*	*-0.08(0.03)*	-0.000 (0.003)			*-0.07(0.03)*	-0.000 (0.003)
Friend Network												
Low			ref.		ref.				ref.		ref.	
Medium			0.01(0.02)	-0.001 (0.002)	0.03(0.03)	-0.003 (0.002)			0.03 (0.02)	-0.001 (0.003)	0.01(0.03)	0.003 (0.003)
High			*0.07(0.03)*	*-0.004 (0.002)*	*0.04(0.02)*	*-0.005 (0.002)*			0.05 (0.03)	-0.000 (0.003)	0.04(0.03)	0.004 (0.003)
Relative Network												
Low			ref.						ref.			
Medium			0.01(0.02)	-0.000 (0.002)					0.04 (0.03)	-0.001 (0.003)		
High			-0.00(0.02)	0.003 (0.002)					0.00 (0.03)	0.002 (0.003)		
Marital Status												
Married/Cohabiting			ref.						ref.			
Single			-0.05(0.03)	0.003 (0.002)					-0.00 (0.03)	0.000 (0.003)		
Divorced			-0.04(0.04)	0.000 (0.003)					0.07 (0.04)	-0.006 (0.004)		
Widowed			-0.03(0.06)	-0.005 (0.004)					-0.02 (0.07)	0.002 (0.007)		

[a] Analyses were based on participants who had all measures of social relationships (n = 5,984). All models adjusted for birth cohort, sex, ethnicity, socioeconomic and health status.
[b] Only includes social relationships measures that were significantly associated with cognitive ageing in previous models.
Italic figures indicate P-value < 0.05.
SE: standard error.

5.3.4 Supplementary analyses

Practice effects

Practice effects were better modelled as non-linear patterns with fixed effects only (Table 5-8) (standard error cannot be computed when allowing practice effects to be random). Observed rates of cognitive decline were positively biased by practice effects, such that cognitive scores of the second test were improved by 0.12 SD for executive function and 0.19 SD for memory, with a similar improvement for three times or more practice.

Unexpectedly, cohort effects at age 60 years became significantly negative for executive function once practice effects were controlled for. Participants from later birth cohorts were more likely to take multiple repeat cognitive tests. In this study sample, those born between 1940s to 1950s were 1.58 times more likely to take 3 times or more cognitive tests than those born in 1930s (result not shown). The incremental effects of birth cohort thus may be explained by extra practice. Alternatively, the negative cohort effects apparent after adjusting for practice effects may indicate selective attrition, that is, participants capable of taking cognitive tests from earlier birth cohorts were not random subsamples, who instead had comparatively greater cognition (Rabbitt *et al.*, 2001). Changes in parameter estimations thus may reflect complex interactions between practice effects, cohort effects and selective attrition (Ferrer and Ghisletta, 2011), and increase the difficulty in interpreting the cognitive ageing trajectory (Hofer and Sliwinski, 2006). Nevertheless, additional adjustments for practice effects did not alter the associations of social relationships and cognitive ageing.

Table 5-8 Model Selection for Practice Effects (PE)

	Executive function (n = 7,469)			Memory (n = 7,481)		
	Linear PE	Quadratic PE	Categorical PE	Linear PE	Quadratic PE	Categorical PE
	Beta (SE)	Beta (SE)	Beta (SE)	Beta (SE)	Beta (SE)	Beta (SE)
Fixed Effects:						
Intercept	-0.16 (0.02)	-0.20 (0.03)	-0.07 (0.02)	-0.27 (0.02)	-0.43 (0.04)	-0.21 (0.02)
Year of Birth	-0.02 (0.003)	-0.02 (0.003)	-0.02 (0.003)	-0.001(0.003)	-0.003 (0.003)	-0.002 (0.003)
Female	-0.29 (0.02)	-0.29 (0.02)	-0.29 (0.02)	0.09 (0.02)	0.09 (0.02)	0.09 (0.02)
Non-white	-1.19 (0.03)	-1.19 (0.03)	-1.19 (0.03)	-0.54 (0.03)	-0.54 (0.03)	-0.54 (0.03)
Linear Practice effects	0.11 (0.01)	0.14 (0.02)		0.10 (0.01)	0.26 (0.03)	
Quadratic practice effects		-0.01 (0.003)			-0.03 (0.005)	
Categorical practice effects						
1			ref.			ref.
2			0.12 (0.01)			0.19 (0.02)
3			0.24 (0.02)			0.25 (0.03)
4			0.36 (0.03)			0.29 (0.04)
5			0.40 (0.04)			0.40 (0.06)
Age (centred at 60)	-0.07 (0.002)	-0.07 (0.002)	-0.07 (0.002)	-0.04 (0.003)	-0.04 (0.003)	-0.04 (0.003)
Age squared (centred at 60)	0.001 (0.0002)	0.001 (0.0002)	0.001 (0.0002)	-0.002 (0.0003)	-0.002 (0.0003)	-0.002 (0.0003)
Year of birth*Age	0.004 (0.0003)	0.004 (0.0003)	0.004 (0.0003)	-0.003 (0.0005)	-0.003 (0.0005)	-0.003 (0.0005)
Non-white*Age	0.009 (0.002)	0.009 (0.002)	0.009 (0.002)	0.02 (0.004)	0.01 (0.004)	0.01 (0.004)
Random Effect:						
Intercept Variance	0.62 (0.01)	0.62 (0.01)	0.62 (0.01)	0.36 (0.01)	0.36 (0.01)	0.36 (0.01)
Linear Variance	0.0005 (0.000)	0.0005 (0.000)	0.0005 (0.000)	0.0002 (0.000)	0.0002 (0.000)	0.0002 (0.000)
Intercept-Linear Covariance	-0.003(0.001)	-0.003(0.001)	-0.003(0.001)	-0.003(0.001)	-0.003(0.001)	-0.003(0.001)
Residual Variance	0.11 (0.002)	0.11 (0.002)	0.11 (0.002)	0.50 (0.007)	0.50 (0.007)	0.50 (0.007)
Goodness-of-fit						
-Log likelihood (Δdf)	16501	16498 (1)	16497 (2)	23615	23595 (1)	23588 (2)
BIC	33118	33122	33136	47345	47316	47318
LR test		0.02	0.15		<0.0001	0.0005

SE: standard error; Δdf: differences in number of parameters; LR test: likelihood ratio test.

Reverse causation

Similar results were obtained after excluding potential dementia cases (57 participants had MMSE scores less than 23 over the 10-year follow-up). Reverse causation was further assessed via using Phase 5 cognitive function to predict subsequent ageing trajectories of functional measures of social relationships from Phase 5 to Phase 9. This analysis tested whether participants with initial higher cognition would have improved quality of social support during follow-up, namely, encountering more positive and less negative social exchanges. Table 5-9 indicates that cognitive function at Phase 5 did not influence the annual rate of changes in social relationships with age (P-values for *executive function*age*: 0.34~0.87; for *memory*age*: 0.16~0.92). Therefore, reverse causation can be largely excluded as an explanation for the observed associations in the main analysis.

Table 5-9 Association between Phase 5 Cognitive Function and Age-Based Trajectories of Functional Measures of Social Relationships from Phase 5 to Phase 9

	Confiding Support			**Practical Support**			**Negative Support**		
	Beta	95% CI		Beta	95% CI		Beta	95% CI	
Executive Function	0.06	-0.07	0.18	0.01	-0.06	0.08	-0.01	-0.06	0.04
Executive Function* Age	0.05	-0.06	0.16	-0.01	-0.08	0.06	-0.03	-0.08	0.03
Memory	-0.02	-0.12	0.08	0.02	-0.03	0.08	-0.04	-0.08	0.00
Memory* Age	0.00	-0.1	0.09	0.04	-0.02	0.10	0.01	-0.04	0.05

Beta coefficient indicates one standard deviation difference in cognitive scores at Phase 5 in relation to intercept (age 60) or 10-year changes in functional social relationships (*Age).
All models adjusted for birth cohort, sex, ethnicity, education and employment grade.
CI: confidence interval.

Time-in-study model

Although all analyses above were adjusted for birth cohort to account for age non-convergence, it is possible associations obtained still reflect some combination of ageing and cohort effects (Hoffman, 2012). Therefore, cognitive trajectories were estimated using time since study baseline in place of age. Consistent patterns of negative support and larger friend networks with executive function were found as in the main analyses. Moreover, three-way interactions between time, birth cohort and social relationships were non-significant (P-value = 0.24~0.68), indicating the estimated effect of mid-life social relationships on cognitive decline did not vary by birth cohorts.

5.4 Interim discussion

The current chapter examined ***Objective one*** regarding the cognitively beneficial components of social relationships. Findings indicated that higher cumulative *negative support* but not confiding or practical support at middle age was associated with lower memory scores at age-60 and accelerated declines in executive function. As for structural aspects of social relationships, larger *friend network* showed a positive association with executive function at age 60 years but not the rate of cognitive decline. Neither relative network nor marital status at middle age was associated with cognitive ageing once controlled for socioeconomic and health status. Functional and structural measures of social relationships seem to influence cognitive ageing independently, as when both measures were considered statistically significant associations remained. Further, in the restricted sample of participants who had all measures of social relationships (n = 5,984), those reporting a large friend network at middle age tended to experience faster declines in executive function. Findings above were not subject to practice effects or reverse causation.

MLM was adopted to estimate age-based cognitive trajectories. Both age and age squared were used to describe a non-linear trend of cognitive decline, where the shape of cognitive trajectory is determined by the centre point of age. Previous studies indicate the effect of risk factor on cognitive decline could be age-sensitive (Gale *et al.*, 2012; Muniz-Terrera *et al.*, 2012). Modelling an overall polynomial cognitive trajectory, the current analysis postulated the impact of social relationships on cognitive ageing applies to all age groups. This assumption was confirmed via the time-in-study model, showing similar patterns of significant associations with no evidence of age-sensitivity.

Objective one studied midlife social relationships as risk factors for subsequent declines in cognition, with the intention of clarifying the temporality. This approach, however, overlooks changes in social relationships during late adulthood, which will be addressed in the next chapter.

Chapter 6. Objective two: social relationship transitions from middle to old age and cognitive ageing

Summary

Following the assessment of mid-life social relationships on subsequent decline in cognitive function, this chapter investigates how longitudinal changing patterns of social relationships from middle to early old age are associated with cognitive ageing. Growth mixture modelling (GMM) was used to uncover longitudinal latent classes of social relationships. These derived classes of social relationships were then used as dummy indicators to assess differences in their corresponding cognitive ageing trajectories by multilevel models (MLM).

6.1 Introduction

Although no one is immune to ageing and disease (Bowling and Dieppe, 2005), those who have adequate social relationships may be more resilient in coping with the challenges of ageing by proactively anticipating and adapting to inexorable changes (Ouwehand *et al.*, 2007). As such, older individuals who are capable of optimizing psychosocial resources could better buffer the negative effects of physiological declines (Young *et al.*, 2009). Cognitive reserve also highlights that social environmental complexity may contribute to individual variations in the capacity to compensate for brain changes with age (Stern, 2002). The extent to which divergent social ageing patterns may project onto different cognitive ageing trajectories is under-investigated (Thomas, 2011b). Examining longitudinal trajectories of social relationships and cognitive function thus provide important leverage to understand how psychosocial and cognitive factors coevolve over time.

6.1.1 Heterogeneity in longitudinal trajectories of social relationship in late life

As discussed in Chapter 2 (Section 2.1.3, Page 24), older people may actively prune their social relationships to optimize emotionally rewarding relationships and avoid negative social encounters given the perceived limitations of future time (Carstensen *et al.*, 2003).

Although evidence generally supports socioemotional selectivity theory, heterogeneity in age-related trajectories of social relationships has been identified (Martire *et al.*, 1999; van Tilburg and Broese van Groenou, 2002; Mavandadi *et al.*, 2007; Shaw *et al.*, 2007). In a nationally representative sample of American adults aged 65 and over, Krause (1999) estimated that at least 91% of the total difference in social support was due to between-individual variation, which was later quantified as the substantial random effect around the average age-based growth curve by using MLM (Shaw *et al.*, 2007). Heterogeneity in trajectories of social relationships have also been found amongst older Dutch adults (van Tilburg, 1998; van Tilburg and Broese van Groenou, 2002), with nearly 1/3 of the respondents who experienced increases in social network size, 30% reported declines and the rest 37% remained unchanged.

These findings echo early evidence on the heterogeneous social developmental trajectories in a British elderly cohort (Bowling and Browne, 1991).

Recent studies adopted latent curve mixture models to uncover heterogeneous subgroups based on their longitudinal social ageing profiles. Mavandadi and colleagues (2007) identified three latent classes for positive exchanges (PE) and negative exchanges (NE), representing chronically low PE (18%) or NE (44%), moderate increase PE (62%) or NE (11%), and chronically high PE (20%) or absent NE (45%). Thomas (2011b) categorized social engagement patterns over 6 years into five latent classes, identified as high initial levels of engagement with slight (60%) or fast (11%) decreases, high initial levels with increases (13%), medium initial levels with increases (7%), and low initial levels with decreases in social engagement (10%).

6.1.2 Longitudinal latent classes of social relationships and cognitive ageing

Social relationship change over time has been associated with cognitive ageing (Béland *et al.*, 2005; Ellwardt *et al.*, 2013; Ellwardt *et al.*, 2015). As yet, only one study has grouped individuals based on their social engagement trajectories, and revealed that participants identified as having a low and decreasing trend of social engagement tended to experience high levels of cognitive limitations (Thomas, 2011b).

Given most studies overlooked change and heterogeneity in social relationships as people age, evidence on the association between divergent trajectories of social relationships and cognitive function over time, especially in the transitions from middle to old age, would hence provide valuable information.

6.1.3 Introduction to growth mixture modelling

In order to estimate the heterogeneity in longitudinal changing patterns of social relationships, growth mixture modelling (GMM), a person-centred approach was employed.

Basic conceptions of GMM

Similar to MLM (Chapter 5, Page 68), GMM captures individual longitudinal growth curves (i.e. heterogeneity) by allowing random effects around the intercept and the growth slope. On the other hand, while MLM assumes all individuals are drawn from the same single population with common population parameters, GMM relaxes this assumption to allow different parameters across unobserved sub-populations (Muthén, 2004). Therefore, instead of treating individual variation distributed around a single intercept and an average growth curve, GMM introduces latent classes to allow individuals to vary around different mean growth curves. GMM therefore offers more flexibility in comparison with conventional MLM. Table 6-1 summarizes the main differences between these two techniques (Nagin and Tremblay, 2001; Muthén, 2002; Laursen and Hoff, 2006).

Table 6-1 Comparison of Growth Mixture Model (GMM) and Multilevel Model (MLM)

	GMM	**MLM**
Focus	Individuals/ Person-centred approach	Variables/ Variable-centred approach
Purpose	Describe differences among individuals in patterns of development, and how associations vary across unobserved sub-populations	Describe association among variables: the relative importance of predictors in explaining variance in the outcome, applying to the entire population
Goal of Analysis	Categorize individuals with similar characteristics or developmental trajectories into distinct classes	Estimate the average trajectory of change in the outcome, and identify variables that affect quantitative deviation from this trajectory
Application	Questions concerned with differences among individuals: minimize difference within groups and maximize difference between groups.	Questions concerned with relations among variables: estimate strength and reliability of the effects attributed to predictor variables, and apportion variance of outcome into predictors.

Equations & Assumptions of GMM

The equation for a conventional MLM, that is, a single growth curve with no latent classes, is as below,

$$\mathrm{Y}[\mathrm{t}]_n = i_{0n} \cdot \Lambda_0[\mathrm{t}] + S_{1n} \cdot \Lambda_t[\mathrm{t}] + e[\mathrm{t}]_n \qquad (1)$$

The observed repeat measure Y is represented by two latent variables intercept i_{0n} and slope S_{1n}, two sets of corresponding factor loadings Λ_0 and Λ_t, and a time-specific residual $e[\mathrm{t}]_n$. The variances for intercept, slope and error are assumed to follow normal distributions.

As for factor loading, Λ_0 is a fixed vector of **1**s representing the stability over time; while Λ_t captures the time-to-time patterns of change (Bollen and Curran, 2006). For example, the matrix of factor loadings for four repeat measures can be represented as,

$$\Lambda = \begin{pmatrix} 1 & 0 \\ 1 & 1 \\ 1 & \Lambda_3 \\ 1 & \Lambda_4 \end{pmatrix}$$

The shape of the latent curve thus is modelled as a function of Λ_t. A linear growth model Λ_t is fixed as **t-1** (i.e. $\Lambda_3 = 2$, $\Lambda_4 = 3$), and a quadratic function is quantified by squaring the linear factor loadings **(t-1)²** (i.e. $\Lambda_3 = 4$, $\Lambda_4 = 9$). For a nonlinear curve, also referred to as a *spline*, factor loadings are freely estimated to offer the best description of change patterns between any two time points (Bollen and Curran, 2006; Ram and Grimm, 2007; 2009). By setting $\Lambda_0 = 0$ and $\Lambda_1 = 1$, the freed factor loadings of Λ_3 and Λ_4 indicate subsequent changes up to time t (i.e. Time 1 to 3, Time 1 to 4) which are evaluated in reference to the change estimated between the first two time points (i.e. Time 1 to 2) (Bollen and Curran, 2006). As fewer parameters are estimated, models with free factor loadings are more parsimonious compared with other polynomial models (Bollen and Curran, 2006; Ram and Grimm, 2007).

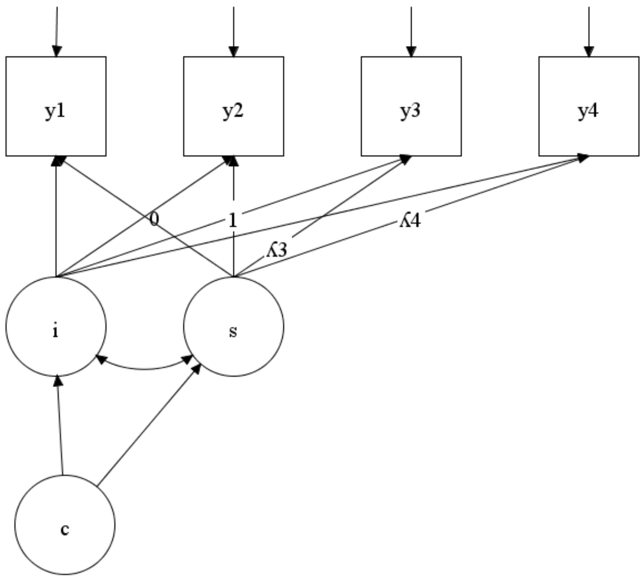
The mathematical equation for GMM is an extension of equation for MLM (1), presenting as a function of the probability of the latent class membership and a multiple-group growth model (Ram and Grimm, 2009).

$$\mathrm{Y}[\mathrm{t}]_n = \sum_{c=1}^{C}\left(\pi_{\mathrm{nc}}(i_{0nc} \cdot \Lambda_{0c}[\mathrm{t}] + S_{1nc} \cdot \Lambda_{tc}[\mathrm{t}] + e[\mathrm{t}]_{nc})\right) \qquad (2)$$

given $0 \leq \pi \leq 1$ and $\sum_{c=1}^{C}(\pi_{\mathrm{nc}}) = 1$

The latent class membership is represented by c subscript, which is conceptualized as the cause rather than the effect of latent developmental patterns (Leoutsakos *et al.*, 2012). Key differences among classes are found on mean intercept (i_{0nc}), slope (S_{1nc}), their variances and covariance, residual variance ($e[\mathrm{t}]_{nc}$), and patterns of change (λ_{tc}) (Muthén, 2004). π_{nc} is the probability of belonging to a certain class, ranging from zero to one and with a sum of one. Therefore, MLM could be seen as GMM with only one class (π = 100%). Figure 6-1 represents an application of equation (2) with freed factor loadings for four repeat measures.

Figure 6-1 Diagram for Unconditional GMM with Four Occasions (Freed Factor Loadings)



Note: Latent variables are represented within ellipses (c = latent classes, i = latent intercept, s = latent slope). Observed variables are presented within rectangles. The one-headed arrows indicate factor loadings ʎ or error, and double-headed arrows indicate correlation.

The main **assumption** for GMM is that for each latent class, the observed continuous variables come from a multivariate normal distribution (Bauer and Curran, 2003a,b; Bollen and Curran, 2006). The normality assumption also applies to the random effects at intra- and inter-individual levels within classes (Muthén, 2004; Kreuter and Muthén, 2008).

6.2 Methods

The research questions of objective two were addressed in 2 steps. First, GMM were used to identify longitudinal latent classes of social relationships. Second, these derived classes of social relationships were related to cognitive ageing trajectories using conventional MLM.

6.2.1 Step 1: Applying GMM to social relationship measures of the Whitehall II cohort

To uncover longitudinal latent classes of social relationship over middle to early old age, GMM was used to estimate the number of latent classes required to categorize individuals into the most likely classes based on their observed measures. Here, four repeat measures of functional social relationships at Phase 2, 5, 7 and 9 were used, covering up to 20 years' follow-up (1989-1990 to 2007-2009). Only three repeat measures of structural social relationships were available at Phase 2, 5 and 7.

The observed data distributions for all measures of social relationships seemed to deviate from the normal distribution (Table 6-2). A variety of transformations (e.g. square, cubic, square root and log) did not improve the normality of the data distribution. These values of skewness and kurtosis are within the range reported in psychometric measures (Micceri, 1989), and represent acceptable levels of deviations from normality for conventional growth models (Bauer and Curran, 2003a). Nevertheless, robust maximum likelihood parameter estimation (MLR) was used in all analyses, which estimates standard errors of the parameters robust to non-normality.

Table 6-2 Univariate Skewness and Kurtosis of Social Relationships Measures [a]

Variables	Skewness	Kurtosis
Confiding Support	-0.16	2.56
Practical Support	-0.01	2.29
Negative Support	1.04	3.97
Friend Network	-0.07	2.34
Relative Network	0.09	2.14

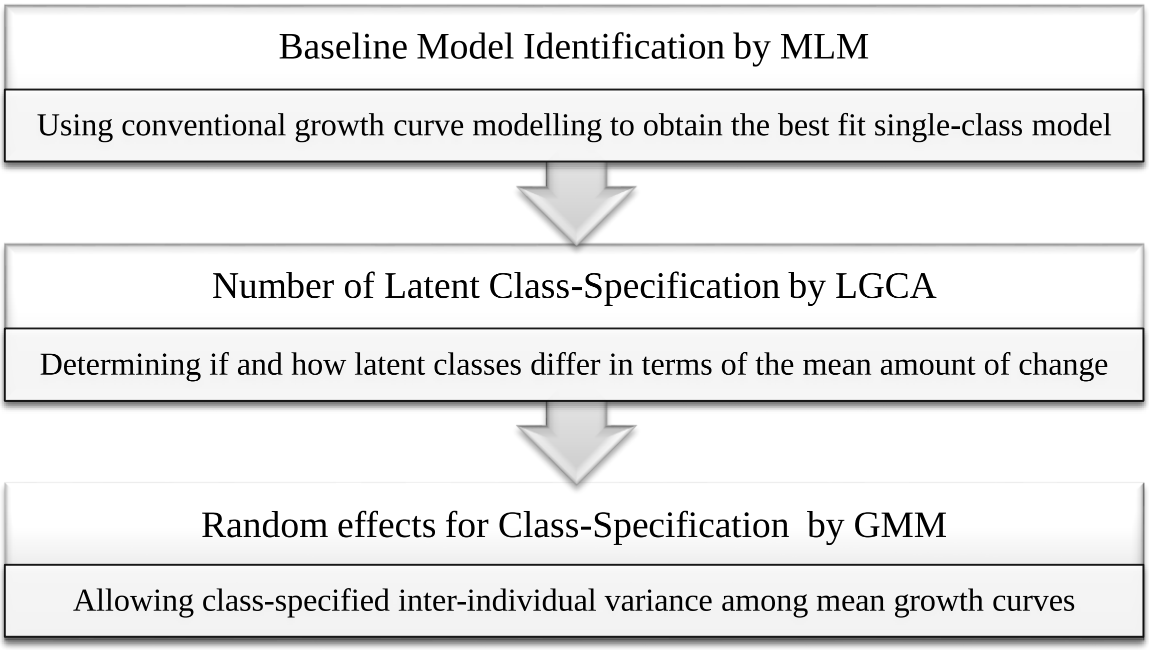
[a] Skewness quantifies how symmetrical the distribution is, and kurtosis compares the shape of the data distribution with the Gaussian distribution. In Stata computation, a normal distribution (i.e. Gaussian distribution) has a skewness of 0 and a kurtosis of 3.

Model specification

Following the recommended procedures (Jung and Wickrama, 2008; Ram and Grimm, 2009), a series of models was specified and estimated sequentially to uncover the longitudinal latent classes of social relationships (Figure 6-2). First, MLM was employed to identify the baseline single-class model that best described longitudinal change, including linear, quadratic and non-linear functions (Ram and Grimm, 2007). Then, via applying the latent growth curve analysis (LGCA), the number of unobserved classes was specified according to differences in the mean amount of change, assuming there was no-within-class variation (Muthén, 2002; Nagin and Nagin, 2009).

Third, the extent of inter-individual differences in change was captured by GMM, which estimated random effects on intercept and slope. Here, residual variances over time were held constant within each class but different between classes (Muthén, 2004). Factor loadings were freely estimated across classes to allow class-specific growth patterns (Ram and Grimm, 2009). This final model relaxed the latent classes to be completely different from each other.

Figure 6-2 Procedures for Implementing GMM to Repeat Measures of Social Relationships



Note: MLM: multilevel model, LGCA: latent growth curve analysis, GMM: growth mixture model.

Model selection

The model fit to the observed data was evaluated by the Tucker-Lewis-index (TLI), the Comparative Fit Index (CFI) and the Root Mean Square Error of Approximation (RMSEA). Cut-off values of 0.95 for TLI and CFI, and 0.06 for RMSEA indicate a good model fit (Hu and Bentler, 1999).

Statistical indexes included in the model selection process were, Bayesian information criterion (BIC), two likelihood ratio test derivatives: Lo-Mendell-Rubin adjusted likelihood ratio test (LMR-LRT) (Lo *et al.*, 2001) and bootstrap likelihood ratio test (BLRT) (McLachlan, 1987; Nylund *et al.*, 2007), posterior probabilities and entropy. These model indexes have been identified as reliable indicators to distinguish a subpopulation mixture distribution from a homogenous non-normal distribution (Nylund *et al.*, 2007; Jung and Wickrama, 2008; Tofighi and Enders, 2008; Peugh and Fan, 2012).

BIC takes into account deviance (-2log-likelihood), the number of estimated model parameters and the sample size. The solution with smaller BIC indicates a better model fit. LMR-LRT and BLRT test the statistical significance of improvement in the model fit when an additional class is extracted. Posterior probabilities quantify the probability with which individuals belong to each latent class alongside classification uncertainty (i.e. classification error) (Asparouhov and Muthén, 2013). Entropy, a summary statistic based on the posterior probabilities (Celeux and Soromenho, 1996; Peugh and Fan, 2012), examines classification accuracy. Entropy ranges from 0 to 1, whereby the closer to 1 indicates improved enumeration accuracy. Entropy is influenced by within-trajectory variance and between-trajectory separation distance (Muthén, 2004). It should be noted that as the number of classes increases, entropy could reduce purely due to chance rather than an indication of raised classification error (Collins and Lanza, 2010).

Other factors, such as relevancy to the research question, parsimony, class size, theoretical justification and interpretability were also considered. Group trajectories were plotted, together with the model parameter estimates to assess sensibility and distinctiveness. All models were estimated using the maximum likelihood robust (MLR) estimator with robust standard errors. The normality assumption of the residuals on intra- and inter-individual levels were examined using histogram and kernel density distribution (Kreuter and Muthén, 2008). Full information maximum likelihood (FIML) was used to handle the missing data under the assumption of missing at random. Missing patterns in each class for all measures of social relationships were also checked to avoid grouping driven by missing observations.

Variations in the longitudinal latent classes of social relationships

To assess sex differences in the longitudinal latent classes of social relationships, model comparison was conducted using male-female multi-group models with or without constraining parameters to be the same across sex. Although there were some indications of sex-specific growth patterns in MLM, GMM suggested the same number of latent classes and similar growth patterns for men and women (Appendix 5). In the main analyses non-significant interactions between sex and latent classes of social relationships were found in relation to cognitive ageing, so models combining male and female were presented. A set of time-invariant covariates (i.e. sex, ethnicity, education and employment grade) and a time-dependent covariate on stability and change in the identity of the closest person were accommodated to examine sociodemographic characteristics across longitudinal latent classes of social relationships.

6.2.2 Step 2: Association between latent classes of social relationship and cognitive ageing

The primary outcomes of objective two were trajectories of cognitive decline, quantified by intercepts and slopes of executive function and memory over a 10- year follow-up from Phase 5 to Phase 9.

MLM was used to estimate cognitive trajectories (refer to Section 5.2 Chapter 5, Page 70 for details about this method). In this chapter, the rate of cognitive decline was modelled as a function of time since baseline, controlled for study baseline age (centred at 55 y). This approach was adopted to separate the effect of being old (i.e. how old was the participant when first joining the cohort) from growing old (i.e. how many extra years did the participant grow during the cohort follow-up) (Hoffman, 2012). Further, in review of the moderate magnitude of the *social relationships-cognitive ageing* association found in the previous chapter, the annual rate of decline in cognition was divided by 10 to obtain cognitive decline over 10 years.

The longitudinal latent classes of social relationships, derived from Step1, were coded as sets of dummy indicators to examine the extent to which the initial levels and changes in cognitive function differ across these latent classes by using MLM. Models were then adjusted for sociodemographic and health covariates previously described (Page 60). Considering changes in health status over the long period of follow-up, analyses were repeated amongst participants with and without chronic diseases over Phase 2 to Phase 9.

In accordance with current practice, the largest class (i.e. the one containing the most average or ‘normal’ individuals) was chosen as reference (Leoutsakos *et al.*, 2012). The classification uncertainty (i.e. classification error) (Bolck *et al.*, 2004) was maintained and weighted by controlling for logged ratios of the adjusted average posterior class membership probabilities, as suggested by the three-step method (Vermunt, 2010; McIntosh, 2013). This adjustment can be automatically computed in the Mplus package (Asparouhov and Muthén, 2013). Robust standard errors were calculated to account for lack of independency of the weighted data across latent classes. All models were estimated using Mplus Version 7 (Muthén and Muthén, 2012).

6.3 Results

6.3.1 Step1: Longitudinal latent classes of social relationships

For each measure of social relationships, a series of MLM, LGCA and GMM as shown in Figure 6-2 were applied sequentially. As the deviation from normal distribution was most evident in the observed scores of negative support (Table 6-2), detailed analytic procedure for this measure was presented, which applies equally to other social relationships measures.

Negative support

Baseline MLM: Alternative time metrics (i.e. individual time score and phase) were considered (Table 6-3). As regards individual time score, the output from Mplus (estimator: MLR) was compared with the ones obtained from STATA (estimator: ML). Identical model fit and parameter estimates were found for the linear models (Model 1.1 vs. 2.1). However, it was rather time-consuming for Mplus to compute the quadratic function using individual time score (Model 1.2). As indicated by models generated in STATA, the quadratic growth model (Model 2.3) with random effects for both intercept, linear and quadratic function fitted the model the best. The spline model (Model1: spline) captured this non-linear change with ideal model fit (TLI = 0.987, CFI = 0.979, RMSEA = 0.033). Given the substantial parsimony spline model offers (Bollen and Curran, 2006), it was chosen to estimate the change of negative support over the study period (Figure 6-3). The normality assumption for random effect of intercept and slope was verified (Figure 6-4).

Table 6-3 Baseline Model Comparison for Negative Support (N = 9,120).

Baseline Model	Software	Shape	RE	LL	No. Par	BIC
Time in study model						
Model 1.1: linear	Mplus	linear	I S	-57148.41	8	114369.8
Model 1.2: quadratic	Mplus	quadratic	I S	/	/	/
Model 1.3: quadratic_2	Mplus	quadratic	I S Q	/	/	/
Model 2.1.: linear	STATA	linear	I S	-57148.41	8	114369.8
Model 2.2: quadratic [a]	STATA	quadratic	I S	-57130.33	9	114342.7
Model 2.3: quadratic_2 [a]	STATA	quadratic	I S Q	-56979.47	12	114068.4
Phase						
Model 1: spline	Mplus	spline	I S	-57017.14	10	114125.5

[a] Log-likelihood ratio test with previous model, P <0.0001
RE: random effect; LL: log likelihood; No. Par: number of parameters; BIC: Bayesian information criterion; I: intercept; S: linear slope; Q: quadratic slope.

Figure 6-3 Estimated (Red Solid Line) and Sample (Blue Dashed Line) Means Levels of Negative Support over Follow-Up, Estimations Based on Spline Model.

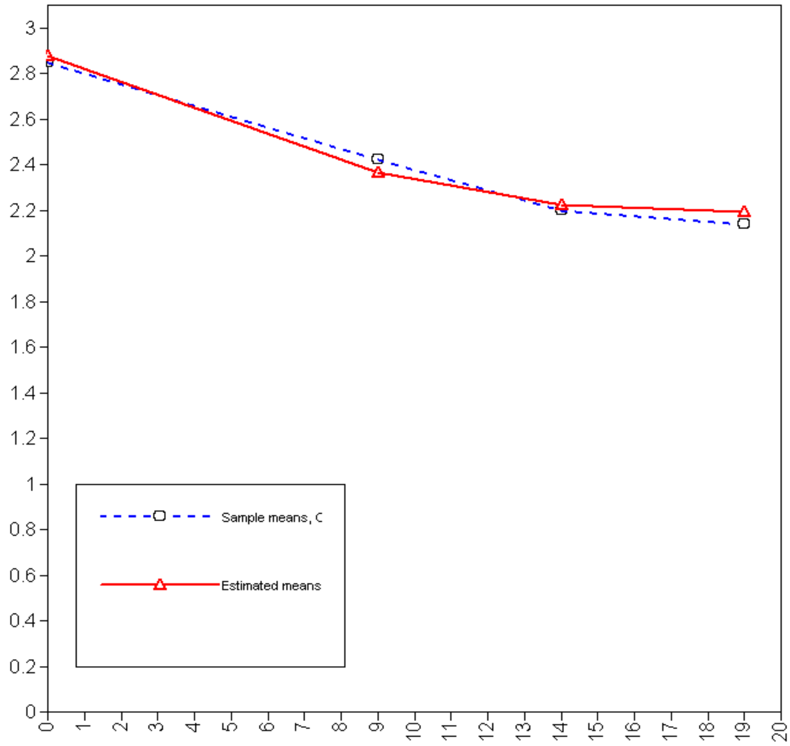
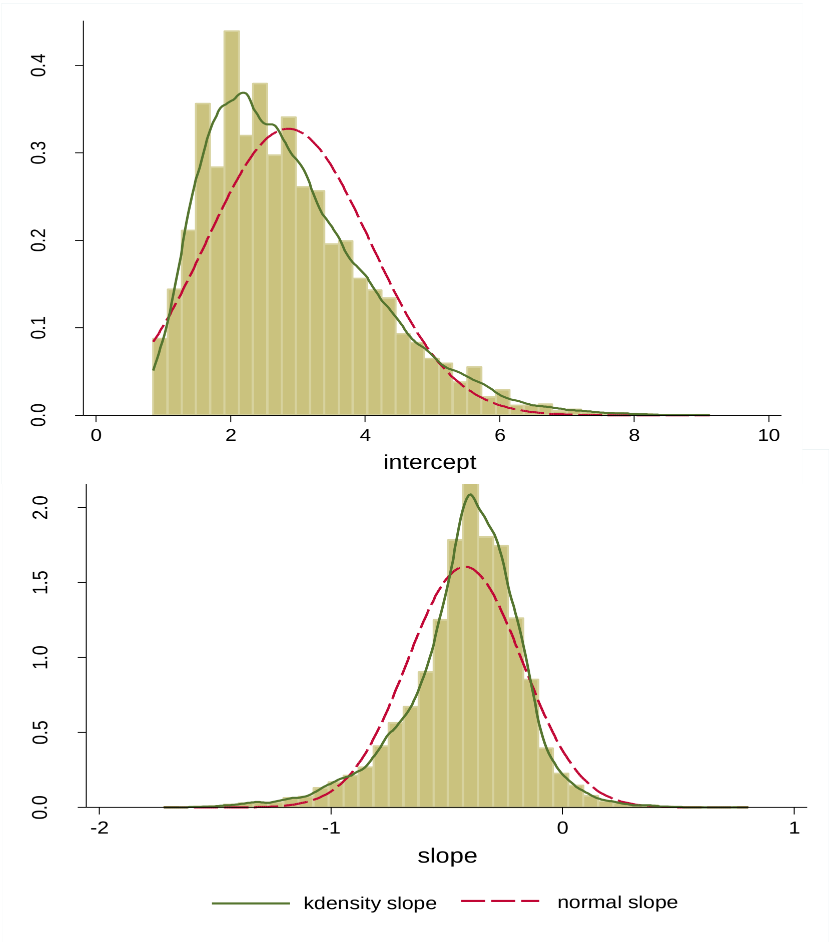


Figure 6-4 Histogram and Kernel Density Distribution of Intercept and Slope Factor Scores for Negative Support, Estimates Derived from the Spline Model.



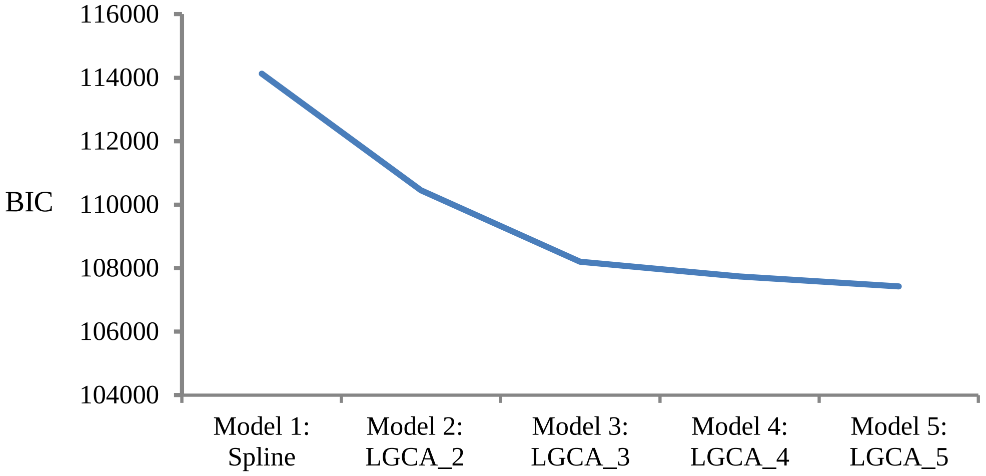
LGCA: As latent-class means were added into the model, BIC improved and LMR-LRT favoured the 4-class solution (Table 6-4). However, 3-class solution (Model 3) showed a similar BIC as 4-class solution (Model 4) (Figure 6-5), with a better entropy (0.66 vs. 0.59). Thus Model 3 with three latent classes was retained for further analysis.

Table 6-4 LGCA Comparison of Negative Support

SEM approach	RE	LL	No. Par	BIC	LMR-LRT	Entropy
Model 2: LGCA_2	I S	-55163.62	14	110454.9	<0.0001	0.69
Model 3: LGCA_3	I S	-54006.72	21	108204.9	<0.0001	0.66
Model 4: LGCA_4	I S	-53740.97	28	107737.3	<0.0001	0.59
Model 5: LGCA_5	I S	-53549.89	35	107419.9	0.27	0.60

RE: random effect; I: intercept, S: slope; LL: log likelihood; No. Par: number of parameters; BIC: Bayesian information criterion; LMR-LRT: Lo-Mendell-Rubin adjusted likelihood ratio test, with P < 0.05 indicates model with additional latent class was preferred.

