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*Till Hanna, William och Jenna!*

DOCTORAL DISSERTATION IN PSYCHOLOGY


Abstract

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The overarching aim of this thesis was to investigate birth cohort differences in level of cognitive functioning and change in later life in three population-based representative samples drawn from the Gerontological and Geriatric Population Studies in Gothenburg (H70), Sweden. We used data from cohorts, born in 1901-02, 1906-07, and 1930, measured at ages 70, 75, and 79 on the same cognitive measures.

In *Study I* we investigated cohort differences in the proportions of individuals showing cognitive decline, stability, or gain. Our findings revealed significant cohort differences on all outcomes (i.e. logical reasoning, spatial ability, verbal meaning, and perceptual-motor-speed). Later born cohorts consisted of larger proportions of participants showing decline and smaller proportions of participants showing gain.

In *Study II* we investigated cohort differences in level of performance and rate of cognitive change on two measures of fluid ability (i.e. logical reasoning and spatial ability). Estimates from multiple-group latent growth curve models (LGCM) revealed substantial cohort differences in levels of performance were later born cohorts outperformed the earlier born. However, later born cohorts also showed, on average, a steeper decline over the study period than the earlier born. Gender and education partially accounted for the observed cohort differences.

In *Study III* we analyzed data concerning four fluid abilities (i.e. perceptual-motor-speed, long-term picture recognition memory, logical reasoning and spatial ability) and one crystallized ability (i.e. verbal ability). We fitted growth curve models to the data within a

Bayesian framework. The results confirmed those reported in Studies I and II indicating, moderate to large cohort differences in levels of performance on all five cognitive outcomes. Later born cohorts showed steeper decline in logical reasoning, spatial ability, and perceptual-motor-speed but we found no differences in rate of decline regarding long-term recognition memory and verbal ability.

In *Study IV* we investigated the moderating effects of birth cohort on the associations between cardiovascular risk (defined as the Framingham Risk Score, FRS) and cognitive functioning and rate of change on two cognitive measures (i.e. spatial ability and logical reasoning). Multiple-group LGCMs revealed relatively weak associations between cardiovascular risk and cognitive functioning and change. These associations were even weaker in the 1930 cohort, especially regarding logical reasoning.

The findings that later born cohorts outperform earlier born cohorts in levels of performance are in line with previous findings and further emphasize the importance of environmental factors in shaping life-span cognitive development. The findings that later born cohorts decline at a faster rate compared to earlier born cohorts on fluid measurements are novel. A potential explanation for the cohort differences in rate of cognitive decline relates to differences in the average age of onset of the cognitive decline due to cohort differences in cognitive reserve. To the extent that later born cohorts on average have higher cognitive reserve compared to earlier born, as indicated by their higher level of performance, they should- in line with the cognitive reserve hypothesis- start to decline at a later stage but then they should decline at a faster rate. Another explanation relates to possible cohort differences in selective survival. As life-expectancy has increased in Sweden, since the 19$^{th}$ century, a relatively higher proportion of more frail individuals may have survived to age 70 in later born cohorts.

Keywords: Aging, cardiovascular risk factors, cognitive decline, cohort differences, fluid and crystallized abilities, Flynn effect, longitudinal

## Svensk sammanfattning

Det kognitiva fungerandet är en viktig komponent med hänseende till hälsa och välbefinnande. Världen över sker ett populationsåldrande, dvs. en allt större andel i befolkningen utgörs av människor i högre ålder. Denna trend beror främst på en minskning i barnafödande men har även påverkats av den gradvisa ökning som skett av den genomsnittliga livslängden. Vilka konsekvenser denna ökade livslängd kommer att få för berörda samhällen beror i hög grad på den hälsomässiga statusen hos de äldre individerna. En viktig faktor här är kognitivt åldrande. I den utsträckning äldre individer är i behov av stöd och assistans på grund av kognitiv försämring så kommer populationsåldrandet innebära ökade resurskrav och belastningar för berörda samhällen. Men på motsvarande vis, i den utsträckning de äldre är kognitivt välfungerande så kan populationsåldrandet även innebära fördelar för berörda samhällen.

Under 1900-talet har en gradvis ökning av den genomsnittliga intelligensen rapporterats. Denna ökning i intelligens, ofta betecknad som Flynn-effekten, utgörs av kohortskillnader, där senare födda kohorter presterar bättre på kognitiva test jämfört med tidigare födda kohorter när de jämförs vid samma åldrar. Det råder fortfarande oenighet med avseende på vilka faktorer som kan förklara Flynn-effekten. De flesta teorier tillskriver effekten till miljömässiga faktorer såsom förbättringar rörande näringsintag, hälsa och sjukvård, längre och bättre utbildning, mer komplexa och stimulerande arbets- och sociala miljöer, som blivit ”mer optimala” för en större andel av populationen i senare födda kohorter.

Flynn-effekter har rapporterats rörande ett flertal kognitiva förmågor såsom episodiskt och semantiskt minne, spatial förmåga, verbal förmåga och logiskt resonerande. Vidare har Flynn-effekter påvisats i ett flertal länder, exempelvis i USA och flera europeiska länder,

inklusive Sverige. Slutligen har Flynn-effekter också påvisats över en rad olika åldrar, från tidig spädbarnsålder till hög ålder.

Med tanke på populationsåldrandet är det särskilt angeläget att undersöka eventuella kohortskillnader rörande kognitiv förändring i samband med åldrande. Förändras senare födda kohorter i samma grad och takt jämfört med tidigare födda kohorter? Trots den samlade kunskapen rörande kohortskillnader beträffande nivå av kognitivt fungerande så råder det brist på forskningsstudier med fokus på eventuella kohortskillnader vad gäller förändring i senare livsfaser. Det saknas således kunskaper om i vilken utsträckning kohortskillnader manifesteras även i grad av kognitiv förändring och inte enbart vad gäller funktionsnivå.

Vidare visar forskning på en betydande heterogenitet rörande kognitivt åldrande, där vissa individer försämras kognitivt medan andra bibehåller, eller förbättrar, sitt kognitiva fungerande även i hög ålder. Med tanke på observerade kohortskillnader är det därför motiverat att även studera om det föreligger kohortskillnader rörande andelen individer som uppvisar kognitiv försämring, stabilitet, respektive förbättring i samband med åldrande.

Då åldrande, även om det är heterogent, innebär ökad risk för såväl kognitiv försämring som utvecklande av demens är det viktigt att försöka identifiera faktorer som kan påverka vårt kognitiva åldrande. Här har intresse särskilt riktats mot kardiovaskulära riskfaktorer (som t.ex. diabetes, och högt blodtryck) då det visat sig att kardiovaskulära riskfaktorer är relaterade till kognitivt fungerande, samtidigt som många kardiovaskulära riskfaktorer är påverkbara (t.ex. via medicin och/eller livsstilsförändringar).

Det övergripande syftet med denna avhandling var att studera födelsekohortskillnader i både nivå av kognitivt fungerande och kognitiv förändring i samband med åldrande. Befolkningsstudierna i Göteborg (H70) har gett oss unika möjligheter för dessa analyser då här har genomförts omfattande undersökningar av representativa urval från tre

födelsekohorter (personer födda 1901-02, 1906-07 samt 1930). Dessa personer har alla undersökts vid 70, 75 och 79 års ålder med samma kognitiva tester.

I *studie I* studerade vi kohortskillnader i andel deltagare som uppvisade kognitiv försämring, stabilitet, respektive förbättring rörande fyra kognitiva test (spatial förmåga, verbal förmåga, perceptuell-motorisk snabbhet, samt logiskt resonerande), från 70 till 79 års ålder. $\chi^2$-test visade på signifikanta kohortskillnader i samtliga kognitiva test. Senare födda kohorter innefattade en högre andel deltagare som uppvisade kognitiv försämring, och en mindre andel som uppvisade förbättring, än tidigare födda kohorter. Det vill säga, även om en signifikant andel av deltagarna uppvisade stabilitet eller förbättring i alla tre studerade kohorter, var andelen högre i tidigare födda kohorter jämfört med senare födda.

I *Studie II* studerade vi kohortskillnader i nivå av fungerande och grad av kognitiv förändring på två mått på flytande förmåga (logiskt resonerande och spatial förmåga). Estimat från flergrupps latenta tillväxtmodeller (LGCM) påvisade, i linje med tidigare studier, påtagliga kohortskillnader rörande nivå av kognitivt fungerande, där senare födda kohorter presterade bättre än tidigare födda kohorter. Dock uppvisade senare födda kohorter också, i genomsnitt, en högre grad av kognitiv försämring från 70 till 79 års ålder jämfört med tidigare födda kohorter. Kön och utbildning kunde till viss del förklara kohortskillnaderna. Våra resultat bekräftar förekomsten av födelsekohorteffekter i högre ålder, där senare födda kohorter presterar bättre än tidigare födda, men indikerar också att senare födda kohorter försämras i snabbare takt än tidigare födda.

I *Studie III* gjordes kohortanalyser av fyra s.k. flytande förmågor (perceptuell-motorisk snabbhet, långtids-bildminne, logiskt resonerande och spatial förmåga) och en s.k. kristalliserad förmåga (verbal förmåga). Här användes latenta tillväxtmodeller baserade på Bayesiansk estimering. Resultaten bekräftade vad som rapporterats i studie I och II, då resultaten indikerade måttliga till stora kohortskillnader i prestationsnivå i alla fem kognitiva

testerna, där senare födda kohorter presterade bättre än tidigare födda. Senare födda kohorter uppvisade även en högre grad av nedgång i logiskt resonerande, spatial förmåga samt perceptuell-motorisk snabbhet. Vi fann dock inga kohortskillnader i grad av försämring rörande långtidsminne (dvs. igenkänning) eller verbal förmåga.

I *studie IV* studerade vi kohortskillnader rörande sambandet mellan kardiovaskulär risk, kognitivt fungerande och förändring i två flytande kognitiva förmågor (spatial förmåga samt logiskt resonerande). Vi använde Framingham risk-index (FRS), baserat på icke-laboratoriemässiga variabler (kön, ålder, systoliskt blodtryck, kroppsmasseindex (BMI), användande av blodtryckssänkande medicin, diabetes-status, samt rökning) för att beräkna kardiovaskulär risk. Estimat från flergrupps latenta tillväxtmodeller (LGCM) visade på relativt svaga samband mellan FRS och kognitivt fungerande och förändring. Dessa samband var än svagare för 1930 kohorten jämfört med tidigare födda kohorter, fr.a. rörande logiskt resonerande. Våra resultat tyder här på att kardiovaskulär risk har något mindre negativa effekter på kognitivt åldrande i senare födda kohorter.

Att senare födda kohorter presterar bättre kognitivt än tidigare födda kohorter, är i linje med tidigare studier och utgör ytterligare bevis för att Flynn-effekten visar sig även i högre åldrar. Det föreligger inte några hittills kända genetiska markörer, eller kombinationer av sådana, med effektstyrkor jämförbara med de som rapporteras i denna avhandling. Våra resultat ger därför ytterligare stöd för betydelsen av miljömässiga faktorer för den kognitiva utvecklingen under hela livet.

Att senare födda kohorter försämrades i högre grad än tidigare födda kohorter på tre kognitiva test (logiskt resonerande, spatial förmåga samt perceptuell-motorisk snabbhet) var något överraskande. En tänkbar förklaring av kohortskillnaderna i grad av kognitiv försämring är relaterad till kohortskillnader rörande den genomsnittliga åldern då kognitiva försämringen startar. På grund av lägre kognitiv reservkapacitet och sämre hälsa kan en större

andel individer i tidigare födda kohorter förmodas ha börjat försämras kognitivt redan före första mätningen vid 70 års ålder. I enlighet med hypotesen rörande kognitiv reservkapacitet kan individer med en högre reservkapacitet använda sina kognitiva processer på ett mer effektivt och flexibelt vis och därmed tolerera mer patologi i hjärna och nervsystem utan försämrad kognitiv funktion jämfört med individer med lägre reservkapacitet. Dock, när individer med högre reservkapacitet väl börjar försämras kommer de, i enlighet med reservkapacitet-hypotesen, försämras i en snabbare takt jämfört med individer med lägre reservkapacitet. I den utsträckning senare födda kohorter uppvisar högre kognitiv reservkapacitet, vilket indikeras av deras bättre prestationer, bör de i enlighet med reservkapacitets-hypotesen uppvisa försämring senare i livet jämfört med tidigare födda kohorter men då också försämras i snabbare takt.

De kohortskillnader avseende kognitiva förmågor som redovisas i denna avhandling är viktiga utifrån ett livsspanns-perspektiv, då utvecklingspsykologiska teorier behöver kunna förklara dessa betydande kohortskillnader. Vidare är de rapporterade kohortskillnaderna i kognitivt fungerande viktiga för praktiker och forskare som använder kognitiva test i samband med utvärderingar rörande exempelvis arbetsförmåga, demensstatus och funktionsnedsättning. I tillämpningar såsom standardisering av kognitiva test, tolkning av testresultat och beslutsfattande baserat på kognitiva bedömningar måste hänsyn tas till kohortskillnader. De här redovisade resultaten är även av betydelse för den pågående debatten rörande pensionsålder. Det populationsåldrande som sker världen över kan potentiellt sett innebära allvarliga ekonomiska belastningar för berörda samhällen. En möjlig strategi för att hantera detta är att höja pensionsåldern, vilket även har gjorts och planeras i ett flertal länder. Sett till det faktum att flera studier, inklusive de som redovisats i denna avhandling, rapporterat betydande kohortskillnader i kognitivt fungerande är detta förståeligt. Dock är det viktigt att också vara medveten om att de här redovisade resultaten i termer av

högre grad av kognitiv försämring indikerar att senare födda kohorter inte är skyddade från kognitiv försämring i samband med åldrande.

Nyckelord: Flynn effekt, flytande och kristalliserade förmågor, Kardiovaskulär risk, kognitiv försämring, kohortskillnader, åldrande

# Preface

This thesis is based on the following studies referred to in the text by their Roman numerals:

I. Karlsson, P., Thorvaldsson, V., Skoog, I., Skoog, J., & Johansson, B. (Submitted). What can we expect of cognition after 70? A study of cognitive decline, stability, and gain between 70 and 79 years in three Swedish birth cohorts.

II. Karlsson, P., Thorvaldsson, V., Skoog, I., Gudmundsson, P., & Johansson, B. (2015). Birth cohort differences in fluid cognition in old age: Comparisons of trends in levels and change trajectories over 30 years in three population-based samples. *Psychology and Aging*, *30*(1), 83-94. doi:10.1037/a0038643

III. Thorvaldsson, V., Karlsson, P., Skoog, J., Skoog, I., & Johansson, B. (2017). Better cognition in new birth cohorts of 70 year olds, but greater decline thereafter. *Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, *72*(1), 16-24. doi:10.1093/geronb/gbw125

IV. Karlsson, P., Johansson, B, Skoog, I., Skoog, J., Rydén, L., &. Thorvaldsson, V. (Submitted). Cohort differences in the association of Cardiovascular Risk and cognitive aging.

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Figures and Tables

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Finally, I want to dedicate this thesis to my wonderful kids, William and Jenna. You are truly the lights of my life!

## Introduction

Cognitive functioning is an essential component of well-being and health (Hofer & Alwin, 2008) as well as managing everyday activities (Drag & Bieliauskas, 2010). Due to the worldwide phenomenon of population aging there is a great need to further our understanding regarding cognitive aging (Alwin & Hofer, 2008; Drag & Bieliauskas, 2010). Population aging refers to a shift across time in the age distribution among individuals in a defined population, often expressed in terms of an increase in the average age of the population and a rise in the proportion of the population consisting of older people, often defined as 65+. This shift in the age distribution is driven mainly by decreasing fertility rates and increasing longevity (Anderson & Hussey, 2000; Moody & Sasser, 2015). Whether the aging population constitutes a burden or a benefit to the affected societies strongly depends on the general health status and vitality of the older persons. One of the most important factors in this respect is intact cognitive function among the older citizens. To the extent that the older individuals, due to cognitive decline and dementia, require help and assistance to manage everyday life, the increasing population age will impose a major burden on society. But likewise, to the extent that they are cognitively "fit" they will likely constitute a benefit and a potential resource to society (Carstensen, 2008).

Cognitive aging refers to time-dependent irreversible changes resulting in a progressive loss of cognitive functional capacity occurring after a point of maturity (Alwin, McCammon, Wray & Rodgers, 2008). The interaction between individual and contextual influences occurring over the lifespan, however, contributes to great variability in cognitive aging. These inter-individual differences' regarding intra-individual change becomes even more complex when comparing different birth cohorts (Willis & Schaie, 2006).

In order to gain a better understanding of the role of environmental influences on cognitive aging it is important to study cohort differences, preferably via longitudinal studies,

as opposed to cross-sectional studies (Finkel, Reynolds, McArdle & Pedersen, 2007; Gerstorf, Ram, Hoppman, Willis & Schaie, 2011; Schaie, 2005). Longitudinal designs provide the possibility to study intra-individual change (Baltes & Nesselroade, 1979; Ferrer & Ghisletta, 2011; Hofer & Sliwinsky, 2006; Hoffman, 2015). As cognitive aging refers to intra-individual changes longitudinal studies represent the essential design in this respect.

**Cohort differences in cognitive abilities**

During the 20th century a steady increase in mean intelligence scores has been reported (e.g. Dickens & Flynn, 2001; Flynn, 1984, 1987; Hiscock, 2007; Lynn, 1982; 2009 a; Russell, 2007; Schaie, Willis & Pennak, 2005). This overall increase in intelligence is often referred to as the Flynn-effect. The Flynn effect constitutes birth cohort differences where later born cohorts typically score higher on cognitive tests compared with earlier born cohorts (e.g. Flynn, 1984; Hiscock, 2007; Lynn, 2009 a; Nettelback & Wilson, 2004; Rodgers & Wänström, 2007; Russell, 2007; Schaie, Willis & Pennak, 2005; for a recent meta-analysis see Trahan, Stuebing, Hiscock & Fletcher, 2014). However, the opposite pattern has been found regarding some cognitive abilities, for instance numeric ability where earlier born cohorts in fact scored higher than later born cohorts (Schaie, 2005, 2008).These cohort differences refer to history-graded influences, that is- influences related to a certain period of time that are experienced, in a similar way, by most members of a certain birth cohort, in certain culture (Johansson, 2008).

Flynn effects have been reported regarding several cognitive functions, such as, mathematic ability (Rodgers & Wänström, 2007), visuospatial ability and verbal knowledge (Rönnlund & Nilsson, 2006), vocabulary (Nettelbeck & Wilson, 2004; Uttl & Van Alstine, 2003), episodic and semantic memory (Rönnlund & Nilsson, 2009), inductive reasoning (Flynn, 2009), and fullscale IQ (Colom, Lluis-Font & Andrés-Pueyo, 2005; Flynn & Weiss,

2007). Flynn effects have been demonstrated in numerous developed countries, for instance the United States (USA) (Flynn, 1984), the United Kingdom (UK) (Flynn, 2009; Lynn, 2009a), Australia (Nettelback & Wilson, 2004), Sweden (Rönnlund, Carlstedt, Blomsted, Nilsson & Weinehall, 2013), Denmark (Christensen et al., 2013), Japan (Lynn, 1982), and in a number of developing countries such as Kenya (Daley, Whaley, Sigman, Espinosa & Neumann, 2003), Sudan (Khaleefa, Abdelwahid, Abdulradi & Lynn, 2008), South Africa (te Nijenhuis, Murphy & van Eeden, 2011), and Brazil (Colom, Flores-Mendoza & Abad, 2007). Notably, Flynn effects have been demonstrated over a wide range of ages, from infants (Lynn, 2009b) to 95 year olds (Christensen et al., 2013).

In sum, a large body of research has indicated substantial birth cohort differences regarding several cognitive abilities, in several countries, and over a wide range of ages.

**Cohort differences in cognitive abilities in old age**

Several studies have found cohort differences concerning cognitive functioning in later life. Finkel et al. (2007) used data from the Swedish Adoption/Twin Study of Aging to compare two different cohorts, younger (born 1926-1948) and older (born 1900-1925), regarding four different cognitive measures (verbal, spatial, memory and processing speed abilities). Finkel et al. (2007) found significant cohort differences for three of the four cognitive measures- verbal, spatial and memory abilities- where the younger cohort scored higher than the older cohort. No cohort differences were, however, found regarding processing speed.