Figure 6-5 Model Fit Evaluation by Bayesian Information Criterion (BIC)



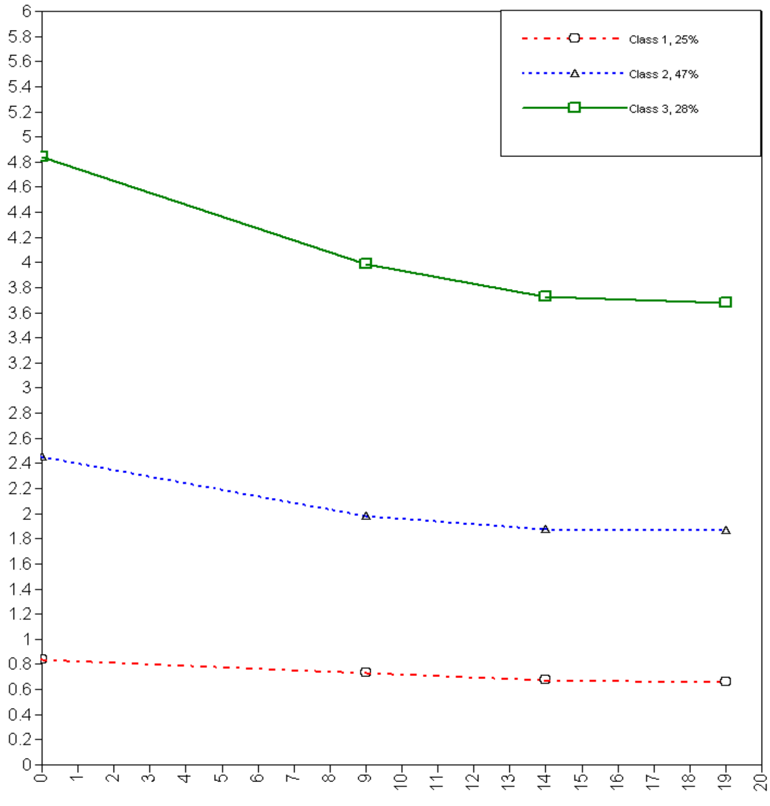
GMM: Allowing for extra within-class variance of this 3-class solution provided a stable classification (log likelihood = -53663.50, BIC = 107601, entropy = 0.61). LMR-LRT and BLRT also endorsed the 3-class GMM solution (P < 0.0001). The class-specific parameter estimates of this model were presented in Table 6-5, with corresponding mean trajectories depicted in Figure 6-6. A quarter of the participants (25%, n = 2,226) perceived *chronically-low* levels of negative support (red dash line in Figure 6-6). Nearly half of the participants (47%, n = 4,295) reported *medium* levels of negative support (blue dotted line).The other 28% (n = 2,599) reported an *initial high level* but a substantial *decrease* in negative support over years, yet having relatively higher overall levels of negative support in comparison with the other two classes (green solid line). As regards sociodemographic characteristics, participants belonging to *high-decline* negative support class, tended to be younger, more likely to be female, ethnic minorities and have a lower employment grade than their counterparts who reported lower levels of negative support.

Table 6-5 Parameter Estimates for the Three-Class GMM of Negative Support

	Negative Support (n = 9,120)		
	Chronically-low	**Medium**	**High-decline**
Sample size [a]	2226 (25%)	4295 (47%)	2599 (28%)
Probability of class membership	0.77	0.79	0.88
Slope factor loadings (ʎ)			
ʎ1	0 (fixed)	0 (fixed)	0 (fixed)
ʎ2	1 (fixed)	1 (fixed)	1 (fixed)
ʎ3	1.57	1.23	1.31
ʎ4	1.69	1.25	1.36
Means			
Intercept	0.84 (0.05)***	2.45 (0.07)***	4.84 (0.11)***
Slope	-0.11 (0.04)*	-0.45 (0.05) ***	-0.85 (0.08)***
Variance estimates			
Intercept	0.24 (0.05)***	0.93 (0.11)***	2.80 (0.20)***
Slope	0.09 (0.06)	0.99 (0.11)***	2.23 (0.25)***
Covariance	-0.11 (0.05)*	-0.88 (0.12)***	-2.06 (0.24)***
Residual variance	0.29 (0.02)***	1.31 (0.07)***	3.91 (0.16)***

[a] Based on the most likely latent class membership
*P<0.05, **P<0.01, ***P<0.001

Figure 6-6 Estimated Class-Specific Mean Trajectories for Negative Support.



The same model specification procedure as described for negative support was applied to other measures of social relationships. For simplicity, model comparisons for the rest of social relationship variables were summarized as Table 6-6 .

Table 6-6 Model Comparison for Social Relationships Measures

Model	Random Effect	LL	BIC	Entropy	LMR-LRT	BLRT
Confiding Support						
Model 1: MLM_1	I S	-75468.50	151009.9	/	/	/
Model 2: LGCA_2	/	-76477.98	153038.0	0.68	<0.0001	<0.0001
Model 3: LGCA_3	/	-75386.20	150890.9	0.69	<0.0001	<0.0001
Model 4: LGCA_4	/	-74972.09	150099.1	0.71	0.12	<0.0001
Model 5: GMM_2	I S	-74866.66	149870.0	0.73	<0.0001	<0.0001
Model 6: GMM_3	I S	-74642.20	149448.5	0.73	<0.0001	<0.0001
Practical Support						
Model 1: MLM_1	I S	-62581.58	125236.1	/	/	/
Model 2: LGCA_2	/	-63278.33	126638.7	0.64	<0.0001	<0.0001
Model 3: LGCA_3	/	-62372.50	124863.6	0.71	<0.0001	<0.0001
Model 4: LGCA_4	/	-62053.10	124261.2	0.71	<0.0001	<0.0001
Model 5: GMM_3	I S	-61759.57	123674.2	0.78	<0.0001	<0.0001
Friend Network						
Model 1: MLM_1	I S	-42543.92	85169.87	/	/	/
Model 2: LGCA_2	/	-42540.12	85198.72	0.59	<0.0001	<0.0001
Model 3: LGCA_3	/	-42450.52	85010.41	0.66	0.002	<0.0001
Model 4: LGCA_4	/	-42245.93	84637.67	0.68	0.06	<0.0001
Model 5: GMM_3	I S	-42189.98	84571.34	0.72	<0.0001	<0.0001
Relative Network						
Model 1: MLM_1	I S	-41127.65	82337.30	/	/	/
Model 2: LGCA_2	/	-41263.42	82645.28	0.87	<0.0001	<0.0001
Model3: LGCA_3	/	-40336.90	80783.14	0.70	<0.0001	<0.0001
Model 4: GMM_3	I S	-39826.30	79825.70	0.66	<0.0001	<0.0001

I: intercept, S: slope. LL: log likelihood; BIC: Bayesian information criterion; LMR-LRT: Lo-Mendell-Rubin adjusted likelihood ratio test; BLRT: bootstrap likelihood ratio test; for both test, P < 0.05 indicates model with additional latent class was preferred.

Confiding support

Model comparisons suggest a 3-class GMM fits the data of confiding support the best (Table 6-6). The parameter estimates of this model are presented in Table 6-7 , whereby relatively large variations around the intercept and slope shown in the *average* class which had the most participants (72%, n = 6,562). This might indicate separation in this 3-class solution is not ideal. However, introducing a fourth latent class did not improve the model fit (entropy = 0.51, P-value for LMR-LRT = 0.26), nor generated a meaningful latent class.

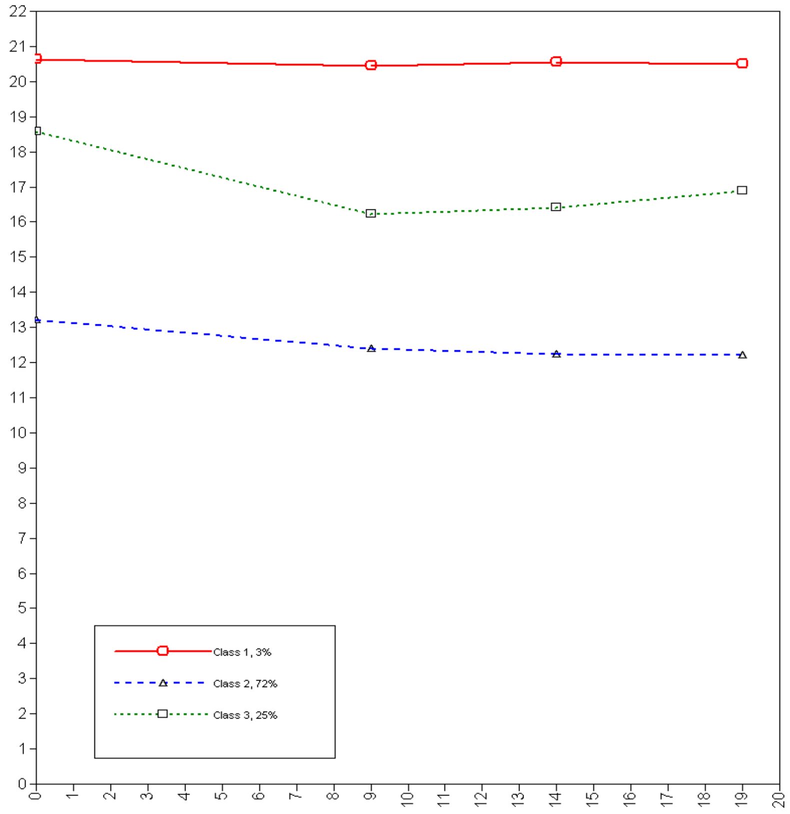
Table 6-7 Parameter Estimates for the Three-Class GMM for Confiding Support

	Confiding support (n = 9,118)		
	Average	**Higher than average**	**Extremely-high**
Sample size [a]	6562 (72%)	2325 (25%)	231 (3%)
Probability of class membership	0.92	0.70	0.83
Slope factor loadings (ʎ)			
ʎ1	0 (fixed)	0 (fixed)	0 (fixed)
ʎ2	1 (fixed)	1 (fixed)	1 (fixed)
ʎ3	1.21	0.92	0.34
ʎ4	1.24	0.72	0.66
Means			
Intercept	13.22 (0.12)***	18.57 (0.14)***	20.62 (0.08)***
Slope	-0.81 (0.10)***	-2.36 (0.16)***	-0.17 (0.07)*
Variance estimates			
Intercept	9.19 (0.31)***	0.00 (0.00)[b]	0.03 (0.02)
Slope	5.29 (0.47)***	4.06 (0.49)***	0.00 (0.00)[b]
Covariance	-3.62 (0.29)	/	/
Residual variance	7.43 (0.16)***	3.72 (0.25)***	0.38 (0.07)***

[a] Based on the most likely latent class membership
[b] Estimate fixed to 0 for model identification
*P<0.05, **P<0.01, ***P<0.001

The estimated mean trajectories of the three latent classes of confiding support are visualized in Figure 6-7. Most of the participants (72%) belonged to the *average* confiding support class, who started with an average level of confiding support, slightly declined in the first 8-9 years (i.e. Phase 2 to 5) and levelled off thereafter (blue dash line), whereas 3% participants (n = 231) experienced consistently *extreme-high* levels of confiding support, who maintained at the top levels throughout (red solid line). The other group (25%, n = 2,325) showed the most fluctuation, who began with a higher than average level, followed by a marked decline and then a gradual increase (green dotted line). Participants who had higher employment grades and always nominated their spouse or partner as the closest person were more likely to be categorized into the *extremely-high* or *higher than average* classes than the *average* class of confiding support.

Figure 6-7 Estimated Class-Specific Mean Trajectories of Confiding Support



Practical support

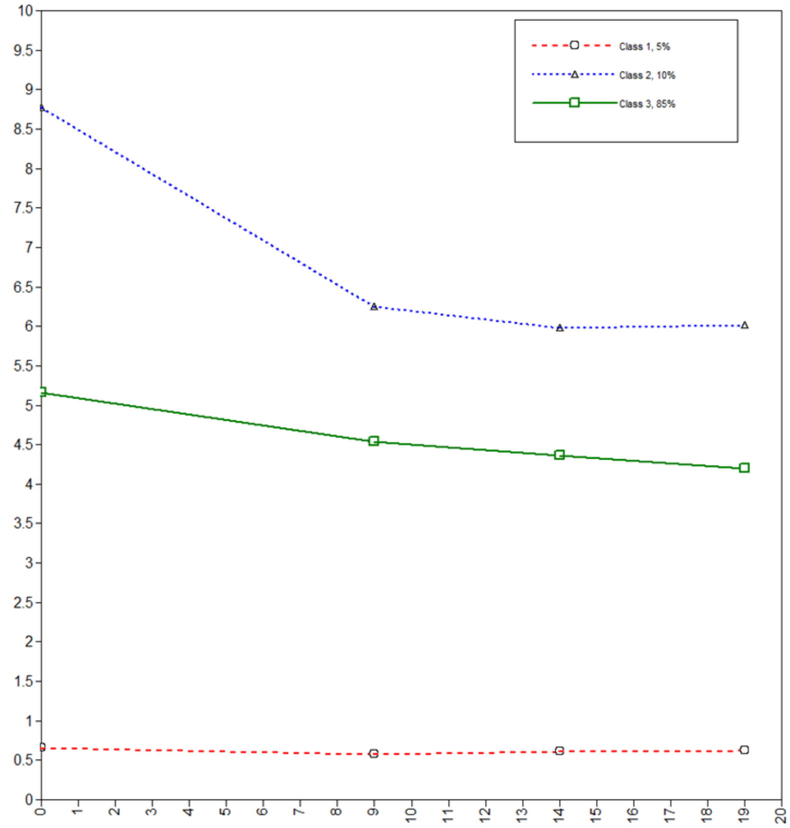
A 3-class solution also applied to practical support (Table 6-6).The covariance matrix cannot be positively defined when a fourth class was introduced. Figure 6-8 presents these class-specific trajectories of practical support based on the parameter estimates in Table 6-8. Five percent of the participants (n = 456) were identified as c*hronically-low*, who perceived consistently low levels of practical support over the follow-up (red dash line). The other 10% (n = 911) were identified as *high-decliners*, whose level of practical support was initially high (8.8), then dropped substantially to around 6.5 and stayed at that level afterwards (blue dotted line). The remaining (85%, n = 7,791) were grouped as *medium-decliners*, who started from an average level and followed by a gradual decline (green solid line). Participants had a high employment grade, high educational attainment or always nominated spouse or partner as the closest person were more likely to be assigned into *high-decline* class. Being a female or nominated the closest person other than spouse or partner was more likely to be grouped as having *chronically-low* practical support.

Table 6-8 Parameter Estimates for the Three-Class GMM for Practical Support

	Practical support (n = 9,128)		
	Chronically-low	**Medium-decline**	**High-decline**
Sample size [a]	456 (5%)	7791 (85%)	911 (10%)
Probability of class membership	0.80	0.95	0.68
Slope factor loadings (ʎ)			
ʎ1	0 (fixed)	0 (fixed)	0 (fixed)
ʎ2	1 (fixed)	1 (fixed)	1 (fixed)
ʎ3	0.54	1.29	1.11
ʎ4	0.48	1.55	1.09
Means			
Intercept	0.66 (0.11)***	5.16 (0.16)***	8.77 (0.21)***
Slope	-0.09 (0.07)	-0.62 (0.08)***	-2.51 (0.34)***
Variance estimates			
Intercept	0[b]	3.13 (0.32)***	0[b]
Slope	0[b]	1.29 (0.20)***	3.72 (1.22)**
Covariance	/	-1.18 (0.15)	-0.13 (0.49)
Residual variance	0.57 (0.10)***	3.07 (0.11)***	0.43 (0.36)***

[a] Based on the most likely latent class membership
[b] Estimate fixed to 0 for model identification
*P<0.05, **P<0.01, ***P<0.001

Figure 6-8 Estimated Class-Specific Mean Trajectories for Practical Support



Structural measures of social relationships

Table 6-9 shows the 3-class GMM for friend- and relative- networks (Table 6-6), with corresponding trajectories shown in Figure 6-9. *Consistently-low* friend (3%, n = 231) or relative (15%, n = 1,395) network classes were identified, showing inapparent changes during follow-up (blue dash lines). The other two classes demonstrated parallel gradual increasing trends starting from *medium* (red solid lines) and *high* levels (green dotted lines) for both friend network (76% vs 21%) and relative network (50% vs 35%). Participants in *high-increase* friend network class were younger and were more likely to have higher employment grades. Those assigned to *high-increase* relative network class were more likely to be female.

Associations between latent classes of social relationships

Chi-square tests were used to investigate associations between these longitudinal latent classes of social relationships. Results showed that participants belonging to the *extreme-high* confiding support class were less likely to fall into the class with *high-decline* in negative support, but were more likely to be grouped into *high-increase* friend- or relative- network classes. Further, no one from this *extreme-high* confiding support class belonged to the *chronically-low* practical support class. Yet participants grouped into the *chronically-low* practical support class were more likely to be in the c*hronically-low* negative support class. The patterns of social network transitions were in high agreement between friend network and relative network, such that participants were most likely to be grouped into a similar latent class for both domains.

Table 6-9 Parameter Estimates for the Three-Class GMM of Structural Measures of Social Relationships

	Friend Network (n = 9,071)			Relative Network (n = 9,054)		
	Consistently-low	**Medium-increase**	**High-increase**	**Consistently-low**	**Medium-increase**	**High-increase**
Sample size [a]	231 (3%)	6958 (76%)	1882 (21%)	1395 (15%)	4526 (50%)	3133 (35%)
Probability of class membership	0.81	0.90	0.71	0.79	0.86	0.79
Means						
Intercept	0.37 (0.07)***	3.38 (0.05)***	5.48 (0.07)***	0.77 (0.02)***	2.54 (0.05)***	4.54 (0.03)***
Slope [c]	0.02 (0.05)	0.40 (0.03)***	0.50 (0.07)***	-0.06 (0.02)***	0.22 (0.04)***	0.16 (0.03)***
Variance estimates						
Intercept	0.07 (0.04)	1.04 (0.08)***	0.94 (0.10)***	0.13 (0.01)***	0.56 (0.08)***	0.56 (0.07)***
Slope	0.00 (0.04)	0.61 (0.08)***	0.45 (0.10)***	0[b]	1.30 (0.11)***	0.39 (0.07)***
Covariance	0.00 (0.03)	-0.24 (0.05)***	-0.36 (0.08)***	/	-0.69 (0.06)***	-0.09 (0.06)
Residual variance	0.18 (0.03)***	1.99 (0.05)***	0.53 (0.07)***	0.15 (0.01)***	1.84 (0.05)***	0.74 (0.04)***

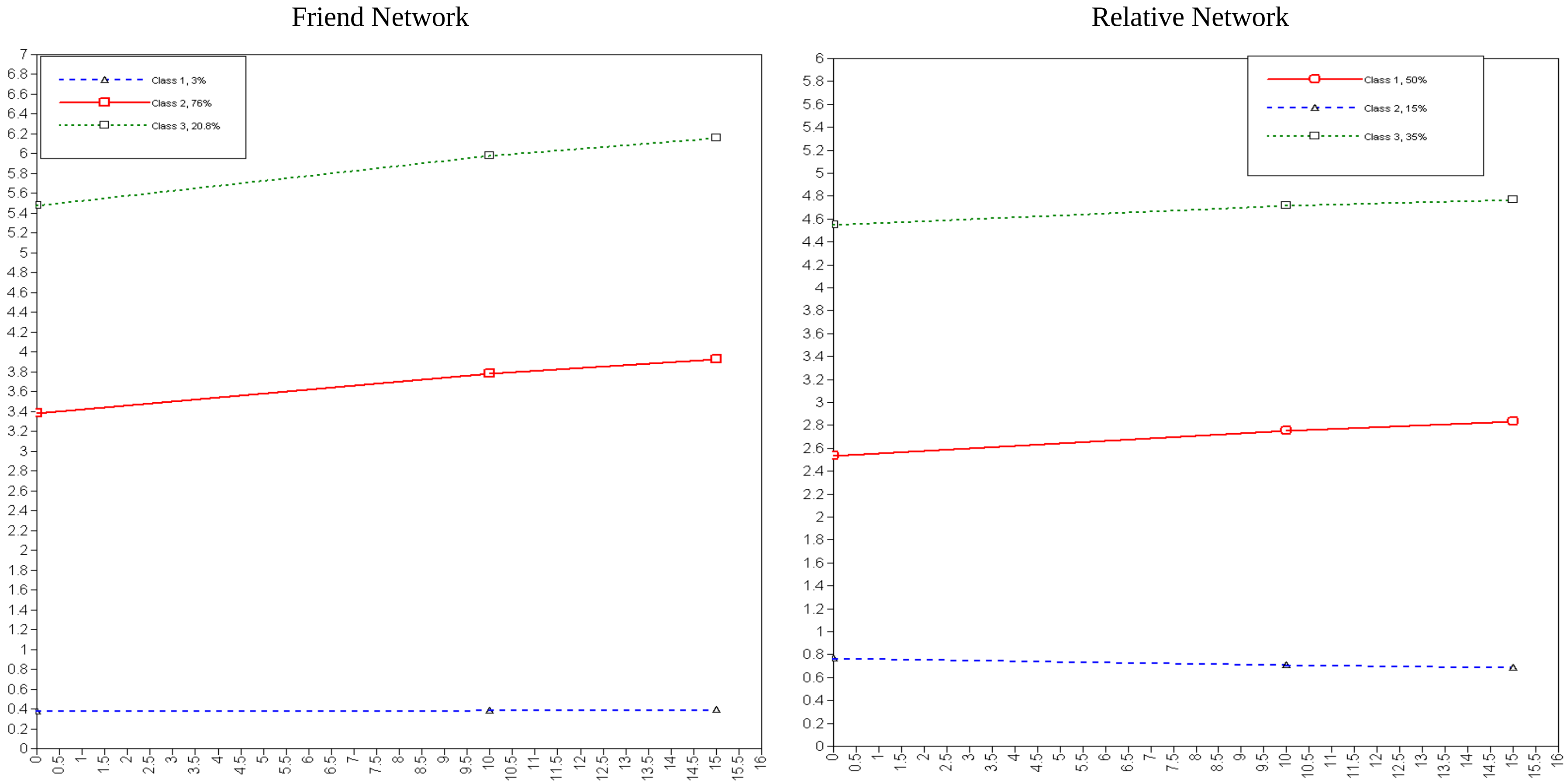
[a] Based on the most likely latent class membership

[b] Estimate fixed to 0 for model identification

[c] Slope factor loadings for friend network were 0 (fixed), 1 (fixed), and 1.36; for relative network were 0 (fixed), 1 (fixed), and 1.34.

*P<0.05, **P<0.01, ***P<0.001

Figure 6-9 Estimated Class-specific Mean Trajectories for Structural Measures of Social Relationships



6.3.2 Step 2: Main analysis: association between latent classes of social relationship and cognitive ageing

The relationships between longitudinal latent classes of social relationships and trajectories of executive function are summarized in Table 6-10, and with trajectories of memory in Table 6-11, alongside parameter estimates plotted in Figure 6-10 and Figure 6-11.

As to the functional measures of social relationships, participants who have a history of high levels of negative support (*high-decliners*) showed the lower score on both executive function and memory tests at Phase 5 compared with those belonging to the *chronically-low* or *medium* negative support classes. When adjusted for other covariates, only the association between low initial memory score and *high* negative support remained statistically significant. The rates of cognitive decline were comparable among those latent negative support classes (Figure 6-10 Column 1). On the other hand, although non-significant associations were found between longitudinal latent classes of confiding support and trajectories of executive function, people perceiving *extremely-high* confiding support presented a significant slower decline in memory compared with those reporting *average* or *higher than average* levels of confiding support over the years (Figure 6-10 Column 2). Notably, decline in memory did not differ between those belonging to *higher-than-average* and *average* confiding support classes, which might indicate a threshold effect. People in different practical support classes showed comparable cognitive ageing trajectories (Figure 6-10 Column 3).

Longitudinal latent classes of structural social relationships were associated with cognitive ageing trajectories differently. In comparison with those classified as *medium-increase* or *consistently-low*, participants reporting a *high-increase* friend network had significantly higher initial executive function and memory scores adjusted for sociodemographic and health status. Contradictorily, those who had a *consistently-low* friend network experienced a more gradual rate of decline in executive function (Figure

6-11 Column 1). However, as only 3% participants were grouped into the *consistently-low* friend network class, the wide confidence interval around the predicted values of executive function over time for this class largely overlapped the one of *medium-increase* friend network class. The initial lower executive function level in participants with a large relative network was explained by socioeconomic characteristics. Trajectories of neither executive function nor memory varied across latent relative network classes (Figure 6-11 Column 2).

Sensitivity analyses stratified by long-term disease status suggested the same number and identical growth patterns for the latent classes of social relationships in those who had *no* chronic disease vs. *any* chronic disease over Phase 2 to 9. Further analyses adjusted for long-term chronic disease status did not alter statistically significant associations identified in the main analysis.

Table 6-10 Associations between Longitudinal Latent Classes of Social Relationships and Executive Function at Phase 5 (Intercept) and 10-Year Declines in Executive Function (Slope) from Phase 5 (1997-1999) to Phase 9 (2007-2009).

	Executive Function (Intercept)						**10-Year Declines in Executive Function (Slope)**					
	Model 1			**Model 2**			**Model 1**			**Model 2**		
	Beta [a]	95% CI		Beta [a]	95% CI		Beta [a]	95% CI		Beta [a]	95% CI	
Negative support												
Chronically-low	0.04	-0.02	0.10	0.02	-0.02	0.07	0.01	-0.02	0.05	0.02	-0.02	0.05
High-decline	-0.12	-0.17	-0.07	-0.01	-0.05	0.04	-0.01	-0.04	0.03	-0.01	-0.04	0.02
P for interaction [b]	*<0.001*			*0.45*			*0.71*			*0.45*		
Confiding support												
Higher than average	0.02	-0.04	0.07	-0.02	-0.06	0.02	0.00	-0.03	0.03	0.00	-0.03	0.04
Extremely-high	0.14	0.00	0.27	0.01	-0.10	0.12	-0.07	-0.16	0.02	-0.06	-0.15	0.03
P for interaction b	*0.14*			*0.69*			*0.31*			*0.36*		
Practical support												
Chronically-low	-0.04	-0.14	0.07	-0.02	-0.10	0.07	0.04	-0.03	0.10	0.04	-0.03	0.10
High-decline	0.07	-0.01	0.15	-0.02	-0.09	0.04	-0.02	-0.07	0.03	-0.02	-0.07	0.03
P for interaction b	*0.15*			*0.75*			*0.34*			*0.36*		
Friend network												
Consistently-low	-0.11	-0.25	0.04	-0.08	-0.20	0.04	0.11	0.02	0.20	0.12	0.02	0.21
High-increase	0.25	0.19	0.30	0.10	0.06	0.15	-0.04	-0.08	-0.01	-0.03	-0.07	0.00
P for interaction b	*<0.0001*			*0.0001*			*0.002*			*0.008*		
Relative network												
Consistently-low	0.03	-0.04	0.10	-0.03	-0.08	0.03	0.02	-0.03	0.06	0.02	-0.02	0.06
High-increase	-0.07	-0.12	-0.02	0.02	-0.02	0.06	0.01	-0.02	0.04	0.01	-0.02	0.04
P for interaction b	*0.01*			*0.27*			*0.64*			*0.57*		

[a] Beta indicates differences in cognitive function or in 10-year cognitive declines in refer to *average* or *medium* class. CI: confidence interval.
[b] Interaction terms assessed whether estimates are different across the three latent classes of social relationships
Model 1: adjusted for age; Model 2: adjusted for age, ethnicity, sex, socioeconomic and health status.

Table 6-11 Associations between Longitudinal Latent Classes of Social Relationships and Memory at Phase 5 (Intercept) and 10-Year Declines in Memory (Slope) from Phase 5 (1997-1999) to Phase 9 (2007-2009)

	Memory (Intercept)						**10-Year Decline in Memory (Slope)**					
	Model 1			**Model 2**			**Model 1**			**Model 2**		
	Beta [a]	95% CI		Beta [a]	95% CI		Beta [a]	95% CI		Beta [a]	95% CI	
Negative support												
Chronically-low	0.04	-0.02	0.10	0.04	-0.02	0.09	0.02	-0.05	0.08	0.02	-0.04	0.09
High-decline	-0.10	-0.16	-0.05	-0.06	-0.11	-0.01	0.05	-0.01	0.10	0.03	-0.03	0.09
P for interaction [b]	*<0.001*			*0.01*			*0.33*			*0.51*		
Confiding support												
Higher than average	0.06	0.01	0.12	0.04	-0.01	0.10	-0.06	-0.12	0.00	-0.06	-0.12	0.00
Extremely-high	0.02	-0.12	0.15	0.05	-0.08	0.18	0.18	0.03	0.34	0.20	0.04	0.36
P for interaction b	*0.07*			*0.11*			*0.005*			*0.005*		
Practical support												
Chronically-low	0.02	-0.08	0.13	0.00	-0.10	0.11	0.02	-0.10	0.14	0.02	-0.10	0.14
High-decline	0.06	-0.02	0.14	0.03	-0.04	0.11	0.00	-0.09	0.09	0.01	-0.08	0.10
P for interaction b	*0.35*			*0.71*			*0.94*			*0.91*		
Friend network												
Consistently-low	0.03	-0.12	0.18	0.04	-0.11	0.18	-0.05	-0.22	0.12	-0.04	-0.21	0.12
High-increase	0.16	0.10	0.21	0.10	0.04	0.15	-0.07	-0.14	-0.01	-0.06	-0.13	0.00
P for interaction b	*<0.0001*			*0.006*			*0.07*			*0.15*		
Relative network												
Consistently-low	0.02	-0.05	0.09	-0.01	-0.08	0.06	0.00	-0.08	0.08	0.01	-0.07	0.09
High-increase	0.00	-0.05	0.05	0.03	-0.02	0.07	0.00	-0.06	0.06	0.00	-0.06	0.06
P for interaction b	*0.78*			*0.52*			*0.99*			*0.98*		

[a] Beta indicates differences in cognitive function or in 10-year cognitive declines in refer to *average* or *medium* class. CI: confidence interval.
[b] Interaction terms assessed whether estimates were different across three latent classes of social relationships
Model 1: adjusted for age; Model 2: adjusted for age, ethnicity, sex, socioeconomic and health status.

Figure 6-10 Predicted Trajectories of Executive Function (Upper Panel) and Memory (Lower Panel) over 10-Years by Longitudinal Latent Classes of Functional Social Relationships, Estimation for White Male Aged 55 at Analysis Baseline (Time = 0), with Low Socioeconomic Status and Had No Illness.

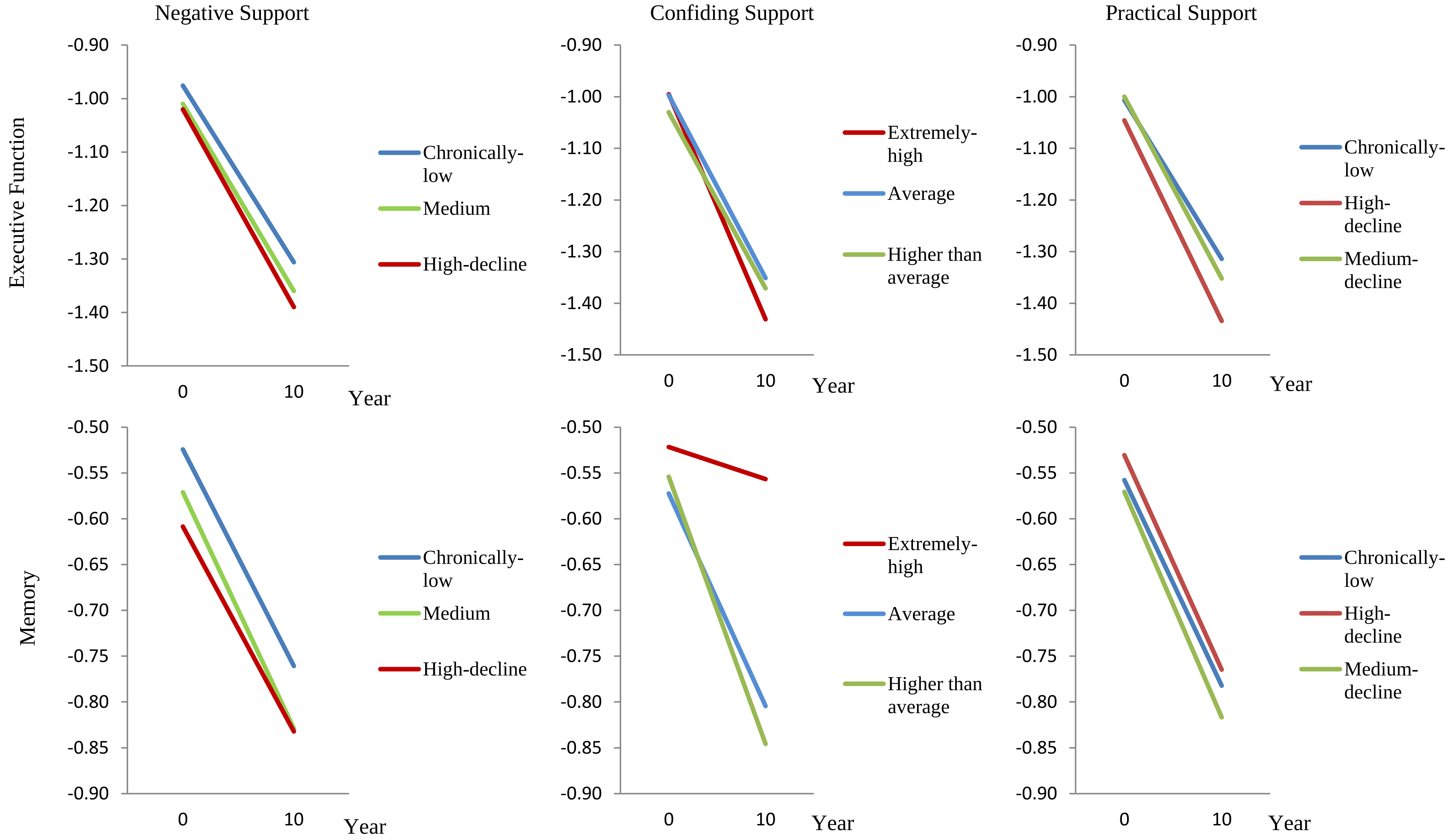
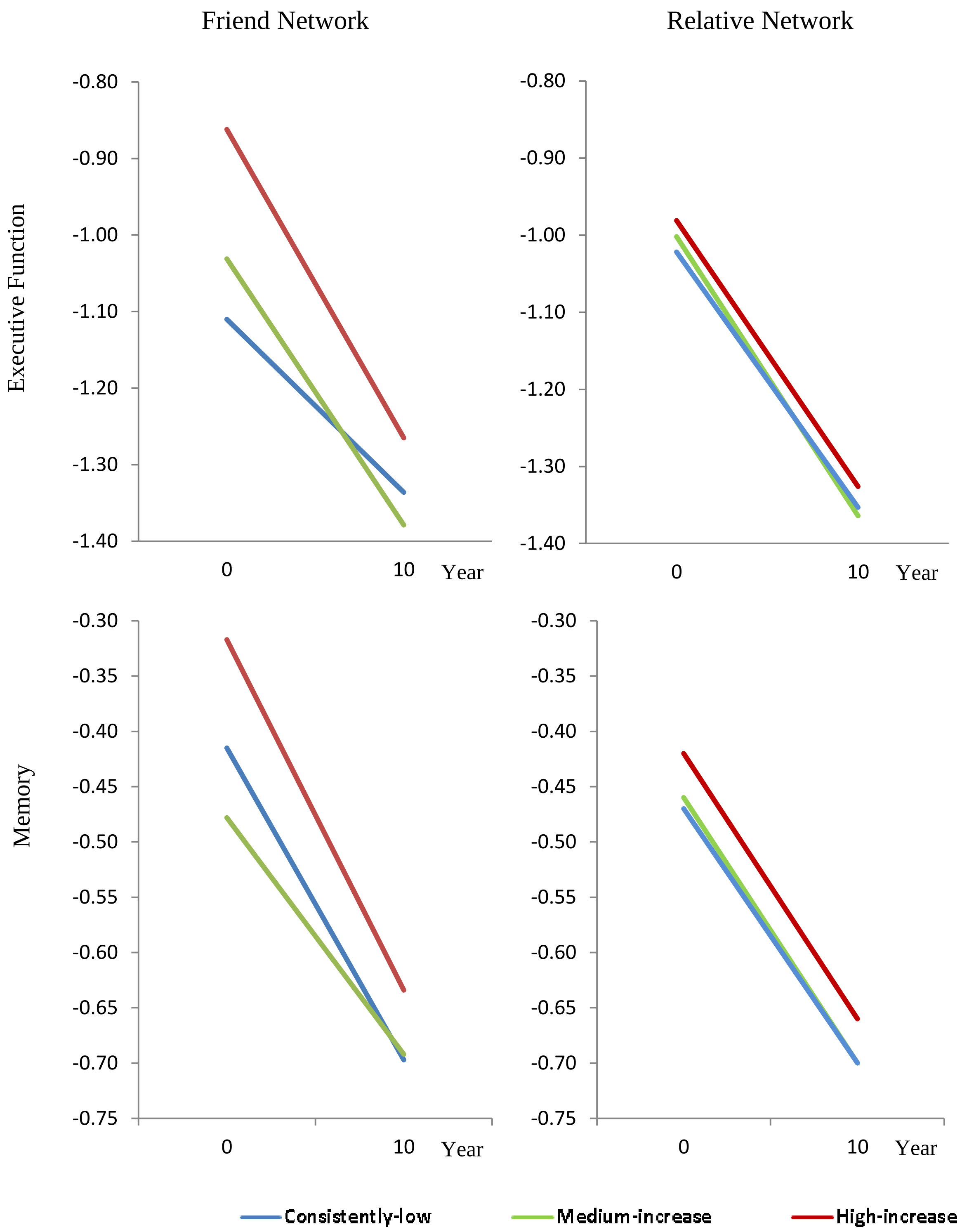


Figure 6-11 Predicted Trajectories of Executive Function (Upper Panel) and Memory (Lower Panel) over 10-years by Longitudinal Latent Classes of Structural Social Relationships, Estimation for White Male Aged 55 at Analysis Baseline (Time = 0), with Low Socioeconomic Status and Had No Illness.



6.4 Interim discussion

This chapter investigated ***Objective two***, examining longitudinal latent classes of social relationships, comprised of heterogeneous subgroups with divergent social ageing patterns as participants moved from middle to early old age; as well as the extent to which their corresponding trajectories of cognitive ageing would differ.

The hypothesized heterogeneity in the longitudinal changing patterns of social relationships was confirmed. For all measures of social relationships considered, three latent classes were identified by GMM as optimal solutions. Although most of the participants (percentages range from 47% to 85%) were grouped into the *average* or *medium* class, some distinct growth patterns were identified. There were around 25% of the participants reporting *higher than average* confiding support with age, plus another 3% consistently perceiving even higher confiding support (*extremely-high* class). Those reporting initial high negative support experienced improved quality of support, indicated by the most evident decline in negative support during the follow-up (28% *high-decliners*). On the other hand, a few participants had *chronically low* levels of practical support (5%), and friend (3%) or relative (15%) network.

In relation to cognitive ageing trajectories, participants perceiving consistently *extremely-high* levels of confiding support appeared to experience the least decline in memory relative to their counterparts in the *average* or *higher than average* classes. Those with a *high-increase* friend network showed significantly higher initial cognitive scores but similar rates of cognitive decline compared with those grouped as the *medium-increase* friend network class, whereas participants having a *chronically-low* friend network seemed to decline more gradually in executive function. However, in view of the amount of uncertainty involved, cautions should be taken in interpreting these significant associations between small latent classes of social relationships (around 3% of the study sample) and trajectories of cognitive ageing.

Methodological caveats of GMM

Although GMM is an advanced statistical technique to distinguish longitudinal latent classes, several methodological caveats should be considered.

First, as disputed by Bauer and Curran (2003a,b), the latent classes suggested by GMM may actually represent homogeneous non-normal data. The within-class multivariate normality assumption appears to be invalidated in the observed data distribution of social relationships. The current analysis used robust maximum likelihood estimation with robust standard errors to adjust for failure to meet this normality assumption (Muthén and Muthén, 2012), as well as a set of validated model indexes to signal subpopulation mixture distribution. Yet the potential of over-extraction simply to capture the non-normal distribution curvature cannot be entirely excluded. Recently, Muthén and colleagues proposed to adopt skew t-distributions (skew-t) in order to relax the assumption of within-class normality (Asparouhov and Muthén, 2014; Muthén and Asparouhov, 2015). Skew-t GMM compensate for deviations from Gaussian distribution by fitting the data with means, co-variances, skewness, kurtosis and the entire distribution. Hence within-class distributions are allowed to be skewed and to have heavy tails. Skew-t GMM advances normal GMM by better fitting the data with more parsimonious models, such reducing the risk of over extracting spurious classes. Despite these advancements, skew-t GMM requires longer computations, larger dataset, more random starts and generates lower entropy than normal GMM (Muthén and Asparouhov, 2015).

Second, as GMM is good at separating individuals with distinct characteristics into sub-groups, the number of participants in these subgroups can be quite small. In the current analysis, the majority of the participants were grouped as the *average* or *medium* classes, while a few participants (less than 5% in some cases) with divergent trajectories were separated into other small classes. These uneven percentages of class memberships identified have been reported in other studies that apply GMM to repeat measures

(Campbell *et al.*, 2009; Terrera *et al.*, 2010; Byers *et al.*, 2012; Silverwood *et al.*, 2013). However, these small numbers in certain latent classes of social relationships may result from chance due to sample characteristics (Bauer and Curran, 2003a), and thus increase the amount of uncertainty in any significant finding in relation to cognitive decline.

Third, the predicted class memberships are influenced by covariates included in the model (Tofighi and Enders, 2008). It has been argued that if covariates have significant direct effects on growth factors (i.e. intercept and slope), the unconditional model will lead to distorted results as the observed items would be incorrectly related to the latent class membership (Muthén, 2004; Jung and Wickrama, 2008). It is analogous to a regression model that additional key covariates would help account for the residual variance, improve the slope estimate and facilitate the assignment into different classes (Muthén, 2004). However, the power loss due to model complexity may outweigh the benefit of including extra covariates (Tofighi and Enders, 2008). In sensitivity analysis, several covariates were considered to test the difference in classification between unconditional and conditional models. Consistent with previous studies (Martire *et al.*, 1999; Shaw *et al.*, 2007), covariates were most likely to explain variations at the initial level of social relationships rather than the rate of change over time. When the same constraints were applied for the sake of model identification, similar classification solutions of social relationships showed in these conditional models. Considering the negligible influence on the trajectory and model complexity of conditional models, the classification derived from unconditional models was retained in the current analysis.

Temporality of the longitudinal social relationships- cognitive decline association

Objective two investigated how social relationships and cognitive ageing coevolve over time, while the temporal direction was not clear. More rigorous analysis is required to understand the temporality, which will be examined in the following chapter.

Chapter 7. Objective three: reciprocity of social relationships and cognitive function in late adulthood

Summary

This chapter investigates the possibility of bidirectional associations between social relationships and cognition in late life. Bivariate dual change score models (BDCSM) were applied to three parallel repeat measures of functional social relationships and cognitive function over Phase 5, 7 and 9, to examine how functional aspects of social relationships at previous phases influence the subsequent 5-year changes in cognitive function, and vice versa. These time-lagged associations were conditional on inter-individual differences and intra-individual changes over time, and adjusted for sociodemographic characteristics and health status at Phase 5. Alternative hypotheses on *social causation* and *health selection* processes were rigorously evaluated.

7.1 Introduction

Previous chapters consider social relationships as risk factors for cognitive ageing, as the predominant literature suggests. Cognitive ageing, however, is likely to curtail social engagement (Shouse *et al.*, 2013) and may strain social relationships (Lang, 2001). In consequence, the neuro-protective effect of social relationships may be produced by reverse causation (Stoykova *et al.*, 2011). As yet, few studies (Thomas, 2011a; Ellwardt *et al.*, 2013; Li and Zhang, 2015) have investigated the bidirectional associations between social relationships and cognitive decline in late life.

7.1.1 Theory and evidence

Two alternative theories, *social causation* and *health selection* apply equally well to the dynamic associations of social relationships and cognitive function (Section 2.3 Chapter 2, Page 32). *Social causation* hypothesizes that better social support (Seeman *et al.*, 2001) and a larger social network (Béland *et al.*, 2005) retard cognitive decline, aligned with social integration and network theory reviewed by Berkman *et al.* (2000). In contrast, *health selection* operates if cognitive limitations endanger structure (Aartsen *et al.*, 2004) and function (Gurung *et al.*, 2003) of social relationships, due to reduced social functioning (Washburn *et al.*, 2003; Bailey *et al.*, 2008) and diminished social reciprocity (van Tilburg and Broese van Groenou, 2002; Lang *et al.*, 2009).

The dynamic interplay between social relationships and cognitive function has been studied in only three population-based longitudinal cohorts. Thomas (2011a) applied cross-lagged models to older people aged 60 and above in the U.S, showing *social causation* among women (i.e. greater social engagement predicted better subsequent cognitive performances), whereas *health selection* in men (i.e. more cognitive limitations led to less social engagement). Using the same statistical technique, Li and Zhang (2015) reported bidirectional associations between diversity in the social network and cognitive maintenance in the Chinese Longitudinal Healthy Longevity Survey (> 64 y). Ellwardt *et al.*, (2013) modelled directional parallel latent growth curves of social support and cognition in the first 3 waves of LASA (> 55 y), and found evidence for *social causation* only, which was especially evident among adults aged 65 years and over.

7.1.2 Dual change score model (DCSM) and its advantages in multivariate longitudinal data analysis

Among statistical models available to detect dynamic interplay between longitudinal repeat measures (McArdle and Hamagami, 2001; Robitaille *et al.*, 2012), DCSM has been proposed to be the most comprehensive and flexible (Ferrer and McArdle, 2003; Lövdén *et al.*, 2005a; Bollen and Curran, 2006; McArdle, 2009; Ferrer and McArdle, 2010). Table 7-1 compares the three statistical models mostly used in the existing literature, including *cross-lagged model*, *parallel latent curves model* (PLCM) and DCSM (Note: information was mainly synthesized from Bollen and Curran (2006); McArdle (2009)).

DCSM combines several features of the cross-lagged model and PLCM, demonstrating advancements over both models. In a conceptual analogy to the cross-lagged model, DCSM evaluates time-lagged relations among variables' status and their subsequent changes. DCSM advances cross-lagged model by explicitly estimating and separating variables' error variances from the true unobserved scores at each measurement occasion (McArdle *et al.*, 2004; Lövdén *et al.*, 2005a). Additionally, similar to PLCM, DCSM estimates intra-individuals' growth curves over time, and thus efficiently utilizes multiple repeat data. On balance, DCSM statistically accounts for different reliabilities (i.e. amount of measurement errors) and stabilities (i.e. amount of inter-individual difference in change) of multivariate longitudinal data, and simultaneously estimates inter-variable lead-lag effects and intra-variable growth patterns. More importantly, this model enables formal statistical evaluation of alternative hypotheses on these time-specific lead-lag associations across multivariate (Lövdén *et al.*, 2005b; Ghisletta *et al.*, 2006).

Table 7-1 Model Comparisons between Cross-Lagged Model, Parallel Latent Curves Model (PLCM) and Dual Change Score Model (DCSM).

Models	Purpose	Application	Pro & Con	Extension
Cross-lagged Model	Estimates **time-lagged associations**: each variable is a combined function of its immediately preceding value, the other variable at previous time and a time-specific residual.	Indicates **inter-individual differences** over time (Piccinin *et al.*, 2011).	Pro: Investigates lead-lag relations across variables simultaneously in one model. Cons: 1) **Not allow systematic growth** components. An inefficient use of multiple waves of data; 2) Using observed scores, where **measurement errors** may confound the results (Rogosa, 1980).	Autoregressive latent trajectory (Bollen and Curran, 2004) combines autoregressive cross-lagged model with latent growth curve.
PLCM	Estimates **correlations** between multivariate growth patterns: each variable has its own latent growth curve, which **co-varies** freely with the other measure.	Investigates how repeat measures '**travel together**' through time, with null hypothesis that there is no correlation between latent curves.	Pro: Accounts for intra-individual change and inter-individual difference. Estimates concurrent correlations of two latent curves. Con: Any correlation in relation to the intercept depends on the location of the intercept (Grimm, 2007). **Does not represent directional dynamic relationships.**	Directional PLCM (Bollen and Curran, 2006) regresses the latent slope parameter of one repeat measure onto the intercept of the other. Latent curve model with structured residuals (Curran *et al.*, 2013) combines latent curve model with an autoregressive residual structure.
DCSM	Estimates **time-lagged dynamics** between multivariate, accounting for **longitudinal growth** pattern and **auto-regression** of each variable.	Predicts how repeat multivariate **change** as a joint function of a constant change (i.e. linear slope), self-feedback (i.e. auto-regression) and the coupling effect from the other measure at the previous occasion.	Pros: **Separates true change from error variance**, and estimates **systematic growth** components. Rigorously assesses the **lead-lag** relationships between variables. Cons: Complicated data requirement and relatively slow in computation.	Unique time-dependent disturbance, multiple-group factorial invariance and non-linear models of change (Lövdén *et al.*, 2005b; Ghisletta *et al.*, 2006).

In light of the plausibility of both *social causation* and *health selection* processes, current mixed findings on the dynamic association between social relationships and cognitive function need to be disentangled by utilizing the best statistical technique available. Therefore, this chapter employed BDCSM to investigate the time-lagged associations between repeat measures of functional social relationships and cognitive function, with alternative hypotheses statistically evaluated.

7.1.3 Equations & Assumptions of DCSM

To express the aforementioned features of DCSM using statistical parameters, this section first defines the latent change scores, and then quantifies these latent change scores via DCSM of a univariate process (e.g. variable *Y*) and of a bivariate dynamic system (e.g. variables *Y* and *X*).

Latent change scores

Under the classical true score theory, each repeat measure *Y* at time point *t* for individual *n* can be decomposed into the sum of a latent true score *y* plus an independent error *e* (McArdle and Nesselroade, 1994), as

$$Y(t)_n = y(t)_n + e(t)_n \qquad (1)$$

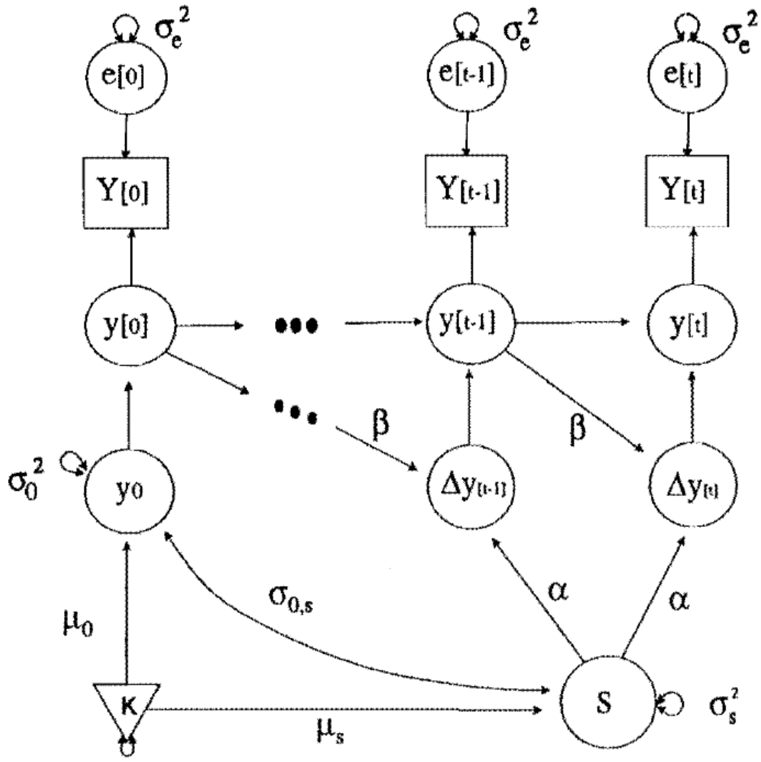
which assumes the error terms 1) have a zero mean ($\mu_e = 0$) and a nonzero variance ($\sigma_e^2 \neq 0$) that is constant over time (i.e. homoscedasticity assumption) (McArdle and Hamagami, 2001; McArdle and Grimm, 2010), and 2) are not part of the accumulated changes in the true score *y* (McArdle, 2009). The time-invariant variances for error terms σ_e^2 indicate that the measurement works comparably well at each occasion.

The latent change scores $\Delta y\ (t)_n$ then can be written as the reliable change between two adjacent true scores, separating from errors (as visualized in the upper part of Figure 7-1),

$$\Delta y\ (t)_n = y\ (t)_n - y(t-1)_n \qquad (2)$$

Modelling latent change scores by DCSM

Figure 7-1 Univariate Dual Change Score Model Cited from McArdle and Hamagami (2001)



Note: squares represent observed variables; circles represent latent variables; triangles represent constants; one-headed arrows represent regression coefficients; double-headed arrows represent variances or co-variances; dots represent repeat measures.

As illustrated in Figure 7-1, for a univariate DCSM, the latent change score can be modelled as,

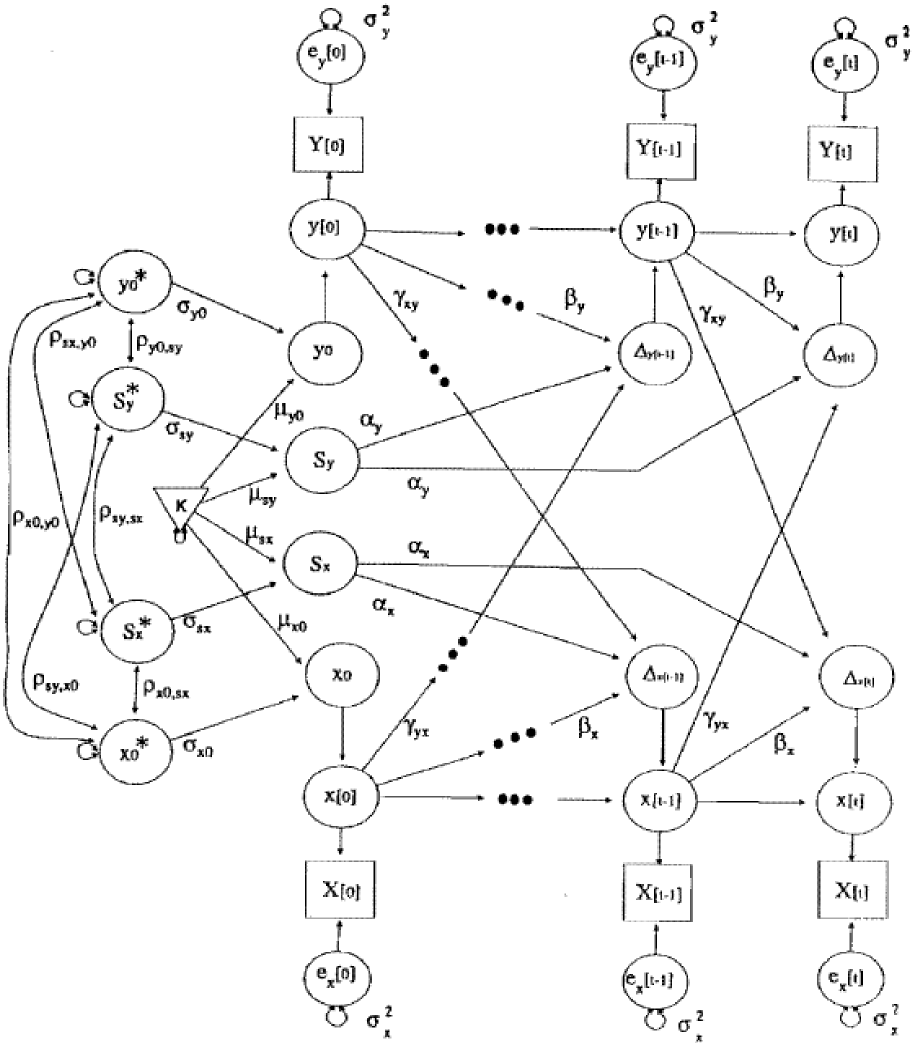
$$\Delta\, y\,(t)_n = \alpha\, \times\, s_n + \beta\, \times y\,(t-1)_n \qquad (3)$$

whereby the latent change score is defined by two additive components, a fixed common slope ($\alpha\, \times\, s_n$) and the previous state $\beta\, \times y\,(t-1)_n$.

There are two key parameters to be estimated 1) a constant regression α which predicts $\Delta y\,(t)_n$ from a common latent linear slope s_n , and 2) an auto-proportion β which predicts $\Delta y\,(t)_n$ proportional to its prior score $y\,(t-1)_n$. Equality constraints are applied to α and β implying a systematic growth pattern. Normally, α is fixed to be one, whereas the same magnitude of βs over time can be relaxed to vary (McArdle and

Hamagami, 2001). When β is set to be zero, the DCSM is equivalent to a classical linear latent growth model (Lövdén *et al.*, 2005b).

Figure 7-2 Bivariate Dual Change Score Model Cited from McArdle and Hamagami (2001)



Note: squares represent observed variables; circles represent latent variables; triangles represent constants; one-headed arrows represent regression coefficients; double-headed arrows represent a correlation or a covariance; dots represent repeat measures; *s represent standardized latent scores.

Bivariate DCSM (BDCSM) expands the univariate foundation. These latent change scores of variable *Y* and *X* modelled by BDCSM in Figure 7-2 can be written as,

$$\Delta y(t)_n = \alpha_y \times s_{yn} + \beta_y \times y(t-1)_n + r_{yx} \times x(t-1)_n$$

and

$$\Delta x(t)_n = \alpha_x \times s_{xn} + \beta_x \times x(t-1)_n + r_{xy} \times y(t-1)_n \qquad (4)$$

where change in one variable is a time-based function of both the variable itself and the other variable, composed of three components: a constant influence (α), an auto-proportional effect of the variable itself (β) and a coupling effect of the other variable (γ) over time. The last component, the coupling parameter γ, captures the time-dependent effect of one variable on the subsequent change in the other (i.e. lead-lag effect); upon which certain constraints can be placed to test specific hypotheses (detailed description in Section 7.2.3, Page 128).

The **assumptions** of BDCSM (McArdle and Hamagami, 2001) are, 1) the separation of the true scores $y(t)$ from the measurement error $e_{(t)}$; 2) a constant time interval ($\Delta[t]$ =1) that guarantees time-invariant scaling of all parameters; 3) the separation of individual scores from group parameters; 4) two simultaneous equations in which the latent changes of $\Delta\, y(t)$ and $\Delta\, x(t)$ are governed separately, where the parameters of one model are embedded in the outcomes of the other variable and vice versa.

7.2 Methods

7.2.1 Repeat measures of functional social relationships and cognitive function

Parallel repeat measures of functional social relationships (i.e. confiding support, practical support and negative support) and cognitive function (i.e. executive function and memory) over Phases 5, 7 and 9 were used.

Measures of functional social relationships were scaled to Z-scores analogous to that of cognitive function, namely, Phase 5 measures of social relationships were scaled to Z-scores (Mean = 0, SD = 1) and the Phase 7 and 9 scores were scaled using the means and standard deviations from Phase 5 as reference values. Standardization does not alter the psychometric properties of these scores, but instead retains longitudinal changes in the mean and variance, and allows for meaningful comparisons on a common metric (Note: it is acknowledged that strict comparison is not possible, as 1SD in cognitive function does not necessary equal 1SD in functional social relationships).

7.2.2 Covariates

Age, sex, ethnicity, socioeconomic and health status measured at Phase 5 were included. See Chapter 4 Section 4.2.3 for the detailed description of these covariates (Page 60).

Considering the potential effect of life events on changes in the identity of the closest person as participants age (Pahl and Pevalin, 2005; Wrzus *et al.*, 2013), an additional variable was used to indicate stability and transitions of marital status from late middle to early old age. Five categories were generated to represent the history of marital status from Phase 5 to Phase 9 (using all available information from Phase 5, 6, 7, 8 and 9): always married 69.8% (reference group), always unmarried 19.5% (i.e. always single, divorced or widowed), became unmarried 4.9% (married at Phase 5 and became single, divorced or widowed in following wave(s)), remarried 2.7% (divorced or widowed at Phase 5 and remarried in subsequent wave(s)) and intermittent patterns 3.1% (moved in and out of marriage more than once during the follow-up). A similar indicator of transitions in the labour market status was also examined. As non-significant associations were found between labour market transitions and trajectories of social relationships or cognitive ageing, it was not included in the present analyses.

7.2.3 Statistical procedures

To investigate the bidirectional time-lagged (5-year) sequential relationships between functional social relationships and cognitive decline, a two-step framework was applied (McArdle and Hamagami, 2001). First, a univariate analysis was carried out separately for each measure of social relationships and cognitive function. The longitudinal trajectory of each variable was indicated by the parameters, which were stepwise introduced in the univariate models as the auto-proportion parameter β, the constant regression parameter α and both parameters together. Second, bivariate models were fitted to describe the dynamic relationships across variables, denoted by the coupling parameter γ (i.e. lead-lag associations). Altogether six separate sets of analyses were carried out, that is, 3 measures of functional social relationships × 2 cognitive variables. Measurement occasions (i.e. Phase 5, 7 and 9) were chosen as the time-metric.

Figure 7-3 illustrates the diagram for BDCSM of the Whitehall II cohort application. Based on formula (1), (2) and (4) in Section 7.1.3, the observed score of functional social relationships (S) and cognitive function (C) at time *t* for individual *n* can be defined as,

$$\mathrm{S}(t)_n = \alpha_s \times \mathrm{S}_{sn} + s(t-1)_n + \beta_s \times s(t-1)_n + r_{c\to s} \times c(t-1)_n + e_s$$

$$= \alpha_s \times S_{sn} + (1+\beta_s) \times s(t-1)_n + r_{c\to s} \times c(t-1)_n + e_s,$$

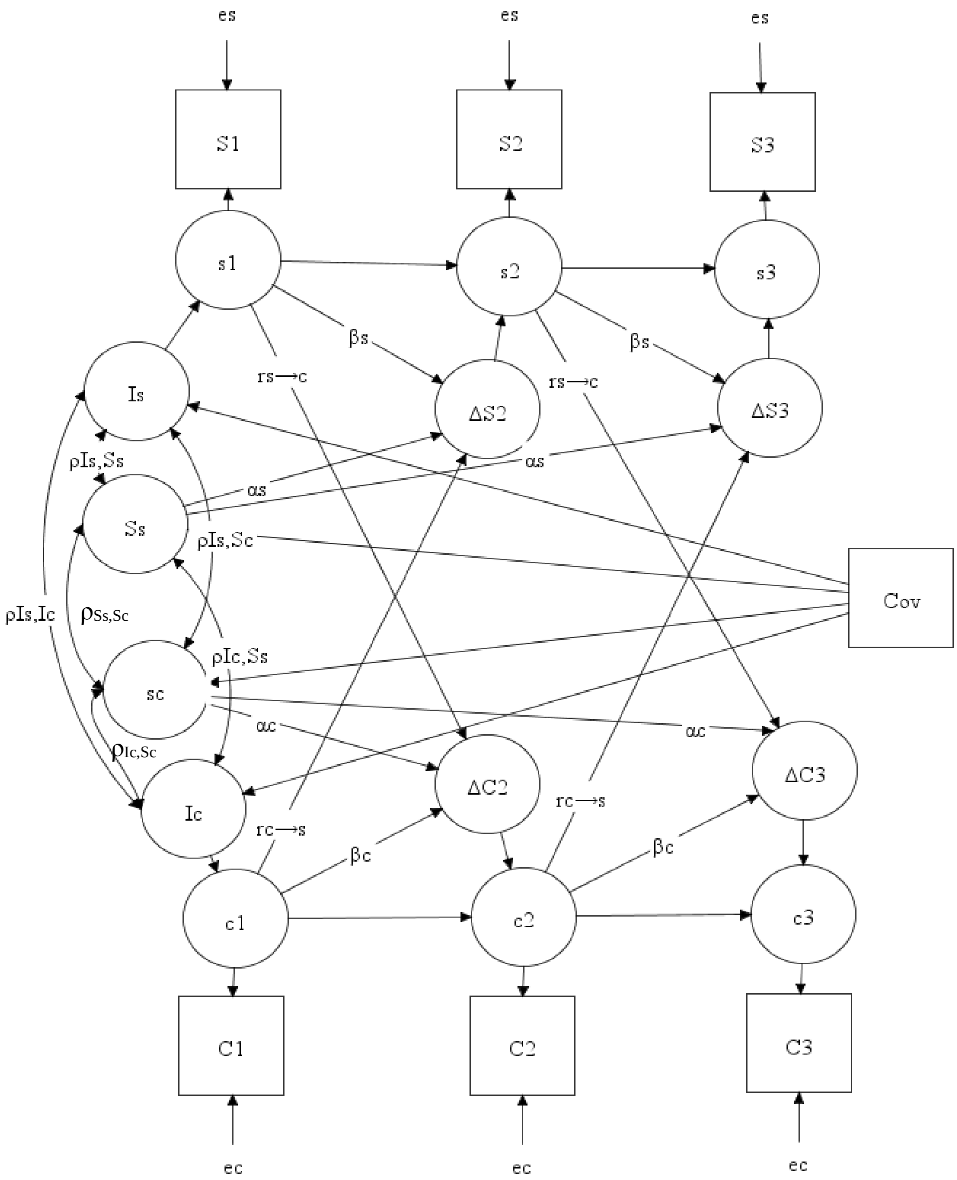
equally,

$$\mathrm{C}(t)_n = \alpha_c \times S_{cn} + (1+\beta_c) \times c(t-1)_n + r_{s\to c} \times s(t-1)_n + e_c \qquad (5)$$

Thus each observed variable at time *t* was an additive result of the constant linear slope (i.e. Ss and Sc, $\alpha_s = \alpha_c = 1$), previous level at time t-1 (contribute to the latent intercept if at Phase 5, s_1 and c_1), plus the effect of self-feedback (i.e. auto-proportion regression βs and βc), the other variable at time *t-1* (i.e. coupling parameter $r_{c\to s}, r_{s\to c}$), and residual errors (e_s, e_c).

Latent intercepts (Is and Ic) and linear slopes (Ss and Sc) were proposed to account for time series information, estimated at both population and individual levels (Lövdén *et al.*, 2005b). Additional acceleration or deceleration in these linear changes was implied by the auto-proportion parameter β and coupling parameter γ. There two dynamic parameters were estimated at population level only (i.e. group development) without predicting inter-individual differences. Thus no random effects were predicted around parameter β or γ. To simplify the estimation and to represent a systematic growth over equal time intervals, β and γ were assumed to be time-invariant. Supplementary analyses supported these constraints, as relaxing the assumption via freeing parameter estimates of β or γ produced similar dynamic structure without significant improvement in the model fits (all P-values for log-likelihood ratio tests > 0.38).

Figure 7-3 Path Diagram for a Conditional Bivariate Dual Change Score Model (BDCSM)



Note: Observed social relationships ($S_{1\text{-}3}$) and cognition ($C_{1\text{-}3}$) are presented by squares, with their corresponding latent true scores ($s_{1\text{-}3}$, $c_{1\text{-}3}$) presented by circles. Time invariant errors are e_s, e_c. ΔS_t and ΔC_t are error-free latent changes at time t. Intercepts (Is, Ic) are anchored at Time1, representing the reliable proportion of variance at Time1. Constant change factors (Slope: Ss,Sc) indicate the common linear component of change scores. Regression pathways are represented by one-headed arrows, and variance and co-variances by two-headed arrows. Unlabelled pathways are fixed to 1, except for the regression paths with the covariates (Cov). α = constant change component, β = auto-proportion, and $r_{c\to s}$ / $r_{s\to c}$ = coupling parameter.

The substantive interpretation of the coupling parameter γ was evaluated on a statistical basis by fitting another three alternative models (Table 7-2).

Table 7-2 Alternative Hypotheses on the Coupling Parameter γ of BDCSM

Alternative models	Hypothesis testing	Coupling parameters $\lvert\gamma_{s\to c}\rvert$	$\lvert\gamma_{c\to s}\rvert$
Full coupling	A form of dynamic associations	> 0	> 0
Social causation	Social relationships are the leading indicators of changes in cognitive function	Only > 0	0
Health selection	Cognitive function is the leading indicator of changes in social relationships	0	Only > 0
No coupling	No dynamic associations between social relationships and cognitive function	0	0

S: social relationships; C: cognitive function.

The first model, labelled as *full coupling*, postulated that mutual influence between functional social relationships and cognitive function, where coupling parameters of both directions ($r_{c\to s}, r_{s\to c}$) were estimated. This model was the least parsimonious, with the other three models nested within it.

The second model tested the *social causation* hypothesis, whereby the coupling parameter $r_{s\to c}$ was freely estimated while $r_{c\to s}$ was constrained to be zero, suggesting there was only unidirectional influence from functional social relationships onto changes in cognition, but no influence the other way around. Likewise, the third model tested the *health selection* hypothesis, where the coupling parameter $r_{c\to s}$ was freely estimated whereas $r_{s\to c}$ was constrained to be zero, indicating unidirectional influence from cognition onto changes in functional social relationships only.

Compared with the full coupling model, a significant loss in goodness-of-fit (method see Section 7.2.5, Page 133) in the second or the third model indicated that the hypothesis of either social relationships or cognitive function being the leading factor of the other (i.e. unidirectional influence) should be rejected. If there was no significant loss in goodness-of-fit, then the more parsimonious model was chosen.

Last, the fourth model, representing *no coupling*, constrained both coupling parameters to be zero ($r_{c \to s} = r_{s \to c} = 0$ suggesting independent growth of these two sets of variables. Statistically rejecting the null hypothesis of the fourth model indicated the necessity to allow bidirectional coupling effects between variables.

All BDCSM tested above were controlled for the effects of age and sex on the intercepts and slopes, as indicated by the regression paths from Cov (i.e. covariates) to Is, Ss, Sc and Ic in Figure 7-3, to avoid spurious associations (Piccinin *et al.*, 2011). The coupling parameters $\gamma_{s \to c}$ and $\gamma_{c \to s}$ thus were conditional on the age- and sex- adjusted effect of systematic growth (slope) and auto-proportional regression (β) of each set of variables. After identifying the best fitting BDCSM via these minimally adjusted models, other time-invariant covariates fixed at Phase 5 and marital history over the 10-year follow-up were then introduced to further control for potential confounding effects.

To facilitate the interpretation of these dynamic associations between functional social relationships and cognitive function over time, the vector field was used to display the direction and magnitude of change in both variables for a given set of starting coordinates (Boker and McArdle, 1995).

7.2.4 Supplementary analyses

Main analyses were rerun restricted to a subsample with complete data for social support and cognition at all three waves. Two approaches were used to verify whether these dynamics would be sensitive to the differences in support providers: analyses were repeated amongst participants who remained always married during the follow-up and consistently nominated their spouse as the closest person; as well as stratified by the change and stability in the identity of the closest person (i.e. always partner, always non-partner, partner to non-partner and non-partner to partner).

To test whether these dynamics found in the main analyses would vary across sex (Thomas, 2011a) and age groups (Ellwardt *et al.*, 2013), supplementary analyses were conducted stratifying by sex and age groups (i.e. ≤ 55 and > 55 years, as 55 years was the mean at analysis baseline Phase 5).

Stratified analyses were also applied to test whether these dynamic patterns would be invariant upon chronic depressive symptom status (Dickinson *et al.*, 2011), and functional limitations, defined as having difficulty with activities of daily living (ADL) (Katz *et al.*, 1970), instrumental activities of daily living (IADL) (Lawton and Brody, 1969) or both by Phase 9.

In light of the evidence that people with different size and composition of social networks may mobilize their social support resources differently (Gurung *et al.*, 2003; Aartsen *et al.*, 2004), the total number of people felt close to (categorized as 0, $1\sim\leq 5$ (reference), $5\sim\leq 10$, $10\sim\leq 20$, 20+), number and frequency of contacting friends (centred at mean score 4) or relatives (centred at mean score 3) measured at Phase 5 were further controlled for.

7.2.5 Model selections

In line with current practice, multiple fit indices were used to assess the difference in model fit: log-likelihood ratio tests (corrected $\chi2$ statistics were used to adjust for non-normal distribution), Bayesian information criterion (BIC), the Tucker-Lewis-index (TLI), the Comparative Fit Index (CFI) and the Root Mean Square Error of Approximation (RMSEA).

Log-likelihood ratio tests compare nested models based on differences in -2 log-likelihood deviance against a Chi-square distribution, with degrees of freedom equal to the number of differences in the number of parameters estimated by the two models compared. The alpha level for all statistical decisions was set at 0.05, where no significant P-values indicate similar model fit. As described in the previous chapter, models with smaller BIC indicate a better model fit and parsimony. Both TLI and CFI access comparative fit, ranging between 0 and 1 with values greater than 0.95 indicating an adequate model fit (Hu and Bentler, 1999). RMSEA provides a measure of discrepancy in model fit as per degree of freedom left in the model approaches zero (Steiger, 1990), with values less than or equal to 0.06 considered as an acceptable model fit (Hu and Bentler, 1999). In addition to point estimate, 90% confidence interval (CI) of RMSEA provides extra information, which takes into account sample size and model complexity.

Models were estimated using Mplus version 7 (Muthén and Muthén, 2012). Missing data were handled with full information maximum likelihood (FIML) procedures, which use both partially and fully complete cases to estimate parameters (Enders and Bandalos, 2001). Robust maximum likelihood (MLR) estimation was used to provide corrected standard errors adjusted for the non-normality of the observed data.

7.3 Results

7.3.1 Univariate DCSM

Cognitive function

Table 7-3 and Table 7-4 present the detailed univariate DCSM of cognitive function. Model fit indexes suggested that the dual change score models allowing both constant change slope (*α*) and auto-proportion (*β*) provided the best solutions.

Table 7-3 Parameter Estimates from Uni-DCSM for Executive Function (n = 7,469)

Parameter and Fits	Model 1 No change score Baseline Beta	SE	Model 2 Proportional change score Beta	SE	Model 3 Constant change score Beta	SE	Model 4 Dual change score Beta	SE
Fixed parameters								
Additive loading α	0[a]		0[a]		1[a]		1[a]	
Auto-proportion β	0[a]		0.03**	0.01	0[a]		-0.55***	0.03
Initial mean μ_I	-0.27***	0.01	-0.27***	0.01	-0.07***	0.01	-0.05***	0.01
Slope mean μ_S	0[a]		0[a]		-0.20***	0.00	-0.31***	0.01
Random parameters								
Initial variance σ^2_I	0.83***	0.02	0.78***	0.02	0.90***	0.02	0.91***	0.02
Slope variance σ^2_S	0[a]		0[a]		0.02***	0.00	0.26***	0.03
Correlation $\rho_{I,S}$	0[a]		0[a]		-0.03***	0.00	0.46***	0.03
Error variance ψ	0.17***	0.00	0.17***	0.00	0.11***	0.00	0.11***	0.00
Model fit								
Number of parameter	3		4		6		7	
Log likelihood	-19258.1		-19234.0		-17774.0		-17658.4	
Corrected χ^2 [b]	/		37.52		2553.88		2780.32	
Lr-test [b]			<0.001		<0.001		<0.001	
BIC	38542.9		38503.6		35601.6		35379.1	
TLI	0.85		0.82		0.98		1.00	
CFI	0.70		0.70		0.98		1.00	
RMSEA	0.24		0.27		0.09		0.00	
90% CI RMSEA	0.24-0.25		0.26-0.28		0.08-0.10		0.00-0.02	

[a] Fixed parameters
[b] Corrected χ2 takes into account of non-normal distribution by adjusting for scaling correlation factor, Lr-test using no-change score model (Model 1) as reference.
Beta: point estimate from univariate dual change score model (Uni-DCSM); SE: standard error.
*P<0.05, ** P<0.01, ***P<0.001

For executive function (Table 7-3, Model 4), the average intercept at Phase 5 was -0.05, standard error (SE) 0.01, with average change over 5-year implied by both the latent linear slope factor (-0.31, SE 0.01) and previous scores (β = -0.55, SE = 0.03). Individual variations on the average scores were estimated at 0.91 (SE 0.02) for the intercept, 0.26 (SE 0.03) for the slope. Intercept and slope were positively correlated

(0.46, SE 0.03) once taking into account auto-regression. The residual variance was estimated as 0.11 (SE 0.00).

Similarly, the average memory score was estimated as 0.02 (SE 0.01) at the initial level with a random effect of 0.49 (SE 0.02) (Table 7-4 Model 4). The average change indicated by the linear slope factor was -0.14 (SE 0.01) without detectable random effect around this average decline. A weak auto-proportion coefficient (β = -0.04, SE = 0.01) was identified.

Table 7-4 Parameter Estimates from Uni-DCSM for Memory (n = 7,481)

	Model 1 **No change score Baseline**		Model 2 **Proportional change score**		Model 3 **Constant change score**		Model 4 **Dual change score**	
Parameter and Fits	Beta	SE	Beta	SE	Beta	SE	Beta	SE
Fixed parameters								
Additive loading α	0[a]		0[a]		1[a]		1[a]	
Auto-proportion β	0[a]		-0.01	0.01	0[a]		-0.04*	0.01
Initial mean μ_I	-0.12***	0.01	-0.12***	0.01	0.02	0.01	0.02	0.01
Slope mean μ_S	0[a]		0[a]		-0.14***	0.01	-0.14***	0.01
Random parameters								
Initial variance σ^2_I	0.44***	0.01	0.45***	0.02	0.45***	0.01	0.49***	0.02
Slope variance σ^2_S	0[a]		0[a]		0[b]		0[b]	
Correlation $\rho_{I,S}$	0[a]		0[a]		/		/	
Error variance ψ	0.53***	0.01	0.53***	0.01	0.51***	0.01	0.51***	0.01
Model fit								
Number of parameter	3		4		4		5	
Log likelihood	-24412.3		-24411.9		-24207.1		-24201.3	
Corrected χ^2 [c]	/		0.52		355.2		324.23	
Lr-test [b]			0.47		<0.001		<0.001	
BIC	48851.3		48859.6		48449.9		48447.3	
TLI	0.88		0.87		0.97		0.96	
CFI	0.77		0.77		0.94		0.95	
RMSEA	0.09		0.10		0.05		0.05	
90% CI RMSEA	0.08-0.10		0.09-0.11		0.04-0.06		0.04-0.06	

[a] Fixed parameter
[b] Allowing random effects for both intercept and slope resulted in negatively defined latent variable covariance matrix. Model that set the random effect of intercept to be zero, showed small random effect for slope (0.06, SE 0.01) and larger residual variance 0.79 (SE 0.01), with worse model fit (i.e. log likelihood = -25009.13, BIC = 50071.8, TLI or CFI = 0.33, RMSEA = 0.19) than the model set the random effect of slope to be zero (Model 3). Therefore Model 3 and 4 with slope random effect fixed at zero were chosen.
[c] Corrected χ2 takes into account non-normal distribution by adjusting for scaling correlation factor, Lr-test using no-change score model (Model 1) as reference.
Beta: point estimate from univariate dual change score model (Uni-DCSM); SE: standard error.
*P<0.05, ** P<0.01, ***P<0.001

Functional aspects of social relationships

Analogous analyses were conducted for functional aspects of social relationships. Table 7-5 summarizes the parameter estimates derived from the best-fit model for each measure of functional social relationships, with model fit indices and model comparison between different change function listed at the bottom of this table.

Table 7-5 Parameter Estimates from Uni-DCSM for Functional Social Relationships

DCSM	Confiding Support n = 7,894		Practical Support n = 7,901		Negative Support n = 7,900	
Parameter and Fits	Beta	SE	Beta	SE	Beta	SE
Fixed parameters						
Additive loading α	1[a]		1[a]		1[a]	
Auto-proportion β	-0.29*	0.13	-0.15	0.16	-0.51***	0.13
Initial mean μ_I	-0.01	0.01	0.00	0.01	0.00	0.01
Slope mean μ_S	0.05***	0.10	-0.08***	0.01	-0.10***	0.01
Random parameters						
Initial variance σ^2_I	0.69***	0.02	0.61***	0.02	0.57***	0.02
Slope variance σ^2_S	0.11*	0.05	0.06**	0.02	0.14*	0.06
Correlation $\rho_{I,S}$	0.15	0.09	0.03	0.09	0.19**	0.07
Error variance ψ	0.33***	0.01	0.40***	0.01	0.44***	0.01
Model fit						
Number of parameter	7		7		7	
Log likelihood	-25095.4		-25884.8		-26071.6	
Lr-test (corrected χ2, P-value)						
vs. constant change (Δdf:1)	3.87	0.05	0.76	0.38	9.13	0.003
vs. proportional change (Δdf:3)	157.15	<0.001	92.69	<0.001	54.66	<0.001
vs. no change (Δdf:4)	173.18	<0.001	212.14	<0.001	212.14	<0.001
BIC	50253.5		51832.3		52206.1	
TLI	0.99		0.99		0.99	
CFI	1.00		0.99		0.99	
RMSEA	0.03		0.03		0.02	
90% CI RMSEA	0.02-0.05		0.02-0.04		0.00-0.03	

[a] Fixed parameter
Beta: point estimate from univariate dual change score model (Uni-DCSM); SE: standard error;
Δdf: differences in number of parameters of the two nested models in comparison.
*P<0.05, ** P<0.01, ***P<0.001

For confiding support, change scores over 5 years were better presented by a mean constant positive slope (0.05, SE 0.10) plus a negative influence from previous status (-0.29, SE 0.13). Similar model structure was observed as regards negative support and practical support, with a negative mean linear slope (negative support: -0.10 SE 0.01; practical support: -0.08 SE 0.01). Whereas negative support was adversely influenced by previous status (β = -0.51, SE 0.13), this influence was non-significant for practical support (β = -0.15, SE 0.16). Model fit index suggested comparable model fit between DCSM and constant change model for practical support (corrected $\Delta\chi^2$ (1, n = 7,901) = 0.76, lr-test P-value = 0.38). Nevertheless, estimates from univariate DCSM of functional social relationships were retained to be verified in bivariate DCSMs, to avoid the risk of biasing the coupling parameter γ (Lövdén *et al.*, 2005b).