Skirbekk, Stonawski, Bonsang and Staudinger (2013) used data from the English Longitudinal Survey on Aging (ELSA) to study possible Flynn effects regarding immediate word recall, delayed word recall and verbal fluency. They included data from two different birth cohorts (born 1930-1949 and 1936-1955), subdivided the cohorts into age groups

ranging from 50 to 74 years of age (i.e. 50-54, 55-59, 60-64, 65-69, 70-74) and compared the cohorts at the same ages. Overall, the later born cohort performed better on immediate word recall, delayed word recall and verbal fluency.

Baxendale (2010) compared data from the norming samples of the Adult Memory and Information Processing Battery, measured in 1985, and the updated version, the BIRT (Brain Injury Rehabilitation Trust) Memory and Information Processing Battery, measured in 2007. Baxendale found evidence for Flynn effects extending into old age regarding memory for visual material, but not for verbal memory leading to the conclusion that the Flynn effect on memory may be material specific (i.e. evident on only some forms of memory tests and not others).

Llewellyn and Matthews (2009) used data from two British cohorts, taken from the Medical Research Council's Cognitive Function and Ageing Study and ELSA, measured on semantic verbal fluency in 1991 and 2002 respectively, at ages 65 years and above. Their results indicated significant cohort differences, with the later born cohort outperforming the earlier born.

Willis and Schaie (2006) also reported cohort differences when examining data from the Seattle Longitudinal Study (SLS), USA. They compared five cohorts (median birth years: 1896, 1903, 1910, 1917, and 1924) at ages 60, 67, and 74 years. Data concerning five cognitive measures were used: inductive reasoning and spatial orientation (representing fluid intelligence); number ability, verbal meaning and word fluency (representing crystallized intelligence). Cohort differences were found for inductive reasoning, spatial orientation, verbal meaning and word fluency, where each successive birth cohort performed at a higher level at each of the three ages of measurement compared to earlier cohorts. When it comes to number ability there were only small differences between the four latest birth cohorts at age 60.

Gerstorf et al. (2011) also used data from the SLS, on the same five cognitive measures as Willis and Schaie (2006), to compare two birth cohorts (born between 1883-1913 and 1914-1948 respectively) at age 70. In line with Willis and Schaie (2006), Gerstorf et al. found significant cohort differences concerning word fluency, verbal meaning, spatial orientation, and inductive reasoning at 70 years of age, where the later born cohort performed at a higher level than the earlier born cohort. There were no cohort differences regarding number ability.

Zelinski and Kennison (2007) used data from two cohorts from the Long Beach Longitudinal Study, USA, (born 1893-1923 and 1908-1940 respectively), measured on five occasions between ages 55 and 87, on four tests of fluid abilities (reasoning, list recall, text recall, and figure and object rotation) and one test of crystallized abilities (vocabulary). They found evidence of cohort effects on all fluid abilities but not regarding crystallized ability (vocabulary).

Rönnlund and Nilsson (2008) studied the generality of the Flynn effects across age on declarative memory (semantic and episodic) and visuospatial ability. They analysed data from the Betula prospective cohort study, Sweden, with measurements taken at ages 35, 40, 45, 50, 55, 60, 65, 70, 75, and 80 years on four measurement occasions (1989, 1994, 1999 and 2003). They found successively higher mean-level performances, where later born cohorts scored higher than earlier born cohorts on all three cognitive measures and at all ages.

Rönnlund and Nilsson (2009) further used the Betula sample to study different sub-factors of episodic memory (recall and recognition) and semantic memory (vocabulary and word fluency). They found significant cohort differences in all the sub-factors, where later born cohorts performed at a higher mean level compared with earlier born cohorts, although the differences seemed to level off for the cohorts born 1950 and later.

Lastly, Bowles, Grimm and McArdle (2005), using data from the General Social Survey, USA, found cohort effects regarding a sub-factor of semantic memory, namely vocabulary knowledge. Their results were somewhat mixed as they found, using non-linear exploratory factor analysis, that vocabulary knowledge consists of two dimensions, basic vocabulary and advanced vocabulary. Bowles et al. (2005) studied three different birth cohorts (born 1920, 1940 and 1960) and found that later born cohorts had lower advanced vocabulary compared to earlier born cohorts. For basic vocabulary the results were reversed, later born cohorts had higher basic vocabulary than earlier born cohorts (Bowles et al., 2005).

In sum, numerous studies demonstrate that there are significant birth cohort differences in cognitive functioning in later life. But, it is also of paramount importance to consider possible cohort differences in trajectories of cognitive decline. Do these cohort differences manifest themselves only in form of cohort differences in level of functioning or do they also become manifest in rate of change?

**Cohort differences in trajectories of cognitive change**

There is an apparent shortage of studies regarding possible cohort differences in trajectories of cognitive decline. To a large extent possible cohort differences in cognitive decline is missing or only touched upon briefly in reviews concerning cohort differences in cognitive aging (see for instance Skirbekk et al., 2013), so there is a lack of knowledge regarding to what extent cohort differences manifest themselves in rate of decline (Gerstorf et al., 2011). One reason for this is due to the fact that there are few studies incorporating large representative samples, followed longitudinally and measured using comparable cognitive measurements.

However, a few studies have in fact investigated cohort differences in cognitive trajectories and the findings are somewhat inconsistent. Willis and Schaie (2006; see also

Schaie, 2005) found cohort differences in cognitive decline, with measurements at 60, 67, and 74 years of age, in addition to cohort differences in levels of functioning (see above). Regarding both the measures of fluid intelligence (inductive reasoning and spatial orientation) and crystallized intelligence (number ability, verbal meaning and word fluency) they report a more gradual rate of decline in later born cohorts compared with earlier born (see also Schaie, Willis & Pennak, 2005).

Gerstorf et al. (2011) also studied cohort differences regarding rate of cognitive aging using data from the SLS. When analyzing the trajectories of change via growth models, Gerstorf et al (2011) found that the later born cohort (birth year between 1914-1948) showed less steep rates of cognitive decline from 50 to 80 years of age then the earlier born cohort (birth year between 1883-1913) for all the measured cognitive abilities (including number ability). But when they modeled the data conditioned on mortality date (i.e. terminal decline) Gerstorf et al. found that the later born cohort showed a steeper, average, decline compared with the earlier born cohort. This indicates that birth cohort effects may not extend into the final stages of life.

Finkel et al. (2007), as well as Zelinski and Kennison (2007), found no or only weak evidence of cohort differences in trajectories of change and significant differences only in levels of performance (as described above).

Hülür, Infurna, Ram, and Gerstorf (2013) took a different approach to studying cohort differences in change trajectories regarding episodic memory, using data from the AHEAD study in the US. Instead of comparing birth cohorts, Hülür et al. compared two death cohorts, one that died earlier (1993-1999) and one that died later (2000-2010). The results revealed that the cohort that died later showed, on average, a steeper cognitive decline.

In sum, there is a shortage of studies regarding possible cohort differences in trajectories of cognitive change. Further, results are somewhat inconsistent, with some studies

indicating no birth cohort differences, some studies indicating less steep decline in later born cohorts, and other studies indicating steeper decline in later born cohorts. These few and inconsistent results necessitates further studies of cohort differences in trajectories of cognitive change.

**Proposed overall explanations for the Flynn effect**

Numerous theories have been proposed regarding the history-graded influences that cause the Flynn effect (Lynn, 2009b) although there is still a debate concerning the role of various influences that are likely to drive the effect (Russell, 2007). Most theories ascribe the effect to a mix of environmental influences such as improved nutrition, better health and health care, changes in parenting styles, smaller families, longer education, and more complex and stimulating work and social environments that have become "more optimal" to a larger proportion of the population in later born cohorts (e.g. Dickens & Flynn, 2001; Flynn, 1984, 2009; Hiscock, 2007; Lynn, 2009b; Russell, 2007; Rönnlund & Nilsson, 2009, Schaie, Willis & Pennak, 2005; te Nijenhuis, 2013; Williams, 1998). Ang, Rodgers and Wänström (2010) and Williams (2013) asserts that there are probably several factors that are driving the Flynn effect, but to various extents under different circumstances and during different periods of time. Rönnlund and Nilsson (2009) assert that most researchers do not propose a genetic explanation because the Flynn effect has been operating over such a short period of time in an evolutionary perspective (maybe 100 years).

But this presents something of a paradox or puzzle (e.g. Dickens & Flynn, 2001; Neisser, 1998). There have been numerous reports of what Flynn (1984) referred to as massive gains in average IQ scores. At the same time IQ is considered highly heritable (e.g. Davies et al., 2011; Deary, Spinath & Bates, 2006; Hunt, 2011). An account of the Flynn

effect therefore needs to solve the puzzle of how environmental influences can contribute to substantial increases in a highly heritable measure such as IQ.

Dickens and Flynn (2001) present a model that allows for large effects of the environment even with very high heritability estimates, thereby supposedly providing an important piece to solve the puzzle. According to Dickens and Flynn (2001) there is a strong reciprocal association between an individual's IQ and the environments experienced by the individual. That is, an individual with a higher IQ is more likely to select, or be selected for, more stimulating environments and experiences. Through a so-called multiplier effect these stimulating environments will lead to further increases in IQ and so on. Over time, even small environmental changes can have a substantial impact on IQ and cognitive functioning (Dickens & Flynn, 2001; Willis & Schaie, 2006). But importantly, Dickens and Flynn (2001) propose one further type of multiplier effect called a social multiplier. A significant aspect of an individual's environment consists of other people with whom the individual interacts. If the IQ of some individuals in a society increases this will affect the environments and experiences of others and increase their IQ through a social multiplier effect (Dickens & Flynn, 2001).

General health has improved globally in the last 150 years (Bloom, Canning & Jamison, 2004), and successive improvements in health since the 18$^{th}$ century have also been reported in Sweden (e.g. Finch & Crimmins, 2004; Gustafsson, Werdelin, Tullberg & Lindenfors, 2007, Willner, 2005), where the studies presented in this thesis were conducted.

Further, educational attainment has increased in several European countries, including Sweden, during the 20th century (Breen, Luijkx, Müller & Pollak, 2010). Traditionally there has been a female disadvantage regarding educational attainment that has decreased continually during the 20$^{th}$ century in Sweden (Breen et al., 2010) but this gender difference first disappeared among people born in the 1950s and1960s.

There have also been reports of decreases in family size in Sweden since the second half of the 19th century (Öberg, 2015), both in terms of median number of children born per mother, and in median sibship size (i.e. number of children in the family during a person's first 10 years).

Body height is often used as a proxy for nutritional health, where greater height is considered indicative of better nutritional intake. Öberg (2014) reported continual increases in the average heights of men born in Sweden from 1797 to 1968, which may then be seen as indicating continuing improvements regarding nutritional intake over this period.

From the above it seems that several of the factors proposed as driving the Flynn effect have been improving in Sweden over an extended period of time. Therefore we may expect to find evidence of substantial cohort differences in cognitive functioning in Swedish samples of older individuals.

To summarize, the following factors and influences have been suggested to account for the Flynn effect: improved nutrition, improved health and health care, changes in parenting styles, smaller families, longer education, increased exposure to testing, more complex and stimulating work and social environments, and multiplier effects. Over time we can assume a considerable interplay among these factors, which makes it difficult to estimate the relative importance of each factor separately as they in fact operate in concert.

**Specific and major influences for observed cohort differences**

Given the demographic trend of population aging, and the importance of cognitive functioning for well-being and performance of daily activities, it is imperative to identify modifiable factors related to both cognitive decline and cognitive maintenance in old age (Arntzen, Schirmer; Wilsgaard, & Mathiesen, 2011; Hendrie et al., 2006). Although it seems impossible to identify and fully disentangle all influences that contribute to observed cohort

differences, some such as education, gender, and overall health- especially cardiovascular health- seem to be of greater significance.

**Education, Gender, and cognitive functioning**

Given the importance of education as a determining factor of individual differences in levels of cognitive functioning, along with secular changes in length and quality of education, many researchers have suggested the importance of evaluating the effects of education on cohort trends.

A positive association is typically found between educational attainment and cognitive functioning in midlife and old age (e.g. Angel, Fay, Bouazzaoui, Baudouin & Isingrini, 2010; Cagney & Lauderdale, 2002; Clouston et al., 2012; Glymour, Kawachi, Jencks & Berkman, 2008; Hatch, Feinstein, Link, Wadsworth & Richards, 2007; Kaplan et al., 2001; Schneeweis, Skirbekk & Winter-Ebmer, 2012; Van Hooren et al., 2007). Results are inconsistent regarding the association between education and rate of cognitive change. Some studies report no association with rate of cognitive change (e.g. Muniz-Terrera et al., 2009; Piccinin et al., 2013; Van Dijk, Van Gerven, Van Boxtel, Van der Elst & Jolles, 2008; Van Gerven, Meijer & Jolles, 2007; Wilson et al., 2009; Zahodne et al., 2011). Other studies suggests a more complex association where the effect of education is related to the cognitive domain in question (e.g. Alley, Suthers & Crimmins, 2007; Ardila, Ostrosky-Solis, Rosselli & Gómez, 2000; Glymour, Tzourio & Dufouil, 2012), where higher levels of educational attainment are related to slower rates of decline on some tests (e.g. general mental status and non-verbal memory), unrelated to rates of decline in others (e.g. working memory) and, even, related to more rapid rates of decline in yet other tests (e.g. verbal memory and verbal fluency). Christensen et al. (1997) found that educational attainment was associated with slower decline

in crystallized intelligence but was not related to rates of decline on tests measuring fluid intelligence.

During the 20th century, work complexity increased quite remarkably. One important criteria used for selecting workers to suitable jobs has been education. We may therefore expect education to be a stronger factor in regards of work complexity in later born cohorts compared to earlier born cohorts. As work complexity is related to cognition in later life, education may therefore also be a stronger predictor of late life cognitive functioning in later born cohorts.

There are also reports of gender differences regarding cognitive functioning in old age (e.g. de Frias, Nilsson & Herlitz, 2006; Jorm, Anstey, Christensen & Rodgers, 2004; Maitland, Intrieri, Schaie & Willis, 2000; Meinz & Salthouse, 1998; Munro et al., 2012; Singer, Verhaeghen, Ghisletta, Lindenberger & Baltes, 2003; Van Exel et al., 2001; Van Hooren et al., 2007) where women tend to perform better on some cognitive tests (e.g. verbal memory, and immediate and delayed recall) while men perform better on others (e.g. visuo-spatial tests, and digit-span backwards). Regarding gender differences in cognitive decline Singer et al. (2003) found no gender differences while Alley et al. (2007) showed that women declined at a faster rate than men on two measures (verbal recall and working memory).

Weber, Skirbekk, Freund and Herlitz (2014) analyzed data from the longitudinal Survey of Health, Aging and Retirement in Europe (SHARE) for participants born between 1923 and 1957 measured in 2006-2007 on three cognitive abilities (i.e. numeracy, category fluency, and episodic memory). Their results indicated that women have benefited more, cognitively, than men from societal improvements in living conditions and educational opportunities. Further, also using data from the SHARE study, Weber, Dekhtyar and Herlitz (2017) reported evidence of larger Flynn effects for women compared to men in Europe from 2004-2005 to 2013 on measures of episodic memory and category fluency.

The above studies suggest that education and gender, among a longer list of potential influences, should be taken into account when studying cohort differences in cognitive performances (Van Hooren et al., 2007).

**Cardiovascular health, brain, and cognitive functioning**

Cardiovascular risk factors have been proposed as important modifiable factors for cognitive health in aging (DeRight, Jorgensen, & Cabral, 2015; Dregan, Stewart & Gulliford 2012; Gunstad et al., 2006; Stephan & Brayne, 2008, Tilvis et al., 2004). Several researchers have also linked between-person variability in cognitive aging to cardiovascular risk factors, such as overall cardiovascular health (Raz & Rodrigue, 2006; Reuter-Lorenz & Lustig, 2005), diabetes (Barnes et al., 2007, Yaffe et al., 2009), hypertension (Barnes et al., 2007; Raz, Ghisletta, Rodrigue, Kennedy & Lindenberger, 2010; Raz & Rodrigue, 2006; Yaffe et al., 2009), body composition (BMI) (Yaffe et al., 2009), and smoking (Barnes et al., 2007; Yaffe et al., 2009).

Even though the human brain comprises only about 2 % of a person's body weight (Allaman & Magistretti, 2013; Carlson, 2013; Kalaria, 2010), it continuously receives about 20 % of the blood flow from the heart (Carlson, 2013), and accounts for about 25 % of total glucose utilization (Allaman & Magistretti, 2013), and 20 % of the body's oxygen and nutrient consumption (Cherubini et al., 2010; Kalaria, 2010). Furthermore, the brain is only capable of storing a small fraction of the fuel it needs (mainly glucose) (Carlson, 2013). In this respect, the brain is highly dependent on the functioning of the vascular system (Carlson, 2013; Cherubini et al., 2010; Kalaria, 2010). Disturbances (structural, chemical, or functional) in macro- or microcirculation in the brain will eventually affect cognitive functioning (Cohen et al., 2009; Forman et al., 2008; Haley et al., 2007; Kalaria, 2010).

A large body of evidence also indicates that cardiovascular risk factors such as hypertension, obesity, and diabetes are related to neurodegenerative processes leading to cognitive decline and eventually to dementia (e.g. Arntzen et al., 2011; Duron & Hanon, 2008; Feigin, Ratnasabapathy & Anderson, 2005; Grodstein, 2007; Gunstad et al., 2006; Kalaria, 2010; Knopman et al. 2001; Nash & Fillit, 2006; Zhong et al., 2012).

Cardiovascular risk factors, such as diabetes and hypertension, increase with age (Cherubini et al., 2010; Goldstein, Levey & Steenland, 2013; Kennelly, Lawlor & Kenny, 2009a; Luchsinger et al., 2005; Qiu, Winblad & Fratiglioni, 2005; Unverzagt et al., 2011). In light of the evidence of an association between cardiovascular risk and cognitive functioning and decline, this necessitates studies of this association also in old age.

Among multiple cardiovascular risk factors identified as contributing to cognitive decline and dementia, hypertension might be the most important modifiable risk factor (Gąsecki, Kwarciany, Nyka & Narkiewics, 2013). The evidence is strongest for an association between midlife blood pressure and cognitive functioning in later life, but regarding the link between late-life blood pressure and cognitive functioning results are more inconsistent (see for instance Qui, Winblad & Fratiglioni, 2005; Waldstein, 2003). Several studies, however, have indicated an association between blood pressure and cognitive functioning in later life. Alosco et al. (2012) found that hypertension was negatively associated with cognitive functioning in a sample of adults with heart failure (mean age 67.7 years). Goldstein et al. (2013) found that high blood pressure was related to faster cognitive decline in several cognitive domains in a sample with mild cognitive impairment (mean age at baseline 72.9 years). Johnson et al. (2008) found that hypertension was associated with both cognitive performance and risk for dementia in a sample of women aged 65 years or older. However, after controlling for various possible confounders this association was no longer significant.

Skoog et al. (1996) also found that high blood pressure in late life (age 70) was associated with an increased risk of subsequent dementia.

Thorvaldsson et al. (2012) found a non-linear association between diastolic blood pressure and cognitive functioning, such that both low and high diastolic pressure was associated with worse cognitive functioning in a population-based sample with baseline at age 70 measured on 12 occasions over 30 years. Kennelly and Collins (2012) and Kennelly, Lawlor and Kenny (2009b) also state that low blood pressure, especially diastolic, in older people confers an increased risk of Alzheimer's disease. This further indicates that the association between blood pressure and cognition in older ages may be U-shaped, rather than linear, suggesting that both low and high blood pressure could constitute cardiovascular risk factors.

A large body of research also indicate that diabetes is associated with cognitive decline and risk for dementia (see for instance Biessels, Deary & Ryan, 2008; Biessels, Staekenborg, Brunner, Brayne & Scheltens, 2006; Cheng, Huang, Deng & Wang, 2012; McCrimmon, Ryan & Frier, 2012; Moran et al. 2013; Tilvis et al., 2004). In a review Kloppenborg, van den Berg, Kappelle and Biessels (2008) compared four cardiovascular risk factors (type 2 diabetes, hypertension, obesity and dyslipidemia) in relation to risk of dementia. Kloppenberg et al. concluded that all four factors were associated with increased risk of dementia in old age, but that hypertension was the strongest predictor in midlife while diabetes was the strongest predictor in old age.