7.3.2 Bivariate DCSM

Age- and sex-adjusted models for the dynamic associations between functional social relationships and cognitive function

The first set of bivariate DCSM analyses was fitted to examine the dynamics between executive function and three measures of functional social relationships. Parameter estimates from *full coupling* models are presented in Table 7-6 , with model fit and statistical comparison between alternative models summarized at the bottom.

The first two columns show the dynamics between confiding support and executive function. Similar estimates for constant slopes ($\mu_{s\ \text{confiding support}}$ = 0.08, $\mu_{s\ \text{executive function}}$ = -0.24), and auto-proportion parameters ($\beta_{\text{confiding support}}$ = -0.37, $\beta_{\text{executive function}}$ = -0.53) showed as in the individual univariate DCSMs, adjusted for age and sex. Beyond and above these effects, the coupling parameter $\gamma_{\text{executive function} \rightarrow \text{confiding support}}$ was significant (-0.11, SE 0.05), whereas the reverse was not ($\gamma_{\text{confiding support} \rightarrow \text{executive function}}$ = -0.05, SE 0.06). Thus, these estimates appeared to indicate preceding executive function was more likely to influence subsequent changes in confiding support, but the opposite did not hold.

Alternative models were then fitted to examine whether one or more of these coupling parameters γ were statistically different from zero. Results from goodness-of-fit model comparisons were consistent with the statistically significant nature of $\gamma_{\text{executive function} \rightarrow \text{confiding support}}$, and the non-significant $\gamma_{\text{confiding support} \rightarrow \text{executive function}}$ estimated in the *full coupling* model. Specially, not allowing for a lagged influence from executive function to changes in confiding support (i.e. *social causation* model $r_{s \rightarrow c} \neq 0$, $r_{c \rightarrow s} = 0$) resulted in significant loss in model fit (i.e. corrected $\Delta\chi^2$ (1, n = 6,859) = 3.76, P = 0.05). In contrast, fixing the lagged influence from confiding support to changes in executive function to be zero (i.e. *health selection* model $r_{s \to c}$ = 0, $r_{c \to s}$ ≠ 0) was not associated with loss in model fit (i.e. corrected $\Delta\chi^2$ (1, n = 6,859) = 0.61, P = 0.44). Additionally, the *no coupling* model ($r_{s \to c}$ = 0, $r_{c \to s}$ = 0) described the data less preciously than the *full coupling* model (corrected $\Delta\chi^2$ (2, n = 6,859) = 4.18, P = 0.04). On the basis of estimates from the *full-coupling* model, alternative models comparisons, parsimony (e.g. BIC for *health selection* model = 75513.9) and goodness-of-fit indices, the *health selection* model was selected.

Likewise, the *health selection* model was also preferred for the dynamic relationships between practical support and executive function (the third and fourth columns of Table 7-6), with a leading effect from executive function on subsequent changes in practical support ($\gamma_{\text{executive function} \rightarrow \text{practical support}}$ = 0.18, SE 0.06). Removing this effect (*social causation* model: corrected $\Delta\chi^2$ (1, n = 6,862) = 6.03, P = 0.004) or both coupling effects (*no coupling* model: corrected $\Delta\chi^2$ (2, n = 6,862) = 9.38, P = 0.009) degraded the model fit considerably.

As suggested by the last two columns of Table 7-6, the coupling parameters between negative support and executive function were virtually zero (γ for both directions -0.04, SE 0.09).The *no coupling* model was preferred (corrected Δχ2 (2, n = 6,862) = 0.36, P = 0.84), implying there was no detectable lagged interrelation between preceding negative support on subsequent changes in executive function, or vice versa.

Similar dynamic relationships showed between functional social relationships and memory (Table 7-7), namely, *health selection* for confiding and practical support, and *no coupling* for negative support in relation to memory. Notably, the influence from memory to confiding support was marginally significant (-0.22, SE 0.11, P = 0.05), rendering comparable model fits among alternative models. As the *health selection* model incurred the least loss of fit (corrected Δχ2 (1, n = 6,859) = 0.09, P = 0.77), it was retained for further analysis.

Table 7-6 Parameter Estimates from BDCSM for Functional Social Relationships and Executive Function, Adjusted for Age and Sex

		Confiding support		**Executive Function**		**Practical support**		**Executive Function**		**Negative support**		**Executive Function**	
		Beta	SE	Beta	SE	Beta	SE	Beta	SE	Beta	SE	Beta	SE
		N = 6,859				**N = 6,862**				**N = 6,862**			
Fixed parameters													
Additive loading α		1[a]		1[a]		1[a]		1[a]		1[a]		1[a]	
Auto-proportion β		-0.37**	0.12	-0.53***	0.03	-0.36*	0.14	-0.51***	0.04	-0.44*	0.22	-0.51***	0.05
Coupling γ		-0.11*	0.05	-0.05	0.06	0.18**	0.06	-0.12	0.08	-0.04	0.09	-0.04	0.09
Initial mean μ_I [b]		-0.02	0.02	0.08***	0.01	0.05**	0.01	0.08***	0.01	-0.02	0.01	0.08***	0.01
Slope mean μ_S[b]		0.08***	0.01	-0.24***	0.01	-0.04***	0.01	-0.24***	0.01	-0.12***	0.02	-0.25***	0.01
Random parameters													
Initial variance σ^2_I		0.69***	0.02	0.78***	0.02	0.60***	0.02	0.78***	0.02	0.55***	0.02	0.78***	0.02
Slope variance σ^2_S		0.15*	0.06	0.19***	0.03	0.13*	0.06	0.19***	0.02	0.11	0.08	0.18***	0.03
Correlation $\rho_{I,S}$		0.20*	0.08	0.34***	0.03	0.14	0.08	0.34***	0.03	0.15	0.11	0.34***	0.03
ρIs,Ic	ρss,sc	0.03*	0.01	0.06*	0.03	0.02	0.08	-0.05	0.03	-0.04**	0.01	0.01	0.04
ρIs,Sc	ρss,Ic	0.04	0.04	0.10**	0.04	0.07	0.04	-0.13**	0.05	-0.01	0.05	0.01	0.08
Error variance ψ		0.32***	0.01	0.11***	0.00	0.40***	0.01	0.11***	0.00	0.44***	0.01	0.11***	0.00
Model fit													
Number of parameter		28				28				28			
Log likelihood		-37637.3				-38379.2				-38446.8			
Lr-test	(corrected χ2, P-value)												
vs. social causation (Δdf:1)		3.76	0.05			6.03	0.004			0.16	0.69		
vs. health selection (Δdf:1)		0.61	0.44			2.46	0.12			0.18	0.68		
vs. no coupling (Δdf:2)		4.18	0.04			9.38	0.009			0.36	0.84		
BIC		75521.98				77005.73				77140.94			
TLI		0.99				0.99				0.99			
CFI		1.00				1.00				1.00			
RMSEA (90%CI RMSEA)		0.02	(0.01-0.03)			0.02	(0.02-0.03)			0.02	(0.02-0.03)		

[a] Fixed parameters.
[b] Intercepts and slopes were for male participants aged 55 at first assessment (Phase 5).
Beta: point estimate from bivariate dual change score models; SE: standard error; Δdf: differences in number of parameters.
Is, intercept for social relationships, Ss, slope for social relationships; Ic, intercept for cognitive function, Sc, slope for cognitive function.
*P<0.05, ** P<0.01, ***P<0.001

Table 7-7 Parameter estimates from BDCSM for Functional Social Relationships and Memory, Adjusted for Age and Sex

	Confiding support		**Memory**		**Practical support**		**Memory**		**Negative support**		**Memory**	
	Beta	SE	Beta	SE	Beta	SE	Beta	SE	Beta	SE	Beta	SE
	N = 6,859				**N = 6,861**				**N = 6,862**			
Fixed parameters												
Additive loading α	1[a]		1[a]		1[a]		1[a]		1[a]		1[a]	
Auto-proportion β	-0.38**	0.13	-0.06***	0.01	-0.39**	0.14	-0.06***	0.01	-0.41	0.21	-0.06***	0.01
Coupling γ	-0.22*	0.11	0.00	0.01	0.40**	0.13	-0.01	0.01	-0.18	0.19	0.01	0.01
Initial mean μ_I [b]	-0.02	0.01	0.01	0.01	0.05**	0.01	0.01	0.01	-0.02	0.01	0.01	0.01
Slope mean μs[b]	0.07***	0.01	-0.15***	0.01	-0.03*	0.01	-0.15***	0.01	-0.13***	0.01	-0.15***	0.01
Random parameters												
Initial variance σ^2_I	0.69***	0.02	0.43***	0.02	0.60***	0.02	0.42***	0.02	0.55*	0.02	0.42***	0.02
Slope variance $\sigma^2 s$	0.16*	0.07	0[c]	/	0.18*	0.08	0[c]	/	0.11*	0.05	0[c]	/
Correlation $\rho_{I,S}$	0.21**	0.08	/	/	0.15	0.08	/	/	0.13	0.11	/	/
ρIs,Ic ρss,sc	0.02	0.01	/	/	0.02	0.01	/	/	-0.05*	0.01	/	/
ρIs,Sc ρss,Ic	/	/	0.09*	0.05	/	/	-0.16**	0.05	/	/	0.06	0.08
Error variance ψ	0.32***	0.01	0.51***	0.01	0.40***	0.01	0.51***	0.01	0.44***	0.01	0.51***	0.01
Model fit												
Number of parameter	24				24				24			
Log likelihood	-43882.9				-44626.7				-44691.0			
Lr-test (corrected χ2 P-value)												
vs. social causation (Δdf:1)	3.34	0.07			8.70	0.003			1.05	0.31		
vs. health selection (Δdf:1)	0.09	0.77			0.33	0.57			0.67	0.41		
vs. no coupling (Δdf:2)	3.53	0.17			8.89	0.01			1.50	0.47		
BIC	87977.86				89465.38				89594.5			
TLI	0.99				0.97				0.98			
CFI	0.98				0.98				0.96			
RMSEA (90% RMSEA)	0.04	(0.03-0.04)			0.04	(0.03-0.04)			0.03	(0.03-0.04)		

[a] Fixed parameter
[b] Intercepts and slopes were for male participants aged 55 at first assessment (Phase 5).
[c] Random effect was not identified for slope of memory.
Beta: point estimate from bivariate dual change score models; SE: standard error; Δdf: differences in number of parameters.
Is, intercept for social relationships, Ss, slope for social relationships; Ic, intercept for cognitive function, Sc, slope for cognitive function.
* P<0.05, ** P<0.01, ***P<0.001

Fully adjusted models for dynamic associations between functional social relationships and cognitive function

Given results from the age and sex adjusted models preferred *health selection*, the non-significant coupling factors from social relationships to cognitive function were removed. Parameter estimates from *health selection* models are presented in Table 7-8 with further adjustments for sociodemographic and health status. As independent change patterns were found between negative support and cognitive function, they were not included in this table.

As shown in Table 7-8, the estimates of auto-proportion parameter β and coupling parameter γ were quite robust to the adjustment, with evident reductions only shown in variances of intercepts and slopes.

As regards confiding support (first and second columns of Table 7-8), negative and significant coupling parameters from either measure of cognitive function indicated that, preceding high levels of cognitive function predicted 5-year negative deviations from the mean linear slope (i.e. less improvement in confiding support) when the influence of the auto-proportion parameter β and other covariates were taken into account. Likewise, high levels of cognitive function tended to positively influence the subsequent 5-year change in practical support, whilst the opposite influence from practical support to change in cognition was not identified (third and fourth columns of Table 7-8).

On the basis of fully adjusted parameter estimates from Table 7-8, the paired equations of latent change (e.g. confiding support and executive function) based on formula (4) in Section 7.1.3 can be written as,

For functional aspects of social relationships and executive function,

$$\mathit{\Delta Confiding}\ (t)_n = \ 0.22 \pm [0.37] - 0.41 Confiding(t-1)_n - 0.11 Executive(t-1)_n$$

$$\mathit{\Delta Executive}(t)_n = \ 0.00 \pm [0.36] - 0.53 Executive\ (t-1)_n\ ,$$

as well as,

$$\Delta Practical\ (t)_n = -0.08 \pm [0.32] - 0.35 Practical(t-1)_n + 0.18 Executive(t-1)_n$$

$$\Delta Executive(t)_n = 0.00 \pm [0.36] - 0.53 Executive\ (t-1)_n\ ,$$

Similarly, the equations for functional aspects of social relationships and memory are,

$$\Delta Confiding\ (t)_n = 0.21 \pm [0.39] - 0.41 Confiding(t-1)_n - 0.22 Memory(t-1)_n$$

$$\Delta Memory\ (t)_n = -0.16 \pm [0.00] - 0.05 Memory\ (t-1)_n\ ,$$

as well as,

$$\Delta Practical\ (t)_n = -0.06 \pm [0.37] - 0.38 Practical(t-1)_n + 0.39\ Memory(t-1)_n$$

$$\Delta Memory\ (t)_n = -0.17 \pm [0.00] - 0.04 Memory\ (t-1)_n\ ,$$

whereby the numbers in the square brackets indicate deviations around the mean slopes, conditional on covariates included.

Table 7-8 Parameter Estimates from Fully Adjusted BDCSM for Functional Social Relationships and Cognitive Function

		Confiding support		**Executive Function**		**Practical support**		**Executive Function**	
		Beta	SE	Beta	SE	Beta	SE	Beta	SE
		N = 6,859				**N = 6,862**			
Auto-proportion β		-0.41**	0.12	-0.53***	0.03	-0.35**	0.12	-0.53***	0.03
Coupling γ		-0.11*	0.05	0[a]	/	0.18**	0.06	0[a]	/
Initial mean μ_I[b]		0.16*	0.02	0.59***	0.02	0.21***	0.02	0.59***	0.02
Slope mean μ_S[b]		0.22***	0.04	0.00	0.02	-0.08*	0.03	0.00	0.02
Initial variance σ^2_I		0.61***	0.02	0.50***	0.01	0.43***	0.02	0.50***	0.01
Slope variance σ^2_S		0.14*	0.05	0.13***	0.01	0.10**	0.03	0.13***	0.01
Correlation $\rho_{I,S}$		0.18**	0.07	0.22***	0.02	0.09	0.05	0.22***	0.02
$\rho Is,Ic$	$\rho ss,sc$	-0.02	0.01	0.02	0.01	-0.02**	0.01	-0.05**	0.02
$\rho Is,Sc$	$\rho ss,Ic$	-0.01*	0.01	0.06*	0.03	-0.02**	0.00	-0.09**	0.03
Error variance ψ		0.32***	0.01	0.11***	0.00	0.40***	0.01	0.11***	0.00
		Confiding support		**Memory**		**Practical support**		**Memory**	
		Beta	SE	Beta	SE	Beta	SE	Beta	SE
		N = 6,859				**N = 6,861**			
Auto-proportion β		-0.41**	0.12	-0.05***	0.02	-0.38**	0.12	-0.04***	0.02
Coupling γ		-0.22*	0.11	0[a]	/	0.39**	0.13	0[a]	/
Initial mean μ_I[b]		0.17***	0.02	0.26***	0.02	0.21***	0.02	0.27***	0.02
Slope mean μ_S[b]		0.21***	0.04	-0.16***	0.01	-0.06*	0.03	-0.17***	0.02
Initial variance σ^2_I		0.61***	0.02	0.36***	0.02	0.43***	0.02	0.35***	0.02
Slope variance σ^2_S		0.15*	0.06	0[c]	/	0.14**	0.05	0[c]	/
Correlation $\rho_{I,S}$		0.19**	0.07	/	/	0.10*	0.05	/	/
$\rho Is,Ic$	$\rho ss,sc$	0.00	0.01	/	/	-0.01	0.01	/	/
$\rho Is,Sc$	$\rho ss,Ic$	/	/	0.08	0.04	/	/	-0.14**	0.05
Error variance ψ		0.32***	0.01	0.51***	0.01	0.40***	0.01	0.51***	0.01

[a] Fixed as zero as no statistically significant effects from any measure of social relationship to subsequent changes in cognitive function was found

[b] Intercepts and slopes were conditional for 55 years, white male, with a university qualification, a high employment grade, had no longstanding illness or chronic disease, and were not depressed at Phase 5, and maintained married over the follow-up (Phase 5-9).

[c] Random effect was not identified for memory slope.

Beta: point estimate from bivariate dual change score models; SE: standard error. * P<0.05, ** P<0.01, ***P<0.001.

7.3.3 Plotting dynamic trajectories

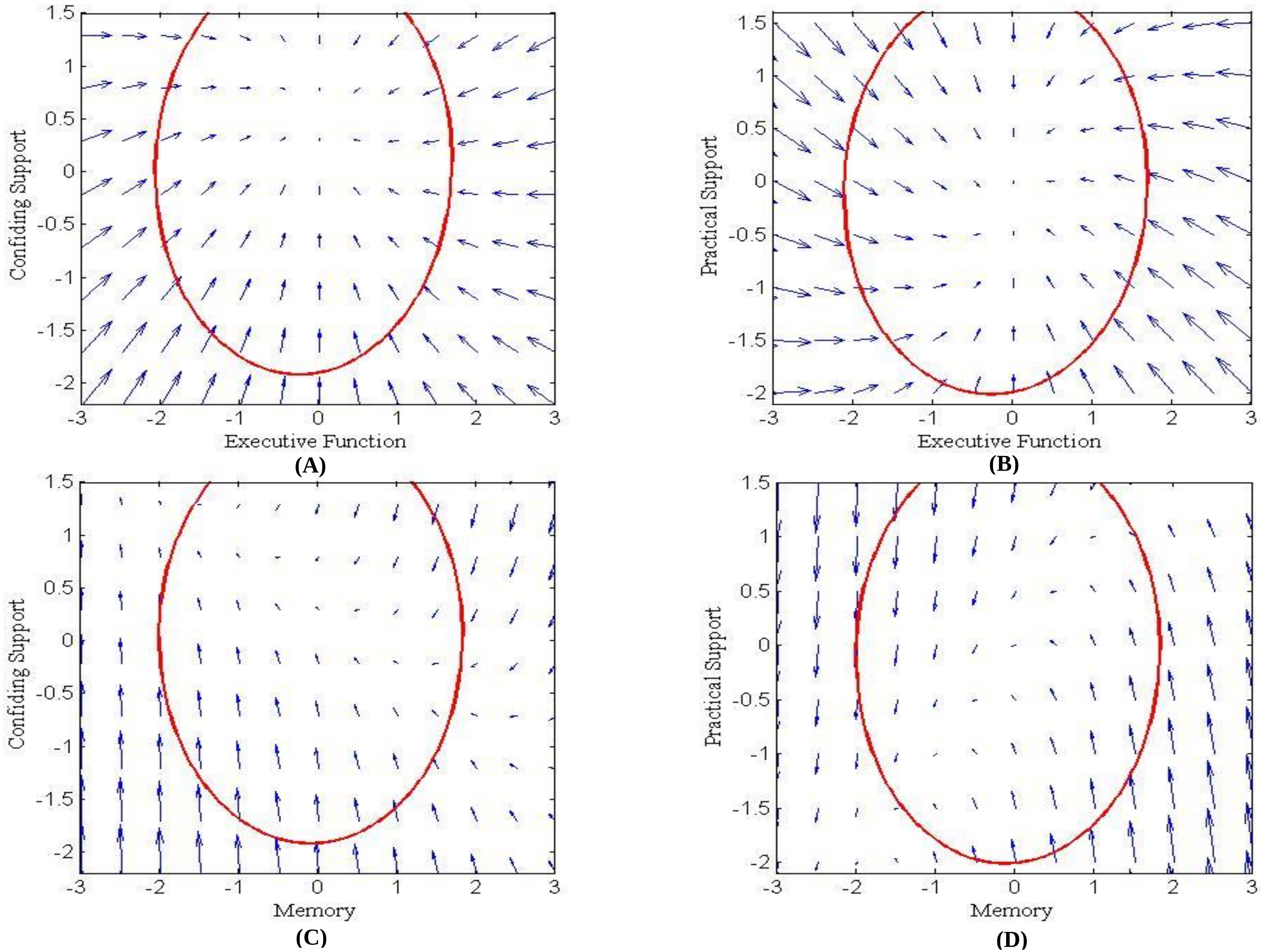
To visualize the complex relationships between functional social relationships and cognitive function, vector fields were plotted to jointly interpret the expected changes alongside within-variables and between-variables' correlations (Boker and McArdle, 1995).

A given pair of coordinates is a bivariate starting point (e.g. intercept for social relationships and cognitive function), and the directional arrow is a display of the expected pair of 5-year changes from this point (McArdle and Grimm, 2010). The direction of the arrow in relation to the x and y axes indicate whether the projected changes are positive, neutral or negative (i.e. increase, maintain or decrease), as the consequence of a combined influence from the linear slope, auto-proportion and coupling parameters (Ferrer and McArdle, 2004). The ellipsoid reflects where 95% of the data lay.

With both variables changing in the bivariate system, the change predictions of a dynamic model depend on the starting point (McArdle and Grimm, 2010). As illustrated by Figure 7-4 (A), participants with initial low levels of executive function and confiding support, perceived marked increases in confiding support as they aged. These increasing trends were more gradual for those with higher starting levels of confiding support (y axis), or higher preceding levels of executive function (x axis). To the extent that, participants with high starting levels of both confiding support and executive function showed slight drops in the confiding support scores (i.e. upper right corner within the ellipsoid). Nevertheless, those participants still perceived higher than average levels of confiding support in the absolute scale. Change patterns in executive function only depended on its own initial scores, with those higher executive functioning participants more likely to decline rapidly to the population average level. Similar dynamic relationships between confiding support and memory can be read from Figure 7-4 (C).

These vector fields are different from the ones for practical support and cognition (Figure 7-4 (B) and (D)). Participants who started with higher levels of practical support were more likely to decline (y axis). Higher preceding levels of cognitive function preceded (x axis), however, decelerated these processes, presenting shallower declines among those with high levels for both variables (i.e. upper right corner within the ellipsoid). Moreover, for those with low initial levels of practical support, high cognition on the previous occasion fuelled the increases in practical support (i.e. lower right corner within the ellipsoid). In contrast, changes in cognitive function were not affected by the levels of practical support.

Figure 7-4 Vector Fields for Bivariate Dynamic System between Function Social Relationships and Executive Function (Upper Panel) and Memory (Lower Panel); the Ellipsoid Encompasses 95% of the Data



7.3.4 Supplementary analyses

Virtually identical estimates for the dynamic associations were obtained from the restricted subsample (n = 4,086) with complete data for three measurement occasions, as well as within participants who remained married during follow-up and consistently nominated their spouse as the closest person (n = 3,623). Stratified analyses by stability and change in the identity of the closest person showed there was no statistically significant difference in the dynamic parameters between those always nominated a non-partner (n = 1,620) vs. those who always nominated their partner (n = 4,197) as the closest person; whereas model parameters cannot be estimated for those who changed the close relationships' nomination from (n = 429) or to (n = 350) a partner due to the small sample sizes.

Similar dynamics were also shown in sex (Table 7-9) and age groups (Table 7-10) stratified analyses. There was some evidence that the *health selection* appeared to be more evident for men regarding changes in practical support (Table 7-9), which was positively influenced by precedent cognition (e.g. $\gamma_{\text{memory} \rightarrow \text{practical support}}$ = 0.61, 95%CI: 0.34,0.89); while a non-significant negative effect was shown in their female counterparts (e.g. $\gamma_{\text{memory} \rightarrow \text{practical support}}$ = -0.33, 95%CI: -1.00, 0.33).

As shown in Table 7-10, despite significant coupling effects being only found in certain age groups, the 95% confidence intervals around these point estimates largely covered each other, indicating it might not be necessary to stratify analysis by age groups. For example, $\gamma_{\text{memory} \rightarrow \text{practical support}}$ was 0.36, 95%CI: -0.09, 0.82 for the age group ≤ 55, while 0.49, 95%CI: 0.15, 0.84 for the age group > 55. Consistent dynamic patterns across age groups thus indicated age-invariant associations. Less than 1/3 participants were categorized as having chronic depressive symptoms (21%, n = 1,221) or functionally limited (18%, n = 1,010), with similar dynamic patterns showing across health status defined subgroups (data not shown).

Table 7-9 Dynamic Associations between Functional Social Relationships and Cognitive Function by Sex

	Men N = 4,859[a]				Women N = 2,003[a]			
	Beta	**SE**	**Beta**	**SE**	**Beta**	**SE**	**Beta**	**SE**
Functional Social Relationships vs Executive Function								
	Confiding Support		**Executive Function**		**Confiding Support**		**Executive Function**	
Auto-proportion β	-0.51***	0.13	-0.50***	0.04	-0.02	0.51	-0.61***	0.06
Coupling γ	-0.15*	0.06	0.00	0.07	-0.17	0.15	0.03	0.17
	Practical Support		**Executive Function**		**Practical Support**		**Executive Function**	
Auto-proportion β	-0.33*	0.02	-0.50***	0.04	-0.41*	0.20	-0.61***	0.06
Coupling γ	0.28***	0.07	-0.05	0.07	-0.08	0.12	-0.03	0.09
	Negative Support		**Executive Function**		**Negative Support**		**Executive Function**	
Auto-proportion β	-0.21	0.31	-0.54***	0.07	-0.54	0.29	-0.60***	0.06
Coupling γ	-0.18	0.13	0.11	0.14	0.09	0.13	-0.07	0.12
Functional Social Relationships vs Memory								
	Confiding Support		**Memory**		**Confiding Support**		**Memory**	
Auto-proportion β	-0.50***	0.13	-0.02	0.02	0.03	0.54	-0.11***	0.03
Coupling γ	-0.26*	0.13	-0.01	0.01	-0.67	0.54	0.03	0.02
	Practical Support		**Memory**		**Practical Support**		**Memory**	
Auto-proportion β	-0.38**	0.14	-0.02	0.02	-0.37	0.23	-0.11***	0.03
Coupling γ	0.61***	0.14	-0.02	0.02	-0.33	0.34	0.01	0.03
	Negative Support		**Memory**		**Negative Support**		**Memory**	
Auto-proportion β	-0.18	0.33	-0.02	0.02	-0.58*	0.27	-0.10***	0.03
Coupling γ	-0.44	0.28	0.02	0.01	0.25	0.29	-0.02	0.03

[a] Numbers for confiding support were men:4,858, women: 2,001; for practical support (vs memory) was 4,858 for men.
Beta: point estimate from bivariate dual change score models, adjusted for age (centred at 55), ethnicity, education, employment grade, longstanding illness, depressive symptoms and prevalent chronic disease at phase 5 and marital history from Phase 5-9.
SE: standard error.
* P<0.05, ** P<0.01, ***P<0.001

Table 7-10 Dynamic Associations between Functional Social Relationships and Cognitive Function by Age Groups

	Age group ≤ 55 at first assessment N = 3,360				**Age group > 55 at first assessment N = 3,502 [a]**			
	Beta	SE	Beta	SE	Beta	SE	Beta	SE
Functional Social Relationships vs Executive Function								
	Confiding support		**Executive Function**		**Confiding support**		**Executive Function**	
Auto-proportion β	-0.51***	0.15	-0.69***	0.04	-0.14	0.26	-0.40***	0.05
Coupling γ	-0.12	0.07	-0.07	0.07	-0.09	0.09	0.05	0.12
	Practical support		**Executive Function**		**Practical support**		**Executive Function**	
Auto-proportion β	-0.40**	0.15	-0.68***	0.04	-0.28	0.22	-0.40***	0.05
Coupling γ	0.14	0.09	-0.03	0.06	0.21*	0.08	0.00	0.10
	Negative support		**Executive Function**		**Negative support**		**Executive Function**	
Auto-proportion β	-0.78***	0.18	-0.68***	0.05	0.05	0.49	-0.38***	0.08
Coupling γ	0.13	0.09	-0.01	0.08	-0.30	0.19	-0.06	0.15
Functional Social Relationships vs Memory								
	Confiding Support		**Memory**		**Confiding Support**		**Memory**	
Auto-proportion β	-0.58***	0.14	-0.05*	0.02	-0.13	0.25	-0.05	0.03
Coupling γ	-0.35*	0.17	-0.02	0.02	-0.12	0.20	0.00	0.02
	Practical Support		**Memory**		**Practical Support**		**Memory**	
Auto-proportion β	-0.43**	0.16	-0.05*	0.03	-0.35	0.22	-0.04	0.03
Coupling γ	0.36	0.23	-0.02	0.02	0.49**	0.18	-0.01	0.02
	Negative Support		**Memory**		**Negative Support**		**Memory**	
Auto-proportion β	-0.74***	0.19	-0.05**	0.02	-0.09	0.39	-0.04	0.03
Coupling γ	0.19	0.21	0.03	0.02	-0.39	0.30	-0.02	0.02

[a] Numbers for Age group > 55 were, 3,499 for confiding support, and 3,501 for practical support (in relation with memory).
Beta: point estimate from bivariate dual change score models, adjusted for age (centred at 51 for age group ≤ 55, at 61 for age group > 55), sex, ethnicity, education, employment grade, longstanding illness, depressive symptoms and prevalent chronic disease at phase 5, and marital history from Phase 5-9.
SE: standard error.
* P<0.05, ** P<0.01, ***P<0.001

Further analyses taking into account the size and structure of social network did not alter the main findings reported above. The total number of people felt close to did not relate to changes in perceived support or cognitive function. Larger size and more frequent contacts with friends or relatives were related to higher rating in confiding and practical support, and lower rating in negative support at the intercept, while no statistically significant effects showed on the change of either measure of functional social relationships. Similarly, only concurrent positive association showed between friend network and cognition, but not with the rate of cognitive decline. There was no evidence that social network characteristics moderated the dynamic associations between functional social relationships and cognition in this analytic sample.

7.4 Interim discussion

This chapter investigated ***Objective three*** regarding the bidirectional associations between functional aspects of social relationships and cognitive function from middle to early-old age. Findings here only partially confirmed the hypothesis of objective three. For both confiding and practical support, results suggest a *health selection* process, namely, a greater cognitive function at the preceding stage was related to less positive changes in confiding support and less negative changes in practical support over the next 5 years, whereas there was no detectable influence from either measure of functional social relationships on subsequent changes in cognition. For negative support, there was no directional relationship either to or from cognitive function. Therefore, *health selection*, not *social causation*, fits the current analysis sample better; indicating cognition is more likely to be the leading modifying factor for subsequent changes in functional social relationships.

As an extension of auto-regression and latent growth curve models, DCSM advances these statistical techniques for multivariate longitudinal data analysis. However, several methodological concerns of DCSM remain. First, DCSM is not a causal model despite the time-lagged association being assessed. Findings based on this observational study do not imply any causal relationship and only suggest cognition may moderate changes in functional social relationships. Second, the developmental patterns of functional social relationships and cognition were restricted by the same set of change equations (i.e. using both constant slope s and auto-proportional parameter β in the univariate DCSM), where additional parameters for modelling the changes in some measures may be unnecessary. Third, the equivalence of structural relations based on inter- and intra-individual variance is difficult to evaluate. The present longitudinal panel only included three measurement occasions, with low power to detect changes in dynamic parameters over time. Extra phases would facilitate investigation on discontinuities in these dynamics (Ferrer and McArdle, 2004; Ferrer *et al.*, 2007).

Chapter 8. Discussion

Summary

This final chapter summarizes the principal findings from the three results chapters. Findings are discussed in comparison with existing literature and between objectives. The strengths and limitations of this thesis are reviewed, followed by its implications. The possibilities for future research are also outlined.

8.1 Summary of principal findings

To investigate the longitudinal dynamic associations between social relationships and cognitive ageing, this thesis used the Whitehall II prospective cohort, which provides multiple repeat measures of *functional* and *structural* aspects of social relationships and cognitive tests assessing *executive function* and *memory* from middle to early old age. Three sequential objectives examined 1) which aspects of social relationships were cognitively beneficial, 2) how social relationships and cognitive function coevolved with age, and 3) what the temporal order of these associations was.

Of the functional and structural aspects of social relationships considered, the findings of ***Objective one*** indicate that mid-life negative aspects of close relationships and a large friend network contributed independently to cognitive ageing. As such, higher cumulative levels of negative aspects of close relationships were associated with lower memory scores at age 60 and accelerated declines in executive function. On the other hand, a positive effect of friend networks on cognition at age 60 faded away with age. There was no evidence that confiding support, practical support, relative network or marital status at middle age influenced cognitive trajectory in the analysis sample.

Objective two identified heterogeneous subgroups with different longitudinal changing patterns of social relationships from middle to early old age. With the majority of the participants grouped into *average* or *medium* class, some divergent growth patterns (e.g. *extremely-high* or *chronically-low*) were found for each measure of social relationships. Consistent with the hypothesis, participants perceiving *extremely-high* levels of confiding support experienced the least decline in memory relative to their counterparts in the *average* or *higher-than-average* class. Those with a *high-increase* friend network showed a higher initial cognitive score but a similar rate of cognitive decline compared with those having a *medium-increase* friend network.

In contrast to the hypothesized bidirectional associations, the findings of ***Objective three*** suggest unidirectional influences from cognition to the subsequent changes in functional aspects of social relationships. For both confiding support and practical support, a greater cognitive function at the preceding stage was related to less positive changes in confiding support and less negative changes in practical support over the next 5 years. On the other hand, there was no detectable influence from either measure of functional social relationships on subsequent changes in cognition.

These principal findings are summarized in Table 8-1. In the next section, findings of each objective are compared with existing literature and are discussed collectively.

Table 8-1 Summary of the principal findings from the thesis

What has been suggested by the existing literature?

- Social relationships, denoted by functional and structural aspects, seem to retard age-related cognitive decline (social causation).
- Cognitive decline with age may jeopardize the structure of social relationships and affect their function (health selection).

What does this thesis add?

- Mid-life negative but not positive aspects of close relationships were associated with accelerated declines in executive function.
- A large friend network was associated with better concurrent cognitive function, but not with age-related cognitive decline.
- Participants with extreme-high levels of confiding support as they transitioned from middle to old age showed the least decline in memory.
- Cognitive function modified subsequent changes in confiding and practical support, not vice versa.

8.2 Interpretation of the results

8.2.1 Comparison with the existing literature

Objective one: mid-life functional and structural aspects of social relationships in relation to subsequent cognitive ageing trajectories

Functional aspects of social relationships and cognitive ageing

Findings on functional social relationships extend previous research on the effect of negative aspects of social relationships on cognitive ageing. Seeman and colleagues (2011) showed that social conflicts (e.g. how often significant others are sources of demands, criticism or tension etc.) were related to lower levels of executive function but not episodic memory, which were assessed on a single occasion 10 years after the measurement of social relationships. The current study extends the evidence of the adverse effect of negative aspects of social relationships by demonstrating their impact on cognitive ageing trajectories. This longitudinal investigation highlights the value of assessing the continuities of cognitive status that are not discerned from cross-sectional studies. Previous studies on the cross-sectional associations of cognitive function and social relationships are also subject to biases related to reverse causation (Seeman *et al.*, 2001; Hughes *et al.*, 2008). In view of the finding that cognitive ability around age 55 did not significantly influence the subsequent age-trajectory of negative aspects of close relationships, this study largely ruled out reverse causation and revealed an association between midlife negative aspects of close relationships with cognitive decline.

The hypothesized salutary impact of confiding support or practical support on cognitive ageing was not found in the current studies, as has been found in some studies (Green *et al.*, 2008; Hughes *et al.*, 2008; Eisele *et al.*, 2012) but not others (Seeman *et al.*, 2001; Dickinson *et al.*, 2011). It has been argued that the absent beneficial effects of social relationships may be due to healthier (Hughes, 2009) and younger-old (Green *et al.*, 2008) participants' characteristics. Given the analytic sample was mainly comprised of relatively healthy early-old age adults, the experience of less confiding support or practical support during middle age may not necessarily influence cognitive decline at this stage. Receipt of more practical support may instead indicate a greater need for assistance signifying poorer health; and further foster dependency and erode self-efficacy (Fuhrer and Stansfeld, 2002; van Tilburg and Broese van Groenou, 2002; Warner *et al.*, 2011; Ellwardt *et al.*, 2013).

Taken together, the results suggest that negative but not positive aspects of social relationships are associated with cognitive ageing, consistent with previous evidence on other health outcomes (Stansfeld *et al.*, 1998b; Rook, 2001; Newsom *et al.*, 2003; De Vogli *et al.*, 2007; Kouvonen *et al.*, 2011). This asymmetrical impact could lie in disproportionate rumination on negative encounters (Taylor, 1991), which evokes strong emotional reactions (Newsom *et al.*, 2005; Golden *et al.*, 2009) and becomes a source of chronic strain (Krause and Rook, 2003; Gleason *et al.*, 2008; Tun *et al.*, 2012). The estimated difference in the rate of cognitive decline over 10 years attributable to negative aspects of close relationships is comparable with one extra year decline in executive function for participants aged 60. This modest magnitude of the difference is consistent with findings from other longitudinal studies (Barnes *et al.*, 2004; Béland *et al.*, 2005; Seeman *et al.*, 2011).

Structural aspects of social relationships and cognitive ageing

A large friend network has previously been related to a slower rate of memory decline (Giles *et al.*, 2012), with some studies suggesting the effect benefited women but not men (Zunzunegui *et al.*, 2003; Béland *et al.*, 2005). The current study did not observe sex-specific associations of friend network and cognition. Moreover, findings obtained here suggest that the cognitively stimulating effects of a friend network appear to be transient. There was also a tendency towards faster declines in executive function among those participants reporting a larger friend network over middle life. Given executive function at the intercept was positively associated with a large friend network, this slightly faster decline may be explained by the effect of regression to the mean (Barnett *et al.*, 2005), that is, participants with better initial cognitive performance tend to have a lower average score in subsequent assessments. Alternatively, this finding may indicate cognitive gains due to friend network are transient instead of long-lasting. Froir and Jager (2012) reported that participants who belonged to a friend-focused network showed an average higher cognitive ability than others; however, the absolute change in cognitive scores over 12 years of this group was not different from those belonging to other network types, for instance, the family-focused network.

The current study find that neither relative network nor marital status was protective for cognitive ageing, in agreement with some studies (Glei *et al.*, 2005; Roth, 2005) but not all (Béland *et al.*, 2005; van Gelder *et al.*, 2006; Karlamangla *et al.*, 2009). Non-significant findings may be rooted in the obligatory nature of the kin relationship, which is ritualized and less mentally stimulating (Keller-Cohen *et al.*, 2006). In this Whitehall II occupational cohort, participants having low employment grades and low educational attainment were more likely to socialize with relatives than friends, and were less likely to have a partner, rendering the inverse associations of a larger relative network or non-married with lower cognitive ability confounded by socioeconomic position. Despite the lack of neuro-protective effects of kin relationships or having a spouse identified by this study, as the main sources of long-term care (Harper, 2006), the importance of relative relationships in old age should not be undervalued (Litwin and Stoeckel, 2014).

Objective two: divergent longitudinal changing patterns of social relationships in relation to cognitive ageing trajectories

Change and stability in the longitudinal patterns of social relationships

Through differentiating longitudinal latent classes of social relationships, the present study provides a nuanced description about the heterogeneity in trajectories of social relationships with age, capturing change and stability over time.

The overall changing patterns of social relationships obtained are consistent with the socioemotional selectivity theory (Carstensen *et al.*, 2003), presenting generally stable or slightly increasing trends of confiding support with age (from 55 y onward) (van Tilburg, 1998; Martire *et al.*, 1999; Gurung *et al.*, 2003), and decreases in negative aspects of close relationships (Boerner *et al.*, 2004).The estimated average decline in confiding support between Phase 2 (mean age 47 y) and Phase 5 (mean 55 y) for participants grouped as *higher -than- average* class was not due to missing data or changes in the closest social partner (data not shown). This trend mirrors the curvilinear wellbeing-age pattern identified in population-based samples from the US (Stone *et al.*, 2010) and several European and developing countries (Blanchflower and Oswald, 2008), probably resulting from middle-life crises that takes place around age 50 (Lachman, 2004).