Being overweight or obese in middle age is also associated with poorer cognitive performance in old age and increased risk of dementia (e.g. Gunstad, Lhotsky, Wendell, Ferrucci & Zonderman, 2010; Gustafson, 2006), but this association may be weaker between late life overweight or obesity and late life cognition (Dahl & Hassing, 2012). Using longitudinal data, Hassing, Dahl, Pedersen and Johansson (2010) found that higher Body

Mass Index (BMI) in midlife was associated with lower level of performance but not rate of cognitive decline over a 30-year period. Cournot et al. (2006) found that a higher BMI was related to worse cognitive functioning (on word-list learning and digit-symbol substitution tests) and steeper decline over five years (on word-list learning) in a healthy, middle-aged sample. Elias, Elias, Sullivan, Wolf, and D'Agostino (2005) found a negative effect of obesity on cognitive performance for men (mean age 65.7 years) but not women (mean age 67.2).

Smoking is recognized as a cardiovascular risk factor and is also negatively related to cognitive functioning. Nooyens, van Gelder, and Verschuren (2008) found that smokers showed worse global cognitive functioning, speed, and flexibility compared to never smokers at baseline (age 43-70 years) and also evidenced a larger decline over a 5-year period. Deary et al. (2003) assessed the effects of smoking on cognitive decline from age 11 to age 80 years and found that current smokers declined more than never smokers and individuals who had quit smoking. Using data from several prospective and population based studies (with participants aged 65 and older), Ott et al. (2004) reported larger declines in Mini-Mental State Examination (MMSE) scores in current smokers compared with never smokers (average length of follow-up: 2.3 years). In a meta-analysis of 19 prospective studies (with an average age at baseline of 74 years and follow-up 2-30 years), Anstey, von Sanden, Salim, and O'Kearney (2007) found that current smokers had greater risk of Alzheimer's disease, vascular dementia, and any dementia, as well as greater declines in MMSE scores compared to never smokers. They also found that current smokers showed an increased risk of Alzheimer's disease and greater decline in MMSE scores compared to former smokers. Former smokers showed greater declines in MMSE scores compared to never smokers but no difference in risk of dementia. Tyas et al. (2003) also reported increased risk of dementia in smokers compared to non-smokers. Reitz, Luchsinger, Tang and Mayeux (2005) found that memory performance declined more rapidly in current smokers over age 75 compared to non-

smokers similar in age. They found no differences in any cognitive domain between smokers and non-smokers under age 75, and no differences between former smokers and never smokers.

Although there is evidence for a significant role of several influences on cardiovascular health it is recognized that cardiovascular risk factors tend to cluster in individuals and interact multiplicatively. These findings have initiated the development of multivariable cardiovascular risk scores (D'Agostino et al., 2008; Harrison et al., 2014; Joosten et al., 2013; Luchsinger et al., 2005). The most commonly used multivariable risk scores, in both clinical and research settings, are the Framingham risk models (FRS) used in predicting the 10-year risk of developing general cardiovascular disease, stroke, or coronary heart disease respectively (Harrison et al., 2014).

Several studies have investigated associations between scores on multivariable risk models and cognitive functioning and decline. Using the FRS general cardiovascular risk profile, Kaffashian et al. (2011) found that higher risk scores were associated with poorer performances in all studied cognitive domains (i.e. reasoning, memory, vocabulary, and phonemic and semantic fluency) in both women and men (mean age = 55 years). Higher risk scores were associated with a steeper 10 year decline on reasoning in men (Kaffashian et al., 2011). Unverzagt et al. (2011) found that scores on the FRS Stroke Risk Profile were associated with incident cognitive impairment in a stroke-free, community-dwelling population followed for an average of four years (mean age at baseline = 64.3 years).

Using a cross-sectional design, Elias et al. (2004) found a negative association between scores on the FRS Stroke Risk Profile and level of performance on tests measuring abstract reasoning, attention, visual-spatial memory, organization, and scanning in a sample with no history of stroke or dementia, drawn from the Framingham Offspring Study (mean age = 60.7 years, SD = 9.4). Llewellyn et al. (2008) also used a cross-sectional design to study

the association between cognitive functioning and scores on the FRS Stroke Risk Profile in a stroke- and dementia-free sample drawn from ELSA (mean age for men = 64.0, SD = 10.5; mean age for women = 65.6, SD = 12.5). Higher stroke risk was associated with worse performance on measures of immediate and delayed verbal memory, processing speed, semantic verbal fluency, and global cognitive functioning (summed z-scores on all the tests used in the study).

In a recent meta-analysis incorporating data from 19 studies that had assessed the association between cognitive functioning and any of the FRS cardiovascular risk models, DeRight et al. (2015) found a mean weighted effect size of r = -.16. DeRight et al. concluded that "composite cardiovascular risk scores can be useful indicators of future cognition" (2015, p. 344). Joosten et al. (2013) investigated, using a cross-sectional design, the association between cardiovascular risk, measured with the FRS for general cardiovascular disease, and cognitive functioning in several age groups (i.e. 35-44, 45-54, 55-64, 65-74, and ≥ 75 years). Joosten et al. found a negative association, of similar strength, in all age groups.

There have been several reports of decreasing secular trends concerning cardiovascular risk factors in countries such as Austria (Ulmer, Kelleher, Fitz-Simon, Diem, & Concin, 2007), England and Wales (Unal, Critchley, & Capewell, 2004), Finland (Vartiainen et al., 2010), Portugal (Pereira et al., 2013), Turkey (Unal et al., 2013), Sweden (Peltonen, Huhtasaari, Stegmayr, Lundberg, & Asplund, 1998), and the USA (Gregg et al., 2005). Notably, there are also reports of decreasing secular trends regarding several cardiovascular risk factors in the Gothenburg region (where the studies presented in this thesis were conducted), over four decades since the early 1960s (e.g. Harmsen, Wilhelmsen, & Jacobsson, 2009; Rosengren et al., 2009; Rosengren et al., 2000; Wilhelmsen et al., 2008). Even though there have been increases in some risk factors, such as the prevalence of diabetes and BMI, the overall risk has decreased (Rosengren et al., 2009; Rosengren et al., 2000;

Wilhelmsen et al., 2008). Given the association between cardiovascular risk factors and cognitive functioning and decline, and evidence of decreasing overall cardiovascular risk in later born cohorts, it may be that the strength of the association between cardiovascular risk and cognition is attenuated in later born cohorts. That is, even though the mechanisms linking cardiovascular risk and cognitive functioning have not changed at the individual level, cardiovascular risk, because it has decreased in general, may be of less relative importance (compared to other determinants) in relation to individual differences in cognitive functioning in later born cohorts.

The exact pathways and underlying mechanisms of the observed associations between cardiovascular risk factors and cognitive performance and decline are not fully elucidated. The associations are proposed to reflect conditions affecting cerebral blood flow (e.g., atherosclerosis and cerebral hypoperfusion) and conditions with negative effects on the neural integrity of the brain (e.g., silent brain infarcts, white matter lesions/hyperintensities, neurodegeneration, oxidative stress, and inflammation) (see for instance Aleman, Muller, de Haan, & van der Schouw, 2005; de la Torre, 2012; Gorelick et al., 2011; Kalaria, 2010; Kivipelto et al., 2001; Qui, Winblad, & Fratiglioni, 2005).

Hypertension has been suggested to affect cognitive functioning through several mechanisms such as cerebral hypoperfusion, i.e. decreased cerebral blood flow, (Cherubini et al., 2010; de la Torre, 2012; Kalaria, 2010;Liu & Zhang, 2012; Waldstein, 2003), neural atrophy (Cherubini et al., 2010; Gąsecki et al., 2013, Qui, Winblad, & Fratiglioni, 2005; Waldstein, 2003), cerebral vascular damage/dysfunction (e.g., atherosclerosis, and structural changes in blood vessels irrigating the white matter) (Cherubini et al., 2010; Gąsecki et al., 2013; Kalaria, 2010; Qui, Winblad, & Fratiglioni, 2005; Waldstein, 2003), oxidative stress (Cherubini et al., 2010; Liu & Zhang, 2012), white matter hyperintensities/lesions (Cherubini

et al., 2010; Gąsecki et al., 2013; Guo et al,. 2009; Kalaria, 2010; Qui, Winblad & Fratiglioni, 2005; de la Torre; 2012; Waldstein, 2003), and silent brain infarcts (Waldstein, 2003).

Several links between diabetes and cognitive functioning have also been reported, such as white matter hyperintensities/lesions (Biessels et al., 2008; Kalaria, 2010; McCrimmon et al., 2012), micro- and macrovascular disease (Beeri, Ravona-Springer, Silverman, & Haroutunian, 2009; Biessels et al., 2006; McCrimmon et al., 2012), neural atrophy (Biessels et al., 2008; Biessels et al., 2006; Brundel, van den Heuvel, de Bresser, Kappelle, & Biessels, 2010; Kalaria, 2010; McCrimmon et al., 2012; Moran et al., 2013), oxidative stress and inflammatory processes (Kalaria, 2010), and silent and lacunar infarcts (Biessels et al., 2008; Biessels et al., 2006; Kalaria, 2010; McCrimmon et al., 2012; Moran et al., 2013).

Obesity and high BMI are thought to be linked to cognitive functioning and decline through factors such as increased gray matter loss/reduced gray matter volume (Gunstad et al.,2008; Taki et al., 2008; Walther, Birdsill, Glisky, & Ryan, 2010), smaller whole brain volume (Gunstad et al., 2008), and increased neural atrophy (Raji et al., 2010)

Smoking has also been linked to cognitive functioning and decline through several factors, such as white matter hyperintensities/lesions (Kalaria, 2010; Swan & Lessov-Schlaggar, 2007), oxidative stress (Tyas et al., 2003; Swan & Lessov-Schlaggar, 2007), inflammatory processes (Swan & Lessov-Schlaggar, 2007), atherosclerosis (Swan & Lessov-Schlaggar, 2007), reduced gray matter volume and density (Brody et al., 2004; Gallinat et al., 2006), cortical thinning (Kühn, Schubert, & Gallinat, 2010), and cerebral infarcts (Ott et al., 2004).

**The co-constructive perspective on life-span development and cognitive aging**

As mentioned above, cohort differences in cognitive abilities have been attributed to history-graded influences. Schaie (2008; 2010) and Willis and Schaie (2006) have proposed a co-constructionist model for cognitive development in adulthood that takes, among other things, history-graded factors into consideration. Central to this co-constructionist model is its emphasis on both neurobiological and sociocultural influences on cognitive development and cognitive aging. This model incorporates two life-span perspectives on development: (a) the co-constructionist perspective by Baltes and colleagues (e.g. Baltes, 1997; Li, 2003) and (b) the dual-intelligence perspective proposed by Horn and Cattell (1967).

It has long been maintained that development obviously is influenced by both biological and sociocultural factors (e.g. Li, 2003; Schaie, 2008; Willis & Schaie, 2006). Within the co-evolutionary perspective it is recognised that cohort differences in cognition (i.e. Flynn effects) are largely attributable to cumulative cultural evolution (Schaie, 2008; Willis & Schaie, 2006). Culture can be defined here as "*ongoing collective social processes that generate social, psychological, linguistic, symbolic, material, and technological resources that influence human development*" (Li, 2003, p. 172). Cumulative cultural evolution then refers to the fact that these cultural resources are not static but continuously developing and changing over time. Li (2003) also suggests a triarchic view of culture incorporating three conjoint aspects, namely resource, process, and developmental relevancy.

Culture as socially inherited resources consists of the knowledge, beliefs, values, technologies and material artefacts accumulated by a society and transferred to future generations. According to Willis and Schaie (2006) these accumulated resources are represented by structural variables such as educational attainment, occupational status, and cognitive functioning. That is, through variables indicating an individual's level of acquisition of these cultural resources.

Culture as an ongoing social process emphasizes the notion that culture is also a time-dependent, dynamic process and driven largely by changes in social interactions. This includes the notion that experiences, activities, etc. in the daily life of individuals are shaped by the social reality shared by a society (Willis & Schaie, 2006). According to Willis and Schaie (2006) an individual's experiences regarding for instance health related behaviours, engagement in cognitively stimulating activities, and work complexity, are aspects of this socially dynamic process that, in turn, influences the individual's cognitive development and functioning. Further, the idea of culture as an ongoing social process also stresses the point that the culture itself is continuously being changed and modified from social interactions and social learning, as well as developments in technology, environment and populations (Li, 2003). This is the basis for cohort differences regarding for instance cognitive functioning which also provides a direct link between the co-constructionist model and the observed Flynn effects.

Culture as an ongoing social process tends to produce cohort differences regarding various sociocultural factors that influence cognitive development. Examples of these sociocultural factors are increases in educational levels, health related behaviours, nutrition, occupational experiences (work complexity) and cognitive stimulation and engagement (Willis & Schaie, 2006). Also, these historical processes (e.g. increasing levels of education and nutrition) determine the changes in both neurobiological and sociocultural influences on development (Schaie, 2008).

Finally, the notion of culture as developmental relevancy attests to the importance that culture has for individual development (Li, 2003). Culture is the mediator of resources and social processes that affects the individual, although these resources and processes differ among people which affect the unique individual development.

The co-constructionist approach by Baltes and colleagues (e.g. Baltes, 1997; Li, 2003) takes a life-span perspective on co-evolutionary theory and postulates three basic principles regarding the relative impact of biological and cultural influences over the life-span. The first principle states that the impact of evolutionary selection processes (i.e. natural selection) decreases with age. That is, the beneficial effects of evolutionary processes are more pronounced early in life and tend to decrease successively as we age.

The second principle states that further advancements in human development (including cognitive development) are dependent on increases in cultural resources. From an individual perspective, this means that the need for cultural resources to promote further development or prevent age-related decline in functioning increases with age. From a historical, or cohort, perspective this means that the cumulative cultural evolution contributes to successive increases in average functioning, including cognitive functioning (i.e. Flynn effects).

The third principle states that the efficacy of cultural resources diminishes with age due mainly to declining biological (including neurobiological) functioning. That is, the effectiveness of for instance technological, social, and psychological resources decreases successively as people get older.

Thus, it is mainly the second principle, that continuing advancements in human development (including cognitive development) are dependent on further increases in cultural resources, that is of relevance for the emergence of birth cohort differences in cognitive aging.

**The dual-intelligence perspective**

Schaie (2008) and Willis and Schaie (2006) have proposed that the co-constructionist perspective is applicable to the dual-intelligence model, in which intelligence is organized into the two main components of Fluid and Crystallized intelligence. Crystallized intelligence

refers to the ability to solve problems by using stored knowledge or learned problem-solving methods, and fluid intelligence refers to the ability to use reasoning to solve novel problems that is relatively independent of previously learned operations or knowledge (Horn & Cattell, 1967; Hunt, 2011; Nisbett et al., 2012). Neurobiological influences particularly affect fluid intelligence, whereas experience and culture-based knowledge mainly affect crystallized intelligence (Schaie, 2008; Willis & Schaie, 2006). There is, however, evidence that suggests that at least some experiential factors, such as education, can affect both fluid and crystallized abilities (Baker et al., 2015; Rönnlund & Nilsson, 2008).

Research shows that fluid abilities start to decline earlier in the lifespan than crystallized abilities (e.g., Alwin, 2008; Alwin & Hofer, 2008; Schaie 2008; Willis & Schaie, 2006). Also, reported Flynn effects have generally been larger regarding fluid abilities compared to crystallized abilities (e.g., Dickens & Flynn, 2001; Hiscock, 2007; Lynn, 2009 b; Pietschnig & Voracek, 2015; Schaie, 2005; Trahan et al., 2014) even though Uttl and Van Alstine (2003), studying vocabulary scores, found that crystallized abilities might be increasing as fast as fluid. Pietschnig, Voracek and Formann (2010) also concludes, in their meta-analysis, that the Flynn effects regarding crystallized abilities are comparable to the ones reported for fluid abilities.

**Implications for cognitive aging and cohort differences**

The historical processes that have been outlined above affects the sociocultural and neurobiological influences that in turn affect cognitive development (Schaie, 2008; 2010). According to the co-constructionist model suggested by Schaie (2008; 2010) and Willis and Schaie (2006) neurobiological influences such as chronic diseases (e.g., hypertension) and biomarkers (e.g., Apo-E e4) primarily affect fluid abilities.

Sociocultural influences have, according to Schaie (2008; 2010) and Willis and Schaie (2006), effects on both crystallized and fluid abilities. Sociocultural influences affect both an individual's current activities (e.g., health related behaviours, cognitive stimulation, work complexity) and accumulated cultural resources (e.g., educational attainment, occupational status, and cognitive functioning) (which also affect current activities) (Schaie 2008; 2010). Current activities and accumulated resources then influence the individual's crystallized abilities. But according to Schaie (2008; 2010) an individual's accumulated resources and crystallized abilities affect the fluid abilities.

Schaie (2008; 2010) further proposes that sociocultural and neurobiological influences differ in the timing of their respective relative impact. The accumulation of sociocultural resources such as educational and occupational attainment, and cognitive ability are attained predominantly during the earlier part of adulthood. Neurobiological influences, such as chronic disease (e.g., hypertension, cardiovascular disease, type 2 diabetes) and effects related to various biomarkers (e.g., c-reactive protein, total plasma homocysteine, Apo-E e4) are proposed to increase with aging.

The co-constructionist model proposes that the positive advancement regarding sociocultural influences and increasing possibilities to control and counter negative neurobiological influences such as chronic diseases should lead to cohort differences in both levels of cognitive functioning and change trajectories. Advancements concerning sociocultural influences are predicted to have positive effects mainly on change trajectories for crystallized abilities in later born cohorts. Cultural advancements should have a limited impact on fluid abilities in old age, due to the increasing negative effects of neurobiological influences with age (Schaie 2008; 2010). However, due to the successively increasing abilities to treat, and delay the onset of, chronic diseases, the deleterious neurobiological effects in old

age should be decreasing in later cohorts leading to positive effects on the change trajectories for fluid abilities in later born cohorts (Schaie 2008; 2010).

**The heterogeneity of cognitive aging**

Just as there have been numerous reports of birth cohort differences in cognitive functioning, a large body of research has indicated between-person differences in cognitive aging within cohorts. Although aging has commonly, and stereotypically, been associated with inevitable cognitive decline (Reuter-Lorenz, 2002; Reuter-Lorenz & Lustig, 2005; Schaie, 2016), there is substantial heterogeneity in cognitive aging (Ardila, 2007; Eyler, Sherzai, Kaup & Jeste, 2011; Habib, Nyberg & Nilsson, 2007; Raz et al., 2010). The proportion of individuals showing cognitive decline increases with age, but a few studies demonstrate that a substantial proportion remain stable, or may even show cognitive gains (Schaie, 2016).

Yaffe et al. (2009) followed 2509 participants (aged 70-79 at baseline) over eight years. Thirty percent of the participants were categorized as showing maintained cognitive function (i.e., showing cognitive gain or no decline), 53% showed minor decline (i.e., decline of no more than 1 SD of the mean of the slopes), while 16% showed major decline (i.e., more than 1 SD of the mean of the slopes).

Josefsson, de Luna, Pudas, Nilsson, and Nyberg (2012) followed 1558 participants, divided into age cohorts with five-year intervals (i.e. 35, 40, 45,…85 years at baseline) for 15 years in a study of episodic memory. Participants were categorized, based on comparison to an average participant, as maintainers (better than average rate of change), decliners (worse than average rate of change), or average. Eighteen percent were categorized as maintainers, 13 % were categorized as decliners, and 68 % as average.

Barnes et al. (2007) followed a sample of 9704 women (aged 65 or older at baseline) for 15 years and found that nine percent evinced either gain or no decline on a modified Mini-Mental state examination.

Using data from the SLS, Schaie (2010) categorized participants from several age groups (i.e., 25-32, 32-39, 39-46, 46-53, 53-60, 60-67, 67-74, 74-81, 81-88 years) as showing either cognitive decline, stability, or gain over a seven year study period. Even though the proportion of participants that were categorized as showing cognitive stability or gain gradually decreased in the older age groups, and proportions categorized as showing decline increased, the majority of participants ($\geq$ 55%) showed stability or gain in all studied age groups, including the oldest.

Several researchers have proposed that the observed heterogeneity in cognitive aging is, partly, related to individual differences in the functioning (e.g., Eyler et al., 2011; Persson et al., 2006; Persson et al., 2012; Pudas et al., 2013; Waiter et al., 2008) and structure of the brain (e.g., Eyler et al., 2011; Kaup, Mirzakhanian, Jeste, & Eyler, 2010; Persson et al., 2006; Persson et al., 2012). Interestingly, Woodley of Menie, Peñaherrera, Fernandes, Becker and Flynn (2016) report secular increases in brain mass, which they assert is an indirect proxy for neuroanatomical changes more directly related to the Flynn effect, in the UK (birth years 1860-1940) and Germany (1861-1978).