Contrary to other studies on the elderly (mean age >73 y) (Martire *et al.*, 1999; Shaw *et al.*, 2007), the current analysis found a decrement rather than increase in practical support, as well as increases instead of decreases in social networks. Disparities could result from cohort differences in terms of age composition and participants' characteristics. It has been suggested that age 75 y could be assumed as the threshold when declines in social integration start (van Tilburg, 2009). The Whitehall II participants were younger-old (mean age was 66 y at last study observation, Phase 9) and relatively healthy, who may require less tangible assistance. Different from earlier generations (Stevens and van Tilburg, 2010; Broese van Groenou *et al.*, 2013), those entering late life in the twenty-first century have better health and socioeconomic circumstances, alongside abundant leisure time after retirement. These conditions facilitate more frequent engagements with friends and relatives (Saczynski *et al.*, 2006; Cornwell *et al.*, 2008), and thus may lead to the increasingly extensive social networks observed.

Nevertheless, against the overall successful social ageing picture, it is apparent that the benefits of social engagement were not uniform (Rook *et al.*, 2011). Consistent with previous studies (van Tilburg and Broese van Groenou, 2002; Mavandadi *et al.*, 2007; Thomas, 2011b), findings here revealed distinct subgroups with divergent social ageing patterns. Beyond the average high levels of confiding support reported in this study sample, a small group of participants (n = 231, 3%) consistently reported *extremely-high* levels of confiding support. In contrast, small (3% - 15%) yet highly isolated groups with chronically low levels of friend or relative networks were identified. There are 5% participants (n = 456) who constantly perceived the lowest level of practical support over the follow-up years, which may reflect limited social sources (this group was more likely to be in low employment grades and unmarried).

Longitudinal latent classes of social relationships and trajectories of cognitive ageing

Using longitudinal latent classes of social relationships as indicators, the findings of this study further suggest the trajectory of confiding support, but not practical support, was associated with cognitive decline, compatible with the findings of Ellwardt and colleagues (2013). Specifically, participants consistently perceiving the highest levels of confiding support over years experienced the least decline in memory. This finding corroborates the importance of social component in defining successful ageing (Young *et al.*, 2009), namely, individuals who were better emotionally supported (Berkman *et al.*, 2000) may effectively cope with (Bowling *et al.*, 2007) and be resilient against (Netuveli *et al.*, 2012) physiological ageing. This association, however, was only evident amongst the small group of participants (referred to above) who constantly benefited from the highest levels of confiding support, which may suggest a threshold effect, though some methodological concerns cannot be entirely ruled out (Page 117). On the other hand, given both social relationships and cognitive function were allowed to change over time, this positive association may also indicate that participants, who had the least cognitive decline, were most likely to maintain positive interactions with their close social partners.

As for the longitudinal classes of structural social relationships, the findings show participants with a *high-increase* friend network had a higher mean cognitive level but the rate of cognitive decline was similar to those with a *medium-increase* friend network. This finding is in contrast to the associations reported in Thomas (2011b), where participants grouped into *high and increasing* social engagement class were related to a decelerated rate of developing cognitive limitations. Different from the present study measuring frequency and number of friend contacts, Thomas (2011b) assessed a wider spectrum of social integration beyond the interpersonal network, where a composite score including community involvement (e.g. church attendance, volunteering) was computed. The extent to which contact with friends may contribute to the positive finding in Thomas (2011b) is not clear. Results from the current study suggest that if there is any cognitive reserve stemming from friend networks, it is more likely to be passive rather than active (Stern, 2002, 2003), that is, the cognitive stimulating effects of having a larger than average friend network may only differentiate the average level of cognition but not noticeably alter the rate of cognitive decline. A similar conclusion has been drawn by Ellwardt and colleagues (2015), proposing the association between social network complexity (i.e. multiple social roles) and cognition is mostly cross-sectional.

Objective three: the bidirectional associations between functional social relationships and cognitive function from middle to early old age

Direction of the dynamic association: health selection

The findings based on the BDCSM buttress *health selection* process between cognition and social support as suggested by some studies (Green *et al.*, 2008; Stoykova *et al.*, 2011; Thomas, 2011a), but not *social causation* (Ellwardt *et al.*, 2013) or bidirectional associations (Li and Zhang, 2015) found by others.

Conflicting findings may result from different statistical approaches applied (Ghisletta *et al.*, 2006). By using BDCSM, this study rigorously evaluated the alternative hypotheses of functional social relationships and cognitive function, taking into account systematic growth and interrelations over time in this bivariate dynamic system. The significant coupling effects of cognition on subsequent 5-year changes in functional social relationships represent deviations from the mean linear slope (i.e. systematic growth over phases) (Lövdén *et al.*, 2005b), beyond and above the auto-proportional effects and covariates included. These results should be interpreted as a modifying effect of cognition on subsequent changes in functional social relationships. Previous studies using cross-lagged regression (Thomas, 2011a; Li and Zhang, 2015) or directional PLCM (Ellwardt *et al.*, 2013) cannot fully capture these dynamic features available in BDCSM. The cross-lagged model is subject to differences in measurement reliability (Rogosa, 1980) of the variables considered and it overlooks systematic growth across multiple waves (Bollen and Curran, 2006). The directional PLCM assumes the intercept is the initial time point where change starts, which is inappropriate in most ageing studies (Robitaille *et al.*, 2012) and any association between intercept and slope is sensitive to the location of the intercept (Grimm, 2007). Based on different change functions, the comparison between alternative statistical methods for multivariate longitudinal data is not straightforward (Ferrer and McArdle, 2003; Grimm, 2007). The BDCSM used in this thesis is an advance on cross-lagged model and PLCM in investigating hypotheses involving dynamics and growths (Lövdén *et al.*, 2005a; Bollen and Curran, 2006; McArdle, 2009; Ferrer and McArdle, 2010).

Furthermore, while previous investigations assessed the structure of social network (Li and Zhang, 2015) or broad terms of social engagement (e.g. volunteering, religious services) (Thomas, 2011a) in relation to cognitive ageing, the current analysis focused on the functional aspects of social relationships, particularly, types of support transmitted and supportive role fulfilment by close social partners. Previous studies indicate that the perceived quality of relationships is more important than the quantitative assessment of social network in preserving cognitive abilities (Gow *et al.*, 2013) and postponing the onset of dementia (Fratiglioni *et al.*, 2000; Amieva *et al.*, 2010). Yet, positive associations derived from these observational studies cannot discern the temporal order. Given the long prodromal phase of dementia (Elias *et al.*, 2000; Amieva *et al.*, 2008), the attempt to minimize reverse causation simply by excluding participants who develop dementia during follow up may be insufficient. The current analysis contributes to the literature by using a more systematic approach, and reveals that perceived support from close relationships is unlikely to influence changes in cognition significantly over a short period (i.e. the next 5 years). Furthermore, as analyses are based on a relatively healthy and younger-old sample with low incidence of cognitive impairment (i.e. only 57 participants with MMSE less than 23 over the 10-year follow-up), the degree to which the observed associations were influenced by dementia cases is likely to be marginal.

Differentiated effects of cognition on subsequent changes in functional social relationships

The findings of the current analyses further suggest that the *health selection* effect of cognition may vary by the type and the `initial level of functional social relationships. One possible explanation may be the perception of supportive actions depends on the specific needs of the recipient (Taylor, 2007). Participants with high cognition may require fewer suggestions and less guidance, and be more aware of the vicissitudes of life and sensitive to negative interpersonal exchanges (Staudinger *et al.*, 2005; Bourne *et al.*, 2007), resulting in the less evident improvements in confiding support over time. Meanwhile, the positive influence from preceding cognition on change in practical support may reflect the accessibility of practical support. Better cognition may facilitate individuals to build a stronger social bank (van Tilburg and Broese van Groenou, 2002; Antonucci *et al.*, 2010), the credit of which can be redeemed (Lang *et al.*, 2009) to fulfil their needs for practical support (van Tilburg and Broese van Groenou, 2002), presenting better maintenance when the initial level of practical support was high, or more rapid response to needs when the initial level of practical support was low.

The self-reported questionnaire of functional social relationships is another factor to be considered. The Close Persons Questionnaire evaluates the 'perceived received quality of support' from close relationships based on past experiences (Stansfeld and Marmot, 1992). Being weakly associated with support actually received (Bolger *et al.*, 2000; Warner *et al.*, 2010), perceived support reflects a combination of truth, personality (Gurung *et al.*, 2003; Bourne *et al.*, 2007; Zammit *et al.*, 2014) and other relational schemas (Reis *et al.*, 2004). Close relationships are central to people's life, where more obligations and greater responsiveness are expected than peripheral social ties (Reis *et al.*, 2004). The findings of this study hence may indicate different expectations in support responsiveness (Gray, 2009). The Whitehall II cohort did not collect personality traits that have been identified as risk factors for cognitive decline (Low *et al.*, 2013; Terracciano *et al.*, 2014); the current analysis thus cannot assess the extent to which individual differences in perception of support may influence these associations obtained.

8.2.2 Integration of objectives

Integration of Objective one & two

Objective one & two examined social relationships as the risk factors for cognitive ageing, based on the *social causation* hypothesis. *Objective one* fixed social relationships at middle age, whereas *objective two* considered changes in social relationships from middle to early old age.

The findings of objective one show mid-life *negative aspects of close relationships* but not *confiding support* were related to cognitive ageing. Although a similar association between high levels of negative support and low initial memory score was observed in both objectives, participants with different longitudinal changing patterns of negative support did not show significant differences in the rate of cognitive decline (objective two). These disparities highlight the importance of modelling individuals' social relationships from a life course perspective (Blieszner, 2006). As revealed by the latent class trajectories (Figure 6-6, Page 103), although average higher levels of negative aspects of close relationships were reported by the *high-decline* group, this group also demonstrated the most evident declines in negative support over time; in other words, improvements in the quality of close relationships as respondents aged. Social relationships fixed at a particular time thus cannot reflect their evolution with age (Thomas, 2011b). In the same vein, the positive association between confiding support and cognition may only be detected when taking the longitudinal perspective into account. That is, only a small group of participants with consistently *extremely-high* confiding support over time (objective two) rather than a high level of confiding support at mid-life only (objective one), experienced the least declines in memory.

Consistent findings were obtained with respect to *friend network* and cognitive ageing in objectives one and two, showing a larger friend network was related to a higher initial level of cognition but not the rate of cognitive decline. These findings may indicate a passive cognitive reserve model, such that the cognitive stimulation offered by friend networks cannot overcome the influence of ageing in the long run (Stern, 2009). Yet, as these positive associations are cross-sectional in nature, it is also plausible that individuals with greater cognitive ability are better at building and utilizing friendships. Both objectives further suggest a more gradual cognitive decline in those with a smaller friend network. Previous evidence indicated that the Whitehall II participants with a less extent social network had an increased death risk (Stringhini *et al.*, 2011). Selective attrition thus may be more evident in those with a smaller friend network, resulting in the observed higher resilience against cognitive decline in this group than their counterparts with adequate friend networks. Nevertheless, given the substantial differences in cognition at the initial level, this relatively gradual decline did not advance participants with a smaller friend network in absolute cognitive scores at later stage (i.e. intercept + slope*time) (Figure 6-11, Page 116).

Integration of Objective three and Objective one & two

Different from the previous two objectives presuming unidirectional effect from social relationships to cognitive ageing, *objective three* investigated the bidirectional associations between functional aspects of social relationships and cognitive function, building upon *social causation* and *health selection* processes.

Similar to objective two, the detrimental effects of *negative aspects of close relationships* on decline in executive function found in objective one were not statistically significant in objective three. In objective one, the estimated difference in decline in executive function over 10 years due to the highest vs. the lowest third of negative support is comparable with one extra year cognitive decline for participants aged 60. In view of this modest effect, it is possible that the adverse effect of negative support on cognitive ageing may need longer time to manifest itself.

Another potential explanation for inconsistent findings may be related to the different statistical approaches used. In objective one, the cumulative scores of negative support over mid-life were divided into three groups based on Phase 2 tertile cut-offs, whereas continuous scores were used in objective three. As regards statistical models, MLM was used in objective one in contrast to DCSM in objective three. Therefore, the interpretation of each analysis is different, namely, objective one estimated the effect of the top third of negative support in reference to the bottom third on the rate of cognitive decline over 10 years; whereas objective three estimated 1SD differences in negative support at the previous stage in relation to subsequent 5-year changes in cognitive function, beyond and above the ageing effects (constant slope) and auto-proportional effects (self-feedback).These two models hence are not directly comparable. Disparate findings further indicate the effect of negative support on cognitive ageing may only demonstrate when a certain threshold is reached, such that a nonlinear association should be modelled (Rook, 1998).

Considering objective one fixed exposure at mid-life while objective two and three captured the longitudinal changes of social relationships from middle to early old age, different results may reveal how the ageing brain processes information (Reed and Carstensen, 2012). The burden and benefit of social relationships may be perceived differently over later adulthood. As people age, they tend to recall more positive interactions and down-regulate emotional response to negative information (Carstensen *et al.*, 2006; Charles and Carstensen, 2010; Fingerman and Charles, 2010; Charles, 2011), with a coping goal to minimize rather than create conflicts (Sorkin and Rook, 2006). Age-related changes in the way of handling interpersonal relationships may result from selective neural degeneration in the amygdala, as well as more neurocognitive resources deployed to process positive stimuli (Reed and Carstensen, 2012). As such, the pernicious effects of mid-age negative aspects of close relationships on cognitive ageing (objective one) may be mitigated once the age-related decline in negative social encounters is taken into account (objective two & three).

On the other hand, objective three found no statistically significant effect of cognition on changes in negative support, further precluding reverse causation as an explanation for the *negative support -cognitive decline* association identified in objective one. Objective three also disentangled the direction of the association between *consistent extremely-high* confiding support and the least decline in memory found in objective two, and provided a more comprehensive picture contingent upon the bivariate starting points of confiding support and memory scores.

Taken together, in spite of different assumptions and statistical methods applied, the three objectives of this thesis progressively investigated the complex interplay between social relationships and cognitive ageing, underscoring the importance of utilizing multiple repeat measures over later adulthood. Findings based on this younger-old civil-servant sample suggest a modest to weak effect of social relationships on cognitive ageing. On the other hand, cognition appears to modify subsequent changes in support from close relationships, suggesting a *health selection* process.

8.3 Strengths and limitations

8.3.1 Strengths

The main strengths of this thesis are its basis in a large longitudinal prospective cohort with low attrition, and repeat measures of social relationships and cognitive function over 10 years' follow-up from participants' middle age. The relatively healthy and younger-old characteristics of the Whitehall II participants minimize the influence of undiagnosed dementia cases on the findings obtained.

Multiple and detailed measures of social relationships and cognitive function enable the use of a sequence of longitudinal analytic methods (McArdle and Grimm, 2010) to study the impact of mid-life social relationships on subsequent decline in cognition (MLM), the heterogeneous longitudinal changing patterns of social relationships (GMM) in relation to concurrent cognitive ageing trajectories, as well as the dynamic and time-dependent relationships of social relationships and cognitive function across later adulthood (DCSM). Each of the statistical methods has its strength and addresses different aspects of the aim of this thesis. Selectively using several statistical approaches allows this thesis to gradually unravel the complexities of the multidimensional ageing process (Tu *et al.*, 2013). The wide range of covariates included facilitates the adjustment of important confounders, including socio-demographic characteristics, depressive symptoms and clinically verified chronic diseases.

This thesis hence extends the existing literature by systematically investigating the longitudinal dynamic associations between social relationships and cognitive function from middle to early old age, based on a healthy ageing cohort with a larger sample size and a longer observational period than most of the studies reviewed.

8.3.2 Limitations

Several limitations should be considered in interpreting the findings of this thesis.

Generalizability of the findings

The findings are based on the Whitehall II occupational cohort, which is comprised predominantly of white-collar male Caucasian civil servants and thus is not representative of the general population. In line with other longitudinal studies, respondents who remained in this cohort were healthier than those who dropped-out or died (Ferrie *et al.*, 2009). As selective attrition may have already occurred before the analysis baseline (Phase 5), the present study sample underrepresents female, ethnic-minority and participants in low socioeconomic positions and less healthy (sample characteristics Page 62).

However, the Whitehall II cohort covers a wide occupational spectrum with a salary difference of more than 10-fold between the top and bottom of the socioeconomic hierarchy. Although the prevalence of adverse risk factors and the incidence of diseases tend to be lower in this occupational cohort, the Whitehall II study appears to provide comparable estimations of the risk factor- disease associations as in other population-based studies (Batty *et al.*, 2014). In comparison with ELSA (50 years and above), similar social relationships' profiles (Stafford *et al.*, 2011) and age-related rate of cognitive decline (Allerhand *et al.*, 2014) were observed in the current analytic sample. The levels of social relationships measured at Phase 1 were not associated with non-response at Phase 5 (P-value range 0.28- 0.85). Thus selective attrition before analysis baseline may not have operated in the associations between social relationships and cognitive ageing.

Measures of social relationships

The assessments of social relationships as most survey methods (Dodge *et al.*, 2014) were self-reported, which may be influenced by respondents' personality traits (Stansfeld and Marmot, 1992). Subjective experience, however, reflects individual interpretation of the social environment and has been shown to modify health behaviours (Kouvonen *et al.*, 2012; Tun *et al.*, 2012). Derived from a well-validated questionnaire, these self-rated measures are relevant indicators of social relationships that have established associations with various health outcomes (Stansfeld *et al.*, 1998a; Kouvonen *et al.*, 2011; Stringhini *et al.*, 2011; Stansfeld *et al.*, 2013).

As the functional measures of social relationships refer to the perceived support from the closest person only, the current study cannot estimate the association between cognition and social support in a more extended social network (Birditt *et al.*, 2009; Stafford *et al.*, 2011). The amount and type of support available may be contingent upon particular social ties (Gurung *et al.*, 2003; Aartsen *et al.*, 2004). Also social interactions may be interpreted and handled source-specifically (Coventry *et al.*, 2004; Rook *et al.*, 2012). The present study examined perceived support and supportive role fulfilment by the closest social tie that provides the most reliable (Harper, 2006) and emotionally rewarding support especially as people age (Kahn and Antonucci, 1980; Carstensen *et al.*, 2003). There was no evidence that the association between support from close relationships and cognition were subject to the identity of the closest person or the wider structure of social network.

The structural measures of social relationships were assessed by the number and frequent contacts with friends and relatives, which capture the current status of social network rather than symbolic or past inactive relationships. However, as the questions of social network were phrased as a mixture of friendship and acquaintanceship (e.g. How many *friends or acquaintances* do you see once a month or more), it is impossible to distinguish these truly supportive friends' ties from superficial acquaintances. In light of the definition of 'real friend' which may broaden as people age (Jerrome and Wenger, 1999), findings obtained here need further verification from studies directly measuring the composition and function of friend networks over time (Uchino, 2009; Stevens and van Tilburg, 2010).

Measures of cognitive function

The scope of the cognitive tests was limited by the 40 minutes' slot allowed in the 3-hour research clinic. Best practice in cognitive epidemiology has been followed, using a cognitive battery of five tests to assess the main components of executive function and memory. The current analysis did not use the *Mill Hill* test as it shows the characteristic age stability of crystallised intelligence, whereas the other four tests employed here to index executive function and memory each shows age-related decline (Singh-Manoux *et* *al.*, 2012). The *verbal memory* test is a standard procedure for testing short-term memory (Lezak, 2004). A composite score of the *inductive reasoning* and *verbal fluency* tests was used to capture the main domains of executive function, namely, coordination, inhibition, set-shifting and goal-orientation (Bryan and Luszcz, 2000; Elliott, 2003). The *verbal fluency* tests involve linguistic (storage and retrieval) and fluent (speed and efficiency) components (Chertkow and Bub, 1990), requiring abilities to sustain attention and suppress inadequate response (Benito-Cuadrado *et al.*, 2002). In spite of their knowledge-based nature (Bryan and Luszcz, 2000), the *verbal fluency* tests are widely used to measure executive function.

Residual confounding

There are potential confounding factors that the current study cannot adjust for, such as, personality and living arrangements.

Personality traits may influence the development and maintenance of social relationships (Langford *et al.*, 1997), as well as the amount of support perceived to be available (Gurung *et al.*, 2003; Bourne *et al.*, 2007; Zammit *et al.*, 2014). As for the association with cognition, two recent systematic reviews indicated that increased risks of cognitive decline and dementia were associated with high neuroticism and low conscientiousness (Low *et al.*, 2013; Terracciano *et al.*, 2014), information about which was not collected in the Whitehall II study. Additional analyses controlled for hostility and optimism measured at Phase 1 did not alter the *social relationships- cognition* associations obtained in the main analyses (results not shown). Given the relative stability in personality, it may not account greatly for the intra-individual change in social relationships with age and its influence on existing relationships may taper off in later life (Lang, 2001).

Living with someone or alone, as well as the geographical proximity between family members may affect the volume, frequency and type of support which can be provided by the significant others, especially in terms of intergenerational support (Murphy *et al.*, 2006; Bourne *et al.*, 2007). Information on living arrangements is not available in the entire Whitehall II dataset (e.g. 44% of participants at Phase 5 had information on whether or not live with children).The analysis of objective three partially addressed this issue by taking into account marital history during the follow-up. More than 2/3 participants were married or cohabiting, for whom the spouse or partner were the most likely choice of the closest person (86%). Thus differences in the perceived level of support due to living arrangements may not have introduced substantial bias in the current study.

Methodologic caveats

The specific limitations of each statistical model have been scrutinized in the corresponding chapters. Here, the common methodologic concerns are discussed.

In all analyses, the missing data were handled with full information maximum likelihood (FIML). FIML calculates the parameters from the model likelihood for each individual in the incomplete sample, alongside the individual misfit from the data likelihood (Ferrer and Ghisletta, 2011). This method uses partially and fully complete cases to estimate parameters (Enders and Bandalos, 2001) in a single step without additional iterations (Hofer and Hoffman, 2007). Under the assumption of MCAR or MAR, FIML can help reduce selection bias in the longitudinal sampling strategy and produce consistent and efficient parameter estimations (Little and Rubin, 2002), equivalent to multiple imputation (Sterne *et al.*, 2009), provided that the same covariates were included (Hofer and Hoffman, 2007).

However, reflecting the natural process of population ageing, non-random participant attrition is ubiquitous (Hofer and Sliwinski, 2006). For this analytic sample (data attrition Page 62), the levels of social relationships did not vary by participation status or the number of cognitive tests taken (Note: the association between married/cohabiting status and number of complete cognitive tests was confounded by socioeconomic circumstance).Yet, given the substantial low initial cognitive scores amongst those who had 1 or 2 waves of cognitive data missing, it is possible that participants who took the successive cognitive tests were not a random subsample; such that the rate of decline may be positively biased and the range of cognitive decline may be limited (Rabbitt *et al.*, 2001; Salthouse *et al.*, 2004; Sabia *et al.*, 2012). Non-random missing dependent on cognitive competency thus may reduce the power to detect the effect of social relationships on cognitive ageing, but not vice versa. That is, selective attrition may be associated with a greater reduction in the variance of cognition than in the variance of social relationships, which may result in the finding of a leading effect of cognition over functional social relationships. Future work could study the potential bias arising from non-random dropout by using joint models (Enders, 2011).

Last, most of the confounding factors were adjusted for as time-invariant covariates, whereas change during the follow-up was possible. Allowing covariates to vary would have increased the modelling complexity substantially. Moreover, change in certain covariates, for example, depressive symptoms, could be a direct consequence of the previous status of social relationships or cognitive function, and hence should be considered as a mediator rather than a confounder.

8.4 **Implications of the findings**

This thesis contributes to evidence for health and social care policy concerning the ageing population (House of Lords, 2013), particularly in terms of leading a healthy and socially engaged later life. In the G8 countries' global action against dementia, the importance of social determinants has been acknowledged (G8 Health and Science Directorate, 2013). The Government pledges to build *age friendly* (World Health Organization, 2007) and *dementia friendly communities* (Alzheimer's Disease International, 2015), aiming to reduce stigma and exclusion, empower older people to participate in society and live independent and fulfilling lives as long as they can in their communities. Meanwhile, public campaigns have been conducted to raise the awareness of the significance of social relationships for health (Goodman and Symons, 2013; Meier, 2013). Age UK, International longevity centre and other charities alike are lobbying the Parliament to ensure the UK will become a great place to grow older (Independent Age, 2014; Linehan *et al.*, 2014; age UK, 2015). This thesis therefore benefits the development of age-integrated societies (Harper, 2006) by providing empirical evidence on the complex dynamic associations between social relationships and cognitive ageing from a longitudinal perspective. Specifically, several implications can be drawn.

First, in the process of encouraging older people to engage fully in social participation, extra attention should be paid to enhance the quality of social relationships. The present study revealed that the negative but not positive aspects of social relationships were related to cognitive decline (*objective one*). This detrimental effect of negative social exchanges has been shown previously in relation to weight gain (Kouvonen *et al.*, 2011), heart diseases (Krause, 2005; De Vogli *et al.*, 2007), compromised mental wellbeing (Stansfeld *et al.*, 1998b; Rook, 2001; Newsom *et al.*, 2003) and functional disability (Krause and Shaw, 2002; Mavandadi *et al.*, 2007). Unsatisfying social relationships may be ascribed to individuals' personality traits and lack of social skills (Krause and Rook, 2003), as well as to unwelcoming social and cultural environments (Akiyama *et al.*, 2003; Berkman *et al.*, 2011). Thus interventions that maintain older people's autonomy and self-esteem (Warner *et al.*, 2011), and improve their ability to minimize social conflicts (Coleman and Stoilova, 2014; The Relationships Alliance, 2014; Jopling, 2015) are most likely to facilitate older people benefiting from social participation (Hogan *et al.*, 2002). The negative stereotype of ageing (Rippon *et al.*, 2013) at societal level must be eradicated to promote positive social interactions (Ready for Ageing Alliance, 2014; Tomas and Milligan, 2015).

Second, the dynamic and heterogeneous features of ageing should be considered in research and practice. This thesis reduces the dearth in literature by demonstrating a long-term and integral view of ageing across social and cognitive domains, incorporating distinct patterns of change and stability in social relationships (*objective two*). Social relationships in late life should be understood from a person-centred life course perspective (Lang *et al.*, 2009), whereby divergent longitudinal changing patterns of social relationships reflect variations in sociodemographic characteristics (Blieszner, 2006) and are related to the course of diseases (Mavandadi *et al.*, 2007; Thomas, 2011b). Highlighting heterogeneity in trajectories of social relationships also embodies the idea of optimization of ageing, namely, instead of a sheer loss, ageing is better viewed as a dynamic balance between gains and losses (Baltes and Baltes, 1990; Lang, 2001) intertwining psychosocial and biological changes. Moreover, adequate support from significant others may assist older people to better anticipate and adapt to inescapable functional deteriorations due to ageing (Liao and Brunner, 2015), leading to more effective coping (Bowling *et al.*, 2007) and higher resilience (Netuveli *et al.*, 2012). Accordingly, interventions should be personalized (Jopling, 2015), aiding old people to take a proactive approach towards ageing (Riediger *et al.*, 2006; Ouwehand *et al.*, 2007).

Another issue worth noting is the availability of sufficient support for older people. This thesis shows that cognitive ability predominantly influenced subsequent change in social support (*objective three*). A recent report reveals that more than two million older people in the UK are struggling in their own home with little or no practical support (Lloyd, 2014). As precisely commented by Gray (2009, Page 7), '*People can choose with whom to associate,…,but they cannot choose how helpful their friends, neighbours and relatives are when needed, or whether these people have the time, physical capacity and above all the inclination to talk, help and visit.*' Support deficit is most evident if older people develop mental and cognitive problems (Aartsen *et al.*, 2004; Broese van Groenou *et al.*, 2013), where the complexity and volume of care may exceed the support that informal carers can provide. The responsibility of informal caregiving is mainly given by family and close friends (Prince *et al.*, 2013b), who are juggling with multiple responsibilities at home and work (Murphy *et al.*, 2006) and thus have difficulties in maintaining their own social networks, let alone the adverse health and financial consequences that may be incurred (Knight and Losada, 2011; Carers UK, 2014). Compounded with shrinking family sizes and greater geographical separations (van Tilburg and Thomése, 2010; Herlofson and Hagestad, 2011; Murphy, 2011), the unmet support needs of older people, particularly those with cognitive impairment, should be supplemented by formal care provision (Sole-Auro and Crimmins, 2014) and well-tailored interventions to reduce caregiving distress (Knight and Losada, 2011; Department of Health, 2014). Comprehensive government leading programs (Beard and Bloom, 2014), such as community-based health services (Muramatsu *et al.*, 2010; South, 2015), should be in place, to help the seniors manage the caregiving burden associated with functional declines.

Last, although this thesis did not find a substantial effect of social relationships on cognitive ageing, it would be unwise to deny the significance of social relationships for health and quality of life in old age. Interpersonal relationships are fundamental in people's life

(Baumeister and Leary, 1995). Interventions targeted at social relationships can influence a wide range of downstream risk factors (Berkman *et al.*, 2000; Umberson and Montez, 2010), the health benefits of which go beyond the target individuals by enhancing the health of others throughout the social network (Christakis and Fowler, 2007; Smith and Christakis, 2008). Interventions of cognitive decline should be comprehensive and sustainable, combining social, cognitive and physical components (Karp *et al.*, 2006; Fratiglioni and Wang, 2007; Agrigoroaei and Lachman, 2011) alongside healthy nutrition (Small *et al.*, 2006; Middleton and Yaffe, 2009; Barnes and Yaffe, 2011). At least, older people will benefit from an overall improved health, and enjoy a socially and cognitively enriched late life (Hertzog *et al.*, 2008; Ybarra *et al.*, 2008; Middleton and Yaffe, 2009).

8.5 Future work

In terms of methodology, future work should take into account MNAR via joint models, such as, the selection model and the pattern mixture model (Enders, 2011). To provide a more precise estimation of the longitudinal latent classes of social relationships, the skew-t GMM may be required to compensate for the non-normal within-class distribution (Muthén and Asparouhov, 2015). It is also interesting to examine the extent to which time-dependent covariates (Robins *et al.*, 2000) may explain the findings obtained from longitudinal analyses.

The additional and new measurement of social relationships is another area for consideration. The self-reported questionnaire of functional social relationships is unidirectional (i.e. perceived ‘received support’), which cannot indicate the support provided to others. It is possible that productive rather than receptive social relationships are cognitively beneficial (Park *et al.*, 2007; Warner *et al.*, 2010), as productive interactions involve new skills whereas only routine schemas are needed in receptive ones. People aged 65 and over in the UK are actively contributing to the economy through employment, informal caregiving and volunteering (Iparraguirre, 2015). It is hence important to consider a wider picture of support exchange (Shaw *et al.*, 2007) in relation to healthy ageing. Advancements in technologies, such as webcams, internet and smartphones (Raento *et al.*, 2009) provide new channels for more objective assessments of social relationships (Dodge *et al.*, 2014). These communication technologies may further trigger cost-effective interventions of social relationships.

The current study used three repeat measures of cognitive function. Additional phases of data will increase the power and gain statistical precision, and provide an estimation of the cognitive ageing trajectory into later-old age. As the incident dementia is increasing with participants growing older, the Whitehall II study will collect information on diagnosed dementia cases. Proxy questions have been implemented in Phase 12 (2015-2016) data collection to detect cognitive capability of participants who are unable to follow the study. Information on ascertained dementia will become available via Hospital Episode Statistics (HES) data linkage, in combination with neuroimaging data in a Whitehall II subset.

Some emerging trends pertinent to social relationships and cognitive ageing are also worth pursuing. Internet and other technologies enable older people to maintain contacts with families and friends geographically apart, and facilitate the development of new social connections (Hagan *et al.*, 2014; Jopling, 2015). However, despite the potential to ameliorate the lack of emotional engagement, current technologies have yet to bridge the physical gap should older people require hands-on care, which critically relies on existing social networks (Roberts *et al.*, 2012). Furthermore, technologies could also exacerbate the social exclusion of older people as a result of reduced face-to-face contacts, and variations in acceptability and affordability to these new technologies (Chen and Chan, 2011; Independent Age, 2014). Future work therefore is needed to understand the role of technology in the association between social relationships and cognitive ageing.

It is also interesting to compare the experience of social relationships and their health impact against different cultural backgrounds (Fiori *et al.*, 2008; Schlecker and Fleischer, 2013), bearing in mind the dramatic changes in modern societies (Gilleard and Higgs, 2000; van Tilburg and Thomése, 2010). In contrast to Western individualism, East Asian cultures are characterised as collectivist and promoting filial piety. Nonetheless, there is evidence instead showing that respondents, with culture emphasizing an interdependent sense of self, would endeavour to maintain social harmony and avoid taxing support system because of their personal problems (Taylor, 2007; Kim *et al.*, 2008; Szawarska, 2013). Furthermore, under the fragmenting pressures of the urban world, traditional family solidarity is threatened in these prototypical collectivistic societies (Cheung and Kwan, 2009). For example, the rapid rural-urban labour migration results in many hollowed-out rural villages in China, with only older people left behind to take care of their grandchildren. This tendency fundamentally disrupts the family-centred support system for older people (He and Ye, 2014). Harmonized nationally-representative ageing cohorts (https://g2aging.org/) will assist the examination of culture-specific effects of social relationships on healthy ageing.

8.6 Conclusions

This thesis aimed to examine the longitudinal dynamic associations between social relationships and cognitive ageing in late life. The effect of social relationships on declines in cognition from middle to early old age is not evident in this British civil servant cohort; or if there is any, as in the case of negative aspects of close relationships, the modest effect may require a relatively high dose of exposure and a long-term to demonstrate. Findings provide empirical evidence for the *health selection* process, showing cognition is more likely to be the leading modifying factor for changes in confiding and practical support, not the other way around. It is concluded that social relationships and cognitive ageing are intertwined and coevolve with age. These dynamic features of ageing deserve careful considerations in constructing our age- and dementia- friendly societies.

References

Aartsen, M. J., van Tilburg, T., Smits, C. H. M., Comijs, H. C. & Knipscheer, K. C. P. M. 2005. Does widowhood affect memory performance of older persons? *Psychological medicine,* 35**,** 217-226.

Aartsen, M. J., van Tilburg, T., Smits, C. H. M. & Knipscheer, K. C. P. M. 2004. A Longitudinal Study of the Impact of Physical and Cognitive Decline on the Personal Network in Old Age. *Journal of Social and Personal Relationships,* 21**,** 249-266.

Adolphs, R. 2009. The social brain: neural basis of social knowledge. *Annual review of psychology,* 60**,** 693-716.

age UK. 2015. *A great place to grow older. Age UK's ambition for the next parliamnet 2015-2020* [Online]. London: Age UK Available: http://www.ageuk.org.uk/Documents/EN-GB/General%20Election%202015/2015_General_Election_Great_Place_to_Grow_Older.pdf?epslanguage=en-GB?dtrk=true [Accessed 1st May 2015].

Agrigoroaei, S. & Lachman, M. E. 2011. Cognitive functioning in midlife and old age: combined effects of psychosocial and behavioral factors. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences,* 66**,** i130-i140.

Ajrouch, K. J., Blandon, A. Y. & Antonucci, T. C. 2005. Social networks among men and women: The effects of age and socioeconomic status. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences,* 60**,** S311-S317.

Akiyama, H., Antonucci, T., Takahashi, K. & Langfahl, E. S. 2003. Negative interactions in close relationships across the life span. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences,* 58**,** P70-P79.

Allan, G. 2001. Personal relationships in late modernity. *Personal Relationships,* 8**,** 325-339.

Allerhand, M., Gale, C. R. & Deary, I. J. 2014. The dynamic relationship between cognitive function and positive well-being in older people: A prospective study using the English Longitudinal Study of Aging. *Psychology and Aging,* 29**,** 306.

Almkvist, O. & Tallberg, I.-M. 2009. Cognitive decline from estimated premorbid status predicts neurodegeneration in Alzheimer's disease. *Neuropsychology,* 23**,** 117.

Alzheimer's Association. 2013. *Alzheimer's disease facts and figures* [Online]. US. Available: https://www.alz.org/downloads/facts_figures_2013.pdf [Accessed 2nd April 2014].

Alzheimer's Association. 2015. *Alzheimer's Disease Facts and Figures* [Online]. Alzheimer's Association. Available: https://www.alz.org/facts/downloads/facts_figures_2015.pdf [Accessed 4th October 2015].

Alzheimer's Disease International. 2015. *Dementia Friendly Communities (DFCs) New domains and global examples* [Online]. London, UK: Alzheimer's Disease International (ADI). Available: https://www.alz.co.uk/adi/pdf/dementia-friendly-communities.pdf [Accessed 5th November 2015].

Amieva, H., Le Goff, M., Millet, X., Orgogozo, J. M., Pérès, K., Barberger‐Gateau, P., Jacqmin‐Gadda, H. & Dartigues, J. F. 2008. Prodromal Alzheimer's disease: successive emergence of the clinical symptoms. *Annals of Neurology,* 64**,** 492-498.

Amieva, H., Stoykova, R., Matharan, F., Helmer, C., Antonucci, T. C. & Dartigues, J.-F. 2010. What aspects of social network are protective for dementia? Not the quantity but the quality of social interactions is protective up to 15 years later. *Psychosomatic medicine,* 72**,** 905-911.

Anstey, K. J., Mack, H. A. & Cherbuin, N. 2009. Alcohol consumption as a risk factor for dementia and cognitive decline: meta-analysis of prospective studies. *The American Journal of Geriatric Psychiatry,* 17**,** 542-555.

Anstey, K. J., von Sanden, C., Salim, A. & O'Kearney, R. 2007. Smoking as a risk factor for dementia and cognitive decline: a meta-analysis of prospective studies. *American journal of epidemiology,* 166**,** 367-378.

Antonucci, T. C., Ajrouch, K. J. & Birditt, K. S. 2013. The convoy model: Explaining social relations from a multidisciplinary perspective. *The Gerontologist,* 54**,** 82-92.

Antonucci, T. C., Birditt, K. S. & Ajrouch, K. 2011. Convoys of social relations: past, present and future. *In:* Fingerman, K. L., Berg, C. A., Smith, J. & Antonucci, T. (eds.) *Handbook of life span development.* New York: Spinger Publishing Company,161-182.

Antonucci, T. C., Fiori, K. L., Birditt, K. & Jackey, L. M. 2010. Convoys of Social Relations: Integrating Life ‐ Span and Life ‐ Course Perspectives. *In:* E., L. M., E., F. M. & M., L. R. (eds.) *The handbook of life-span development, Vol 2: Social and EmotionalDevelopment* Hoboken, NJ: John Wiley & Sons Inc.,193-209.

Ardelt, M. 2011. Wisdom, Age, and Well-Being. *In:* Schaie, K. W. & Willis, S. L. (eds.) *Handbook of the Psychology of Aging.* 7th ed. San Diego, USA: Academic Press,279-291.

Asparouhov, T. & Muthén, B. 2013. *Auxiliary variables in mixture modeling: A 3-step approach using Mplus (Mplus Web Notes)* [Online]. Available: http://statmodel.com/examples/webnotes/AuxMixture_submitted_corrected_webnote [Accessed 2nd December 2014].

Asparouhov, T. & Muthén, B. 2014. Structural equation models and mixture models with continuous non-normal skewed distributions. *Mplus Web Note,* 19**,** 1-49.

Bailey, P. E., Henry, J. D. & Von Hippel, W. 2008. Empathy and social functioning in late adulthood. *Aging and Mental Health,* 12**,** 499-503.

Ballard, C., Gauthier, S., Corbett, A., Brayne, C., Aarsland, D. & Jones, E. 2011. Alzheimer's disease. *Lancet,* 377**,** 1019–1031.

Baltes, P. B. & Baltes, M. M. 1990. Psychological perspectives on successful aging: The model of selective optimization with compensation. *Successful aging: Perspectives from the behavioral sciences,* 1**,** 1-34.

Barefoot, J. C., Grønbæk, M., Jensen, G., Schnohr, P. & Prescott, E. 2005. Social network diversity and risks of ischemic heart disease and total mortality: findings from the Copenhagen City Heart Study. *American journal of epidemiology,* 161**,** 960-967.

Barnes, D. E., Cauley, J. A., Lui, L.-Y., Fink, H. A., McCulloch, C., Stone, K. L. & Yaffe, K. 2007. Women who maintain optimal cognitive function into old age. *Journal of the American Geriatrics Society,* 55**,** 259-264.

Barnes, D. E. & Yaffe, K. 2011. The projected effect of risk factor reduction on Alzheimer's disease prevalence. *The Lancet Neurology,* 10**,** 819-828.

Barnes, L. L., de Leon, C. F. M., Wilson, R. S., Bienias, J. L. & Evans, D. A. 2004. Social resources and cognitive decline in a population of older African Americans and whites. . *Neurology,* 63**,** 2322-2326.