As mentioned above, several researchers have also linked between-person variability in cognitive aging to cardiovascular risk factors (e.g., Barnes et al., 2007; Raz et al., 2010; Raz & Rodrigue, 2006; Reuter-Lorenz & Lustig, 2005; Yaffe et al., 2009), which are related to the functioning and structural integrity of the brain (e.g., Aleman et al., 2005; de la Torre, 2012; Gorelick et al., 2011; Kalaria, 2010; Kivipelto et al., 2001; Qui, et al., 2005).

To summarize, there is convincing evidence supporting the notion of substantial heterogeneity in cognitive aging. This between-person variability has been

suggested to be, at least partly, related to individual differences in the structure and functioning of the brain and also to cardiovascular risk factors. In light of decreasing secular trends concerning cardiovascular risk factors, and secular increases in brain mass, we may therefore expect birth cohort differences regarding heterogeneity in cognitive aging (i.e., in proportions of individuals showing cognitive decline, stability or gain over a certain age range).

**Rational and implications for further studies**

In light of the worldwide trend of population aging it is imperative to gain a better understanding regarding cognitive aging. Aging is typically associated with compromised cognitive functioning, and incidence and prevalence of cognitive impairment and dementia are projected to increase substantially worldwide in coming decades (e.g., Ferri et al., 2006; Llewellyn & Matthews, 2009; Matthews & Dening, 2002; Prince et al., 2013; Wimo, Jönsson, Bond, Prince, & Winblad, 2013). These facts provide strong support for further studies aiming at identifying modifiable factors associated with cognitive functioning in aging. In this respect, analyses of cohort differences seem to be an important research approach.

Hitherto, findings of substantial birth cohort differences (i.e., Flynn effects) in performance levels that extend into advanced ages caused Skirbekk et al. (2013) to project that if the observed Flynn effects continue, they may counterbalance the increase in population age, and even lead to an improvement in cognitive functioning at the population level. But aging is also experienced at the individual level, which makes it of immense importance to consider possible cohort differences in change trajectories. According to Schaie (2008), later born cohorts should be expected to decline less rapidly compared to earlier born cohorts. However, results from the few studies that have investigated cohort differences in

trajectories of change are mixed and so not yet fully conclusive. There is thus a need for further research focusing especially on cohort differences in rates of cognitive decline.

Given recent reports of decreasing overall cardiovascular risk in later born cohorts, it is especially relevant to investigate the possible moderating effect of birth cohort on the associations between cardiovascular risk and cognitive functioning.

## The present studies

### The aims of the present studies

### Study I

The aim of Study I was to investigate the proportions of participants showing cognitive decline, stability, or gain from age 70 to 79 on four cognitive measures (i.e., verbal meaning, perceptual- and motor-speed, logical reasoning, and spatial ability). A further aim was to investigate possible birth cohort differences in the proportions of participants showing cognitive decline, stability, or gain.

### Study II

The aim of Study II was to analyze birth cohort differences in level of cognitive functioning and rate of cognitive change in later life. We used data from the same three cohorts as in Study I, and measurements at ages 70, 75, and 79 years on two fluid cognitive measures (i.e., logical reasoning and spatial ability). We included gender and education as covariates in the analyses. We specifically addressed three main questions. The first was whether there are birth cohort differences in level of cognitive functioning and rate of cognitive change in old age. Based on previous research we hypothesized that later born cohorts would perform at a higher cognitive level than earlier born cohorts. We also hypothesized that later born cohorts would show less decline (even though previous studies are inconsistent in this respect). We further asked whether education could account for observed cohort differences in levels of performance and rates of change. We hypothesized that this was likely, since later born cohorts generally have higher educational attainment, which is associated with higher cognitive functioning. We also investigated possible cohort trends in the effects of education on level of performance and rate of change. As mentioned, we assumed that education is a stronger determinant of work complexity in later born cohorts

and therefore hypothesized that education would be a stronger determinant of levels of performance and rates of change in later born cohorts. Finally, we investigated gender differences in levels of performance and rates of change. Based on previous research, our hypothesis was that men, on average, would outperform women on the two fluid cognitive measures. More importantly, we asked whether there were cohort trends in the effect of gender on level of performance and rate of change. As gender equality in educational and work opportunities increased successively in Sweden during the 20$^{th}$ century, we hypothesized that gender effects would be smaller in later born cohorts compared to earlier born.

**Study III**

The aim of Study III was to further investigate birth cohort differences in levels of cognitive functioning and rates of change. In this study we extended the analyses, compared to study II, to five cognitive measurements: spatial ability, logical reasoning, verbal ability, perceptual- and motor-speed, and long-term picture recognition memory. Further, we present the evidence in the form of conditioned probability distributions using a Bayesian analytical framework.

**Study IV**

The aim of Study IV was to evaluate the moderating effects of birth cohort on the associations between cardiovascular risk and levels of performance and rates of cognitive change from ages 70 to 79 on two fluid cognitive measures (i.e., spatial ability and logical reasoning). We used the Framingham Risk Score, FRS, based on non-laboratory predictors (age, gender, systolic blood pressure [SBP], BMI, smoking, and diabetes status) to approximate cardiovascular risk. As previous research have indicated that cardiovascular risk

have decreased successively in later born cohorts, we hypothesized that the association between FRS and cognition would be weaker in later born cohorts. That is, cardiovascular risk may be of less relative importance (compared to other determinants) in relation to individual differences in cognitive functioning in later born cohorts as a result of the decreased cardiovascular risk, even though the mechanisms linking cardiovascular risk and cognitive functioning have not changed at the individual level.

## Methods

### Participants and sampling design

In the studies presented in this thesis we investigated cohort differences in levels of cognitive functioning and rates of change in a representative sample drawn from the Gerontological and Geriatric Population Studies in Gothenburg (H70) including three birth cohorts born in 1901-02, 1906-07, and 1930, and measured on the same cognitive tests at the same ages (i.e., 70, 75 and 79 years).

The H70 study started in 1971-1972 with a systematic and representative sample of 70-year-old inhabitants of Gothenburg, Sweden (Rinder, Roupe, Steen & Svanborg, 1975; Svanborg, 1977). Subsequently, several more samples of 70-year-olds have been drawn and included in the H70 study. The cohorts included in the studies in this thesis were born in 1901-02, 1906-07, and 1930 and measured at 70, 75, and 79 years of age (see Table 1). For all three birth cohorts, participants were identified and systematically selected from the Swedish Revenue Office Register in a similar manner.

**Cohort 1901-02.** The first cohort was selected in 1971-1972. One-thousand one hundred forty-eight people born from July 1$^{st}$, 1901to June 30$^{th}$, 1902, on dates ending with 2, 5, or 8 where chosen for participation in the H70 study. This sample constituted approximately 30% of the population of 70-year-olds in Gothenburg. The baseline response rate for this sample was 85% yielding a representative sample (Rinder et al., 1975). All participants were randomly given a number between 1 and 5. Participants with numbers 1 and 2 were selected for psychometric testing (N = 460). The participation rate for this subsample at age 70 was 80%. Follow-up rates were 76% at age 75 and 47% at age 79. Attrition rate due to mortality was 14% at age 75 and 21% at age 79, and attrition due to other reasons such as refusal to participate, relocation, or administrational reasons (e.g., shortage of time) was 10% at age 75 and 8% at age 79.

**Cohort 1906-07.** In 1976-1977 a second cohort was included in the H70 study. Using the same sampling procedure as with the first cohort, 1281 individuals born from July 1st, 1906, to June 30th, 1907, were sampled. This sample constituted about 30% of the population of 70-year-old inhabitants of Gothenburg. Baseline response rate was 81% (Jönsson, Rosenhall, Gause-Nilsson & Steen, 1998). This sample also constitutes a representative sample of the population of 70-year-olds in Gothenburg (Dey, Rothenberg, Sundh, Bosaeus & Steen, 2002). Participants in this cohort were randomly given a number from 6 and 10. Participants with numbers 6 and 7 were selected for psychometric testing (N = 513). The participation rate for this subsample was 75% at age 70. Follow-up rates were 74% at age 75 and 56% at age 79. Attrition rates due to mortality were 13% at age 75 and 13% at age 79. Attrition due to other reasons was 13% at age 75 and 5% at age 79. For more information regarding the 1906-07 cohort see Nilsson (1983).

**Cohort 1930.** In the year 2000 all inhabitants of Gothenburg born in 1930 on days 3, 6, 12, 18, 21, 24 or 30 of each month were sampled (N = 767). The baseline response rate for this cohort was 66%. Comparisons indicate that responders and non-responders did not differ in terms of gender, marital status, 3-year mortality rate, or inpatient psychiatric care at baseline age 70 years (Sacuiu et al., 2010) nor regarding specific diagnoses such as cardiovascular disease or dementia (Falk et al., 2014). In 2005, this sample was extended by the inclusion of 75-year-olds born on days 2, 3, 5, 6, 11, 12, 16, 18, 20, 21, 24, 27, and 30 (N = 1250, response rate 63 %) (for details see Wiberg, Waern, Billstedt, Östling & Skoog, 2013). At the measurements at age 70, half of the participants were randomly selected for psychometric testing (N = 254). At the subsequent measurements at age 75 (N = 768) and 79 (N = 597) all participants were invited to perform the psychometric testing. Therefore, the sample proportion eligible for psychometric testing varies over the three measurement occasions. Participation rate at age 70 for the subsample selected for psychometric testing (N

= 254) was 90%. Follow-up rates were 85% at age 75 and 79% at age 79. Attrition rate due to mortality was 4% at age 75 and 8% at age 79. Attrition due to other reasons was 27% at age 75 and 27% at age 79.

In order to minimise biasing influences of floor effects on estimates of change in the psychometric measures, due to factors such as severe dementia, we omitted all participants with a score of zero on the cognitive measures at baseline (i.e., age 70). We also omitted measurements at age 79 for participants with a score of zero on both the 75- and 79-year measures. This way both initial level of functioning and decline for these participants could be included in the analyses, but the risk of incorporating further measures from seriously demented participants was reduced. In total, scores from 60 individuals were omitted from the analyses (25 from cohort 1901-02, 14 from cohort 1906-07, and 21 from cohort 1930).

**Cognitive measures**

A broad battery of cognitive measurements was used in the H70 study.

-Logical reasoning was measured with a Figure Logic test (see Dureman, Eriksson, Kebbon & Österberg, 1971). In this test participants are presented with geometrical figures, organized in rows with five figures per row. Participants are asked to identify, as quickly as possible, which figure differs in some aspect from the other figures. Participants' raw scores are calculated as Total number of correct items – (Total number of wrong items/4) in order to penalize for guessing and wrong answers. The test consists of 30 rows of figures, with an 8-minute time limit and a maximum score of 30.

-Spatial ability was measured with a Swedish version of the Block Design test (Wechsler, 1981). In this test participants are asked to organize colored wooden blocks in accordance with seven different patterns presented on cards. The test has a 20-minute time limit and a maximum score of 42.

-Perceptual- and motor- speed, or perceptual speed, was measured with a Figure Identification test. Participants were presented with figures organized in rows of six figures per row. Participants were instructed to match, as quickly as possible, the target figure (the first figure in each row) with an identical figure in the same row. The entire test consists of 60 rows of figures. Participants' raw scores are calculated as Total number of correct items – (Total number of wrong items/4) in order to penalize for guessing and wrong answers. The test has a time limit of 4 minutes and a maximum score of 60.

-Verbal ability was measured with a synonym test. Participants were asked to match a target word with a synonym word among five alternatives. The time limit was 7 minutes; maximum score was 30. All words were presented in an enlarged form to compensate for potential deficiencies in vision.

- Long-term picture recognition memory was measured with Thurstone's picture memory test. In this test participants are presented with 28 pictures of familiar objects at a rate of five seconds per picture. After a delay of 30 seconds each presented picture is shown again, but together with three distractors. Participants are instructed to select the picture that had been presented earlier. All pictures were in enlarged form to compensate for possible deficiencies in vision. Maximum score on this test was 28.

The Block Design and Figure Identification tests were administered on all measurement occasions (i.e., at ages 70, 75, and 79) for all three birth cohorts. The Figure Logic test was omitted at ages 75 and 79 for the 1906-07 cohort. Thurstone's Picture memory test was omitted at age 70 for the 1901-02 and 1930 cohorts, and at age 75 for the 1906-07 cohort. The Synonym test was omitted at age 75 for the 1930 cohort. At age 70, half of the sample in the 1901-02 cohort was randomly selected to take only the Figure Logic and the Synonym tests. At age 75, the 1930 cohort received a shorter version of the Figure Identification test (with a maximum score of 30 instead of 60). For more information

regarding the tests and their psychometric properties see Dureman et al. (1971). For more information concerning the usage of the tests in the H70 study, see Berg (1980). Reliability coefficients for the cognitive measures range from 0.82 split-half reliability for Thurstone's Picture memory test to 0.96 split-half reliability for the Figure identification test.

**Cardiovascular risk**

To assess cardiovascular risk in Study IV we used the FRS based on simple office-based non-laboratory predictors (D'Agostino et al., 2008). This constitutes a composite measure of the risk of developing any cardiovascular disease event within 10 years of assessment (i.e., it is a global assessment of cardiovascular risk rather than a measure of the risk for a specific type of cardiovascular disease event such as stroke). The FRS was developed based on 1174 cardiovascular disease events observed over a 12-year follow-up of 8491 participants in the Framingham study (D'Agostino et al., 2008).

This simple non-laboratory based composite score is based on predictors that do not require any laboratory analyses. The predictors are age, sex, systolic blood pressure (SBP), BMI, current smoking status (non-smoker = 0, current smoker = 1) and diabetes status (non-diabetic = 0, diabetic = 1), and use of anti-hypertensive medication (D'Agostino et al., 2008). The equations used to calculate the cardiovascular risk differs between women and men, and SBP is weighted differently depending on the use of anti-hypertensive medication (Framingham Heart Study, 2017). For women not using anti-hypertensive medication the FRS is calculated as

$$1 - 0.94833^{\exp([2.72107\times\log(Age)+0.51125\times\log(BMI)+2.81291\times\log(SBP)+0.61868\times Smoking+0.77763\times Diabetes]-26.0145)}$$

For women using anti-hypertensive medication, the SBP beta weight is $2.88267 \times \log(SBP)$. For men not using anti-hypertensive medication the FRS is calculated as

$$1 - 0.88431^{\exp([3.11296\times\log(Age)+0.79277\times\log(BMI)+1.85508\times\log(SBP)+0.70953\times Smoking+0.53160\times Diabetes]-23.9388)}$$

For men using anti-hypertensive medication, the SBP weight is $1.92672 \times \log(SBP)$.

Blood pressure was measured using a mercury sphygmomanometer on the right arm after a 5-minute rest in a seated position. Blood pressure was registered to the nearest 5 mmHg. The same measurement procedure was used across all three cohorts.

BMI was calculated as weight (kg) divided by height squared ($m^2$). Standing height was recorded to the nearest centimeter and weight to the nearest 0.1 kg. Measurements were taken in the morning with participants wearing light clothing. To minimize methodological differences in the measurements, all investigators received the same training and instructions.

Data regarding smoking, diabetes status, and use of anti-hypertensive medication was obtained through self-reports during the examinations.

**Statistical analyses**

For Study I we used the standard error of measurement ($SE_M = SD\sqrt{1 - r_{xx}}$) at baseline (i.e., 70 years of age) to categorize participants as showing cognitive decline (if scores decreased by >1 $SE_M$ from age 70 to 79), cognitive stability (if change was ≤1$SE_M$), or cognitive gain (if scores increased by >1 $SE_M$). This was done for the four cognitive measures analyzed in Study I (i.e., verbal meaning, perceptual- and motor-speed, logical reasoning, and spatial ability). When calculating the $SE_M$ we used the reliabilities reported in Dureman et al. (1971), and the standard deviation (SD), for each respective cognitive test, of the total sample at age 70. The reported reliabilities were 0.89 for the Figure Logic test (split-half), 0.91 for the Block Design test (test-retest), 0.96 for the Figure Identification test (split-half), and 0.88 for the Synonym test (test-retest) (Dureman et al., 1971).

We used $\chi^2$-tests to analyze cohort differences in the proportion of participants showing cognitive decline, stability, and gain, and estimated effect sizes using Cramer's V.

In order to evaluate the robustness of our results to the specific cut-off used to categorize participants, we performed a sensitivity analysis. For this purpose we tested several

alternative cut-offs. First, we used the $SE_M$, in the same manner as described above, but used 0.80 and 0.70 as reliability when calculating $SE_M$. We also used the SDs of the total sample at baseline, i.e. age 70 to categorize participants. Here we used both a change of >1 and >0.5 SD to categorize participants as showing decline or gain respectively (otherwise showing stability). No matter the specific cut-off used, our results remained the same. Therefore, we chose to report only the results from the analyses using $SE_M$ based on the reliabilities reported in Dureman et al. (1971).

In study II we fitted multiple-groups Latent Growth Curve Models (LGCM) within structural equation modelling (SEM) to the data (see e.g., McArdle & Anderson, 1990; McArdle & Nesselroade, 2002). The basic model can be presented in a hierarchical form with level 1

$$y_{ij}^{(c)} = \alpha_{ij}^{(c)} + \lambda_{ij}^{(c)}\beta_{ij}^{(c)} + e_{ij}^{(c)}$$

and level 2

$$\alpha_i^{(c)} = \mu_\alpha^{(c)} + \zeta_{\alpha i}^{(c)}$$

$$\beta_i^{(c)} = \mu_\beta^{(c)} + \zeta_{\beta i}^{(c)}$$

where *y* is an observed outcome variable (i.e., reasoning or spatial ability) for individual *i* at time *j* and *(c)* refers to birth cohort (i.e., cohorts 1901-02, 1906-07, and 1930). The $\alpha$ and $\beta$ are latent intercepts and slopes, respectively, and $\lambda$ reflects the time structure of the slope component and was specified as 0, 5, and 9 for all cohorts in the present analyses, and *e* are residuals. The second level $\mu_\alpha$ and $\mu_\beta$ are mean estimates (i.e., fixed effects) for the intercepts and slopes and $\zeta_\alpha$ and $\zeta_\beta$ are between-person variability components (i.e., random effects) assumed to be normally distributed with a mean of zero and estimated variance and covariance across the components. Essentially, the main deviation of this model from the more common latent growth curve model (or mixed model, see e.g., Raudenbush & Bryk, 2002) is the inclusion of *(c)* which allows comparisons across birth cohorts on all parameters

in the model. We further included Gender and Education as covariates in the models. We used maximum likelihood estimation to derive parameters and tested cohort differences estimates using deviance tests.

For Study III we fitted linear growth curve models to the data from each of the outcome variables separately within a Bayesian framework (see e.g. Gelman et al., 2014) using non-informative prior distributions. Growth curve models are essentially multilevel models (e.g., Snijders & Bosker, 2012), sometimes referred to as hierarchal linear models (e.g., Raudenbush & Bryk, 2002), with the repeated measurements at level 1, or time, nested within the individuals at level 2. In all models, we specified the time variable as chronological age centered at the baseline value of age 70, the cohort variable was dummy coded using the 1901-02 birth cohort as reference group, and we included both gender and education as mean centered time constant covariates into the models. We then modeled the time and individual specific data points using a normal prior distribution with the mean derived from the linear combinations of the level 1 variables by coefficients, and the precision, or the reciprocal of the residuals, using a uniform prior in the range of 0 to 10 raised to the power of -2. We estimated all level 2 mean values (i.e., fixed effects) using a normal prior distribution with mean of 0 and a low precision of 0.01. The variance and covariance matrix (i.e., random effects) of the intercept and the age slope were estimated using a scaled inverse Wishart prior distribution with 3 degrees of freedom. The parameter estimates were derived through a numerical approximation using a Markov Chain Monte Carlo (MCMC) Gibbs sampling in JAGS (Plummer, 2003). For each model we used 3 chains, each with 150000 iterations, a burn-in of 75000, and a thinning factor of 5, resulting in 15000 sampling steps per chain, and a total of 45000. To evaluate convergence of each chain on the target distribution we plotted the trace, autocorrelations, and the marginal posterior density plots for each of the reported parameters (see online appendix). Occasional missing data on the outcome variables were

defined, modeled, and thereby handled in the integration of the posterior distribution across the parameter space under the assumption that missing data is missing at random as conventionally defined (Little & Rubin, 1987). There were no missing data for the age, gender, and education variables.