Barnett, A. G., Van Der Pols, J. C. & Dobson, A. J. 2005. Regression to the mean: what it is and how to deal with it. *International Journal of Epidemiology,* 34**,** 215-220.

Barrera, M. 1986. Distinctions between social support concepts, measures, and models. *American Journal of Community Psychology,* 14**,** 413-445.

Bassuk, S. S., Glass, T. A. & Berkman, L. F. 1999. Social disengagement and incident cognitive decline in community-dwelling elderly persons. *Annals of Internal Medicine,* 131**,** 165-173.
Batty, G. D., Shipley, M., Tabák, A., Singh-Manoux, A., Brunner, E., Britton, A. & Kivimäki, M. 2014. Generalizability of Occupational Cohort Study Findings. *Epidemiology,* 25**,** 932-933.
Bauer, D. J. & Curran, P. J. 2003a. Distributional assumptions of growth mixture models: implications for overextraction of latent trajectory classes. *Psychological methods,* 8**,** 338.
Bauer, D. J. & Curran, P. J. 2003b. Overextraction of Latent Trajectory Classes: Much Ado About Nothing? Reply to Rindskopf (2003), Muthén (2003), and Cudeck and Henly (2003).
Baumeister, R. F. & Leary, M. R. 1995. The need to belong: desire for interpersonal attachments as a fundamental human motivation. *Psychological bulletin,* 117**,** 497.
Beard, J. R. & Bloom, D. E. 2014. Towards a comprehensive public health response to population ageing. *Lancet,* 385**,** 658-661.
Beauchamp, M. H. & Anderson, V. 2010. SOCIAL: an integrative framework for the development of social skills. *Psychological bulletin,* 136**,** 39.
Béland, F., Zunzunegui, M. V., Alvarado, B., Otero, A. & Del Ser, T. 2005. Trajectories of cognitive decline and social relations. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences,* 60**,** P320-P330.
Beluche, I., Carrière, I., Ritchie, K. & Ancelin, M. L. 2010. A prospective study of diurnal cortisol and cognitive function in community-dwelling elderly people. *Psychological medicine,* 40**,** 1039.
Benito-Cuadrado, M., Esteba-Castillo, S., Böhm, P., Cejudo-Bolivar, J. & Peña-Casanova, J. 2002. Semantic verbal fluency of animals: a normative and predictive study in a Spanish population. *Journal of Clinical and Experimental Neuropsychology,* 24**,** 1117-1122.
Bennett, D. A., Arnold, S. E., Valenzuela, M. J., Brayne, C. & Schneider, J. A. 2014. Cognitive and social lifestyle: links with neuropathology and cognition in late life. *Acta neuropathologica,* 127**,** 137-150.
Bennett, D. A., Schneider, J. A., Tang, Y., Arnold, S. E. & Wilson, R. S. 2006. The effect of social networks on the relation between Alzheimer's disease pathology and level of cognitive function in old people: a longitudinal cohort study. *Lancet Neurology,* 5**,** 406-412.
Berkman, L., Ertel, K. & Glymour, M. 2011. Aging and social intervention: Life course perspectives. *In:* Binstock, R. & George, L. (eds.) *Handbook of aging and the social sciences.* San Diego, CA: Academic Press,337-351.
Berkman, L. F., Glass, T., Brissette, I. & Seeman, T. E. 2000. From social integration to health: Durkheim in the new millennium. *Social science & medicine,* 51**,** 843-857.
Berkman, L. F., Melchior, M., Chastang, J.-F., Niedhammer, I., Leclerc, A. & Goldberg, M. 2004. Social Integration and Mortality: A Prospective Study of French Employees of Electricity of France–Gas of France The GAZEL Cohort. *American journal of epidemiology,* 159**,** 167-174.
Berkman, L. F. & Syme, S. L. 1979. Social networks, host resistance, and mortality: a nine-year follow-up study of Alameda County residents. *American journal of epidemiology,* 109**,** 186-204.
Berscheid, E. & Ammazzalorso, H. 2004. Emotional experience in close relationships. *In:* Brewer, M. B. & Hewstone, M. (eds.) *Emotion and motivation: persepectives on social psychology.* Malden., MA: Blackwell handbook 47-69.

Beswick, A., Gooberman-Hill, R., Smith, A., Wylde, V. & Ebrahim, S. 2010. Maintaining independence in older people. *Reviews in Clinical Gerontology,* 20**,** 128-153.

Bickart, K. C., Wright, C. I., Dautoff, R. J., Dickerson, B. C. & Barrett, L. F. 2010. Amygdala volume and social network size in humans. *Nature neuroscience,* 14**,** 163-164.

Bielak, A. A. M. 2010. How can we not 'lose it' if we still don't understand how to 'use it'? Unanswered questions about the influence of activity participation on cognitive performance in older age-A mini-review. *Gerontology,* 56**,** 507-519.

Binstock, R. H. & George, L. K. 2011. *Handbook of aging and the social sciences,* San Diego, CA, Elsevier Academic Press.

Birditt, K. S., Jackey, L. M. & Antonucci, T. C. 2009. Longitudinal patterns of negative relationship quality across adulthood. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences,* 64**,** 55-64.

Black, D., Morris, J., Smith, C. & Townsend, P. 1980. Inequalities in health: report of a research working group London: the Department of Health and Social Security (DHSS).

Blanchflower, D. G. & Oswald, A. J. 2008. Is well-being U-shaped over the life cycle? *Social science & medicine,* 66**,** 1733-1749.

Blane, D., Smith, G. D. & Bartley, M. 1993. Social selection: what does it contribute to social class differences in health? *Sociology of Health & Illness,* 15**,** 1-15.

Blieszner, R. 2006. A lifetime of caring: Dimensions and dynamics in late ‐ life close relationships. *Personal Relationships,* 13**,** 1-18.

Boerner, K., Reinhardt, J. P., Raykov, T. & Horowitz, A. 2004. Stability and change in social negativity in later life: Reducing received while maintaining initiated negativity. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences,* 59**,** S230-S237.

Boker, S. M. & McArdle, J. 1995. Statistical vector field analysis applied to mixed cross-sectional and longitudinal data. *Experimental aging research,* 21**,** 77-93.

Bolck, A., Croon, M. & Hagenaars, J. 2004. Estimating latent structure models with categorical variables: One-step versus three-step estimators. *Political Analysis,* 12**,** 3-27.

Bolger, N., Zuckerman, A. & Kessler, R. C. 2000. Invisible support and adjustment to stress. *Journal of Personality and Social Psychology,* 79**,** 953.

Bollen, K. A. & Curran, P. J. 2004. Autoregressive latent trajectory (ALT) models a synthesis of two traditions. *Sociological methods & research,* 32**,** 336-383.

Bollen, K. A. & Curran, P. J. 2006. *Latent curve models: A structural equation perspective,* Hoboken, NJ, John Wiley & Sons.

Bourne, V. J., Fox, H. C., Starr, J. M., Deary, I. J. & Whalley, L. J. 2007. Social support in later life: Examining the roles of childhood and adulthood cognition. *Personality and Individual Differences,* 43**,** 937-948.

Bowling, A. & Browne, P. D. 1991. Social networks, health, and emotional well-being among the oldest old in London. *Journal of Gerontology,* 46**,** S20-S32.

Bowling, A. & Dieppe, P. 2005. What is successful ageing and who should define it? *BMJ,* 331**,** 1548-1551.

Bowling, A., Seetai, S., Morris, R. & Ebrahim, S. 2007. Quality of life among older people with poor functioning. The influence of perceived control over life. *Age and ageing,* 36**,** 310-315.

Brayne, C. 2007. The elephant in the room—healthy brains in later life, epidemiology and public health. *Nature reviews neuroscience,* 8**,** 233-239.

Brayne, C. & Calloway, P. 1988. Normal ageing, impaired cognitive function, and senile dementia of the Alzheimer's type: a continuum? *The Lancet,* 331**,** 1265-1267.

Britton, A., Milne, B., Butler, T., Sanchez-Galvez, A., Shipley, M., Rudd, A., Wolfe, C. D., Bhalla, A. & Brunner, E. J. 2012. Validating self-reported strokes in a longitudinal UK cohort study (Whitehall II): Extracting information from hospital medical records versus the Hospital Episode Statistics database. *BMC medical research methodology,* 12**,** 83.

Broese van Groenou, M. I., Hoogendijk, E. O. & van Tilburg, T. G. 2013. Continued and New Personal Relationships in Later Life Differential Effects of Health. *Journal of aging and health,* 25**,** 274-295.

Broese van Groenou, M. I. & van Tilburg, T. 2003. Network size and support in old age: Differentials by socio-economic status in childhood and adulthood. *Ageing and Society,* 23**,** 625-645.

Brookmeyer, R., Johnson, E., Ziegler-Graham, K. & Arrighi, H. M. 2007. Forecasting the global burden of Alzheimer’s disease. *Alzheimer's and Dementia,* 3**,** 186-191.

Bryan, J. & Luszcz, M. A. 2000. Measurement of executive function: Considerations for detecting adult age differences. *Journal of Clinical and Experimental Neuropsychology,* 22**,** 40-55.

Byers, A. L., Vittinghoff, E., Lui, L.-Y., Hoang, T., Blazer, D. G., Covinsky, K. E., Ensrud, K. E., Cauley, J. A., Hillier, T. A. & Fredman, L. 2012. Twenty-Year Depressive Trajectories Among Older WomenTwenty-Year Depressive Trajectories in Older Women. *Archives of general psychiatry,* 69**,** 1073-1079.

Cacioppo, J. T. & Hawkley, L. C. 2009. Perceived social isolation and cognition. *Trends in cognitive sciences,* 13**,** 447-454.

Campbell, S. B., Morgan-Lopez, A. A., Cox, M. J. & McLoyd, V. C. 2009. A latent class analysis of maternal depressive symptoms over 12 years and offspring adjustment in adolescence. *Journal of abnormal psychology,* 118**,** 479.

Carers UK. 2014. *Facts about carers* [Online]. London. Available: https://www.carersuk.org/for-professionals/policy/policy-library/facts-about-carers-2014 [Accessed 29th June 2015].

Carstensen, L. L. 2006. The influence of a sense of time on human development. *Science,* 312**,** 1913-1915.

Carstensen, L. L., Fung, H. H. & Charles, S. T. 2003. Socioemotional selectivity theory and the regulation of emotion in the second half of life. *Motivation and emotion,* 27**,** 103-123.

Carstensen, L. L., Mikels, J. A. & Mather, M. 2006. Aging and the intersection of cognition, motivation, and emotion. *In:* Birren, J., E. & Schaie, K. W. (eds.) *Handbook of the Psychology of Aging.* Amsterdam: Amsterdam,343-362.

Cassel, J. 1976. The contribution of the social environment to host resistance. *American Journal of Epidemology***,** 107-123.

Celeux, G. & Soromenho, G. 1996. An entropy criterion for assessing the number of clusters in a mixture model. *Journal of classification,* 13**,** 195-212.

Chandola, T., Bartley, M., Sacker, A., Jenkinson, C. & Marmot, M. 2003. Health selection in the Whitehall II study, UK. *Social science & medicine,* 56**,** 2059-2072.

Charles, S. T. 2011. Emotional experience and regulation in later life. *In:* Schaie, K. W. & Willis, S. L. (eds.) *Handbook of the Psychology of Aging.* 7th ed. San Diego, USA: Academic Press,295-310.

Charles, S. T. & Carstensen, L. L. 2010. Social and emotional aging. *Annual review of psychology,* 61**,** 383-409.

Chen, K. & Chan, A. 2011. A review of technology acceptance by older adults. *Gerontechnology,* 10**,** 1-12.
Chertkow, H. & Bub, D. 1990. SEMANTIC MEMORY LOSS IN DEMENTIA OF ALZHEIMER'S TYPE WHAT DO VARIOUS MEASURES MEASURE? *Brain,* 113**,** 397-417.
Cheung, C.-K. & Kwan, A. Y.-h. 2009. The erosion of filial piety by modernisation in Chinese cities. *Ageing and society,* 29**,** 179-198.
Christakis, N. A. & Fowler, J. H. 2007. The spread of obesity in a large social network over 32 years. *New England Journal of Medicine,* 357**,** 370-379.
Christensen, H. 2001. What cognitive changes can be expected with normal ageing? *Australian and New Zealand Journal of Psychiatry,* 35**,** 768-775.
Cobb, S. 1976. Social support as a moderator of life stress. *Psychosomatic medicine,* 38**,** 300-314.
Cohen, S. 2004. Social relationships and health. *American psychologist,* 59**,** 676.
Cohen, S., Doyle, W. J., Skoner, D. P., Rabin, B. S. & Gwaltney Jr, J. M. 1997. Social ties and susceptibility to the common cold. *JAMA: The Journal of the American Medical Association,* 277**,** 1940-1944.
Cohen, S., Gottlieb, B. H. & Underwood, L. G. 2001. Social relationships and health: Challenges for measurement and intervention. *Advances in Mind-Body Medicine,* 17**,** 129 –141.
Cohen, S. & Janicki-Deverts, D. 2009. Can we improve our physical health by altering our social networks? *Perspectives on Psychological Science,* 4**,** 375-378.
Cohen, S. & Wills, T. A. 1985. Stress, social support, and the buffering hypothesis. *Psychological bulletin,* 98**,** 310-357.
Colcombe, S. & Kramer, A. F. 2003. Fitness effects on the cognitive function of older adults a meta-analytic study. *Psychological science,* 14**,** 125-130.
Coleman, L. & Stoilova, M. 2014. *Opportunities for Relationship Support: A set of diverse case studies* [Online]. London: The Relationships Alliance. Available: http://www.oneplusone.org.uk/wp-content/uploads/2014/05/Opportunities-for-Relationship-Support-A-set-of-diverse-case-studies-by-Lester-Coleman-Mariya-Stoilova1.pdf [Accessed 30th May 2015].
Collins, L. M. & Lanza, S. T. 2010. *Latent class and latent transition analysis: With applications in the social, behavioral, and health sciences,* Hoboken, NJ, John Wiley & Sons.
Cornwell, B., Laumann, E. O. & Schumm, L. P. 2008. The social connectedness of older adults: A national profile. *American Sociological Review,* 73**,** 185-203.
Cosentino, S. A., Brickman, A. M. & Manly, J. J. 2011. Neuropsychological Assessment of the Dementias of Late Life. *In:* Schaie, K. W. & Willis, S. L. (eds.) *Handbook of the Psychology of Aging.* 7th ed. San Diego, USA: Academic Press,339-352.
Coventry, W., Gillespie, N., Heath, A. C. & Martin, N. 2004. Perceived social support in a large community sample. *Social psychiatry and psychiatric epidemiology,* 39**,** 625-636.
Craik, F. I. M. & Bialystok, E. 2006. Cognition through the lifespan: mechanisms of change. *Trends in cognitive sciences,* 10**,** 131-138.
Curran, P. J., Howard, A. L., Bainter, S. A., Lane, S. T. & McGinley, J. S. 2013. The Separation of Between-Person and Within-Person Components of Individual Change Over Time: A Latent Curve Model With Structured Residuals. *Journal of Clinical and Consulting Psychology,* 82**,** 879-894.
Daviglus, M. L., Plassman, B. L., Pirzada, A., Bell, C. C., Bowen, P. E., Burke, J. R., Connolly Jr, E. S., Dunbar-Jacob, J. M., Granieri, E. C. & McGarry, K. 2011.

Risk factors and preventive interventions for Alzheimer disease: state of the science. *Archives of neurology,* 68**,** 1185.
De Ruiter, J., Weston, G. & Lyon, S. M. 2011. Dunbar's number: Group size and brain physiology in humans reexamined. *American Anthropologist,* 113**,** 557-568.
De Vogli, R., Chandola, T. & Marmot, M. G. 2007. Negative aspects of close relationships and heart disease. *Archives of Internal Medicine,* 167**,** 1951-1957.
Deary, I. J. & Batty, G. D. 2007. Cognitive epidemiology. *Journal of Epidemiology and Community Health,* 61**,** 378-384.
Deary, I. J., Corley, J., Gow, A. J., Harris, S. E., Houlihan, L. M., Marioni, R. E., Penke, L., Rafnsson, S. B. & Starr, J. M. 2009. Age-associated cognitive decline. *British Medical Bulletin,* 92**,** 135-152.
Debette, S., Seshadri, S., Beiser, A., Au, R., Himali, J., Palumbo, C., Wolf, P. & DeCarli, C. 2011. Midlife vascular risk factor exposure accelerates structural brain aging and cognitive decline. *Neurology,* 77**,** 461-468.
Department of Health. 2014. *Care and support statutory gudiance* [Online]. Available: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/315993/Care-Act-Guidance.pdf [Accessed 1st August 2015].
Depp, C. A. & Jeste, D. V. 2006. Definitions and predictors of successful aging: a comprehensive review of larger quantitative studies. *American Journal of Geriatric Psych,* 14**,** 6-20.
Dickens, W. T. & Flynn, J. R. 2001. Heritability estimates versus large environmental effects: the IQ paradox resolved. *Psychological review,* 108**,** 346.
Dickinson, W. J., Potter, G. G., Hybels, C. F., McQuoid, D. R. & Steffens, D. C. 2011. Change in stress and social support as predictors of cognitive decline in older adults with and without depression. . *International Journal of Geriatric Psychiatry,* 26**,** 1267-1274.
Dodge, H. H., Ybarra, O. & Kaye, J. A. 2014. Tools for advancing research into social networks and cognitive function in older adults. *International psychogeriatrics,* 26**,** 533-539.
Dregan, A., Stewart, R. & Gulliford, M. C. 2012. Cardiovascular risk factors and cognitive decline in adults aged 50 and over: a population-based cohort study. *Age and ageing***,** afs166.
DSM-5 2013. *Diagnostic and statistical manual of mental disorders, (DSM-5®),* Arlington, VA, American Psychiatric Association.
Duff, K., Beglinger, L. J., Moser, D. J., Paulsen, J. S., Schultz, S. K. & Arndt, S. 2010. Predicting cognitive change in older adults: The relative contribution of practice effects. *Archives of Clinical Neuropsychology,* 25**,** 81-88.
Dunbar, R. I. 1998. The Social Brain Hypothesis. *Evolutionary Anthropology,* 6**,** 178-190.
Eisele, M., Zimmermann, T., Kohler, M., Wiese, B., Heser, K., Tebarth, F., Weeg, D., Olbrich, J., Pentzek, M., Fuchs, A., Weyerer, S., Werle, J., Leicht, H., Konig, H.-H., Luppa, M., Riedel-Heller, S., Maier, W., Scherer, M. & AgeCoDe Study, G. 2012. Influence of social support on cognitive change and mortality in old age: results from the prospective multicentre cohort study AgeCoDe. *BMC Geriatrics,* 12**,** 9.
Elias, M. F., Beiser, A., Wolf, P. A., Au, R., White, R. F. & D'Agostino, R. B. 2000. The preclinical phase of alzheimer disease: A 22-year prospective study of the Framingham Cohort. *Archives of neurology,* 57**,** 808.
Elliott, R. 2003. Executive functions and their disorders Imaging in clinical neuroscience. *British Medical Bulletin,* 65**,** 49-59.

Ellwardt, L., Aartsen, M., Deeg, D. & Steverink, N. 2013. Does loneliness mediate the relation between social support and cognitive functioning in later life? *Social science & medicine*.

Ellwardt, L., van Tilburg, T. G. & Aartsen, M. J. 2015. The mix matters: Complex personal networks relate to higher cognitive functioning in old age. *Social science & medicine,* 125**,** 107-115.

Elovainio, M., Ferrie, J. E., Singh-Manoux, A., Shipley, M., Batty, G. D., Head, J., Hamer, M., Jokela, M., Virtanen, M. & Brunner, E. 2011. Socioeconomic differences in cardiometabolic factors: social causation or health-related selection? Evidence from the Whitehall II Cohort Study, 1991–2004. *American journal of epidemiology,* 174**,** 779-789.

Elwood, P., Galante, J., Pickering, J., Palmer, S., Bayer, A., Ben-Shlomo, Y., Longley, M. & Gallacher, J. 2013. Healthy Lifestyles Reduce the Incidence of Chronic Diseases and Dementia: Evidence from the Caerphilly Cohort Study. *PLoS one,* 8**,** e81877.

Enders, C. K. 2011. Missing not at random models for latent growth curve analyses. *Psychological methods,* 16**,** 1.

Enders, C. K. & Bandalos, D. L. 2001. The relative performance of full information maximum likelihood estimation for missing data in structural equation models. *Structural Equation Modeling,* 8**,** 430-457.

Engelhart, M. J., Geerlings, M. I., Meijer, J., Kiliaan, A., Ruitenberg, A., van Swieten, J. C., Stijnen, T., Hofman, A., Witteman, J. & Breteler, M. 2004. Inflammatory proteins in plasma and the risk of dementia: the Rotterdam study. *Archives of neurology,* 61**,** 668.

Ertel, K. A., Glymour, M. M. & Berkman, L. F. 2008. Effects of social integration on preserving memory function in a nationally representative US elderly population. *American Journal of Public Health,* 98**,** 1215-1220.

Ferrer, E. & Ghisletta, P. 2011. Methodological and analytical issues in the psychology of aging. *In:* Birren, J., E. & Schaie, K. W. (eds.) *Handbook of the Psychology of Aging.* Amsterdam: Elseriver Academic Press,25-39.

Ferrer, E. & McArdle, J. 2003. Alternative structural models for multivariate longitudinal data analysis. *Structural Equation Modeling,* 10**,** 493-524.

Ferrer, E. & McArdle, J. J. 2004. An experimental analysis of dynamic hypotheses about cognitive abilities and achievement from childhood to early adulthood. *Developmental psychology,* 40**,** 935.

Ferrer, E. & McArdle, J. J. 2010. Longitudinal modeling of developmental changes in psychological research. *Current Directions in Psychological Science,* 19**,** 149-154.

Ferrer, E., McArdle, J. J., Shaywitz, B. A., Holahan, J. M., Marchione, K. & Shaywitz, S. E. 2007. Longitudinal models of developmental dynamics between reading and cognition from childhood to adolescence. *Developmental psychology,* 43**,** 1460.

Ferrer, E., Salthouse, T. A., Stewart, W. F. & Schwartz, B. S. 2004. Modeling age and retest processes in longitudinal studies of cognitive abilities. *Psychology and Aging,* 19**,** 243-259.

Ferrie, J. E., Kivimäki, M., Singh-Manoux, A., Shortt, A., Martikainen, P., Head, J., Marmot, M., Gimeno, D., De Vogli, R. & Elovainio, M. 2009. Non-response to baseline, non-response to follow-up and mortality in the Whitehall II cohort. *International Journal of Epidemiology,* 38**,** 831-837.

Ferrie, J. E., Langenberg, C., Shipley, M. J. & Marmot, M. G. 2006. Birth weight, components of height and coronary heart disease: evidence from the Whitehall II study. *International Journal of Epidemiology,* 35**,** 1532-1542.

Fingerman, K. L. & Charles, S. T. 2010. It Takes Two to Tango Why Older People Have the Best Relationships. *Current Directions in Psychological Science,* 19**,** 172-176.

Fingerman, K. L., Hay, E. L. & Birditt, K. S. 2004. The best of ties, the worst of ties: Close, problematic, and ambivalent social relationships. *Journal of Marriage and Family,* 66**,** 792-808.

Fiocco, A. J. & Yaffe, K. 2010. Defining successful aging: the importance of including cognitive function over time. *Archives of neurology,* 67**,** 876-880.

Fiori, K. L., Antonucci, T. C. & Akiyama, H. 2008. Profiles of social relations among older adults: A cross-cultural approach. *Ageing and Society,* 28**,** 203-231.

Fiori, K. L. & Jager, J. 2012. The impact of social support networks on mental and physical health in the transition to older adulthood: A longitudinal, pattern-centered approach. *International Journal of Behavioral Development,* 36**,** 117-129.

Flynn, J. R. 1987. Massive IQ gains in 14 nations: What IQ tests really measure. *Psychological bulletin,* 101**,** 171-191.

Folstein, M. F., Folstein, S. E. & McHugh, P. R. 1975. Mini-Mental State: a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res.***,** 12189-12198.

Fratiglioni, L., Paillard-Borg, S. & Winblad, B. 2004. An active and socially integrated lifestyle in late life might protect against dementia. *The Lancet Neurology,* 3**,** 343-353.

Fratiglioni, L. & Wang, H.-X. 2007. Brain reserve hypothesis in dementia. *Journal of Alzheimer's disease,* 12**,** 11-22.

Fratiglioni, L., Wang, H. X., Ericsson, K., Maytan, M. & Winblad, B. 2000. Influence of social network on occurrence of dementia: a community-based longitudinal study. *Lancet,* 355**,** 1315-1319.

Fries, J. F. 1983. The compression of morbidity. *The Milbank Memorial Fund Quarterly. Health and Society***,** 397-419.

Fries, J. F. 2005. The compression of morbidity. *Milbank Quarterly,* 83**,** 801-823.

Frith, U. & Frith, C. D. 2003. Development and neurophysiology of mentalizing. *Philosophical Transactions of the Royal Society of London B: Biological Sciences,* 358**,** 459-473.

Fuhrer, R. & Stansfeld, S. A. 2002. How gender affects patterns of social relations and their impact on health: a comparison of one or multiple sources of support from "close persons". *Social science & medicine,* 54**,** 811-825.

Fuhrer, R., Stansfeld, S. A., Chemali, J. & Shipley, M. J. 1999. Gender, social relations and mental health: prospective findings from an occupational cohort (Whitehall II study). *Social science & medicine,* 48**,** 77-87.

G8 Health and Science Directorate 2013. G8 Dementia Summit Communique. Prime Minister's Office, 10 Downing Street, London: Deparment of Helath, Gov.UK.

Gale, C. R., Allerhand, M. & Deary, I. J. 2012. Is there a bidirectional relationship between depressive symptoms and cognitive ability in older people? A prospective study using the English Longitudinal Study of Ageing. *Psychological Medicine,* 42**,** 2057-2069.

Gallacher, J., Bayer, A. & Ben-Shlomo, Y. 2005. Commentary: Activity each day keeps dementia away—does social interaction really preserve cognitive function? *International Journal of Epidemiology,* 34**,** 872-873.

Ghisletta, P., Bickel, J.-F. & Lövdén, M. 2006. Does activity engagement protect against cognitive decline in old age? Methodological and analytical considerations. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences,* 61**,** P253-P261.

Giles, L. C., Anstey, K. J., Walker, R. B. & Luszcz, M. A. 2012. Social Networks and Memory over 15 Years of Followup in a Cohort of Older Australians: Results from the Australian Longitudinal Study of Ageing. *Journal of Aging Research,* 2012.

Gilleard, C. J. & Higgs, P. 2000. *Cultures of ageing: Self, citizen, and the body,* Prentice Hall, London, Pearson Education.

Gillette-Guyonnet, S., Van Kan, G. A., Andrieu, S., Barberger-Gateau, P., Berr, C., Bonnefoy, M., Dartigues, J., De Groot, L., Ferry, M. & Galan, P. 2007. IANA task force on nutrition and cognitive decline with aging. *Journal of Nutrition Health and Aging,* 11**,** 132.

Gilmour, H. 2011. Cognitive performance of Canadian seniors. *Health Reports,* 22**,** 27-31.

Glass, T. A., De Leon, C. F. M., Seeman, T. E. & Berkman, L. F. 1997. Beyond single indicators of social networks: a LISREL analysis of social ties among the elderly. *Social science & medicine,* 44**,** 1503-1517.

Gleason, M. E. J., Iida, M., Shrout, P. E. & Bolger, N. 2008. Receiving support as a mixed blessing: evidence for dual effects of support on psychological outcomes. *Journal of Personality and Social Psychology,* 94**,** 824.

Glei, D. A., Landau, D. A., Goldman, N., Chuang, Y.-L., Rodriguez, G. & Weinstein, M. 2005. Participating in social activities helps preserve cognitive function: an analysis of a longitudinal, population-based study of the elderly. *International Journal of Epidemiology,* 34**,** 864-871.

Glymour, M. M., Weuve, J., Berkman, L. F., Kawachi, I. & Robins, J. M. 2005. When is baseline adjustment useful in analyses of change? An example with education and cognitive change. *American journal of epidemiology,* 162**,** 267-278.

Glymour, M. M., Weuve, J., Fay, M. E., Glass, T. & Berkman, L. F. 2008. Social ties and cognitive recovery after stroke: Does social integration promote cognitive resilience? . *Neuroepidemiology,* 31**,** 10-20.

Golden, J., Conroy, R. M., Bruce, I., Denihan, A., Greene, E., Kirby, M. & Lawlor, B. A. 2009. Loneliness, social support networks, mood and wellbeing in community ‐ dwelling elderly. *International journal of geriatric psychiatry,* 24**,** 694-700.

Goodman, A. & Symons, M. 2013. Evidence-based campaigning on loneliness in older age: an update from the Campaign to End Loneliness. *Working with Older People,* 17**,** 146-156.

Gottlieb, B. H. & Bergen, A. E. 2010. Social support concepts and measures. *Journal of psychosomatic research,* 69**,** 511-520.

Gouldner, A. W. 1960. The norm of reciprocity: A preliminary statement. *American Sociological Review***,** 161-178.

Gow, A. J., Corley, J., Starr, J. & Deary, I. 2013. Which Social Network or Support Factors are Associated with Cognitive Abilities in Old Age. *Gerontology,* 59**,** 454-463.

Gow, A. J., Corley, J., Starr, J. M. & Deary, I. J. 2012. Reverse causation in activity-cognitive ability associations: the Lothian Birth Cohort 1936. *Psychology and Aging,* 27**,** 250.

Grant, N., Hamer, M. & Steptoe, A. 2009. Social isolation and stress-related cardiovascular, lipid, and cortisol responses. *Annals of Behavioral Medicine,* 37**,** 29-37.

Gray, A. 2009. The social capital of older people. *Ageing and Society,* 29**,** 5-31.

Green, A. F., Rebok, G. & Lyketsos, C. G. 2008. Influence of social network characteristics on cognition and functional status with aging. *International Journal of Geriatric Psychiatry,* 23**,** 972-978.

Grimm, K. J. 2007. Multivariate longitudinal methods for studying developmental relationships between depression and academic achievement. *International Journal of Behavioral Development,* 31**,** 328-339.

Grundy, E. & Farquhar, M. 1995. Changes in network composition among the very old living in inner London. *Journal of Cross-Cultural Gerontology,* 10**,** 331-347.

Gurung, R. A. R., Taylor, S. E. & Seeman, T. E. 2003. Accounting for changes in social support among married older adults: Insights from the MacArthur Studies of Successful Aging. . *Psychology and Aging,* 18**,** 487-496.

Hagan, R., Manktelow, R., Taylor, B. J. & Mallett, J. 2014. Reducing loneliness amongst older people: a systematic search and narrative review. *Aging & mental health,* 18**,** 683-693.

Håkansson, K., Rovio, S., Helkala, E. L., Vilska, A. R., Winblad, B., Soininen, H., Nissinen, A., Mohammed, A. H. & Kivipelto, M. 2009. Association between mid-life marital status and cognitive function in later life: population based cohort study. *British Medical Journal,* 339**,** b24642.

Hall, B. H., Mairesse, J. & Turner, L. 2007. Identifying age, cohort, and period effects in scientific research productivity: Discussion and illustration using simulated and actual data on French physicists. *Econ. Innov. New Techn.,* 16**,** 159-177.

Hamer, M. & Chida, Y. 2009. Physical activity and risk of neurodegenerative disease: a systematic review of prospective evidence. *Psychological medicine,* 39**,** 3.

Harper, S. 2006. Chapter 11: Mature societies: planning for our future selves. *In:* Harper, S. (ed.) *Ageing Societies: Myths, Challenges and Opportunities.* London: Hodder Arnold,271-299.

Harvey, I. S. & Alexander, K. 2012. Perceived Social Support and Preventive Health Behavioral Outcomes among Older Women. *Journal of Cross-Cultural Gerontology***,** 1-16.

Hayden, K. M., Reed, B. R., Manly, J. J., Tommet, D., Pietrzak, R. H., Chelune, G. J., Yang, F. M., Revell, A. J., Bennett, D. A. & Jones, R. N. 2011. Cognitive decline in the elderly: an analysis of population heterogeneity. *Age and Ageing,* 40**,** 684-689.

He, C. & Ye, J. 2014. Lonely Sunsets: Impacts of Rural–urban Migration on the Left‐behind Elderly in Rural China. *Population, Space and Place,* 20**,** 352-369.

Hedden, T. & Gabrieli, J. D. 2004. Insights into the ageing mind: a view from cognitive neuroscience. *Nature reviews neuroscience,* 5**,** 87-96.

Hemingway, H. & Marmot, M. 1999. Evidence based cardiology: psychosocial factors in the aetiology and prognosis of coronary heart disease: systematic review of prospective cohort studies. *BMJ: British Medical Journal,* 318**,** 1460.

Heritage, Z., Wilkinson, R. G., Grimaud, O. & Pickett, K. E. 2008. Impact of social ties on self reported health in France: Is everyone affected equally? *BMC Public Health,* 8**,** 243.

Herlofson, K. & Hagestad, G. O. 2011. Challenges in moving from macro to micro: Population and family structures in ageing societies. *Demographic Research,* 25**,** 337-370.

Hertzog, C., Kramer, A. F., Wilson, R. S. & Lindenberger, U. 2008. Enrichment Effects on Adult Cognitive Development Can the Functional Capacity of Older Adults Be Preserved and Enhanced? *Psychological Science in the Public Interest,* 9**,** 1-65.

Higgs, P., Hyde, M., Wiggins, R. & Blane, D. 2003. Researching quality of life in early old age: the importance of the sociological dimension. *Social Policy & Administration,* 37**,** 239-252.

Hofer, S. M. & Hoffman, L. 2007. Statistical analysis with incomplete data: A developmental perspective. *In:* Little, T., Bovaird, J. & Card, N. (eds.) *Modeling* *ecological and contextual effects in longitudinal studies of human development.* Mahwah, NJ:LEA: Lawrence Erlbaum Associates Publishers,13-32.

Hofer, S. M. & Sliwinski, M. J. 2001. Understanding ageing. *Gerontology,* 47**,** 341-352.

Hofer, S. M. & Sliwinski, M. J. 2006. Design and analysis of longitudinal studies of aging. *In:* Birren, J., E. & Schaie, K. W. (eds.) *Handbook of the Psychology of Aging.* Amsterdam: Elseriver Academic Press,15-37.

Hoffman, L. 2012. Considering alternative metrics of time: Does anybody really know what "time" is? *Advances in longitudinal methods in the social and behavioral sciences* In J. Harring & G. Hancock ed. Charlotte, NC: Information Age Publishing.,255-287.

Hoffman, L., Hofer, S. M. & Sliwinski, M. J. 2011. On the confounds among retest gains and age-cohort differences in the estimation of within-person change in longitudinal studies: A simulation study. *Psychology and Aging,* 26**,** 778-791.

Hogan, B. E., Linden, W. & Najarian, B. 2002. Social support interventions: Do they work? *Clinical Psychology Review,* 22**,** 381-440.

Holt-Lunstad, J., Smith, T. B. & Layton, J. B. 2010. Social relationships and mortality risk: a meta-analytic review. *PLoS Medicine,* 7**,** e1000316.

Holtzman, R. E., Rebok, G. W., Saczynski, J. S., Kouzis, A. C., Wilcox Doyle, K. & Eaton, W. W. 2004. Social network characteristics and cognition in middle-aged and older adults. *Journals of Gerontology Series B-Psychological Sciences & Social Sciences,* 59**,** P278-284.

Horn, J. L. & Cattell, R. B. 1967. Age differences in fluid and crystallized intelligence. *Acta psychologica,* 26**,** 107-129.

House, J. S. 1981. *Work stress and social support,* MA, Addison-Wesley Publishing Company Reading.

House, J. S. Social support and social structure. Sociological Forum, 1987. Springer, 135-146.

House, J. S., Landis, K. R. & Umberson, D. 1988a. Social relationships and health. *Science,* 241**,** 540-545.

House, J. S., Umberson, D. & Landis, K. R. 1988b. Structures and processes of social support. *Annual Review of Sociology,* 14**,** 293-318.

House of Lords. 2013. *Ready for Ageing?* [Online]. London: Select Committee on Public Service and Demographic Change. Available: http://www.cpahq.org/cpahq/cpadocs/UK%20Parliament%20HOL%20Ready%20for%20the%20Ageing.pdf [Accessed 3rd November 2014].

Hu, L. t. & Bentler, P. M. 1999. Cutoff criteria for fit indexes in covariance structure analysis: Conventional criteria versus new alternatives. *Structural Equation Modeling: A Multidisciplinary Journal,* 6**,** 1-55.

Hughes, T. F. 2009. The role of lifestyle factors in cognitive aging and dementia. *Dissertation Abstracts International Section A: Humanities and Social Sciences,* 70**,** s.652.

Hughes, T. F., Andel, R., Small, B. J., Borenstein, A. R. & Mortimer, J. A. 2008. The association between social resources and cognitive change in older adults: evidence from the Charlotte County Healthy Aging Study. *Journals of Gerontology Series B-Psychological Sciences & Social Sciences,* 63**,** P241-P244.

Hultsch, D. F., Hertzog, C., Small, B. J. & Dixon, R. A. 1999. Use it or lose it: engaged lifestyle as a buffer of cognitive decline in aging? *Psychology and Aging; Psychology and Aging,* 14**,** 245.

Hyde, M., Wiggins, R. D., Higgs, P. & Blane, D. B. 2003. A measure of quality of life in early old age: the theory, development and properties of a needs satisfaction model (CASP-19). *Aging & mental health,* 7**,** 186-194.

Independent Age. 2014. *2030 Vision: what we have learnt* [Online]. London, UK: Independent Age. Available: http://ageactionalliance.org/wordpress/wp-content/uploads/2014/12/2030-Vision-what-we-have-learnt.pdf [Accessed 4th August 2015].

Institute of Medicine 2015. *Cognitive Aging: Progress in Understanding and Opportunities for Action,* Washington, DC, The National Academies Press.

Iparraguirre, J. 2015. *Age UK Chief Economist's Report* [Online]. UK,London: Age UK. Available: http://www.ageuk.org.uk/Documents/EN-GB/For-professionals/Research/Chief_Economist's_Report_summer_2015.pdf?dtrk=true [Accessed 30th May 2015].

Jerrome, D. & Wenger, G. C. 1999. Stability and change in late-life friendships. *Ageing and Society,* 19**,** 661-676.

Johnson, J. G., Cohen, P., Dohrenwend, B. P., Link, B. G. & Brook, J. S. 1999. A longitudinal investigation of social causation and social selection processes involved in the association between socioeconomic status and psychiatric disorders. *Journal of abnormal psychology,* 108**,** 490-499.

Jopling, K. 2015. *Promising apporaches to reducing loneliness and isolation in later life* [Online]. UK:London: Campaing to end loneliness, Age UK Available: http://www.campaigntoendloneliness.org/wp-content/uploads/Promising-approaches-to-reducing-loneliness-and-isolation-in-later-life.pdf [Accessed 1st February 2015].

Jorm, A. F. 2001. History of depression as a risk factor for dementia: an updated review. *Australian and New Zealand Journal of Psychiatry,* 35**,** 776-781.

Jung, T. & Wickrama, K. 2008. An introduction to latent class growth analysis and growth mixture modeling. *Social and Personality Psychology Compass,* 2**,** 302-317.

Kaffashian, S., Dugravot, A., Nabi, H., Batty, G. D., Brunner, E., Kivimäki, M. & Singh-Manoux, A. 2011. Predictive utility of the Framingham general cardiovascular disease risk profile for cognitive function: evidence from the Whitehall II study. *European heart journal,* 32**,** 2326-2332.

Kahn, R. L. & Antonucci, T. C. 1980. Convoys over the life course: Attachment, roles, and social support. *In:* Baltes, P. B. & Brim, O. G. (eds.) *Life-span development and behavior.* New York: Academic Press,253-286.

Kaniasty, K. & Norris, F. H. 2008. Longitudinal linkages between perceived social support and posttraumatic stress symptoms: Sequential roles of social causation and social selection. *Journal of Traumatic Stress,* 21**,** 274-281.

Karlamangla, A. S., Miller-Martinez, D., Aneshensel, C. S., Seeman, T. E., Wight, R. G. & Chodosh, J. 2009. Trajectories of cognitive function in late life in the United States: demographic and socioeconomic predictors. *American journal of epidemiology,* 170**,** 331-342.

Karp, A., Kåreholt, I., Qiu, C., Bellander, T., Winblad, B. & Fratiglioni, L. 2004. Relation of education and occupation-based socioeconomic status to incident Alzheimer's disease. *American journal of epidemiology,* 159**,** 175-183.