In Study IV we used multiple-groups LGCM within SEM (McArdle & Anderson, 1990; McArdle & Nesselroade, 2002) to evaluate the moderating effects of birth cohorts on the associations between the FRS and both level and change in cognitive performance from age 70 to 79. Gender and Education were included as covariates in all models, but in order to reduce model complexity we constrained the effects of these covariates to be equal across birth cohorts. Gender was coded as women = 0 and men = 1, and education was coded as compulsory education (i.e. 6 years or less for cohorts 1901-02 and 1906-07, 7 years or less for the 1930 cohort) = 0 and more than compulsory education = 1. We note that 6 years of education (7 years for the 1930 cohort) refers to "Folkskola" which was the compulsory level of education for these birth cohorts. The FRS variable was grand mean-centered and scaled such that the estimates would refer to change in the outcome per 10 % increase in cardiovascular risk.

In the analyses we fitted three types of LGCM to the data from each of the two cognitive outcomes. In all models we estimated average level of performance at age 70 and average linear rate of change from age 70 to 79 (counting in years) as unique parameters for each of the three birth cohorts. In Model 1 all effects of the FRS were constrained to zero, and this model was used mainly for comparative purposes. In Model 2, we estimated the effects of FRS on both the level and the change factors, but these parameters were constrained as equal across the birth cohorts. Finally, in Model 3, we released these parameter constraints across the birth cohorts such that the effects of FRS on both the level and change factors were free parameters. Occasional missing data were assumed to be missing at random, as

conventionally defined (Little & Rubin, 1987) and handled using full-information maximum likelihood estimation.

## Results

### Study I

Descriptive statistics for the cognitive measures analyzed in Study I are presented in Table 1, stratified by birth cohort and age at measurement. The proportion of participants categorized as showing cognitive decline, stability, or gain from age 70 to 79 are presented in Table 2, stratified by birth cohort and cognitive measure. As could be expected, a substantial proportion of participants showed cognitive decline from age 70 to 79, especially evident on the perceptual speed test. However, there were also significant proportions showing stability or even gain on all four tests (see Table 2 and Figure 1). This was particularly manifest on the verbal meaning test.

There were significant birth cohort differences in the distributions for all four cognitive measures, with weak to moderate effect sizes (for verbal meaning: $\chi^2(4) = 11.28$ $p = 0.024$, Cramer's V = 0.11; logical reasoning: $\chi^2(2) = 19.38$ $p = 0.000$, Cramer's V = 0.26; spatial ability: $\chi^2(4) = 9.52$ $p = 0.049$, Cramer's V = 0.11; perceptual speed: $\chi^2(4) = 27.99$ $p = 0.000$, Cramer's V = 0.18).

As evident in Figure 1 (for details see Table 2), there was a distinctive pattern common to all four cognitive measures. Earlier born cohorts had of a higher proportion of participants showing cognitive gain, and a smaller proportion of participants showing cognitive decline compared to later born cohorts. This pattern is especially evident when comparing the 1901-02 and 1930 cohorts.

Table 1. Sample characteristics in the H70 study stratified by birth cohort, gender, and measurement occasions.

| | | Gender | | Measurement occasions | |
|---|---|---|---|---|---|
| Cognitive test | N | Women (%) | Men (%) | Age 70 M (SD) | Age 79 M (S) |
| Verbal Meaning | | | | | |
| Cohort 1901-02 | 175 | 70.29 | 29.71 | 17.51 (6.37) | 17.53 (7.30) |
| Cohort 1906-07 | 207 | 60.87 | 39.13 | 18.85 (6.35) | 16.64 (7.82) |
| Cohort 1930 | 104 | 46.15 | 53.85 | 21.48 (5.26) | 21.36 (4.94) |
| Total | 486 | 61.11 | 38.89 | 19.02 (6.29) | 19.39 (6.65) |
| Logical Reasoning[a] | | | | | |
| Cohort 1901-02 | 165 | 69.70 | 30.30 | 12.61 (4.60) | 12.41 (4.93) |
| Cohort 1930 | 119 | 45.38 | 54.62 | 16.80 (4.60) | 14.49 (5.30) |
| Total | 284 | 59.51 | 40.49 | 14.24 (5.03) | 13.93 (5.28) |
| Spatial Ability | | | | | |
| Cohort 1901-02 | 87 | 70.11 | 29.89 | 13.38 (6.64) | 11.73 (7.28) |
| Cohort 1906-07 | 209 | 59.81 | 40.19 | 15.94 (6.90) | 11.57 (7.43) |
| Cohort 1930 | 110 | 44.55 | 55.45 | 19.65 (6.83) | 15.74 (6.41) |
| Total | 406 | 57.88 | 42.12 | 16.47 (7.19) | 13.84 (7.16) |
| Perceptual Speed | | | | | |
| Cohort 1901-02 | 81 | 71.60 | 28.40 | 16.45 (8.54) | 14.91 (6.81) |
| Cohort 1906-07 | 206 | 59.71 | 40.29 | 19.51 (6.79) | 14.77 (7.50) |
| Cohort 1930 | 127 | 45.67 | 54.33 | 25.79 (7.83) | 21.38 (7.04) |
| Total | 414 | 57.73 | 42.27 | 20.69 (8.29) | 18.59 (7.80) |

[a] Data for cohort 1906-07 on the Logical reasoning test were not collected at age 75 and 79 and are therefore omitted from the present analyses.

Table 2. Proportions of participants categorized as showing cognitive decline, stability, and gain, stratified by birth cohort and cognitive measure.

| Cognitive measure | Cohort 1901-02 | | | Cohort 1906-07 | | | Cohort 1930 | | |
|---|---|---|---|---|---|---|---|---|---|
| | Decline N (%) | Stability N (%) | Gain N (%) | Decline N (%) | Stability N (%) | Gain N (%) | Decline N (%) | Stability N (%) | Gain N (%) |
| Verbal Meaning | 43 (24.6) | 97 (55.4) | 35 (20.0) | 77 (37.2) | 105 (50.7) | 25 (12.1) | 32 (30.8) | 61 (58.7) | 11 (10.6) |
| Logical Reasoning[a] | 80 (48.5) | 28 (17.0) | 57 (34.5) | | | | 71 (57.3) | 37 (29.8) | 16 (12.9) |
| Spatial Ability | 49 (56.3) | 27 (31.0) | 11 (12.6) | 145 (69.4) | 49 (23.4) | 15 (7.2) | 83 (75.5) | 22 (20.0) | 5 (4.5) |
| Perceptual Speed | 49 (60.5) | 5 (6.2) | 27 (33.3) | 148 (71.8) | 34 (16.5) | 24 (11.7) | 100 (78.7) | 13 (10.2) | 14 (11.0) |

[a] Data for cohort 1906-07 on the Logical Reasoning test were not collected at ages 75 and 79 and are therefore omitted from the present analyses.

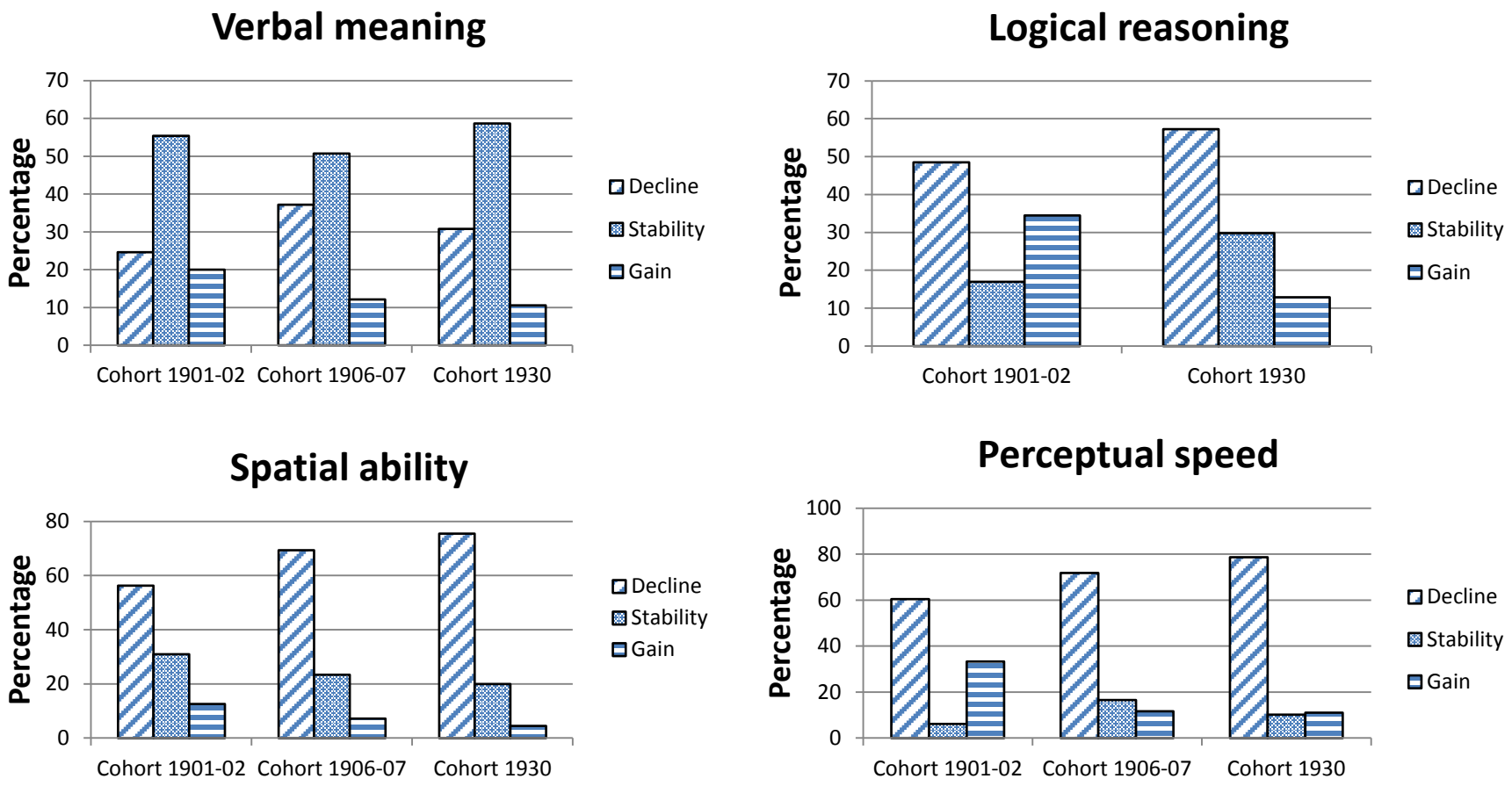



*Figure 1.* Proportions of participants showing cognitive decline, stability, and gain from 70 to 79 years stratified by cohort.

**Study II**

Descriptive statistics for the two cognitive outcoms variables analyzed in study II, stratified by age at measurement and birth cohort, are presented in Table 3. The parameter estimates from selected multiple-group LGCM are shown in Table 4 for spatial ability and Table 5 for reasoning. First, presented under Model 1 in Tables 4 and 5, we constrained all parameters to be equal across cohorts and we constrained the covariates, i.e. gender and education, to zero. The intercept in this model refer to estimated average performance at age 70, i.e. baseline measurement occasion, and the linear slope refer to estimated one-year change in the outcome variable over the study period. The linear slope was negative for both spatial ability and logical reasoning, indicating an average decline in cognitive functioning over time. The variability component estimates are significant for both measures, indicating substantial between-person differences in both level of baseline performance and rate of change.

Next, we released cohort constraints on the intercept parameters and estimated cohort differences for the average intercepts. This resulted in a significant improvement in model fit for both cognitive measures (spatial ability: $\chi^2(2) = 119.89$, $p < .001$; reasoning: $\chi^2(1) = 112.69$, $p < .001$ ). We then also released cohort constraints on the slope parameters and estimated cohort differences regarding average linear slopes. This resulted in yet another significant improvement in model fit for both cognitive measures (spatial ability: $\chi^2(2) = 13.57$, $p = .001$; reasoning $\chi^2(1) = 6.78$, $p = .009$). The estimates from these models, shown in Table 4 and Table 5 under Model 2, indicate cohort differences in both level of baseline performance and rate of linear decline. For both spatial ability and logical reasoning, later born cohorts performed at a higher level, but showed a faster average rate of cognitive decline. Fixed effects estimates for these models are plotted in Figure 2 for the respective birth cohorts and cognitive measures.

Table 3. Sample characteristics in the H70 study stratified by birth cohort, gender, education, and measurement occasions.

| Cognitive test | N | Gender | | Education | | Measurement occasions | | |
|---|---|---|---|---|---|---|---|---|
| | | Women (%) | Men (%) | Compulsory (%) | More than Compulsory (%) | Age 70 M (SD) | Age 75 M (SD) | Age 79 M (SD) |
| Spatial Ability | | | | | | | | |
| Cohort 1901 | 314 | 58.60 | 41.40 | 85.00 | 15.00 | 13.38 (6.64) | 12.83 (6.45) | 11.73 (7.28) |
| Cohort 1906 | 383 | 55.90 | 44.10 | 82.20 | 17.80 | 15.94 (6.90) | 14.61 (6.83) | 11.57 (7.43) |
| Cohort 1930 | 783 | 58.60 | 41.40 | 54.00 | 46.00 | 19.65 (6.83) | 16.67 (6.93) | 15.74 (6.41) |
| Total | 1480 | 57.90 | 42.10 | 67.90 | 32.10 | 16.47 (7.19) | 15.27 (6.97) | 13.84 (7.16) |
| Logical Reasoning[a] | | | | | | | | |
| Cohort 1901 | 372 | 58.30 | 41.70 | 85.50 | 14.50 | 12.61 (4.60) | 12.56 (5.14) | 12.41 (4.93) |
| Cohort 1930 | 804 | 57.60 | 42.40 | 54.60 | 45.40 | 16.80 (4.60) | 14.65 (4.78) | 14.49 (5.30) |
| Total | 1176 | 57.80 | 42.20 | 64.40 | 35.60 | 14.24 (5.03) | 14.03 (4.98) | 13.93 (5.28) |

Note. [a] Data for cohort 1906 on the Logical Reasoning test was not collected at ages 75 and 79 and therefore omitted from the present analyses.

Table 4. Parameter estimates from multiple-group growth curve models fitted to the spatial ability (Block Design test) data from three birth cohort in the H70 study and measured at ages 70, 75, and 79 (N=1480)

| | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|---|---|---|---|---|---|---|---|---|---|---|
| Parameters | Estimates | 95% CI | Estimates | 95% CI | Estimates | 95% CI | Estimates | 95% CI | Estimates | 95% CI |
| | | | | | Average effects | | | | | |
| Intercept | 17.12*** | [16.72, 17.52] | | | | | | | | |
| Cohort 1901 | | | 13.80*** | [12.97, 14.63] | 12.59*** | [11.73, 13.45] | 12.69*** | [11.78, 13.59] | 13.12*** | [12.08, 14.16] |
| Cohort 1906 | | | 16.13*** | [15.46, 16.80] | 14.75*** | [14.02, 15.48] | 14.41*** | [13.64, 15.18] | 14.54*** | [13.68, 15.40] |
| Cohort 1930 | | | 19.31*** | [18.70, 19.92] | 16.71*** | [15.94, 17.49] | 17.19*** | [16.34, 18.04] | 16.60*** | [15.74, 17.46] |
| Gender | | | | | 1.31*** | [0.56, 2.06] | 1.31*** | [0.56, 2.06] | | |
| Education | | | | | 4.52*** | [3.65, 5.38] | | | 4.50*** | [3.64, 5.37] |
| Cohort 1901 x Education | | | | | | | 3.88*** | [1.67, 6.08] | | |
| Cohort 1906 x Education | | | | | | | 6.47*** | [4.82, 8.13] | | |
| Cohort 1930 x Education | | | | | | | 3.47*** | [2.29, 4.65] | | |
| Cohort 1901 x Gender | | | | | | | | | 0.04 | [-1.56, 1.64] |
| Cohort 1906 x Gender | | | | | | | | | 1.79** | [0.52, 3.07] |
| Cohort 1930 x Gender | | | | | | | | | 1.58* | [0.38, 2.77] |
| Linear slope | -0.44*** | [-0.49,-0.39] | | | | | | | | |
| Cohort 1901 | | | -0.31*** | [-0.40, -0.21] | -0.27*** | [-0.37, -0.16] | -0.27*** | [-0.38, -0.16] | -0.28*** | [-0.41, -0.16] |
| Cohort 1906 | | | -0.49*** | [-0.57, -0.42] | -0.45*** | [-0.53, -0.36] | -0.42*** | [-0.51, -0.33] | -0.45*** | [-0.54, -0.35] |
| Cohort 1930 | | | -0.53*** | [-0.61, -0.45] | -0.46*** | [-0.56, -0.36] | -0.52*** | [-0.63, -0.41] | -0.45*** | [-0.56, -0.34] |
| Gender | | | | | -0.06 | [-0.15, 0.03] | -0.06 | [-0.15, 0.03] | | |
| Education | | | | | -0.11* | [-0.22, -0.00] | | | -0.11* | [-0.22, -0.00] |
| Cohort 1901 x Education | | | | | | | -0.10 | [-0.37, 0.16] | | |
| Cohort 1906 x Education | | | | | | | -0.26*** | [-0.45, -0.07] | | |
| Cohort 1930 x Education | | | | | | | 0.03 | [-0.12, 0.18] | | |
| Cohort 1901 x Gender | | | | | | | | | -0.03 | [-0.22, 0.16] |
| Cohort 1906 x Gender | | | | | | | | | -0.07 | [-0.21, 0.08] |
| Cohort 1930 x Gender | | | | | | | | | -0.07 | [-0.23, 0.08] |
| | | | | | Variability components | | | | | |
| Intercept | 38.47 | [33.94, 42.99] | 33.53 | [29.37, 37.68] | 28.95 | [25.14, 32.76] | 28.71 | [24.92, 32.50] | 28.82 | [25.01, 32.62] |
| Slope | 0.06 | [0.00, 0.12] | 0.04 | [0.00, 0.10] | 0.04 | [0.00, 0.09] | 0.03 | [-0.03, 0.09] | 0.03 | [0.00, 0.09] |
| Covariance | .0.33 | [-0.72, 0.08] | -0.12 | [-0.50, 0.26] | 0.01 | [0.00, 0.37] | 0.05 | [-0.31, 0.40] | 0.01 | [-0.35, 0.37] |
| Residual | 11.68 | [10.40, 12.96] | 11.85 | [10.57, 13.14] | 11.90 | [10.62, 13.19] | 11.92 | [10.63, 13.20] | 11.91 | [10.63, 13.20] |

| | | | Model fit indices | | |
|---|---|---|---|---|---|
| $\chi^2(df)$ | 183.14 (21) | 49.68 (17) | 69.65 (31) | 59.42 (27) | 66.02(27) |
| CFI | 0.86 | 0.97 | 0.97 | 0.97 | 0.97 |
| RMSEA [90% *CI*] | 0.07 [0.06-0.08] | 0.04 [0.03-0.05] | 0.03 [0.02-0.04] | 0.03 [0.02-0.04] | 0.03 [0.02-0.04] |

Note. CI= confidence interval.
* p < .05. ** p < .01. *** p < .001.