Karp, A., Paillard-Borg, S., Wang, H.-X., Silverstein, M., Winblad, B. & Fratiglioni, L. 2006. Mental, physical and social components in leisure activities equally contribute to decrease dementia risk. *Dementia and geriatric cognitive disorders,* 21**,** 65-73.

Katz, S., Downs, T. D., Cash, H. R. & Grotz, R. C. 1970. Progress in development of the index of ADL. *The Gerontologist,* 10**,** 20-30.

Kawachi, I. & Berkman, L. 2000. Social cohesion, social capital, and health. *In:* Berkman Lf & I, K. (eds.) *Social epidemiology.* New York: Oxford University Press,174-190.

Kawachi, I. & Berkman, L. F. 2001. Social ties and mental health. *Journal of Urban health,* 78**,** 458-467.

Keller-Cohen, D., Fiori, K., Toler, A. & Bybee, D. 2006. Social relations, language and cognition in the'oldest old'. *Ageing and Society,* 26**,** 585-606.

Ki, M., Sacker, A., Kelly, Y. & Nazroo, J. 2011. Health selection operating between classes and across employment statuses. *Journal of Epidemiology and Community Health,* 65**,** 1132-1139.

Kiecolt-Glaser, J. K., Gouin, J. P. & Hantsoo, L. 2010. Close relationships, inflammation, and health. *Neuroscience & Biobehavioral Reviews,* 35**,** 33-38.

Kim, H. S., Sherman, D. K. & Taylor, S. E. 2008. Culture and social support. *American psychologist,* 63**,** 518.

Knecht, S., Wersching, H., Lohmann, H., Bruchmann, M., Duning, T., Dziewas, R., Berger, K. & Ringelstein, E. B. 2008. High-normal blood pressure is associated with poor cognitive performance. *Hypertension,* 51**,** 663-668.

Knight, B. G. & Losada, A. 2011. Family caregiving for cognitively or physically frail older adults: Theory, research and practice. *In:* Schaie, K. W. & Willis, S. L. (eds.) *Handbook of the Psychology of Aging.* 7th ed. San Diego, USA: Academic Press,353-365.

Knopman, D., Boland, L., Mosley, T., Howard, G., Liao, D., Szklo, M., McGovern, P. & Folsom, A. 2001. Cardiovascular risk factors and cognitive decline in middle-aged adults. *Neurology,* 56**,** 42-48.

Kohli, M., Hank, K. & Künemund, H. 2009. The social connectedness of older Europeans: patterns, dynamics and contexts. *Journal of European Social Policy,* 19**,** 327-340.

Kouvonen, A., De Vogli, R., Stafford, M., Shipley, M. J., Marmot, M. G., Cox, T., Vahtera, J., Väänänen, A., Heponiemi, T. & Singh-Manoux, A. 2012. Social support and the likelihood of maintaining and improving levels of physical activity: the Whitehall II Study. *The European Journal of Public Health,* 22**,** 514-518.

Kouvonen, A., Stafford, M., De Vogli, R., Shipley, M. J., Marmot, M. G., Cox, T., Vahtera, J., Väänänen, A., Heponiemi, T. & Singh-Manoux, A. 2011. Negative Aspects of Close Relationships as Predictor of Increase in Body Mass Index and Waist Circumference: the Whitehall II Study. *American Journal of Public Health,* 101**,** 1474-1480.

Kramer, A. F., Bherer, L., Colcombe, S. J., Dong, W. & Greenough, W. T. 2004. Environmental influences on cognitive and brain plasticity during aging. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences,* 59**,** M940-M957.

Krause, N. 1999. Assessing change in social support during late life. *Research on aging,* 21**,** 539-569.

Krause, N. 2005. Negative Interaction and Heart Disease in Late Life Exploring Variations by Socioeconomic Status. *Journal of aging and health,* 17**,** 28-55.

Krause, N. & Rook, K. S. 2003. Negative interaction in late life: Issues in the stability and generalizability of conflict across relationships. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences,* 58**,** P88-P99.

Krause, N. & Shaw, B. A. 2002. Negative interaction and changes in functional disability during late life. *Journal of Social and Personal Relationships,* 19**,** 339-359.

Kreuter, F. & Muthén, B. 2008. Analyzing criminal trajectory profiles: Bridging multilevel and group-based approaches using growth mixture modeling. *Journal of Quantitative Criminology,* 24**,** 1-31.

Kuh, D., Cooper, R., Richards, M., Gale, C., von Zglinicki, T. & Guralnik, J. 2012. A life course approach to healthy ageing: the HALCyon programme. *Public health,* 126**,** 193-195.

Kumar, S., Calvo, R., Avendano, M., Sivaramakrishnan, K. & Berkman, L. F. 2012. Social support, volunteering and health around the world: Cross-national evidence from 139 countries. *Social science & medicine*.

Kumari, M. & Marmot, M. 2005. Diabetes and cognitive function in a middle-aged cohort Findings from the Whitehall II study. *Neurology,* 65**,** 1597-1603.

Lachman, M. E. 2004. Development in midlife. *Annu. Rev. Psychol.,* 55**,** 305-331.

Lachman, M. E. & Agrigoroaei, S. 2010. Promoting functional health in midlife and old age: Long-term protective effects of control beliefs, social support, and physical exercise. *PLoS one,* 5**,** e13297.

Lakey, B. & Cassady, P. B. 1990. Cognitive processes in perceived social support. *Journal of Personality and Social Psychology,* 59**,** 337.

Landy, R. 2012. *The influence of life course socioeconomic position on cognitive function and cognitive decline in older age: the impact of missing data.* PhD thesis, University College London.

Lang, F. R. 2001. Regulation of social relationships in later adulthood. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences,* 56**,** P321-P326.

Lang, F. R., Rieckmann, N. & Baltes, M. M. 2002. Adapting to aging losses: do resources facilitate strategies of selection, compensation, and optimization in everyday functioning? *Journals of Gerontology Series B-Psychological Sciences & Social Sciences,* 57**,** P501-509.

Lang, F. R., Wagner, J. & Neyer, F. J. 2009. Interpersonal functioning across the lifespan: Two principles of relationship regulation. *Advances in life course research,* 14**,** 40-51.

Langford, C. P. H., Bowsher, J., Maloney, J. P. & Lillis, P. P. 1997. Social support: a conceptual analysis. *Journal of advanced nursing,* 25**,** 95-100.

Laslett, P. 1991. *Fresh map of life: the emergence of the Third Age,* Cambridge, MA, Harvard University Press.

Laursen, B. P. & Hoff, E. 2006. Person-centered and variable-centered approaches to longitudinal data. *Merrill-Palmer Quarterly,* 52**,** 377-389.

Lawton, M. P. & Brody, E. M. 1969. Assessment of older people: self-maintaining and instrumental activities of daily living. *The Gerontologist,* 9**,** 179-186.

Layte, R., Sexton, E. & Savva, G. 2013. Quality of life in older age: evidence from an Irish cohort study. *Journal of the American Geriatrics Society,* 61**,** S299-S305.

Lee, Y., Back, J. H., Kim, J., Kim, S.-H., Na, D. L., Cheong, H.-K., Hong, C. H. & Kim, Y. G. 2010. Systematic review of health behavioral risks and cognitive health in older adults. *International psychogeriatrics,* 22**,** 174-187.

Lee, Y., Kim, J. & Back, J. H. 2009. The influence of multiple lifestyle behaviors on cognitive function in older persons living in the community. *Preventive medicine,* 48**,** 86-90.

Lenehan, M. E., Summers, M. J., Saunders, N. L., Summers, J. J. & Vickers, J. C. 2015. Relationship between education and age ‐ related cognitive decline: a review of recent research. *Psychogeriatrics*.

Leoutsakos, J. M. S., Muthen, B. O., Breitner, J. & Lyketsos, C. G. 2012. Effects of non ‐ steroidal anti ‐ inflammatory drug treatments on cognitive decline vary by phase of pre ‐ clinical Alzheimer disease: findings from the randomized controlled Alzheimer's Disease Anti ‐ inflammatory Prevention Trial. *International journal of geriatric psychiatry,* 27**,** 364-374.

Lewis, P. A., Rezaie, R., Brown, R., Roberts, N. & Dunbar, R. I. M. 2011. Ventromedial prefrontal volume predicts understanding of others and social network size. *Neuroimage,* 57**,** 1624-1629.

Lezak, M. D., Howieson, D.B., Loring, D.W 2004. *In:* Hannay, J. H., Fischer, J.S. (ed.) *Neuropsychological assessment.* 4 th ed. New York: Oxford university press, pp. 429-498.

Li, T. & Zhang, Y. 2015. Social Network Types and the Health of Older Adults: Exploring Reciprocal Associations. *Social science & medicine*.

Liao, J. & Brunner, E. J. 2015. Structural and functional measures of social relationships and quality of life among older adults: does chronic disease status matter? *Quality of Life Research***,** 1-12.

Lieberman, M. D. 2007. Social cognitive neuroscience: a review of core processes. *Annu. Rev. Psychol.,* 58**,** 259-289.

Linehan, T., Bottery, S., Kaye, A., Millar, L., Sinclair, D. & Waston, J. 2014. *2030 visions, The best-and the worst-futures for older people in the UK* [Online]. Independent Age, the International Longevity Center-UK (ILC-UK), the Ready for Ageing Alliance's Available: http://www.ilcuk.org.uk/index.php/publications/publication_details/2030_vision_the_best_and_worst_futures_for_older_people_in_the_uk [Accessed 21st May 2015].

Little, R. J. & Rubin, D. B. 2002. *Statistical analysis with missing data,* New York, Wiley

Litwin, H. & Stoeckel, K. J. 2014. Confidant network types and well-being among older Europeans. *The Gerontologist,* 54**,** 762-772.

Lloyd, J. 2014. *The Bigger Picture, Policy insights and recommendations* [Online]. London,UK: the Strategic Society Centre and Independent Age. Available: http://www.independentage.org/media/847199/biggerpicture_policyfinal.pdf [Accessed 21st June 2015].

Lo, Y., Mendell, N. R. & Rubin, D. B. 2001. Testing the number of components in a normal mixture. *Biometrika,* 88**,** 767-778.

Lövdén, M., Bergman, L., Adolfsson, R., Lindenberger, U. & Nilsson, L.-G. 2005a. Studying individual aging in an interindividual context: typical paths of age-related, dementia-related, and mortality-related cognitive development in old age. *Psychology and Aging,* 20**,** 303.

Lövdén, M., Ghisletta, P. & Lindenberger, U. 2005b. Social participation attenuates decline in perceptual speed in old and very old age. *Psychology and Aging,* 20**,** 423.

Low, L.-F., Harrison, F. & Lackersteen, S. M. 2013. Does Personality Affect Risk for Dementia? A Systematic Review and Meta-Analysis. *The American Journal of Geriatric Psychiatry*.

Marmot, M., Banks, J., Blundell, R., Lessof, C. & Nazroo, J. 2003. *Health, wealth and lifestyles of the older population in England: the 2002 English Longitudinal study of ageing,* London, Institute for Fiscal Studies.

Marmot, M. & Brunner, E. 2005. Cohort profile: the Whitehall II study. *International journal of epidemiology,* 34**,** 251-256.

Marsiske, M. & Margrett, J. A. 2006. Everyday problem solving and decision making. *In:* Birren, J., E. & Schaie, K. W. (eds.) *Handbook of the Psychology of Aging.* 6th ed. Amsterdam: Elseriver Academic Press,315-342.

Martire, L. M., Schulz, R., Mittelmark, M. B. & Newsom, J. T. 1999. Stability and change in older adults' social contact and social support: the Cardiovascular Health Study. *J Gerontol B Psychol Sci Soc Sci,* 54**,** S302-311.

Marzano, R. J., Kendall, J.S., Paynter, D.E 2005. Appendix: a list of essential words by grade level. *In:* Paynter, D. E., Bodrova, E.,Doty,J.K. (ed.) *For the Love of Words: Vocabulary Instruction that Works, Grades K-6.* Jossey-Bass, San Francisco pp. 127-202.

Mavandadi, S., Rook, K. S. & Newsom, J. T. 2007. Positive and negative social exchanges and disability in later life: an investigation of trajectories of change. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences,* 62**,** S361-S370.

McArdle, J. & Nesselroade, J. 1994. Structuring data to study development and change. *In:* Cohen.S.H. & Reese, H. W. (eds.) *Life-span developmental psychology: Methodological innovations.* Hillsdale,NJ: Erlbaum 223-267.

McArdle, J. J. 2009. Latent variable modeling of differences and changes with longitudinal data. *Annual review of psychology,* 60**,** 577-605.

McArdle, J. J. & Grimm, K. J. 2010. Five steps in latent curve and latent change score modeling with longitudinal data. *Longitudinal research with latent variables.* Springer,245-273.

McArdle, J. J. & Hamagami, F. 2001. Latent difference score structural models for linear dynamic analyses with incomplete longitudinal data. *In:* Collins, L. M. & Sayer, A. G. (eds.) *New methods for the analysis of change* Washington, DC: American Psychological Association,139-175.

McArdle, J. J., Hamgami, F., Jones, K., Jolesz, F., Kikinis, R., Spiro, A. & Albert, M. S. 2004. Structural modeling of dynamic changes in memory and brain structure using longitudinal data from the normative aging study. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences,* 59**,** P294-P304.

McIntosh, C. N. 2013. Pitfalls in subgroup analysis based on growth mixture models: a commentary on van Leeuwen et al.(2012). *Quality of Life Research***,** 1-5.

McLachlan, G. J. 1987. On bootstrapping the likelihood ratio test stastistic for the number of components in a normal mixture. *Applied statistics***,** 318-324.

McLaughlin, D., Vagenas, D., Pachana, N. A., Begum, N. & Dobson, A. 2010. Gender differences in social network size and satisfaction in adults in their 70s. *Journal of Health Psychology,* 15**,** 671-679.

Meaney, M. J., Aitken, D. H., Bhatnagar, S. & Sapolsky, R. M. 1991. Postnatal handling attenuates certain neuroendocrine, anatomical, and cognitive dysfunctions associated with aging in female rats. *Neurobiology of aging,* 12**,** 31-38.

Meaney, M. J., Aitken, D. H., Van Berkel, C. & Bhatnagar, S. 1988. Effect of neonatal handling on age-related impairments associated with the hippocampus. *Science*.

Meier, R. 2013. *Relationships: the mssing link in public health.* [Online]. London,UK Relationships Alliance. Available: http://www.relate.org.uk/files/relate/publication-relationships-missing-link-2013.pdf [Accessed 23rd June 2015].

Micceri, T. 1989. The unicorn, the normal curve, and other improbable creatures. *Psychological bulletin,* 105**,** 156.

Middleton, L. E. & Yaffe, K. 2009. Promising strategies for the prevention of dementia. *Archives of neurology,* 66**,** 1210-1215.

Mirza, S. S., de Bruijn, R. F., Direk, N., Hofman, A., Koudstaal, P. J., Ikram, M. A. & Tiemeier, H. 2014. Depressive symptoms predict incident dementia during short-but not long-term follow-up period. *Alzheimer's & Dementia*.

Mitchell, J. C. 1974. Social networks. *Annual Review of Anthropology,* 3**,** 279-299.

Muniz-Terrera, G., Matthews, F., Dening, T., Huppert, F. A. & Brayne, C. 2009. Education and trajectories of cognitive decline over 9 years in very old people: methods and risk analysis. *Age and ageing,* 38**,** 277-282.

Muniz-Terrera, G., van den Hout, A., Piccinin, A. M., Matthews, F. E. & Hofer, S. M. 2012. Investigating Terminal Decline: Results From a UK Population-Based Study of Aging. *Psychol Aging,* 28**,** 377-385.

Muramatsu, N., Yin, H. & Hedeker, D. 2010. Functional declines, social support, and mental health in the elderly: Does living in a state supportive of home and community-based services make a difference? *Social science & medicine,* 70**,** 1050-1058.

Murphy, M. 2011. Long‐Term Effects of the Demographic Transition on Family and Kinship Networks in Britain. *PoPulation and develoPment review,* 37**,** 55-80.

Murphy, M., Martikainen, P. & Pennec, S. 2006. Demographic change and the supply of potential family supporters in Britain, Finland and France in the period 1911–2050/Changements démographiques et disponibilité des soutiens familiaux en Grande-Bretagne, en Finlande et en France entre 1911 et 2050. *European Journal of Population/Revue européenne de Démographie,* 22**,** 219-240.

Muthén, B. 2004. Latent variable analysis: Growth mixture modeling and related techniques for longitudinal data. *In:* Kaplan, D. (ed.) *Handbook of quantitative methodology for the social sciences.* . Newbury Park, CA: : Sage Publications,345-368.

Muthén, B. & Asparouhov, T. 2015. Growth mixture modeling with non‐normal distributions. *Statistics in medicine,* 34**,** 1041-1058.

Muthén, B. O. 2002. Beyond SEM: General latent variable modeling. *Behaviormetrika,* 29**,** 81-118.

Muthén, L. & Muthén, B. 2012. *Mplus Users' Guide. 7th edition,* Los Angeles, CA;.

Nagin, D. & Nagin, D. 2009. *Group-based modeling of development*, Harvard University Press.

Nagin, D. S. & Tremblay, R. E. 2001. Analyzing developmental trajectories of distinct but related behaviors: a group-based method. *Psychological methods,* 6**,** 18.

Netuveli, G., Pikhart, H., Bobak, M. & Blane, D. 2012. Generic quality of life predicts all-cause mortality in the short term: evidence from British Household Panel Survey. *Journal of Epidemiology and Community Health,* 66**,** 962-966.

Newsom, J. T., Nishishiba, M., Morgan, D. L. & Rook, K. S. 2003. The relative importance of three domains of positive and negative social exchanges: a longitudinal model with comparable measures. *Psychology and Aging,* 18**,** 746-754.

Newsom, J. T., Rook, K. S., Nishishiba, M., Sorkin, D. H. & Mahan, T. L. 2005. Understanding the relative importance of positive and negative social exchanges: Examining specific domains and appraisals. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences,* 60**,** P304-P312.

Nylund, K. L., Asparouhov, T. & Muthén, B. O. 2007. Deciding on the number of classes in latent class analysis and growth mixture modeling: A Monte Carlo simulation study. *Structural Equation Modeling,* 14**,** 535-569.

Orth-Gomér, K. & Undén, A. L. 1987. The measurement of social support in population surveys. *Social science & medicine,* 24**,** 83-94.

Ouwehand, C., de Ridder, D. T. & Bensing, J. M. 2007. A review of successful aging models: Proposing proactive coping as an important additional strategy. *Clinical psychology review,* 27**,** 873-884.

Ownby, R. L., Crocco, E., Acevedo, A., John, V. & Loewenstein, D. 2006. Depression and risk for Alzheimer disease: systematic review, meta-analysis, and metaregression analysis. *Archives of general psychiatry,* 63**,** 530-538.
Pahl, R. & Pevalin, D. J. 2005. Between family and friends: a longitudinal study of friendship choice. *The British journal of sociology,* 56**,** 433-450.
Park, D. C., Gutchess, A. H., Meade, M. L. & Stine-Morrow, E. A. 2007. Improving cognitive function in older adults: nontraditional approaches. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences,* 62**,** 45-52.
Petersen, R. C., Doody, R., Kurz, A., Mohs, R. C., Morris, J. C., Rabins, P. V., Ritchie, K., Rossor, M., Thal, L. & Winblad, B. 2001. Current concepts in mild cognitive impairment. *Archives of neurology,* 58**,** 1985.
Peugh, J. & Fan, X. 2012. How Well Does Growth Mixture Modeling Identify Heterogeneous Growth Trajectories? A Simulation Study Examining GMM's Performance Characteristics. *Structural Equation Modeling: A Multidisciplinary Journal,* 19**,** 204-226.
Piccinin, A. M., Muniz, G., Sparks, C. & Bontempo, D. E. 2011. An evaluation of analytical approaches for understanding change in cognition in the context of aging and health. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences,* 66**,** i36-i49.
Pinquart, M. & Duberstein, P. R. 2010. Associations of social networks with cancer mortality: a meta-analysis. *Critical reviews in oncology/hematology,* 75**,** 122.
Pinquart, M. & Sörensen, S. 2000. Influences of socioeconomic status, social network, and competence on subjective well-being in later life: a meta-analysis. *Psychology and Aging,* 15**,** 187.
Plassman, B. L., Williams Jr, J. W., Burke, J. R., Holsinger, T. & Benjamin, S. 2010. Systematic review: factors associated with risk for and possible prevention of cognitive decline in later life. *Annals of internal medicine,* 153**,** 182.
Pope, S. K., Shue, V. M. & Beck, C. 2003. Will a healthy lifestyle help prevent Alzheimer's disease? *Annual Review of Public Health,* 24**,** 111-132.
Power, M., Champion, L. & Aris, S. 1988. The development of a measure of social support: the Significant Others (SOS) Scale. *British Journal of Clinical Psychology,* 27**,** 349-358.
Prince, M., Guerchet, M. & Prina, M. 2013a. The Global Impact of Dementia 2013-2050. London,UK: Alzheimer's Disease International.
Prince, M., Prina, M., Guerchet, M. & Alzheimer’s Disease International 2013b. Journey of Caring: An analysis of long-term care for dementia. *World Alzheimer Report 2013.* London: Alzheimer’s Disease International.
Qiu, C., Winblad, B. & Fratiglioni, L. 2005. The age-dependent relation of blood pressure to cognitive function and dementia. *The Lancet Neurology,* 4**,** 487-499.
Rabbitt, P. 1993. Does it all go together when it goes? The Nineteenth Bartlett Memorial Lecture. *The Quarterly Journal of Experimental Psychology,* 46**,** 385-434.
Rabbitt, P., Diggle, P., Holland, F. & McInnes, L. 2004. Practice and drop-out effects during a 17-year longitudinal study of cognitive aging. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences,* 59**,** P84-P97.
Rabbitt, P., Diggle, P., Smith, D., Holland, F. & Mc Innes, L. 2001. Identifying and separating the effects of practice and of cognitive ageing during a large longitudinal study of elderly community residents. *Neuropsychologia,* 39**,** 532-543.
Rabbitt, P., Lunn, M., Ibrahim, S. & McInnes, L. 2009. Further analyses of the effects of practice, dropout, sex, socio-economic advantage, and recruitment cohort differences during the University of Manchester longitudinal study of cognitive

change in old age. *The Quarterly Journal of Experimental Psychology,* 62**,** 1859-1872.

Raento, M., Oulasvirta, A. & Eagle, N. 2009. Smartphones an emerging tool for social scientists. *Sociological methods & research,* 37**,** 426-454.

Ram, N. & Grimm, K. 2007. Using simple and complex growth models to articulate developmental change: Matching theory to method. *International Journal of Behavioral Development,* 31**,** 303-316.

Ram, N. & Grimm, K. J. 2009. Methods and measures: growth mixture modeling: a method for identifying differences in longitudinal change among unobserved groups. *International Journal of Behavioral Development,* 33**,** 565-576.

Ready for Ageing Alliance 2014. Getting Ready for Ageing: a manifesto for action. Age UK, Alzheimer's Society, Anchor, Carers UK, Centre for Policy on Ageing, the International Longevity Centre – UK (ILC-UK), Independent Age and Joseph Rowntree Foundation.

Rechel, B., Grundy, E., Robine, J.-M., Cylus, J., Mackenbach, J. P., Knai, C. & McKee, M. 2013. Ageing in the European Union. *The Lancet,* 381**,** 1312-1322.

Reed, A. E. & Carstensen, L. L. 2012. The theory behind the age-related positivity effect. *Frontiers in psychology,* 3**,** 339.

Reis, H. T., Clark, M. S. & Holmes, J. G. 2004. Perceived partner responsiveness as an organizing construct in the study of intimacy and closeness. *Handbook of closeness and intimacy***,** 201-225.

Richards, M. & Deary, I. J. 2005. A life course approach to cognitive reserve: A model for cognitive aging and development? *Annals of Neurology,* 58**,** 617-622.

Richards, M. & Hatch, S. L. 2011. A life course approach to the development of mental skills. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences,* 66**,** i26-i35.

Richards, M. & Sacker, A. 2003. Lifetime antecedents of cognitive reserve. *Journal of Clinical and Experimental Neuropsychology,* 25**,** 614-624.

Riediger, M., Li, S.-C. & Lindenberger, U. 2006. Selection, optimization, and compensation as developmental mechanisms of adaptive resource allocation: Review and preview. *In:* Birren, J., E. & Schaie, K. W. (eds.) *Handbook of the Psychology of Aging.* 6th ed. Amsterdam: Elseriver Academic Press,289-313.

Rippon, I., Kneale, D., de Oliveira, C., Demakakos, P. & Steptoe, A. 2013. Perceived age discrimination in older adults. *Age and ageing,* 43**,** 379-386.

Ritchie, S. J., Bates, T. C., Der, G., Starr, J. M. & Deary, I. J. 2012. Education Is Associated With Higher Later Life IQ Scores, but Not With Faster Cognitive Processing Speed. *Psychology and Aging,* 28**,** 515-521.

Roberts, C., Mort, M. & Milligan, C. 2012. Calling for Care:'Disembodied'work, teleoperators and older people living at home. *Sociology,* 46**,** 490-506.

Robins, J. M., Hernan, M. A. & Brumback, B. 2000. Marginal structural models and causal inference in epidemiology. *Epidemiology,* 11**,** 550-560.

Robitaille, A., Muniz, G., Piccinin, A. M., Johansson, B. & Hofer, S. M. 2012. Multivariate longitudinal modeling of cognitive aging: Associations among change and variation in processing speed and visuospatial ability. *GeroPsych: The Journal of Gerontopsychology and Geriatric Psychiatry,* 25**,** 15.

Rogosa, D. 1980. A critique of cross-lagged correlation. *Psychological bulletin,* 88**,** 245.

Rook, K. S. 1984. The negative side of social interaction: impact on psychological well-being. *Journal of Personality and Social Psychology,* 46**,** 1097.

Rook, K. S. 1994. Assessing the health-related dimensions of older adults' social relationships. *Annual review of gerontology and geriatrics,* 14**,** 142-142.

Rook, K. S. 1998. Investigating the positive and negative sides of personal relationships: Through a lens darkly? *In:* Spitzberg, B. H. & Cupach, W. R. (eds.) *The dark side of close relationships.* Mahwah, NJ: Erlbaum,369-393.

Rook, K. S. 2001. Emotional health and positive versus negative social exchanges: A daily diary analysis. *Applied Developmental Science,* 5**,** 86-97.

Rook, K. S. 2009. Gaps in social support resources in later life: An adaptational challenge in need of further research. *Journal of Social and Personal Relationships,* 26**,** 103-112.

Rook, K. S., August, K. & Sorkin, D. H. 2011. Social network functions and health. *In:* Contrada, R. & Baum, A. (eds.) *The handbook of stress science: Biology, psychology, and health.* New York: Springer,123-135.

Rook, K. S., Luong, G., Sorkin, D. H., Newsom, J. T. & Krause, N. 2012. Ambivalent versus problematic social ties: Implications for psychological health, functional health, and interpersonal coping. *Psychology and Aging,* 27**,** 912.

Ross, C. E. & Mirowsky, J. 2002. Family relationships, social support and subjective life expectancy. *Journal of Health and Social Behavior***,** 469-489.

Roth, A. E. 2005. Sources of individual differences in cognitive functioning (sweden). *Dissertation Abstracts International Section A: Humanities and Social Sciences,* 66.

Roth, G. & Dicke, U. 2005. Evolution of the brain and intelligence. *Trends in cognitive sciences,* 9**,** 250-257.

Rowe, J. W. & Kahn, R. L. 1997. Successful aging. *The Gerontologist,* 37**,** 433-440.

Royall, D. R., Palmer, R., Chiodo, L. K. & Polk, M. J. 2005. Normal rates of cognitive change in successful aging: the freedom house study. *Journal of the International Neuropsychological Society,* 11**,** 899-909.

Sabia, S., Elbaz, A., Dugravot, A., Head, J., Shipley, M., Hagger-Johnson, G., Kivimaki, M. & Singh-Manoux, A. 2012. Impact of smoking on cognitive decline in early old age: the Whitehall II cohort study. *Archives of general psychiatry,* 69**,** 627--635.

Sabia, S., Guéguen, A., Marmot, M. G., Shipley, M. J., Ankri, J. & Singh-Manoux, A. 2010. Does cognition predict mortality in midlife? Results from the Whitehall II cohort study. *Neurobiology of aging,* 31**,** 688-695.

Sabia, S., Nabi, H., Kivimaki, M., Shipley, M. J., Marmot, M. G. & Singh-Manoux, A. 2009. Health behaviors from early to late midlife as predictors of cognitive function the Whitehall II Study. *American journal of epidemiology,* 170**,** 428-437.

Saczynski, J. S., Pfeifer, L. A., Masaki, K., Korf, E. S., Laurin, D., White, L. & Launer, L. J. 2006. The Effect of Social Engagement on Incident Dementia The Honolulu-Asia Aging Study. *American journal of epidemiology,* 163**,** 433-440.

Salthouse, T. A. 1991. *Theoretical perspectives on cognitive aging*, Lawrence Erlbaum.

Salthouse, T. A. 2007. Implications of within-person variability in cognitive and neuropsychological functioning for the interpretation of change. *Neuropsychology,* 21**,** 401.

Salthouse, T. A. 2009. When does age-related cognitive decline begin? *Neurobiology of aging,* 30**,** 507-514.

Salthouse, T. A. 2010a. Influence of age on practice effects in longitudinal neurocognitive change. *Neuropsychology,* 24**,** 563.

Salthouse, T. A. 2010b. Selective review of cognitive aging. *Journal of the International Neuropsychological Society,* 16**,** 754-760.

Salthouse, T. A., Schroeder, D. H. & Ferrer, E. 2004. Estimating retest effects in longitudinal assessments of cognitive functioning in adults between 18 and 60 years of age. *Developmental psychology,* 40**,** 813-822.

Savva, G. M. & Stephan, B. C. 2010. Epidemiological studies of the effect of stroke on incident dementia a systematic review. *Stroke*, 41**,** e41-e46.
Scanlan, J. M., Binkin, N., Michieletto, F., Lessig, M., Zuhr, E. & Borson, S. 2007. Cognitive impairment, chronic disease burden, and functional disability: a population study of older Italians. *American Journal of Geriatric Psych,* 15**,** 716-724.
Schaefer, C., Coyne, J. C. & Lazarus, R. S. 1981. The health-related functions of social support. *Journal of behavioral medicine,* 4**,** 381-406.
Schlecker, M. & Fleischer, F. 2013. *Ethnographies of social support*, Palgrave Macmillan.
Schmidt, R., Schmidt, H., Curb, J. D., Masaki, K., White, L. R. & Launer, L. J. 2002. Early inflammation and dementia: A 25 - year follow - up of the Honolulu - Asia aging study. *Annals of Neurology,* 52**,** 168-174.
Seeman, T. E. & Berkman, L. F. 1988. Structural characteristics of social networks and their relationship with social support in the elderly: who provides support. *Social science & medicine,* 26**,** 737-749.
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 Psychology; Health Psychology,* 20**,** 243-255.
Seeman, T. E., Miller-Martinez, D. M., Stein Merkin, S., Lachman, M. E., Tun, P. A. & Karlamangla, A. S. 2011. Histories of social engagement and adult cognition: midlife in the U.S. study. *Journals of Gerontology Series B-Psychological Sciences & Social Sciences,* 66 Suppl 1**,** i141-152.
Settersten, J. & Richard , A. 2002. Social sources of meaning in later life. *In:* R. A. Weiss & Bass, S. A. (eds.) *Challenges of the third age: Meaning and purpose in later life.* New York: Oxford University Press,55-79.
Shankar, A., Hamer, M., McMunn, A. & Steptoe, A. 2013. Social Isolation and Loneliness: Relationships With Cognitive Function During 4 Years of Follow-up in the English Longitudinal Study of Ageing. *Psychosomatic Medicine,* 75**,** 161-170.
Shankar, A., Rafnsson, S. B. & Steptoe, A. 2014. Longitudinal associations between social connections and subjective wellbeing in the English Longitudinal Study of Ageing. *Psychology & health,* 30**,** 686-698.
Shaw, B. A., Krause, N., Liang, J. & Bennett, J. 2007. Tracking changes in social relations throughout late life. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences,* 62**,** S90-S99.
Shouse, J., Rowe, S. V. & Mast, B. T. 2013. Depression and cognitive functioning as predictors of social network size. *Clincial Gerontologist,* 36**,** 147-161.
Silverstein, M., Chen, X. & Heller, K. 1996. Too much of a good thing? Intergenerational social support and the psychological well-being of older parents. *Journal of Marriage and the Family,* 58**,** 970-982.
Silverwood, R. J., Pierce, M., Hardy, R., Thomas, C., Ferro, C., Savage, C., Sattar, N., Kuh, D. & Nitsch, D. 2013. Early-life overweight trajectory and CKD in the 1946 British Birth Cohort Study. *American journal of kidney diseases,* 62**,** 276-284.
Sims, R. C., Hosey, M., Levy, S.-A., Whitfield, K. E., Katzel, L. I. & Waldstein, S. R. 2014. Distinct Functions of Social Support and Cognitive Function Among Older Adults. *Experimental aging research,* 40**,** 40-59.
Singer, J. D. & Willett, J. B. 2003. *Applied longitudinal data analysis: Modeling change and event occurrence*, Oxford University Press, USA.

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,* 83**,** 486-493.

Singh-Manoux, A., Kivimaki, M., Glymour, M. M., Elbaz, A., Berr, C., Ebmeier, K. P., Ferrie, J. E. & Dugravot, A. 2012. Timing of onset of cognitive decline: results from Whitehall II prospective cohort study. *BMJ,* 344**,** (d7622):7621–7628.

Singh-Manoux, A. & Marmot, M. 2005. High blood pressure was associated with cognitive function in middle-age in the Whitehall II study. *Journal of clinical epidemiology,* 58**,** 1308-1315.

Singh-Manoux, A., Sabia, S., Lajnef, M., Ferrie, J. E., Nabi, H., Britton, A. R., Marmot, M. G. & Shipley, M. J. 2008. History of coronary heart disease and cognitive performance in midlife: the Whitehall II study. *European heart journal,* 29**,** 2100-2107.

Singh ‐ Manoux, A., Marmot, M. G., Glymour, M., Sabia, S., Kivimäki, M. & Dugravot, A. 2011. Does cognitive reserve shape cognitive decline? *Annals of Neurology,* 70**,** 296-304.

Sliwinski, M., Hoffman, L. & Hofer, S. M. 2010. Evaluating convergence of within-person change and between-person age differences in age-heterogeneous longitudinal studies. *Research in human development,* 7**,** 45-60.

Small, B. J. & Bäckman, L. 2007. Longitudinal trajectories of cognitive change in preclinical Alzheimer's disease: a growth mixture modeling analysis. *Cortex,* 43**,** 826-834.

Small, B. J., Dixon, R. A., McArdle, J. J. & Grimm, K. J. 2012. Do changes in lifestyle engagement moderate cognitive decline in normal aging? Evidence from the Victoria Longitudinal Study. *Neuropsychology,* 26**,** 144.

Small, G. W., Silverman, D. H., Siddarth, P., Ercoli, L. M., Miller, K. J., Lavretsky, H., Wright, B. C., Bookheimer, S. Y., Barrio, J. R. & Phelps, M. E. 2006. Effects of a 14-day healthy longevity lifestyle program on cognition and brain function. *American Journal of Geriatric Psych,* 14**,** 538-545.

Smith, K. P. & Christakis, N. A. 2008. Social networks and health. *Annu. Rev. Sociol,* 34**,** 405-429.

Sole-Auro, A. & Crimmins, E. M. 2014. Who cares? A comparison of informal and formal care provision in Spain, England and the USA. *Ageing and society,* 34**,** 495-517.

Sonnenberg, C., Deeg, D., van Tilburg, T., Vink, D., Stek, M. & Beekman, A. 2013. Gender differences in the relation between depression and social support in later life. *International psychogeriatrics,* 25**,** 61-70.

Sorensen, G., Stoddard, A. M., Dubowitz, T., Barbeau, E. M., Bigby, J., Emmons, K. M., Berkman, L. F. & Peterson, K. E. 2007. The influence of social context on changes in fruit and vegetable consumption: results of the healthy directions studies. *American Journal of Public Health,* 97**,** 1216.

Sorkin, D. H. & Rook, K. S. 2006. Dealing with negative social exchanges in later life: coping responses, goals, and effectiveness. *Psychology and Aging,* 21**,** 715.

South, J. 2015. A guide to community-centered approaches for health and wellbeing. *Protecting and improving the nation's health.* London: Public Health England and National Health System.

Stafford, M., McMunn, A., Zaninotto, P. & Nazroo, J. 2011. Positive and negative exchanges in social relationships as predictors of depression: Evidence from the English longitudinal study of aging. *Journal of aging and health,* 23**,** 607-628.

Stansfeld, S., Fuhrer, R. & Shipley, M. 1998a. Types of social support as predictors of psychiatric morbidity in a cohort of British Civil Servants (Whitehall II Study). *Psychological medicine,* 28**,** 881-892.

Stansfeld, S. & Marmot, M. 1992. Deriving a survey measure of social support: the reliability and validity of the Close Persons Questionnaire. *Social science & medicine,* 35**,** 1027-1035.

Stansfeld, S. A. 2006. Social support and social cohesion. *In:* Marmot, M. & Wilkinson, R. (eds.) *Social determinants of health.* 2 ed. New York, US: Oxford University Press,148-171.

Stansfeld, S. A., Bosma, H., Hemingway, H. & Marmot, M. G. 1998b. Psychosocial work characteristics and social support as predictors of SF-36 health functioning: the Whitehall II study. *Psychosomatic medicine,* 60**,** 247-255.

Stansfeld, S. A., Marmot, M. & Wilkinson, R. 2006. Social support and social cohesion. *Social determinants of health,* 2**,** 148-171.

Stansfeld, S. A., Shipley, M. J., Head, J., Fuhrer, R. & Kivimaki, M. 2013. Work Characteristics and Personal Social Support as Determinants of Subjective Well-Being. *PLoS one,* 8**,** e81115.

Staudinger, U. M., Dörner, J. & Mickler, C. 2005. Wisdom and personality. *In:* Sternberg, R. J. & Jordan, J. (eds.) *A handbook of wisdom: Psychological perspectives.* New York: Cambridge University Press,191-219.

Steiger, J. H. 1990. Structural model evaluation and modification: An interval estimation approach. *Multivariate behavioral research,* 25**,** 173-180.

Steptoe, A., Shankar, A., Demakakos, P. & Wardle, J. 2013. Social isolation, loneliness, and all-cause mortality in older men and women. *Proceedings of the National Academy of Sciences*.

Stern, Y. 2002. What is cognitive reserve? Theory and research application of the reserve concept. *Journal of the International Neuropsychological Society,* 8**,** 448-460.

Stern, Y. 2003. The concept of cognitive reserve: a catalyst for research. *Journal of Clinical and Experimental Neuropsychology,* 25**,** 589-593.

Stern, Y. 2009. Cognitive reserve. *Neuropsychologia,* 47**,** 2015-2028.

Sterne, J. A., White, I. R., Carlin, J. B., Spratt, M., Royston, P., Kenward, M. G., Wood, A. M. & Carpenter, J. R. 2009. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. *BMJ,* 338.

Stevens, N. L. & van Tilburg, T. G. 2010. Cohort differences in having and retaining friends in personal networks in later life. *Journal of Social and Personal Relationships,* 28**,** 24-43.

Steverink, N. & Lindenberg, S. 2006. Which social needs are important for subjective well-being? What happens to them with aging? *Psychology and Aging,* 21**,** 281.

Stokes, J. P. 1985. The relation of social network and individual difference variables to loneliness. *Journal of Personality and Social Psychology,* 48**,** 981.

Stone, A. A., Schwartz, J. E., Broderick, J. E. & Deaton, A. 2010. A snapshot of the age distribution of psychological well-being in the United States. *Proceedings of the National Academy of Sciences,* 107**,** 9985-9990.

Stoykova, R., Matharan, F., Dartigues, J. F. & Amieva, H. 2011. Impact of social network on cognitive performances and age-related cognitive decline across a 20-year follow-up. *International Psychogeriatrics,* 23**,** 1405-1412.

Stringhini, S., Berkman, L., Dugravot, A., Ferrie, J. E., Marmot, M., Kivimaki, M. & Singh-Manoux, A. 2011. Socioeconomic Status, Structural and Functional Measures of Social Support, and Mortality The British Whitehall II Cohort Study, 1985–2009. *American journal of epidemiology,* 175**,** 1275-1283.

Szawarska, D. 2013. "Who will love you if they have to look after you?": Sakhalin Koreans Caring from a distance. *In:* Schlecker, M. & Fleischer, F. (eds.) *Ethnographies of social support.* New York: Palgrave Macmillan,39-58.

Taylor, S. E. 1991. Asymmetrical effects of positive and negative events: the mobilization-minimization hypothesis. *Psychological bulletin,* 110**,** 67-85.

Taylor, S. E. 2007. Social support. *In:* Friedman, H. & Silver, R. (eds.) *Foundations of health psychology.* New York: Oxford University Press,145-171.

Terracciano, A., Sutin, A. R., An, Y., O'Brien, R. J., Ferrucci, L., Zonderman, A. B. & Resnick, S. M. 2014. Personality and risk of Alzheimer's disease: New data and meta-analysis. *Alzheimer's & Dementia,* 10**,** 179-186.

Terrera, G. M., Brayne, C. & Matthews, F. 2010. One size fits all? Why we need more sophisticated analytical methods in the explanation of trajectories of cognition in older age and their potential risk factors. *International psychogeriatrics,* 22**,** 291-299.

The Relationships Alliance 2014. The Relationships Manifesto: Strengthening Relationships. London,UK: The Relationships Alliance.

Thoits, P. A. 1982. Conceptual, methodological, and theoretical problems in studying social support as a buffer against life stress. *Journal of Health and Social Behavior,* 23**,** 145-159.

Thoits, P. A. 2011. Mechanisms linking social ties and support to physical and mental health. *Journal of Health and Social Behavior,* 52**,** 145-161.

Thomas, P. A. 2011a. Gender, social engagement, and limitations in late life. *Social Science & Medicine,* 73**,** 1428-1435.

Thomas, P. A. 2011b. Trajectories of social engagement and limitations in late life. *Journal of Health & Social Behavior,* 52**,** 430-443.

Thorvaldsson, V., Hofer, S. M., Berg, S. & Johansson, B. 2006. Effects of repeated testing in a longitudinal age-homogeneous study of cognitive aging. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences,* 61**,** P348-P354.

Tofighi, D. & Enders, C. K. 2008. Identifying the correct number of classes in growth mixture models. *In:* Hancock, G., R & Samuelsen, K., M (eds.) *Advances in latent variable mixture models.* Charlotte, NC: Information Age,317-341.

Tomas, C. & Milligan, C. 2015. *How can and should UK society adjust to dementia?* [Online]. London: Joseph Rowntree Foundation (JRF). Available: https://www.jrf.org.uk/report/how-can-and-should-uk-society-adjust-dementia [Accessed 23rd June 2015].

Trippel, M., Kulikov, D., Davidov, Z. & Groth, H. A truly impossible equation: the future of welfare states in times of demographic ageing. World Demographic and Ageing Forum, 2011 St Gallen.

Tu, Y.-K., Tilling, K., Sterne, J. A. & Gilthorpe, M. S. 2013. A critical evaluation of statistical approaches to examining the role of growth trajectories in the developmental origins of health and disease. *International Journal of Epidemiology,* 42**,** 1327-1339.

Tuligenga, R. H., Dugravot, A., Tabák, A. G., Elbaz, A., Brunner, E. J., Kivimäki, M. & Singh-Manoux, A. 2014. Midlife type 2 diabetes and poor glycaemic control as risk factors for cognitive decline in early old age: a post-hoc analysis of the Whitehall II cohort study. *The Lancet Diabetes & Endocrinology,* 2**,** 228-235.

Tun, P. A., Miller-Martinez, D., Lachman, M. E. & Seeman, T. 2012. Social strain and executive function across the lifespan: The dark (and light) sides of social engagement. *Aging, Neuropsychology, and Cognition,* 20**,** 320-338.

Uchino, B. N. 2006. Social support and health: a review of physiological processes potentially underlying links to disease outcomes. *Journal of behavioral medicine,* 29**,** 377-387.

Uchino, B. N. 2009. Understanding the links between social support and physical health: A life-span perspective with emphasis on the separability of perceived and received support. *Perspectives on Psychological Science,* 4**,** 236-255.

Umberson, D., Crosnoe, R. & Reczek, C. 2010. Social relationships and health behavior across life course. *Annual Review of Sociology,* 36**,** 139.

Umberson, D. & Montez, J. K. 2010. Social Relationships and Health A Flashpoint for Health Policy. *Journal of Health and Social Behavior,* 51**,** S54-S66.

Undén, A. L. & Orth-Gomér, K. 1989. Development of a social support instrument for use in population surveys. *Social science & medicine,* 29**,** 1387-1392.

United Nations Population Division 2013. Department of Economic and Social Affairs. Population Division (2013) World population ageing 2013. New York: United Nations.

Valenzuela, M. J., Matthews, F. E., Brayne, C., Ince, P., Halliday, G., Kril, J. J., Dalton, M. A., Richardson, K., Forster, G. & Sachdev, P. S. 2012. Multiple biological pathways link cognitive lifestyle to protection from dementia. *Biological psychiatry,* 71**,** 783-791.

Valenzuela, M. J. & Sachdev, P. 2006. Brain reserve and cognitive decline: a non-parametric systematic review. *Psychological medicine,* 36**,** 1065-1073.

van Gelder, B., Tijhuis, M., Kalmijn, S., Giampaoli, S. & Kromhout, D. 2007. Decline in cognitive functioning is associated with a higher mortality risk. *Neuroepidemiology,* 28**,** 93-100.

van Gelder, B. M., Tijhuis, M., Kalmijn, S., Giampaoli, S., Nissinen, A. & Kromhout, D. 2006. Marital status and living situation during a 5-year period are associated with a subsequent 10-year cognitive decline in older men: the FINE Study. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences,* 61**,** P213-P219.

van Tilburg, T. 1998. Losing and gaining in old age: Changes in personal network size and social support in a four-year longitudinal study. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences,* 53**,** S313-S323.

van Tilburg, T. 2009. Social integration/isolation, later life. *In:* D. Carr, R. Crosone, M.E. Hughes & A. Pienta (eds.) *Encyclopeida of the life course and human development.* Detroit: Macmillan,378-381.

van Tilburg, T. & Broese van Groenou, M. 2002. Network and health changes among older Dutch adults. *Journal of Social Issues,* 58**,** 697-713.

van Tilburg, T. & Thomése, G. 2010. Societal dynamics in personal networks. *The Sage handbook of social gerontology.* SAGE publications,215-225.

Vermunt, J. K. 2010. Latent class modeling with covariates: Two improved three-step approaches. *Political Analysis,* 18**,** 450-469.

Walen, H. R. & Lachman, M. E. 2000. Social support and strain from partner, family, and friends: Costs and benefits for men and women in adulthood. *Journal of Social and Personal Relationships,* 17**,** 5-30.

Warner, L. M., Schüz, B., Wurm, S., Ziegelmann, J. P. & Tesch-Römer, C. 2010. Giving and taking—Differential effects of providing, receiving and anticipating emotional support on quality of life in adults with multiple illnesses. *Journal of Health Psychology,* 15**,** 660-670.

Warner, L. M., Ziegelmann, J. P., Schüz, B., Wurm, S., Tesch-Römer, C. & Schwarzer, R. 2011. Maintaining autonomy despite multimorbidity: self-efficacy and the two faces of social support. *European Journal of Ageing,* 8**,** 3-12.

Warren, J. R. 2009. Socioeconomic status and health across the life course: A test of the social causation and health selection hypotheses. *Social Forces,* 87**,** 2125-2153.

Washburn, A. M., Sands, L. P. & Walton, P. J. 2003. Assessment of Social Cognition in Frail Older Adults and Its Association With Social Functioning in the Nursing Home. *The Gerontologist,* 43**,** 203-212.

Watson, R., Deary, I. & Shipley, B. 2008. A hierarchy of distress: Mokken scaling of the GHQ-30. *Psychological medicine,* 38**,** 575-579.

Weuve, J., Tchetgen, E. J. T., Glymour, M. M., Beck, T. L., Aggarwal, N. T., Wilson, R. S., Evans, D. A. & de Leon, C. F. M. 2012. Accounting for bias due to selective attrition: the example of smoking and cognitive decline. *Epidemiology (Cambridge, Mass.),* 23**,** 119.

Whalley, L. J., Dick, F. D. & McNeill, G. 2006. A life-course approach to the aetiology of late-onset dementias. *The Lancet Neurology,* 5**,** 87-96.

WHO 2006. Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia: report of a WHO/IDF consultation. *Geneva: World Health Organization.*

Wiggins, R. D., Higgs, P. F., Hyde, M. & Blane, D. B. 2004. Quality of life in the third age: key predictors of the CASP-19 measure. *Ageing and Society,* 24**,** 693-708.

Wilson, R., Evans, D., Bienias, J., De Leon, C. M., Schneider, J. & Bennett, D. 2003. Proneness to psychological distress is associated with risk of Alzheimer’s disease. *Neurology,* 61**,** 1479-1485.

Wilson, R., Hebert, L., Scherr, P., Barnes, L., de Leon, C. M. & Evans, D. 2009. Educational attainment and cognitive decline in old age. *Neurology,* 72**,** 460-465.

Wilson, R., Leurgans, S., Boyle, P., Schneider, J. & Bennett, D. 2010. Neurodegenerative basis of age-related cognitive decline. *Neurology,* 75**,** 1070-1078.

Wilson, R. S., Beckett, L. A., Barnes, L. L., Schneider, J. A., Bach, J., Evans, D. A. & Bennett, D. A. 2002. Individual differences in rates of change in cognitive abilities of older persons. *Psychology and Aging,* 17**,** 179.

Wilson, R. S., Li, Y., Bienias, J. L. & Bennett, D. A. 2006. Cognitive decline in old age: separating retest effects from the effects of growing older. *Psychology and Aging,* 21**,** 774.

Winningham, R. & Pike, N. 2007. A cognitive intervention to enhance institutionalized older adults’ social support networks and decrease loneliness. *Aging & mental health,* 11**,** 716-721.

World Health Organization 2007. Global Age-Freindly Cities: a guide. Geneva, Switzerland: WHO.

Wrzus, C., Hänel, M., Wagner, J. & Neyer, F. J. 2013. Social network changes and life events across the life span: A meta-analysis. *Psychological bulletin,* 139**,** 53.

Yaffe, K., Blackwell, T., Kanaya, A., Davidowitz, N., Barrett-Connor, E. & Krueger, K. 2004a. Diabetes, impaired fasting glucose, and development of cognitive impairment in older women. *Neurology,* 63**,** 658-663.

Yaffe, K., Fiocco, A., Lindquist, K., Vittinghoff, E., Simonsick, E., Newman, A., Satterfield, S., Rosano, C., Rubin, S. & Ayonayon, H. 2009. Predictors of maintaining cognitive function in older adults The Health ABC Study. *Neurology,* 72**,** 2029-2035.

Yaffe, K., Kanaya, A., Lindquist, K., Simonsick, E. M., Harris, T., Shorr, R. I., Tylavsky, F. A. & Newman, A. B. 2004b. The metabolic syndrome, inflammation, and risk of cognitive decline. *Jama,* 292**,** 2237-2242.

Ybarra, O., Burnstein, E., Winkielman, P., Keller, M. C., Manis, M., Chan, E. & Rodriguez, J. 2008. Mental exercising through simple socializing: Social interaction promotes general cognitive functioning. *Personality and Social Psychology Bulletin,* 34**,** 248-259.

Young, Y., Frick, K. D. & Phelan, E. A. 2009. Can successful aging and chronic illness coexist in the same individual? A multidimensional concept of successful aging. *Journal of the American Medical Directors Association,* 10**,** 87-92.

Zammit, A. R., Starr, J. M., Johnson, W. & Deary, I. J. 2014. Patterns and associates of cognitive function, psychosocial wellbeing and health in the Lothian Birth Cohort 1936. *BMC geriatrics,* 14**,** 53.

Zettel, L. A. & Rook, K. S. 2004. Substitution and compensation in the social networks of older widowed women. *Psychology and Aging,* 19**,** 433.

Zhao, J., Brunner, E., Kumari, M., Singh-Manoux, A., Hawe, E., Talmud, P., Marmot, M. & Humphries, S. 2005. APOE polymorphism, socioeconomic status and cognitive function in mid-life. *Social psychiatry and psychiatric epidemiology,* 40**,** 557-563.

Zunzunegui, M. V., Alvarado, B. E., Del Ser, T. & Otero, A. 2003. Social networks, social integration, and social engagement determine cognitive decline in community-dwelling Spanish older adults. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences,* 58**,** S93-S100.

Appendices

Appendix 1. Longitudinal Studies Association between Social Relationships and Cognition Decline in Late Life.

First-author Year	Country/Cohort	Follow-up (years)[a]	Sample size (Female %)	Baseline Mean Age / Range	Social Relationships Measures	Cognitive Assessment	Findings
Social Causation							
Andrew and Rockwood, 2010	Canada/ the Canadian Study of Health and Aging	5	2,468 (60.7%)	79.1	Combined (baseline)	3MS (range:0-100)	Each additional social deficit increased the odds of CD by 1.03. Individual with the highest social vulnerability increased the risk of CD by 36%.
Bassuk *et al*., 1999	US/ the Established Population for Epidemiologic studies of Elderly (EPESE)	3,6,12	2,412 (48.7%)	> 65	Combined	10-item Short Portable Mental Status Questionnaire (SPMSQ)	Participants reporting less social ties had higher chance of subsequent CD, especially those consistently without social ties, independent of emotional support.
Dickinson 2011	US/ the Neurocognitive Outcomes of Depression in Elderly and community dwellers	1	213 (67%)	69	Combined	The Consortium to Establish a Registry in Alzheimer's Disease: MMSE, language tasks and geometric designs and verbal learning and memory	Decreases in instrumental support and social interaction were associated with faster CD in the following year.

[a] Interval between baseline and repeated follow-up assessments

CF: cognitive function; CD: cognitive decline; MMSE: Mini-Mental State Examination; 3MS: The Modified Mini-mental State Examination.

Appendix1. Continued

First-author Year	Country/Cohort	Follow-up (years)[a]	Sample size (Female %)	Baseline Mean Age / Range	Social Relationships Measures	Cognitive Assessment	Findings
Fiori and Jager, 2012	US/ the Wisconsin Longitudinal study (WLS)	11	6,824 (54%)	53	Combined (baseline)	Verbal reasoning and concept formation comprehension	Though CF at wave 2 was highest in the friend-focused network, no significant differences in cognitive changes over time for different network types.
Holtzman *et al.*, 2004 (H); Green *et al.*, 2008 (G)	US / the Epidemiologic Catchment Area (ECA) survey; H: wave1 and 3; G: wave 3 and 4.	H: 12.4 G: 10.9	H: 354 (68.6%) G: 874 (62.9%)	H: 61.3 G: 47.3	Combined (Functional measure from wave 3)	MMSE (0-30) :wave 1,3 & 4; A delayed recall task: wave 3 & 4.	Social network and emotional support were positively related to concurrent CF in wave 3. While either measure was related with CD in Green et al. 2008, while in the early waves 1-3 larger social network was related to reduce odds of CD Holtzman et al. 2004.
Hughes *et al.*, 2008	US/ the Charlotte County Healthy aging study	5	217 (51.8%)	72.4	Combined (baseline)	3MS, the Stroop Test, Trail making Test (perceptual speed) and the Hopkins Verbal Learning Tests (recall)	Satisfactory support was associated with less memory decline. Negative support and satisfaction with support were related to better CF.

[a] Interval between baseline and repeated follow-up assessments

CF: cognitive function; CD: cognitive decline; MMSE: Mini-Mental State Examination; 3MS: The Modified Mini-mental State Examination.

Appendix 1 Continued

First-author Year	Country/Cohort	Follow-up (years)[a]	Sample size (Female %)	Baseline Mean Age / Range	Social Relationships Measures	Cognitive Assessment	Findings
Seeman *et al.*, 2011	US/ the national Midlife in the US (MIDUS)	10	3,525 (55.3%)	56.3	Combined	The Brief test of adult cognition by telephone (BTACT): memory, executive function, , reasoning and speed of processing (wave2)	Cumulative social contacts and social support were positively associated with executive function and episodic memory. Social conflicts were only related to worse executive function. Those declines in social contacts exhibited poorer CF.
Stoykova *et al.*, 2011	France/ PAQUID study	1,3,5,8,10, 13,15,20	2,055 (54.2%)	75	Combined (baseline)	MMSE-30,semantic verbal fluency, memory, speed and learning ability	No statistically significant association was found regarding CD after excluding all incident dementia cases.
Yaffe *et al.*, 2009	US/ Health, Aging and Body composition (Health ABC) study	2,4,7	2,509 (53%)	73.6	Combined (baseline)	3MS (range:0-100)	Cognition maintainers got better support than cognitive decliner. No effect showed regarding social network.
Eisele *et al.*, 2012	Germany/ AgeCoDe	1.5	1,869 (65.9%)	82.4	Functional (baseline)	DSMIII-R, DSM-IV and ICD-10 (SIDAM)	Perceived social support did not have a significant association with cognitive change after adjustment.

[a] Interval between baseline and repeated follow-up assessments
CF: cognitive function; CD: cognitive decline; MMSE: Mini-Mental State Examination; 3MS: The Modified Mini-mental State Examination.

Appendix 1 Continued

First-author Year	Country/Cohort	Follow-up (years)[a]	Sample size (Female %)	Baseline Mean Age / Range	Social Relationships Measures	Cognitive Assessment	Findings
Kim *et al.*, 2007	Korea	5	136 (61%)	>65	Functional (baseline)	Korean MMSE	Social relationships were related to slower CD and lower risk of cognitive impairment
Barnes *et al.*, 2004	US/ Chicago Health and Aging project	3, 6	6,102 (62.2%)	73.9	Structural (baseline)	Episodic memory (immediate/delayed recall), perceptual speed and MMSE	Per social network was associated with a 0.003 unit increase in baseline global CF, and a 0.002 unit reduction in rate of CD.
Barnes et al., 2007	US/ Study of Osteoporotic Fractures	6,8,10,15	9,704 (100%)	71.7	Structural (baseline)	3MS (0-26)	Cognitive maintainers had better social network than minor cognitive decliners
Zunzunegui *et al.*, 2003 (Z) Béland *et al.*, 2005 (B)	Spain / The study Aging in Legane´s (Envejecer en Legane´s)	Z: 4 B: 2, 4, 6	557 (47.4%) 1,165 (58%)	>65 75.6	Structural	The Legane´s' Cognitive Test**:** Orientation & memory index.	Engagement with relatives was associated with slower CD. Having friends is protective for CD for women but not men.
Bennett *et al.*, 2006	US/ the Rush Memory and Aging Project	till death	89 (55.1%)	84.3	Structural (baseline)	Memory, perceptual speed and spatial ability.	Social network size modified the association between pathology and cognitive function.

[a] Interval between baseline and repeated follow-up assessments
CF: cognitive function; CD: cognitive decline; MMSE: Mini-Mental State Examination; 3MS: The Modified Mini-mental State Examination.

Appendix 1 Continued

First-author Year	Country/Cohort	Follow-up (years)[a]	Sample size (Female %)	Baseline Mean Age / Range	Social Relationships Measures	Cognitive Assessment	Findings
Ertel *et al*., 2008	US/ Health and Retirement Study (HRS)	2,4,6	16,638 (57.8%)	64.5	Structural (baseline)	Memory: immediate and delayed recall of 10-word list	Higher social integration predicted slower rate of memory decline, especially those with lower education or vascular condition.
Giles *et al*., 2012	Australia/ the Australian Longitudinal Study of Aging (ALSA)	2,8,11,15	706 (32.1%)	78.6	Structural (baseline)	Memory & MMSE	A positive effect of friend network on decline in memory was found among women.
Glei *et al*., 2005	China/ Study of Health and Living Status of the elderly in Taiwan	3,6,7	2,387(43.5%)	71.8	Structural (baseline)	the Short Portable Mental Status Questionnaire	None of the social network measures was related to the number of failed cognitive tasks.
Ho *et al*., 2001	China	3	988 (47.5%)	>70	Structural (baseline)	the information/ orientation part of the Clifton Assessment Procedure for the elderly (CAPE)	Male participants with the least social network tripled the risk of cognitive impairment compared with those in the highest tertile. No effect showed in female.

[a] Interval between baseline and repeated follow-up assessments
CF: cognitive function; CD: cognitive decline; MMSE: Mini-Mental State Examination; 3MS: The Modified Mini-mental State Examination.

Appendix 1 Continued

First-author Year	Country/Cohort	Follow-up (years)[a]	Sample size (Female %)	Baseline Mean Age / Range	Social Relationships Measures	Cognitive Assessment	Findings
Roth 2005	Sweden/ Health-70 study	5,9	995 (58.6%)	70	Structural (baseline)	Space, speed, digits backwards & forwards and verbal meaning	No significant association was showed in terms of marital status, or contact with children with any cognitive tests.
Shankar *et al*., 2013	UK/ the English Longitudinal Study of Aging (ELSA)	4	6,034 (54.7%)	65.9	Structural (baseline)	Memory & Executive function (follow-up)	Higher social isolation was related with lower verbal function, immediate and delayed recall at follow-up.
Thomas 2011 b	US/ the Americans' Changing Lives survey	3,5,8	1,667 (67.1%)	70.1	Structural	Short Portable Mental Status Questionnaire: time orientation, memory, inductive reasoning	Individuals with trajectories of high and increasing social engagement had lower levels of cognitive limitations.
Ellwardt *et al*., 2015	Netherlands/ Longitudinal Aging Study Amsterdam (LASA)	3,6,9,12, 15,18	2,959 (51.6%)	67.9	Structural	MMSE	A reduction in network size or complexity was associated with a reduction in cognition. The effect on cognitive decline was marginal.
Aartsen *et al*., 2005	Netherlands/ LASA	3,6	1,144 (40.7%)	70.3	Structural	Memory	Widowhood during follow-up was related to greater memory decline.

[a] Interval between baseline and repeated follow-up assessments
CF: cognitive function; CD: cognitive decline; MMSE: Mini-Mental State Examination; 3MS: The Modified Mini-mental State Examination.

Appendix 1 Continued

First-author Year	Country/Cohort	Follow-up (years)[a]	Sample size (Female %)	Baseline Mean Age / Range	Social Relationships Measures	Cognitive Assessment	Findings
Håkansson *et al.*, 2009	Finland/ the Cardiovascular Risk Factors Aging and Dementia study	21	1,448 (39.1%)	50.4	Structural	MMSE (range: 0-30) DSM-IV (Screening +clinical phases) (follow-up)	Widowhood at mid-life increased the risk of cognitive impairment in later life. The risk was even higher for those without partner at both mid and later-life.
Karlamangla *et al.*, 2009	US/ the study of Assets and Health Dynamics Among the Oldest old	2,5,7,9	6,467 (61.3%)	77.1	Structural	Telephone Interview for Cognitive Status: recall; serial 7's subtraction and other mental items.	Widowhood and being single were associated with faster overall CD and memory decline.
Van Gelder *et al.*, 2006	Finland, Italy & Netherlands/ FINE Study	5,10	1,042 (0)	76	Structural (5-year ahead of baseline MMSE)	MMSE (0-30)	Men lost a partner or unmarried had twice faster CD in the subsequent 10-years.
Health Selection							
Van Tilburg *et al.*, 2002 (V); Aartsen *et al.*, 2004 (A); Broese van Groenou *et al.*, 2013 (B)	Netherlands/ Longitudinal Aging Study Amsterdam (LASA)	V: 1,4,7 A: 6 B:3,6,9,13 ,16	V: 2,302 (51%) A: 1,552 (?) B: 2,960 (52%)	V: 72 A: 55-85 B: 70.3	V: Combined A: Structural B: Structural	MMSE (0-30)	Greater cognition and cognitive maintenance were related to larger network size over time, but not with change in practical support.

[a] Interval between baseline and repeated follow-up assessments
CF: cognitive function; CD: cognitive decline; MMSE: Mini-Mental State Examination; 3MS: The Modified Mini-mental State Examination.

Appendix 1 Continued

First-author Year	Country/Cohort	Follow-up (years)[a]	Sample size (Female %)	Baseline Mean Age / Range	Social Relationships Measures	Cognitive Assessment	Findings
Bourne *et al.*, 2007	UK/ The Scottish Mental Survey	11-year & recruited again at 64 years	266 (51%)	64	Functional	Moray House Test 11year-old/ Raven's standard progressive matrices 64 year	Cognition at age-11 not age-64, predicted less practical and emotional support at age-64
Gurung *et al.*, 2003	US/ MacArthur Studies of aging	23 month	439 (35%)	76	Combined	Memory test recognition and inductive reasoning	Participants with lower cognition reported more negative interactions.
Social Causation and Health Selection							
Ellwardt *et al.*, 2013	Netherlands/ Longitudinal Aging Study Amsterdam (LASA)	3,6	2,255(54%)	63	Functional	MMSE, Coding task and Raven Colored progressive matric	Emotional support and increases in emotional support were related to better CF and cognitive performance over follow-up. Higher baseline practical support was related to faster CD.
Thomas 2011a	US/ the Americans' Changing Lives survey	3,5,8	1,667 (67.1%)	70.1	Structural	Short Portable Mental Status Questionnaire: time orientation, name (recall /memory), inductive reasoning (mathematics)	For women, greater social engagement predicted better cognitive function; for men, more cognitive limitations predicted less social engagement.

[a] Interval between baseline and repeated follow-up assessments
CF: cognitive function; CD: cognitive decline; MMSE: Mini-Mental State Examination; 3MS: The Modified Mini-mental State Examination.

Appendix 1 Continued

First-author Year	Country/Cohort	Follow-up (years)[a]	Sample size (Female %)	Baseline Mean Age / Range	Social Relationships Measures	Cognitive Assessment	Findings
Li and Zhang, 2015	China/ the Chinese Longitudinal Healthy Longevity Survey (CLHLS)	3,7	4,190 (53.7%)	77.6	Structural	MMSE (0-30) (Chinese version)	Reciprocity showed social network types and health indicators. A diverse network yielded better subsequent cognition; whereas lower cognition was related to withdraw from a more diversified network.

[a] Interval between baseline and repeated follow-up assessments

CF: cognitive function; CD: cognitive decline; MMSE: Mini-Mental State Examination; 3MS: The Modified Mini-mental State Examination.

Appendix 2. The Close Persons Questionnaire (CPQ)

Functional measures of social relationships

Confiding/emotional support

1. How much in the last 12 months did this person give you information, suggestions and guidance that you found helpful?
2. How much in the last12 months did this person make you feel good about yourself?
3. How much in the last 12 months did you share interests, hobbies and fun with this person?
4. How much in the last 12 months did you want to confide in (talk frankly, share feelings with) this person?
5. How much in the last 12 months did you confide in this person?
6. How much in the last 12 months did you trust this person with your most personal worries and problems?
7. How much in the last 12 months did he/she talk about his/her personal worries with you?

Practical support

1. How much in the last 12 months did you need practical help from this person with major things (e.g. look after you when ill, help with finances, children)?
2. How much in the last 12 months did this person give you practical help with major things?
3. How much in the last12 months did this person give you practical help with small things when you needed it? (e.g. chores, shopping, watering plants etc.)

Negative aspects of close relationships

1. How much in the last12 months did this person give you worries, problems and stress?
2. How much in the last 12 months would you have liked to have confided more in this person?
3. How much in the last 12 months did talking to this person make things worse?
4. How much in the last 12 months would you have liked more practical help with major things from this person?

Structural measures of social relationships

Relative network

a. Are there any relatives outside your household with whom you have regular contact (either by visit, telephone or letters)? (Not necessarily the same person each time)
b. How many relatives do you see once a month or more?

Friend network

a. Are there any friends or acquaintances with whom you have regular contact (either by visit, telephone, e-mail or letters)? (Not necessarily the same person each time)
b. How many friends and acquaintances do you see once a month or more?

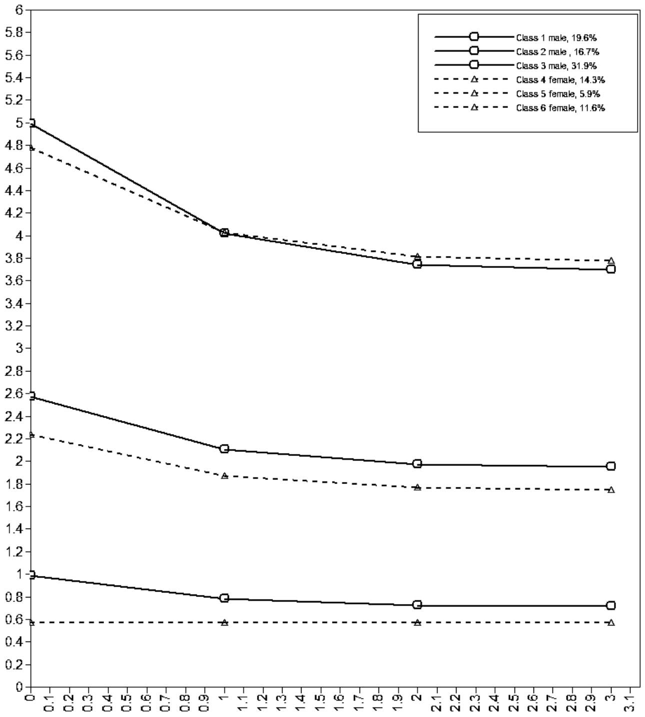
Appendix 3. Confirmation Factor Analysis for Types of Functional Social Relationships from the Closest Person: Factor Loading Coefficients (Varimax Rotation)

Items	**Phase 2** n = 7,436	**Phase 5** n = 6,498	**Phase 7** n = 6,456	**Phase 9** n = 6,296
Factor 1: Confiding/Emotional support				
Information, suggestions, guidance	0.55	0.52	0.52	0.51
Make you feel good	0.51	0.51	0.50	0.48
Share interest	0.41	0.41	0.42	0.44
Want to confide in	0.78	0.81	0.82	0.84
Did you confide in	0.86	0.89	0.89	0.88
Trusting with most personal worries	0.74	0.74	0.73	0.70
Reciprocity	0.47	0.51	0.52	0.50
Factor 2: Practical support				
Need practical support	0.81	0.75	0.69	0.69
Major practical support	0.89	0.81	0.79	0.79
Minor practical support	0.56	0.61	0.63	0.58
Factor 3: Negative aspects of close relationships				
Give worries, problems, stress	0.50	0.50	0.47	0.49
Like to confide more	0.54	0.53	0.55	0.52
Talking makes things worse	0.62	0.61	0.62	0.61
Like more practical help	0.59	0.62	0.62	0.64

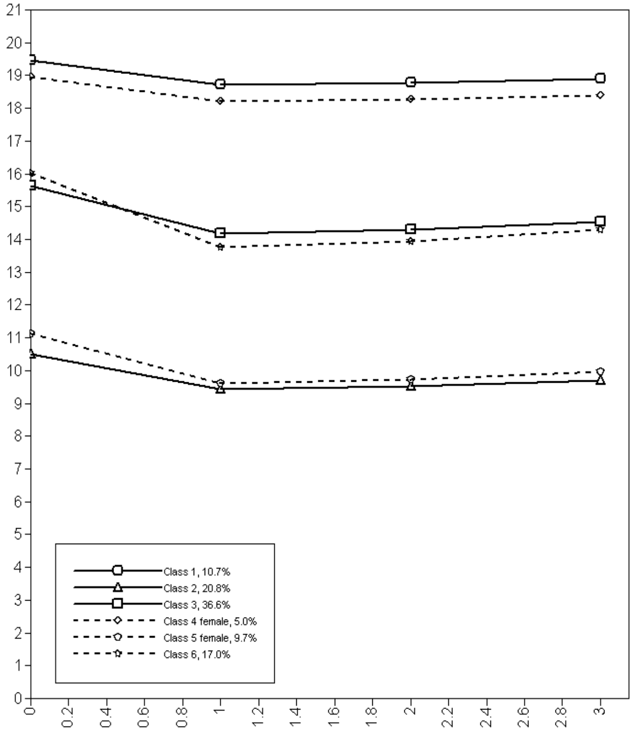
Appendix 4. Sex-specific Growth Patterns of Social Relationships by Longitudinal Latent Classes (Male: Solid Lines; Female: Dash Lines)

Functional measures of social relationships from Phase 2 (1989-1990) to Phase 9 (2007-2009)

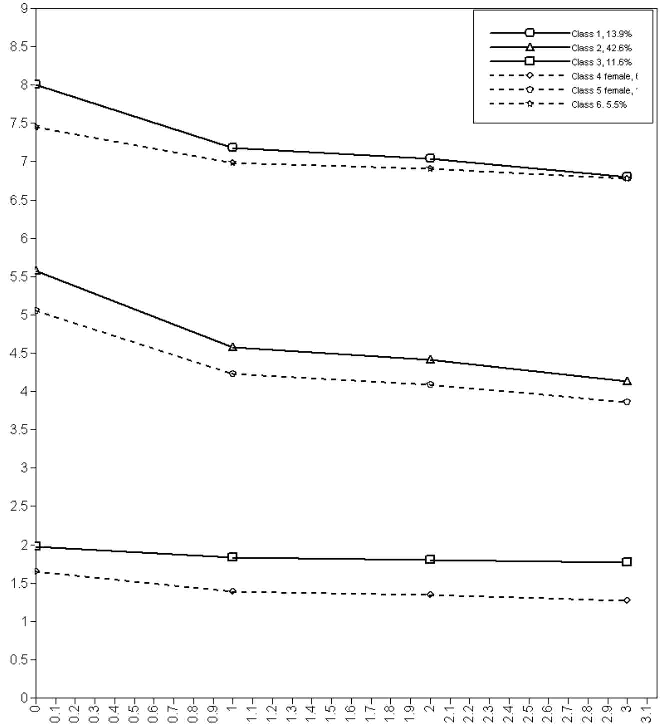
Negative Support



Confiding Support

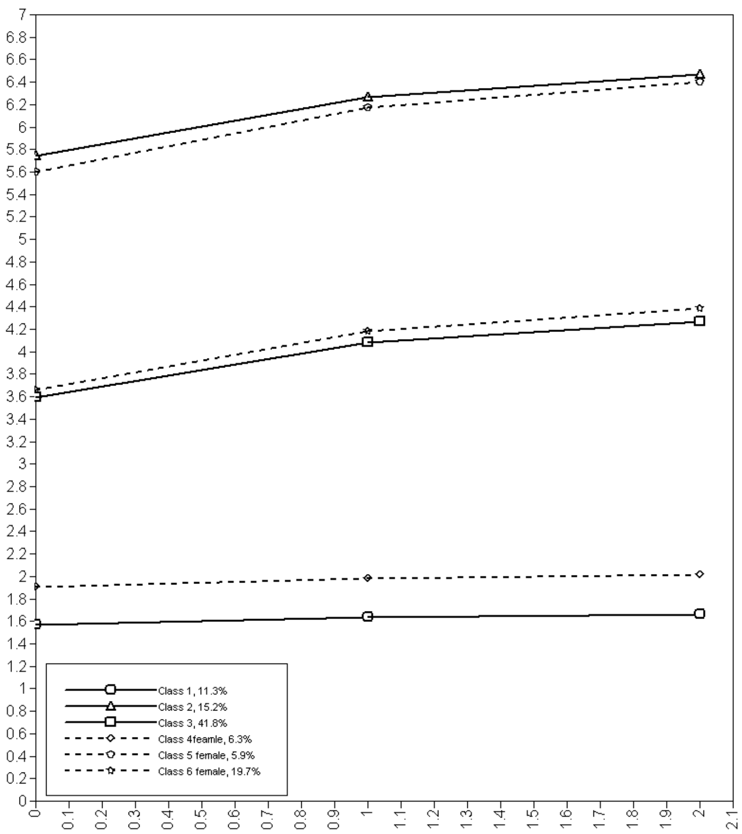


Practical Support

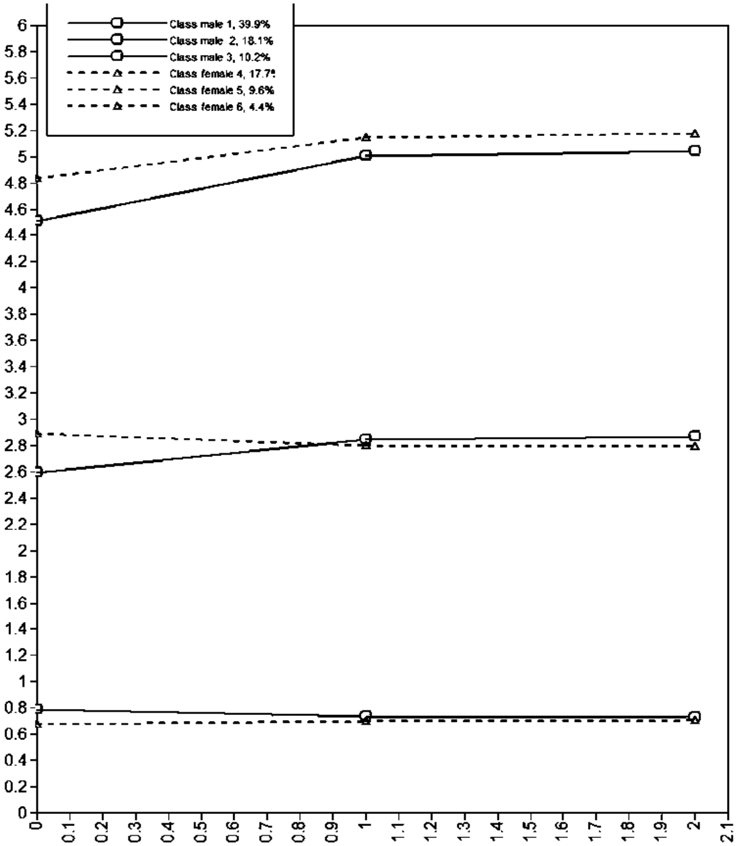


Structural measures of social relationships from Phase 2 (1989-1990) to Phase 7 (2002-2004)

Friend Network



Relative Network



Appendix 5. Research output

Publications

Liao J, Brunner EJ (2015) Structural and Functional Measures of Social Relationships and Quality of Life among Older Adults, Does Chronic Disease Status matter? Quality of Life Research. DOI: 10.1007/s11136-015-1052-1

Liao J, Head J, Kumari M, Stansfeld S, Kivimaki M, Singh-Manoux A , Brunner EJ (2014) Negative aspects of close relationships as risk factors for cognitive aging. American Journal of Epidemiology. 1;180(11):1118-25. doi: 10.1093/aje/kwu236, http://www.ncbi.nlm.nih.gov/pubmed/25342204

Liao J, Brunner EJ, Kumari M (2013) Is There an Association between Work Stress and Diurnal Cortisol Patterns? Findings from the Whitehall II Study. PLoS ONE 8(12): e81020. doi:10.1371/journal.pone.0081020

Conferences

Oral presentation at the symposium ‘Re-examination of Cognitive Reserve and its Role on Trajectories of Cognitive Decline’ in the Gerontological Society of America's 68th Annual Scientific Meeting, 18th-22nd Nov, 2015, Orlando, Florida US.

Poster presentation at the Wellcome Trust conference of Longitudinal Studies: Maximising their Value for Ageing Research, Cambridge, UK, 21st-23rd July 2015, Title: *Dynamic longitudinal associations between social support and cognitive function*.

Oral presentation at the International Festival of Public Health UK, Manchester, UK, 2nd July 2015, Title*: Dynamic longitudinal associations between social support and cognitive function: losing and gaining in late life.*

Poster presentation at the Canadian Institutes of Health Research (CIHR) summer program in ageing 2015, ‘More Years, Better Lives: The Health, Wellness and Participation of Older Adults in the World of Work’, Toronto, Canada, 1st -5th June; Title: *The longitudinal dynamic association between social support and cognitive ageing*.

Oral presentation at the conference symposia, ‘Mission possible: IMPACT-BAM model for evaluating alternative mid-life approaches to promote better ageing’ at the Society for Longitudinal and Life Course Studies (SLLS) international conference, ‘Lives in Transition: Life Course Research and Social Policies’, Lausanne, Switzerland, 9th -11th

October 2014, Title: *The psychosocial approach: Social relationships in mid-life and cognitive decline*

Poster presentation at Society for Social Medicine (SSM) 58th Annual Scientific Meeting, Oxford UK, 10th -12th September 2014; Title: *Impact of negative aspects of close relationships on cognitive ageing, the dark side of social relationships*

Media coverage

"Stressful relationships tied to mental decline"
http://www.reuters.com/article/2014/11/19/us-mental-decline-relationships-idUSKCN0J322N20141119