Table 5. Parameter estimates from multiple-group growth curve models fitted to the reasoning ability (Figure Logic test) data from three birth cohort in the H70 study and measured at ages 70, 75, and 79 (N=1176)

| | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|---|---|---|---|---|---|---|---|---|---|---|
| Parameters | Estimates | 95% CI | Estimates | 95% CI | Estimates | 95% CI | Estimates | 95% CI | Estimates | 95% CI |
| | | | | | Average effects | | | | | |
| Intercept | 14.51*** | [14.16, 14.87] | | | | | | | | |
| Cohort 1901 | | | 12.67*** | [12.21, 13.14] | 11.96*** | [11.42, 12.50] | 12.05*** | [11.49, 12.61] | 12.44*** | [11.84, 13.03] |
| Cohort 1930 | | | 16.19*** | [15.71, 16.66] | 14.83*** | [14.19, 15.47] | 14.72*** | [14.03, 15.41] | 14.29*** | [13.59, 14.98] |
| Gender | | | | | 1.00*** | [0.35, 1.66] | 1.00*** | [0.34, 1.65] | | |
| Education | | | | | 2.09*** | [1.33, 2.84] | | | 2.07*** | [1.32, 2.82] |
| Cohort 1901 x Education | | | | | | | 1.50** | [0.21, 2.78] | | |
| Cohort 1930 x Education | | | | | | | 2.34*** | [1.40, 3.28] | | |
| Cohort 1901 x Gender | | | | | | | | | -0.15 | [-1.06, 0.76] |
| Cohort 1930 x Gender | | | | | | | | | 2.16*** | [1.22, 3.10] |
| Linear slope | -0.12*** | [-0.18, -0.07] | | | | | | | | |
| Cohort 1901 | | | -0.11*** | [-0.19, -0.03] | -0.09 | [-0.18, 0.00] | -0.09 | [-0.18, 0.13] | -0.12* | [-0.23, -0.01] |
| Cohort 1930 | | | -0.26*** | [-0.33, -0.18] | -0.25*** | [-0.35, -0.15] | -0.24*** | [-0.35, -0.13] | -0.19*** | [-0.29, -0.08] |
| Gender | | | | | -0.05 | [-0.15, 0.06] | -0.05 | [-0.15, 0.06] | | |
| Education | | | | | 0.01 | [-0.11, 0.13] | | | 0.01 | [-0.11, 0.13] |
| Cohort 1901 x Education | | | | | | | -0.02 | [-0.24, 0.21] | | |
| Cohort 1930 x Education | | | | | | | -0.01 | [-0.15, 0.14] | | |
| Cohort 1901 x Gender | | | | | | | | | 0.02 | [-0.14, 0.18] |
| Cohort 1930 x Gender | | | | | | | | | -0.17* | [-0.32, -0.03] |
| | | | | | Variability components | | | | | |
| Intercept | 12.71 | [9.64, 15.78] | 9.17 | [6.43, 11.91] | 8.08 | [5.44, 10.73] | 8.06 | [5.41, 10.70] | 7.66 | [5.06, 10.27] |
| Slope | 0.11 | [0.03, 0.18] | 0.09 | [0.01, 0.16] | 0.08 | [0.01, 0.15] | 0.8 | [0.01, 0.15] | 0.08 | [0.00, 0.15] |
| Covariance | -0.26 | [-0.65, 0.12] | -0.01 | [-0.36, 0.35] | -0.01 | [-0.35, 0.34] | -0.01 | [-0.36, 0.34] | 0.03 | [-0.32, 0.37] |
| Residual | 12.03 | [10.56, 13.49] | 12.17 | [10.71, 13.62] | 12.21 | [10.75, 13.66] | 12.20 | [10.74, 13.65] | 12.22 | [10.76, 13.67] |
| | | | | | Model fit indices | | | | | |
| $\chi^2(df)$ | 151.70 (12) | | 32.22 (10) | | 52.22 (18) | | 50.45 (16) | | 39.95 (16) | |
| CFI | 0.46 | | 0.91 | | 0.90 | | 0.90 | | 0.93 | |
| RMSEA [90% CI] | 0.10 [0.09-0.11] | | 0.04 [0.03-0.06] | | 0.04 [0.03-0.05] | | 0.04 [0.03-0.06] | | 0.04 [0.02-0.05] | |

Note. CI= confidence interval.
* p < .05. ** p < .01. *** p < .001.

In the next step in the analyses we released cohort constraints on the variability and covariability components. This did not significantly improve the model fit in either of the cognitive measures (spatial ability: $\chi^2(6) = 2.17$, $p = .90$; reasoning: $\chi^2(3) = 2.96$, $p = .40$), indicating lack of cohort differences in the conditioned variability components for both the spatial ability level of baseline performance (cohort 1901 = 30.93, *SE* = 4.09 ; cohort 1906 = 36.05, *SE* = 3.45; cohort 1930 = 33.67, *SE* = 3.48) and rate of linear change (cohort 1901 = 0.06, *SE*= 0.05; cohort 1906 = 0.03, *SE* = 0.04; cohort 1930 = 0.05, *SE* = 0.05), and logical reasoning level of baseline performance (cohort 1901 = 9.31, *SE*= 1.68; cohort 1930 = 8.38, *SE* = 1.93) and rate of linear change (cohort 1901 = 0.13, *SE*= 0.05; cohort 1930 = 0.03, *SE* = 0.04).

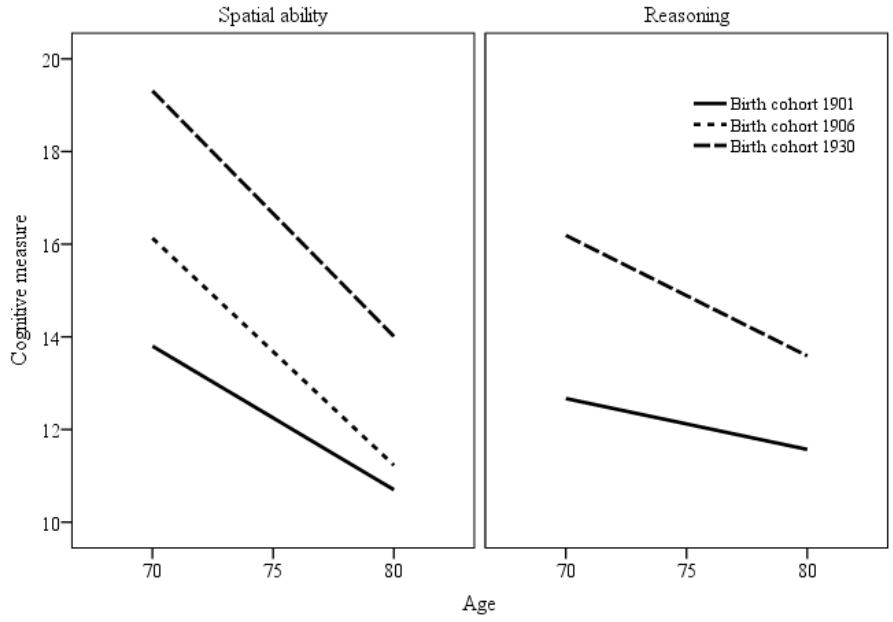



*Figure 2*. Estimated change trajectories from multiple-group LGCMs fitted to spatial ability and reasoning data from the H70. Groups are defined by birth cohorts.

Next, we released cohort constraints on the residuals. Here the variability and covariability components were constrained equal across cohorts (since there were no significant cohort differences). This did not lead to significant improvements in model fit for

either of the two measures (spatial ability: $\chi^2(2) = 0.93$, $p = .63$; reasoning: $\chi^2(1) = 1.29$, $p = .26$). Therefore, we decided to constrain the variability and residual components equal across cohorts in further analyses.

In the next step in the analyses we included gender and education as covariates. This enabled the estimation of main effects of gender and education as well as gender by time and education by time two-way interaction effects. Parameter estimates from these models are presented in Tables 4 and 5 under Model 3. As can be seen in Tables 4 and 5, controlling for gender and education resulted in a partial effect on the estimated cohort differences in both level of performance and rate of linear change regarding both spatial ability and logical reasoning. But even after controlling for education and gender, later born cohorts performed at a higher level but declined at a faster rate compared with earlier born. There was a significant effect of gender on level of performance for both cognitive measures. The estimated baseline performance at age 70 was 1.31 points higher on the raw scale (i.e., 18% of the total sample baseline *SD*) for men as compared with women on the spatial ability measure and 1.00 point higher (i.e., 20% of baseline *SD*) on the reasoning test. The effect of gender on rate of change was non-significant for both cognitive measures, indicating no gender differences in rate of cognitive decline. The effect of education on level of performance was significant regarding both spatial ability and logical reasoning. The expected baseline value for individuals with more than compulsory education was 4.52 points higher (i.e., 63% of baseline *SD*) as compared with those with compulsory education (or less) on the spatial ability test and 2.09 points higher (i.e., 42% of baseline *SD*) on the reasoning test. Longer education was associated with a steeper decline on the spatial ability test but not on the reasoning test.

Next, we released cohort constraints on the effects of education on both intercept and slope (while constraining the effects of gender equal across cohorts). This enabled the estimation of the cohort by education two-way interactions and the time by cohort by

education three-way interactions. Estimates from these models are shown in tables 4 and 5 under Model 4, and the fixed effects are plotted in Figure 3.

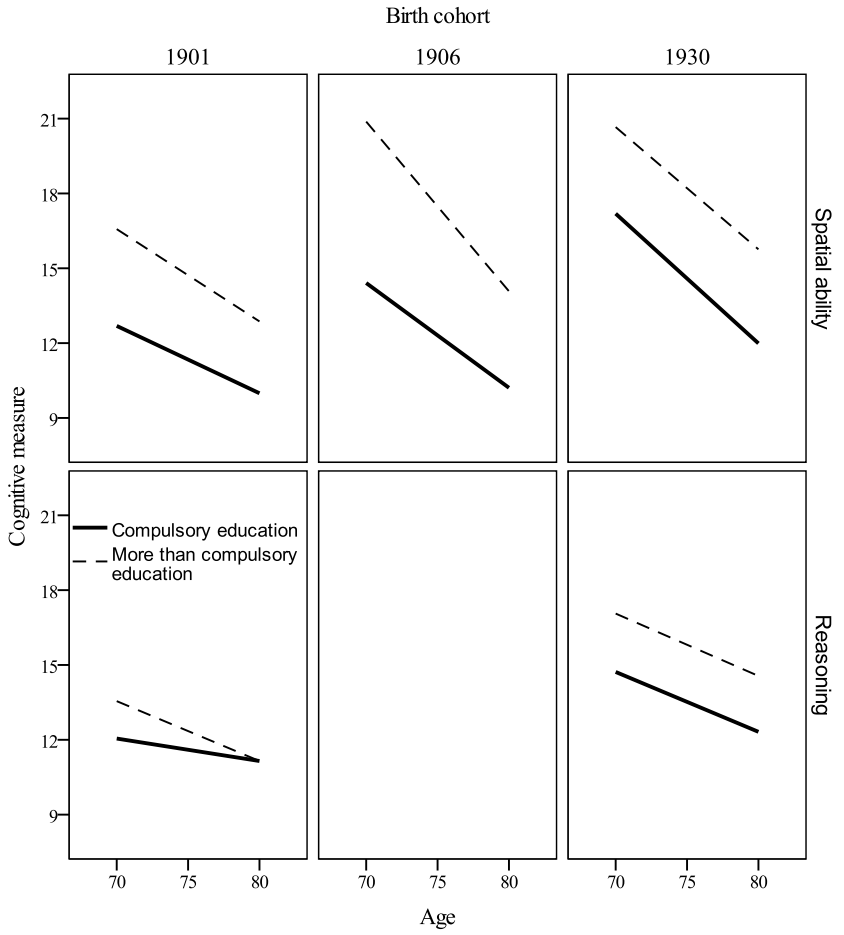



*Figure 3*. Estimated change trajectories from multiple-group LGCMs, conditioned on education, and fitted to spatial ability and reasoning data from the H70. Groups are defined by birth cohorts.

In all three cohorts, individuals with more than compulsory education performed at a higher level than individuals with compulsory education or less. Cohort differences in the effects of education, tested simultaneously, on both level of performance and rate of change were significant for the spatial ability measure ($\chi^2(4) = 10.23$, $p = .04$), but not for reasoning ($\chi^2(2) = 1.78$, $p = .41$). Education had the largest effect, concerning both level of performance and rate of change in the spatial ability test in the 1906-07 cohort, where individuals with more than compulsory education had an expected baseline value of 6.47 points higher (i.e.,

90% of baseline *SD*) than individuals with compulsory education or less. Estimates for the 1901-02 and 1930 birth cohorts were 3.88 (i.e., 54% of baseline *SD*) and 3.47 (i.e., 48% of baseline *SD*) respectively. Since both the earliest and latest born cohorts showed smaller estimates compared with the 1906-07 cohort there is no clear cohort trend regarding the effect of education. The effect of education on rate of change in spatial ability was significant for the 1906-07 cohort, where more than compulsory education was associated with a faster rate of change, but non-significant for the other two cohorts.

Finally, we extended Model 3 by releasing cohort constraints on the effects of gender on both intercept and slope (while constraining the effects of education equal across cohorts). This enabled the estimation of cohort by gender two-way interactions and time by cohort by gender three-way interactions. Estimates from these models are shown in Model 5 in Tables 4 and 5, and fixed effects are plotted in Figure 4. As can be seen in Table 4 there were significant gender differences in baseline performance on the spatial ability test in birth cohorts 1906-07 and 1930 (see table 4). In cohort 1906-07 men had an expected baseline value of 1.79 points higher (i.e., 25% of baseline *SD*) than women. In cohort 1930 men had an expected baseline value of 1.58 points higher (i.e., 22% of baseline *SD*) than women. For the reasoning test there were significant gender differences in birth cohort 1930, where men had an expected baseline value of 2.16 points higher (i.e., 43% of baseline *SD*) than women, but they also showed a significantly steeper rate of average decline as compared with women. There were no significant gender differences in either baseline performance or rate of change in the 1901-02 birth cohort. Cohort trends in gender effects were significant when tested simultaneously on both level of performance and rate of change in the reasoning measure ($\chi^2(2) = 12.27$ $p < .001$ ) but not on spatial ability ($\chi^2(4) = 3.63$ $p = 0.26$).

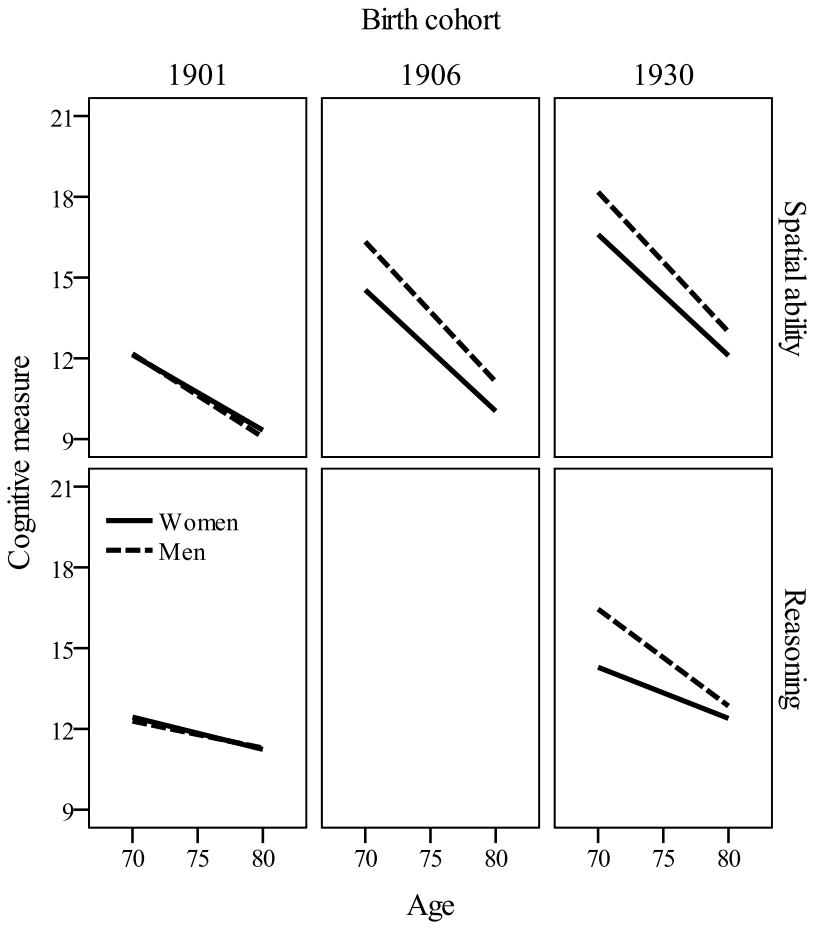



*Figure 4*. Estimated change trajectories from multiple-group LGCMs, conditioned on gender, and fitted to spatial ability and reasoning data from the H70. Groups are defined by birth cohorts.

**Study III**

Descriptive statistics for each of the cognitive outcome variables stratified by birth cohort and age at measurement are shown in Table 6 along with the standardized and unconditioned effect sizes (i.e., Cohen's d). The standardized and jittered data points are plotted in Figure 5. The boxes refer to ± 1 SD from the mean value. By simply eyeballing the data in Figure 5, it is obvious that there are large birth cohort differences in level of performance for most of the cognitive outcomes. This is particularly evident at age 70 on the spatial ability, reasoning, and the perceptual-and- motor speed measures (see Table 6 for exact effect sizes). The most informative comparisons, in terms of birth cohort effects, are those

between the 1901-02 and 1930 birth cohorts. At age 70 these comparisons have effect sizes in the range between 0.63-1.19, at age 75 between 0.42-0.87, and at age 79 between 0.50-0.80. On all measures, except picture recognition memory, there is a reduction in the cohort effect sizes across time. The patterns of cohort effect are smaller and more stable across time for the picture recognition memory and verbal ability measures.

The raw score change trajectories for each of the cognitive outcomes are plotted in Figure 6. The overlaid red lines refer to the estimated average change trajectory for the specific birth cohort as obtained from the growth curve models. Fixed effect estimates from the growth curve models are shown in Table 7. In all models, except picture recognition memory, we used cohort 1901-02 as comparison group. Other group estimates, within the same model, are therefore interpreted as deviation from the 1901-02 estimate. For example, the estimated central tendency (i.e., the mean) for birth cohort 1901-02 at age 70 for the spatial ability measure was 12.90, 95% HDI [12.06, 13.74], points. This estimate was 2.20, 95% HDI [1.18, 3.21], and 4.72, 95% HDI [3.65, 5.79], points, higher for cohorts 1906-07 and 1930, respectively. Similar interpretations apply for the slope (i.e., the age interaction) estimates. The estimated central tendency of a linear rate of change from age 70 to 79 for birth cohort 1901-02 was -0.31, 95% HDI [-0.41, -0.21], points a year. This estimate was -0.19, 95% HDI [-0.31, -0.06], and -0.28, 95% HDI [-0.41, -0.15], points lower for cohort 1906-07 and 1930, respectively, indicating a reliably steeper average decline in the later born cohorts. Parameter estimates from the other models are interpreted in a similar manner, however, as we only had one measure of picture recognition memory for cohort 1901-02 we used cohort 1906-07 as reference group for that model.

Table 6. Standardized (Cohen's d effect sizes) mean differences in cognitive performance across cohorts born in 1901-02, 1906-07, and 1930, and measured at ages 70, 75, and 79 as part of the H70 study.

| | Age 70 | | | | | Age 75 | | | | | Age 79 | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | d effect size | | | | | d effect size | | | | | d effect size | | | | |
| Cohorts | 1906/07 | 1930 | M | SD | n | 1906/07 | 1930 | M | SD | n | 1906/07 | 1930 | M | SD | n |
| | | | | | | | Spatial ability | | | | | | | | |
| 1901/02 | 0.36 | **0.92** | 13.38 | 6.64 | 174 | 0.25 | **0.58** | 12.83 | 6.45 | 274 | -0.02 | **0.55** | 11.73 | 7.28 | 191 |
| 1906/07 | - | 0.56 | 15.94 | 6.90 | 383 | - | 0.33 | 14.61 | 6.83 | 259 | - | 0.57 | 11.57 | 7.43 | 209 |
| 1930 | | - | 19.95 | 6.68 | 222 | | - | 17.01 | 7.04 | 332 | | - | 15.67 | 6.88 | 266 |
| | | | | | | | Reasoning | | | | | | | | |
| 1901/02 | 0.25 | **0.81** | 12.95 | 4.56 | 297 | **-** | **0.42** | 12.78 | 5.02 | 270 | **-** | **0.50** | 12.15 | 5.22 | 178 |
| 1906/07 | - | 0.57 | 14.13 | 4.64 | 378 | - | **-** | - | - | - | - | **-** | - | - | - |
| 1930 | | - | 16.86 | 4.54 | 220 | | - | 14.82 | 5.23 | 348 | | - | 14.57 | 5.18 | 272 |
| | | | | | | | Perceptual-motor-speed | | | | | | | | |
| 1901/02 | 0.40 | **1.19** | 16.17 | 8.73 | 175 | 0.21 | **0.87** | 16.27 | 6.95 | 268 | -0.01 | **0.80** | 14.71 | 6.94 | 178 |
| 1906/07 | - | 0.80 | 19.51 | 6.79 | 375 | - | 0.66 | 18.05 | 6.74 | 256 | - | 0.81 | 14.63 | 7.60 | 211 |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1930 | | - | 26.14 | 7.58 | 221 | | - | 23.54 | 4.62 | 363 | | - | 21.43 | 7.04 | 302 |
| | | | | | | | Picture recognition memory | | | | | | | | |
| 1901/02 | - | - | | | | - | **0.58** | 18.17 | 5.05 | 271 | - | - | - | - | - |
| 1906/07 | - | 0.45 | 18.96 | 4.52 | 375 | - | - | - | - | - | - | 0.62 | 17.40 | 5.88 | 211 |
| 1930 | | - | 21.07 | 4.53 | 222 | | - | 20.84 | 4.66 | 356 | | - | 20.27 | 4.64 | 284 |
| | | | | | | | Verbal ability | | | | | | | | |
| 1901/02 | 0.21 | **0.63** | 17.51 | 6.36 | 295 | 0.05 | - | 17.76 | 6.87 | 270 | -0.15 | **0.58** | 17.53 | 7.30 | 186 |
| 1906/07 | - | 0.43 | 18.80 | 6.42 | 373 | - | - | 18.01 | 6.55 | 255 | - | 0.73 | 16.58 | 7.85 | 211 |
| 1930 | | - | 21.50 | 5.23 | 204 | | - | - | - | - | | - | 21.18 | 5.18 | 277 |

*Note*. The d effect sizes are standardized based on the baseline (i.e. age 70) distribution of the respective test.

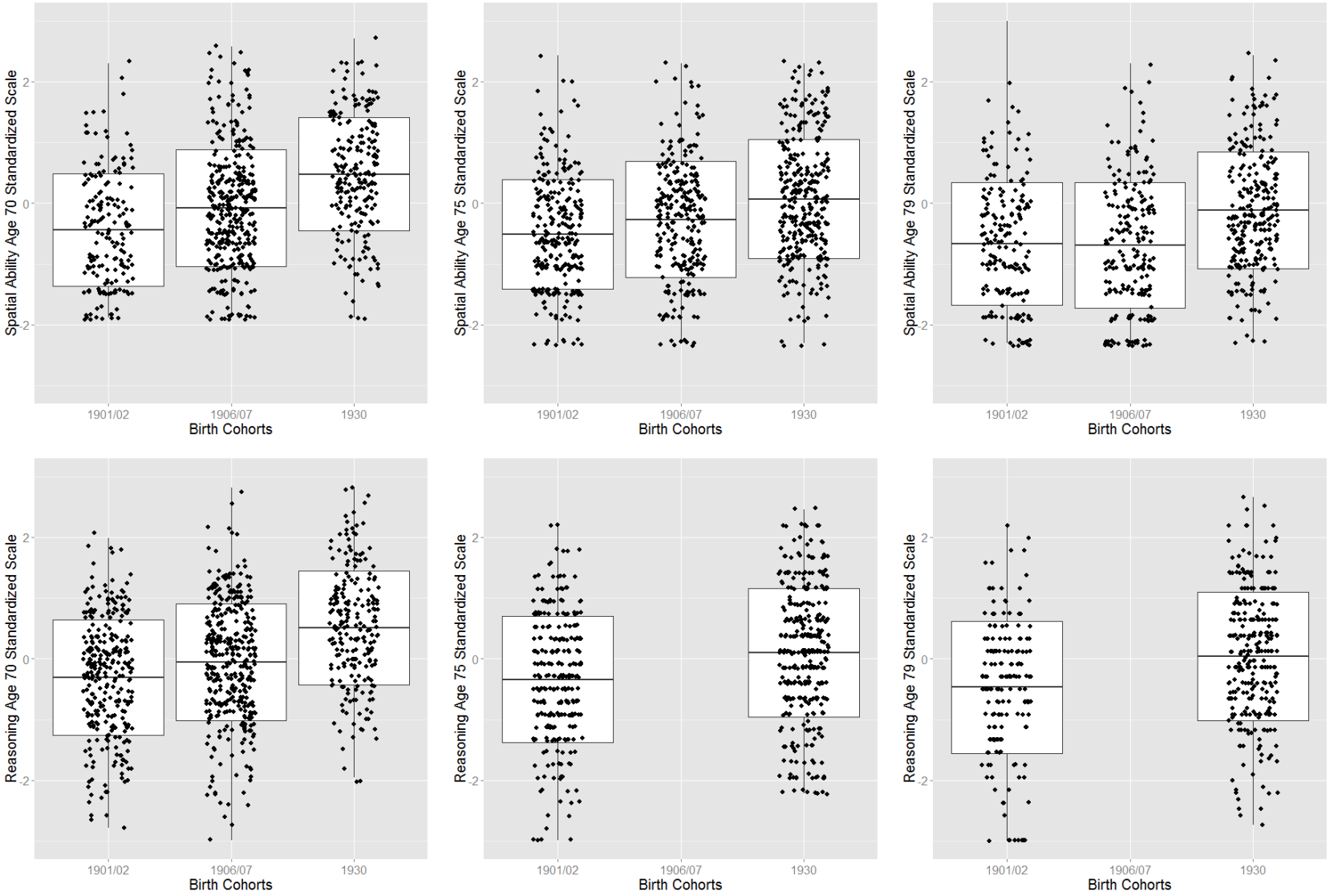
Table 7. Estimates from growth curve models fitted to data from the three birth cohort in the H70 study

| Cognitive ability | Parameters[a] | Marginal posterior median | 95% HDI[b] |
|---|---|---|---|
| Spatial ability (Block Design) | Level at age 70 | | |
| | Cohort 1901/02 | 12.90 | [12.06, 13.74] |
| | Cohort 1906/07 | 2.20 | [1.18, 3.21] |
| | Cohort 1930 | 4.72 | [3.65, 5.79] |
| | Slope age 70-79 | | |
| | Cohort 1901/02 | -0.31 | [-0.41, -0.21] |
| | Cohort 1906/07 | -0.19 | [-0.31, -0.06] |
| | Cohort 1930 | -0.28 | [-0.41, -0.15] |
| Reasoning (Figure Logic) | Level at age 70 | | |
| | Cohort 1901/02 | 12.47 | [11.94, 12.99] |
| | Cohort 1906/07 | 1.03 | [0.37, 1.68] |
| | Cohort 1930 | 2.81 | [2.11, 3.52] |
| | Slope age 70-79 | | |
| | Cohort 1901/02 | -0.13 | [-0.21, -0.06] |
| | Cohort 1906/07 | - | - |
| | Cohort 1930 | -0.16 | [-0.26, -0.05] |
| Perceptual-motor-speed (Figure Identification) | Level at age 70 | | |
| | Cohort 1901/02 | 16.87 | [15.91, 17.81] |
| | Cohort 1906/07 | 2.75 | [1.62, 3.89] |
| | Cohort 1930 | 8.89 | [7.28, 9.69] |
| | Slope age 70-79 | | |

| | | | |
|---|---|---|---|
| | Cohort 1901/02 | -0.29 | [-0.41, -0.16] |
| | Cohort 1906/07 | -0.25 | [-0.41, -0.10] |
| | Cohort 1930 | -0.31 | [-0.47, -0.15] |
| Picture recognition | Level at age 70 | | |
| memory | Cohort 1901/02 | -0.15 | [-0.87, 0.58] |
| (Thurstone's) | | | |
| | Cohort 1906/07 | 19.47 | [18.78, 20.15] |
| | Cohort 1930 | 1.60 | [0.79, 2.41] |
| | Slope age 70-79 | | |
| | Cohort 1901/02 | - | - |
| | Cohort 1906/07 | -0.20 | [-0.27, -0.13] |
| | Cohort 1930 | 0.06 | [-0.04, -0.13] |
| Verbal ability | Level at age 70 | | |
| (Synonyms) | Cohort 1901/02 | 16.92 | [16.21, 17.63] |
| | Cohort 1906/07 | 1.06 | [0.21, 1.92] |
| | Cohort 1930 | 2.44 | [1.47, 3.42] |
| | Slope age 70-79 | | |
| | Cohort 1901/02 | -0.09 | [-0.16, -0.02] |
| | Cohort 1906/07 | -0.17 | [-0.25, -0.07] |
| | Cohort 1930 | -0.01 | [-0.11, 0.09 ] |

*Notes*. [a]Birth cohort 1901/02 is the reference group in all models except in the picture recognition memory model where cohort 1906/07 is the reference group. Education and gender are included as covariates in all models. [b]Highest density interval.

The marginal posterior probability density distributions of the differences between cohort 1901-02 and 1930 on level of cognitive performance at age 70 are plotted in Figure 7. Confirming the descriptive data, these plots demonstrate strong evidence for birth cohort differences in level of cognitive performance at age 70 on all cognitive measures. An integral over the posterior distribution close to the parameter value of zero is extremely small and almost non-existent on all cognitive outcomes. The marginal posterior probability density distributions of the differences between cohort 1901-02 and 1930 on rate of change from age 70 to 79 are plotted in Figure 8. The data also provide strong evidence for cohort differences in rate of change for the spatial ability, reasoning, and perceptual-motor-speed measures, where cohort 1930 shows a steeper decline than the other cohorts. This difference is however close to zero for the picture recognition memory and verbal ability measures, indicating no cohort difference in rate of change on these measures.


Spatial Ability Age 70 Standardized Scale
Spatial Ability Age 75 Standardized Scale
Spatial Ability Age 79 Standardized Scale
Reasoning Age 70 Standardized Scale
Reasoning Age 75 Standardized Scale
Reasoning Age 79 Standardized Scale
2
0
-2
1901/02
1906/07
1930
Birth Cohorts

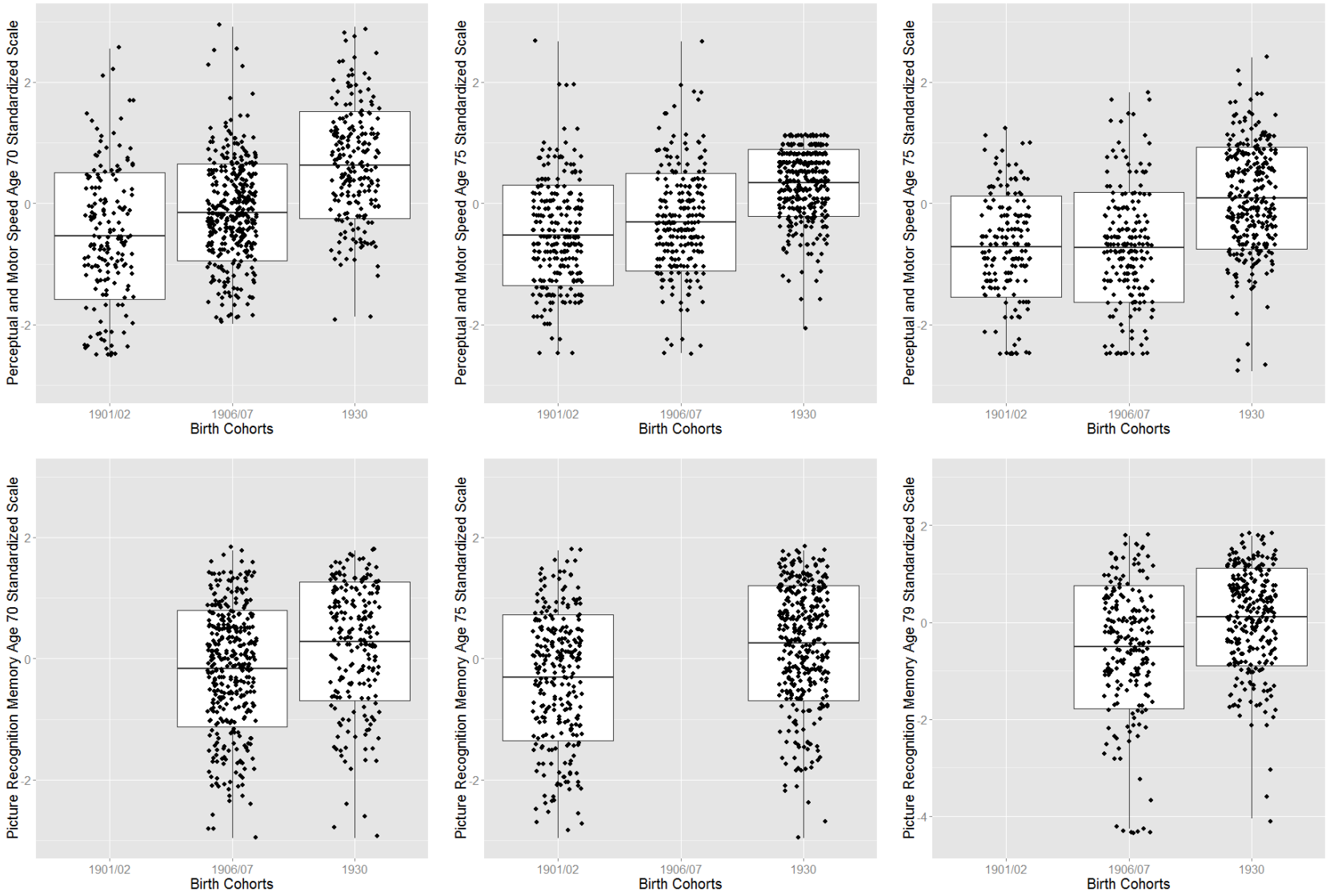
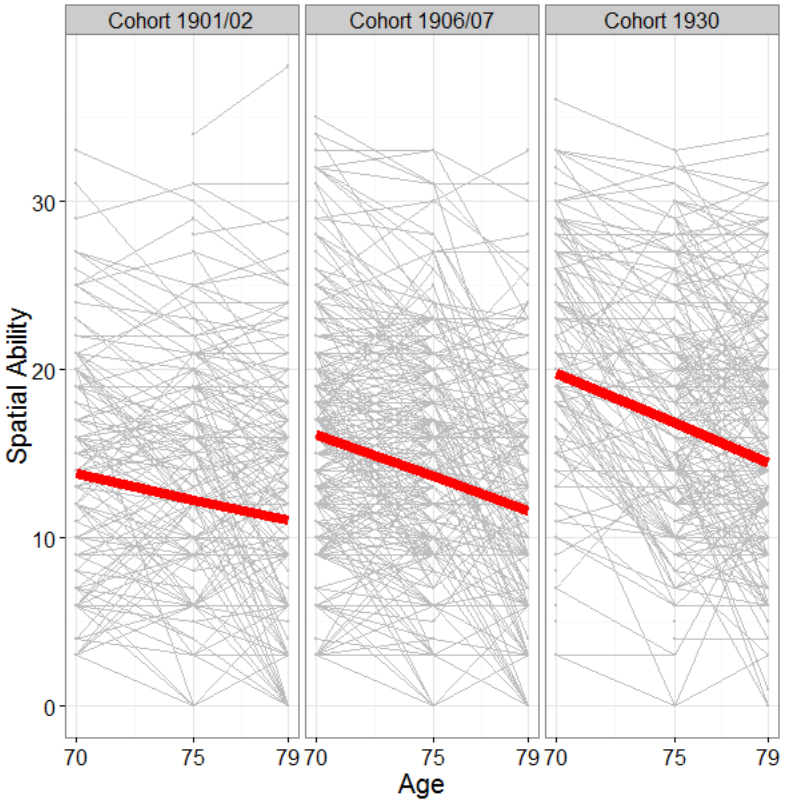
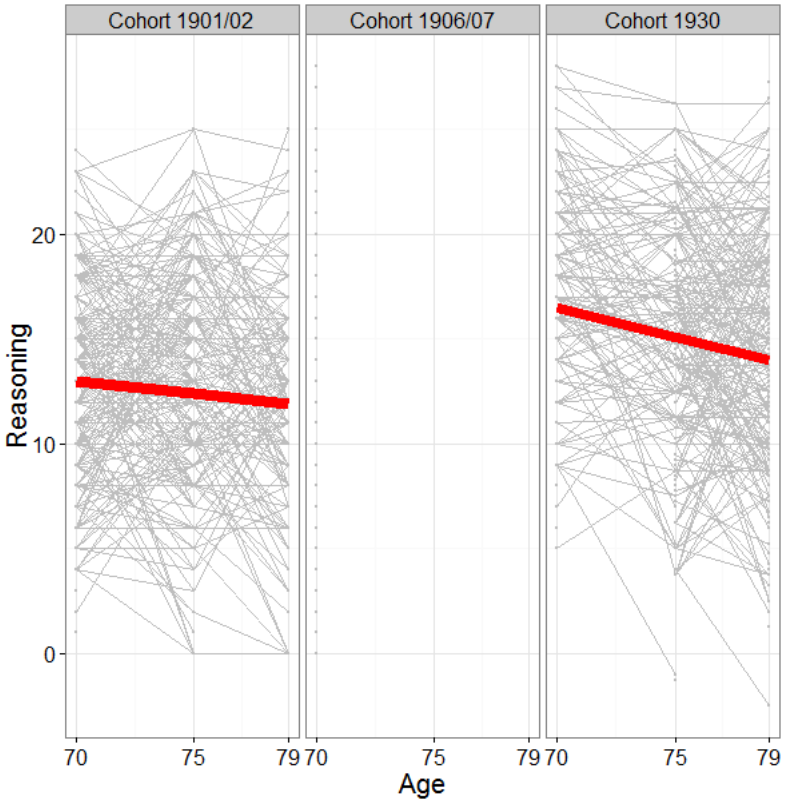
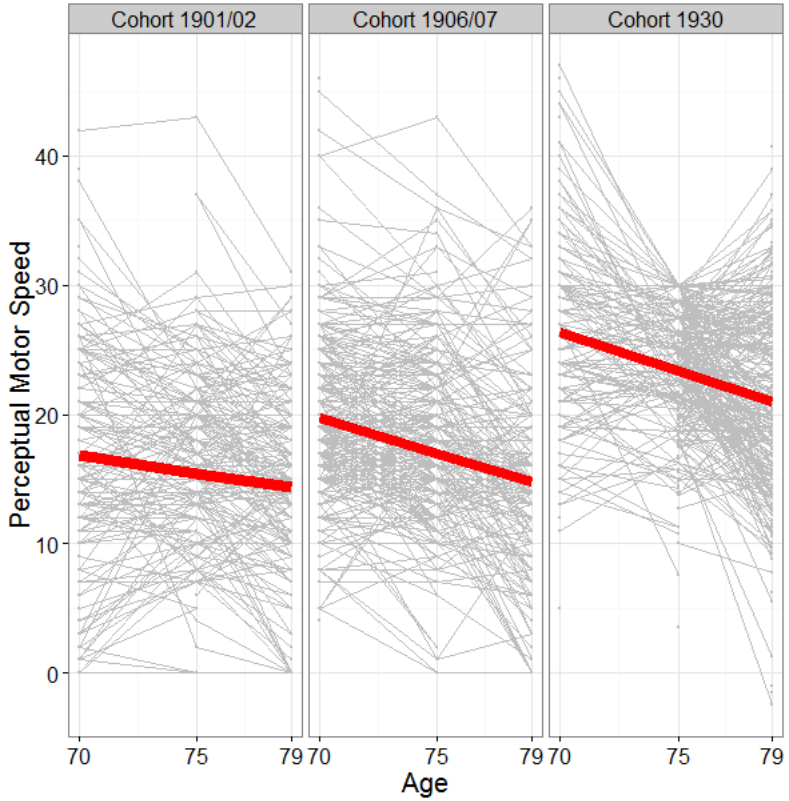
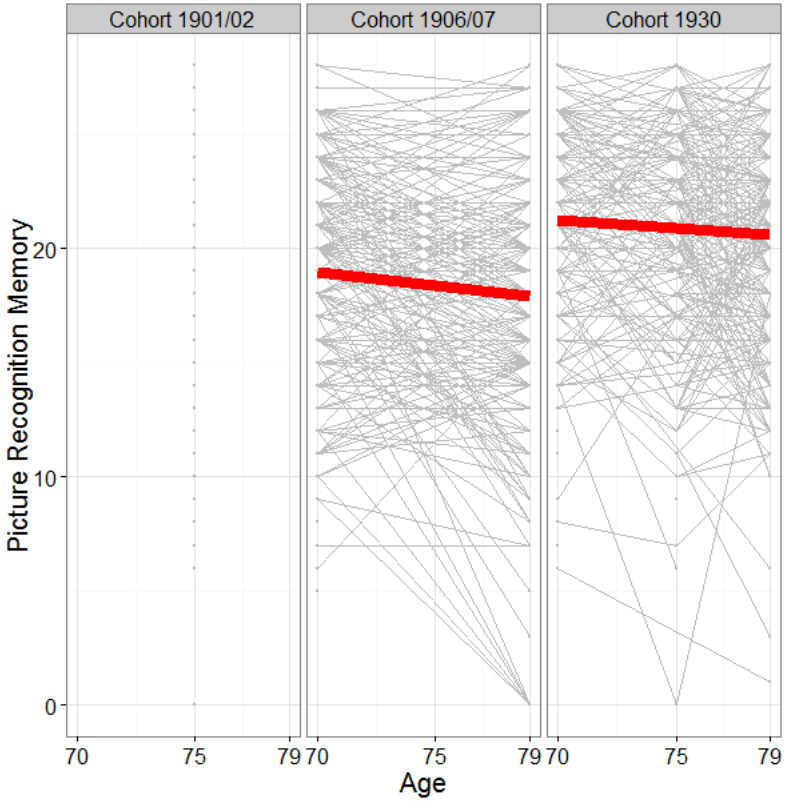

Perceptual and Motor Speed Age 70 Standardized Scale
Perceptual and Motor Speed Age 75 Standardized Scale
Perceptual and Motor Speed Age 75 Standardized Scale
Picture Recognition Memory Age 70 Standardized Scale
Picture Recognition Memory Age 75 Standardized Scale
Picture Recognition Memory Age 79 Standardized Scale
2
0
-2
-4
1901/02
1906/07
1930
Birth Cohorts


*Figure 5*.Standardized and jittered data points from the cognitive tests for cohorts born 1901/02, 1906/07, and 1930 and measured at ages 70, 75, and 79 as part of the H70 study. The boxes refer to ± 1 standard deviation from the mean.


Cohort 1901/02
Cohort 1906/07
Cohort 1930
Spatial Ability
0
10
20
30
70
75
79
Age


Cohort 1901/02
Cohort 1906/07
Cohort 1930
Reasoning
0
10
20
70
75
79
Age


Cohort 1901/02
Cohort 1906/07
Cohort 1930
Perceptual Motor Speed
0
10
20
30
40
70
75
79
Age


Cohort 1901/02
Cohort 1906/07
Cohort 1930
Picture Recognition Memory
0
10
20
70
75
79
Age

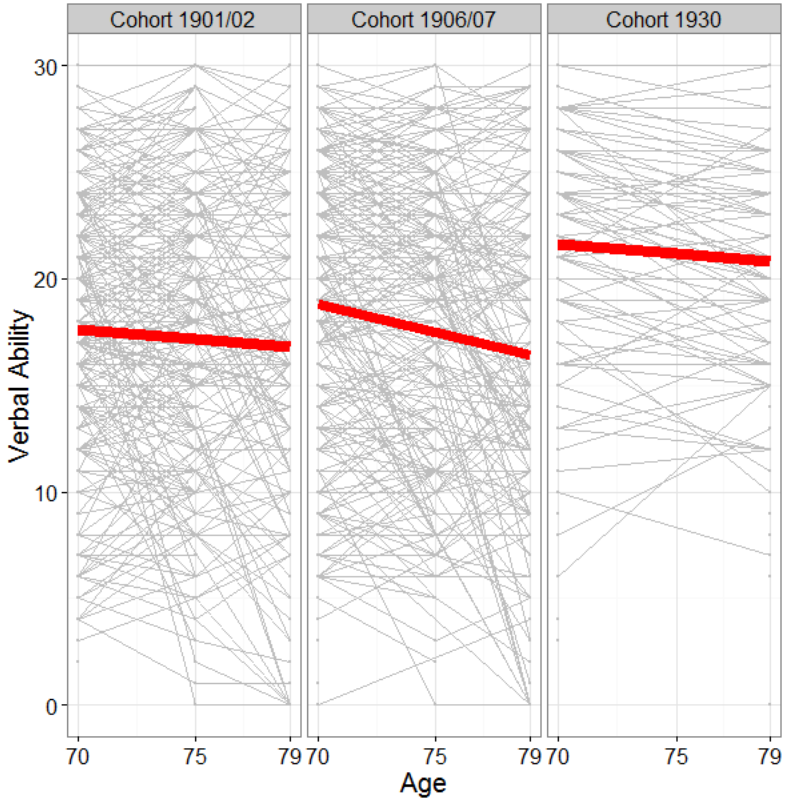
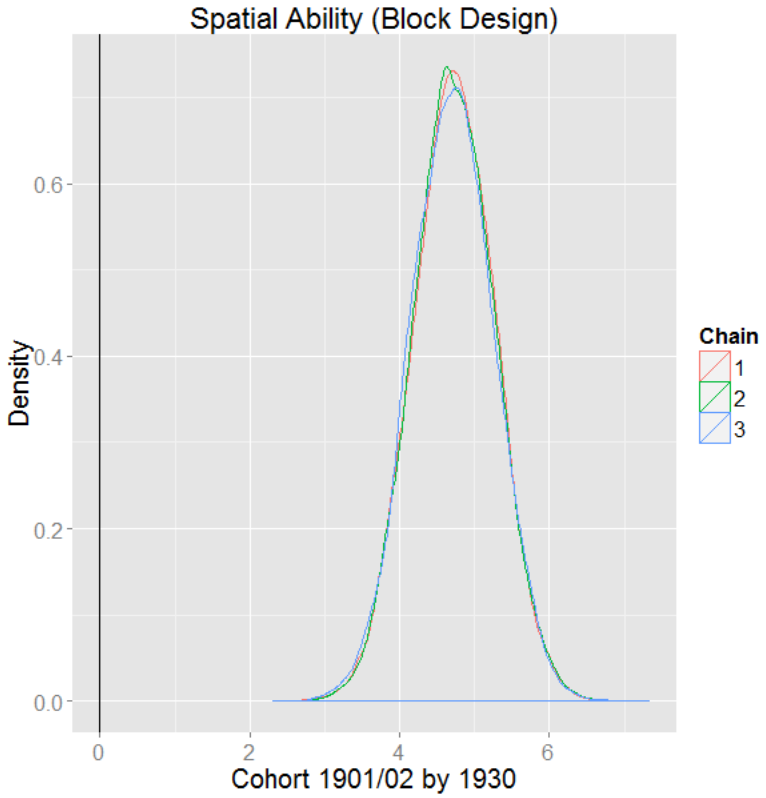
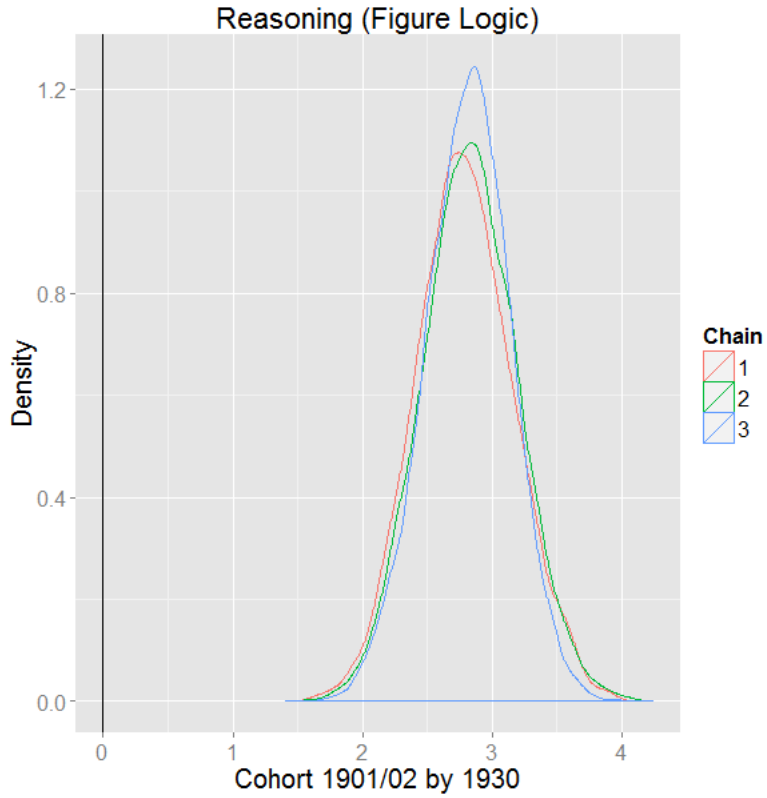
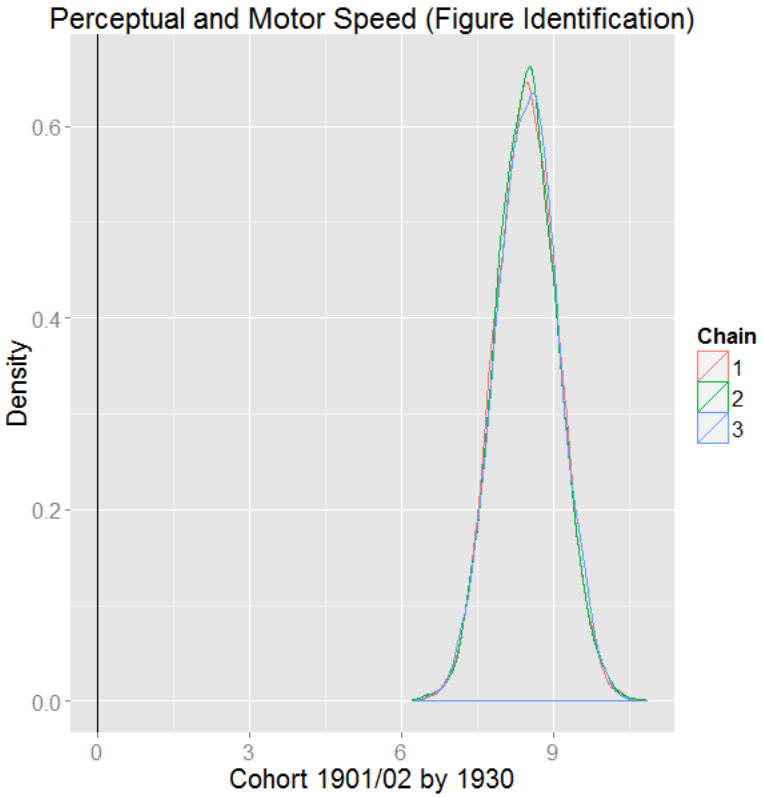
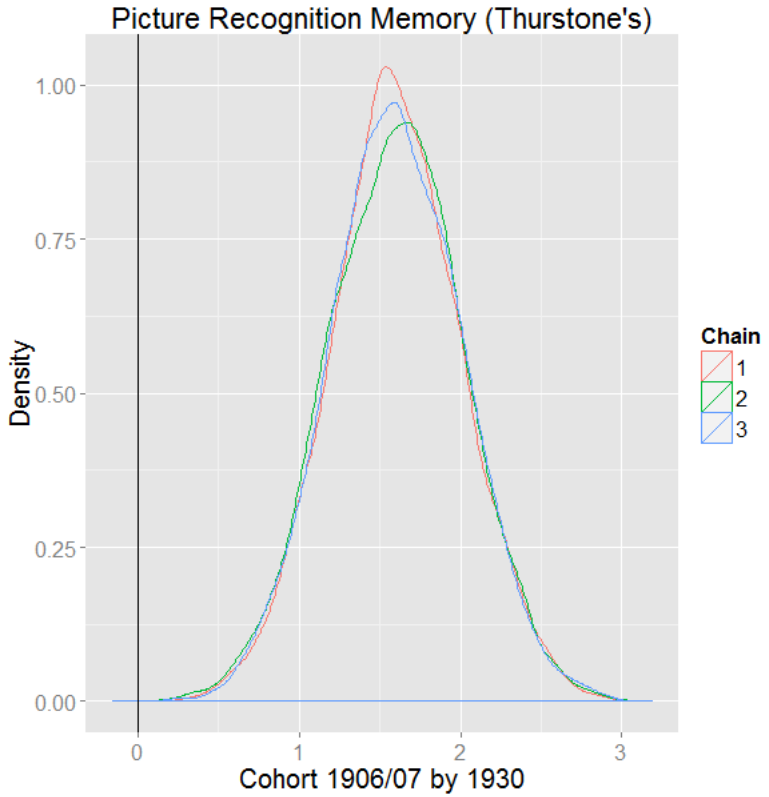



*Figure 6*. Raw score trajectories from the cognitive tests for cohorts born 1901/02, 1906/07, and 1930 and measured at ages 70, 75, and 79 as part of the H70 study. The red lines refer to the estimated average change trajectories.


Spatial Ability (Block Design)
Density
0.0
0.2
0.4
0.6
0
2
4
6
Cohort 1901/02 by 1930
Chain
1
2
3


Reasoning (Figure Logic)
Density
0.0
0.4
0.8
1.2
0
1
2
3
4
Cohort 1901/02 by 1930
Chain
1
2
3


Perceptual and Motor Speed (Figure Identification)
Density
0.0
0.2
0.4
0.6
0
3
6
9
Cohort 1901/02 by 1930
Chain
1
2
3


Picture Recognition Memory (Thurstone's)
Density
0.00
0.25
0.50
0.75
1.00
0
1
2
3
Cohort 1906/07 by 1930
Chain
1
2
3

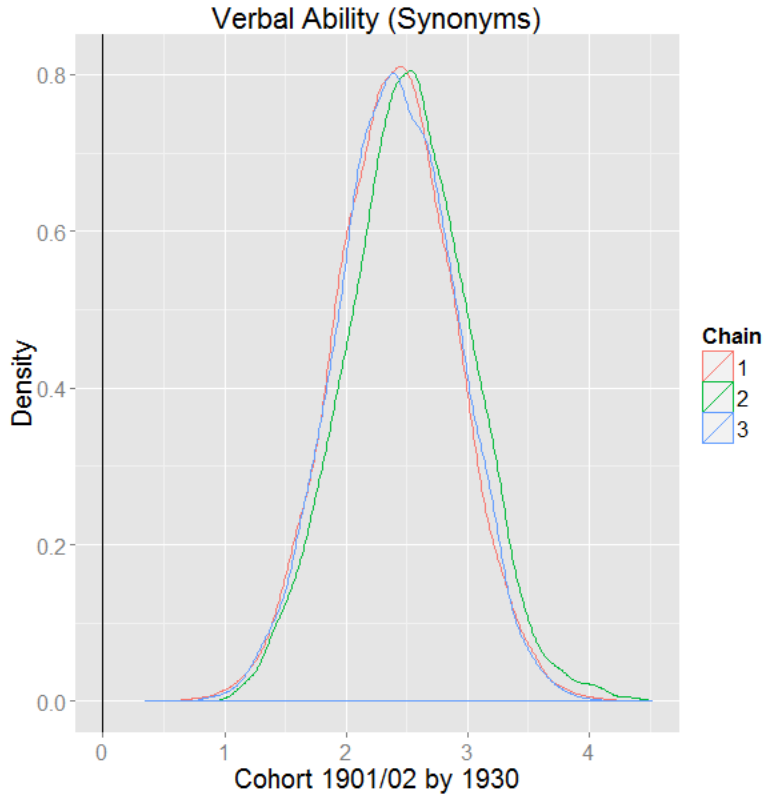
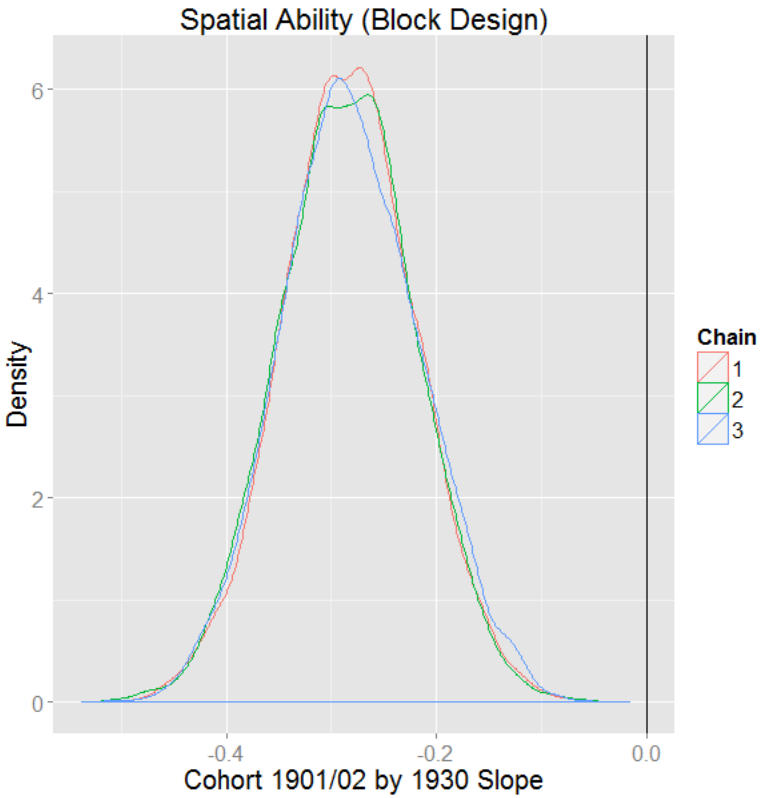
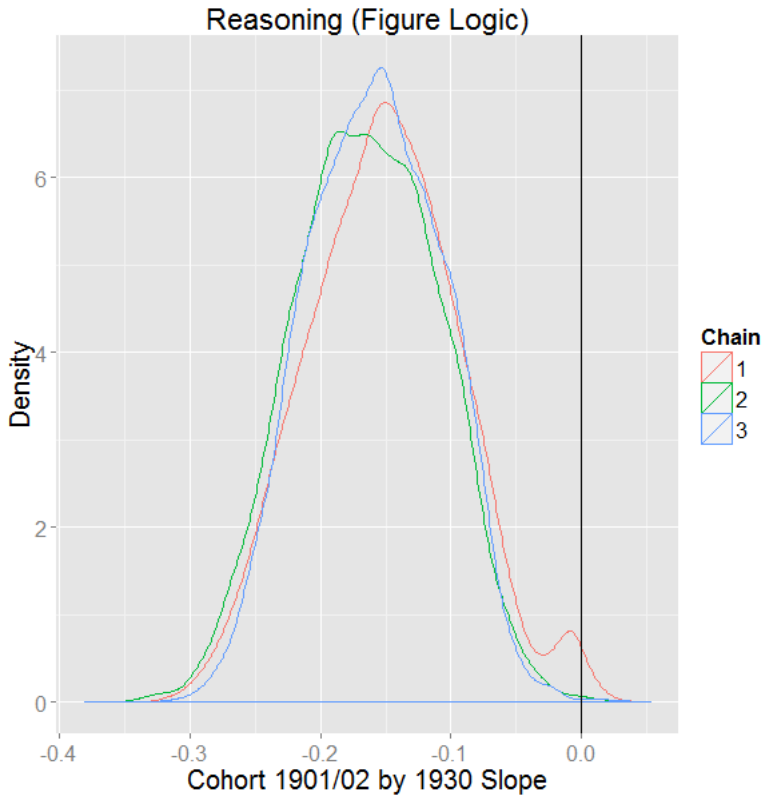
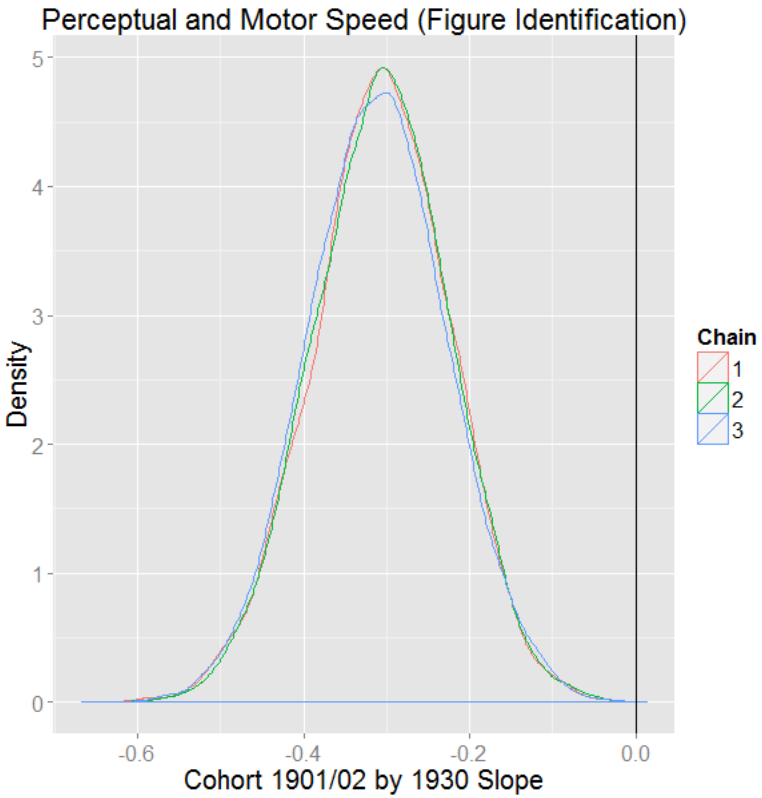
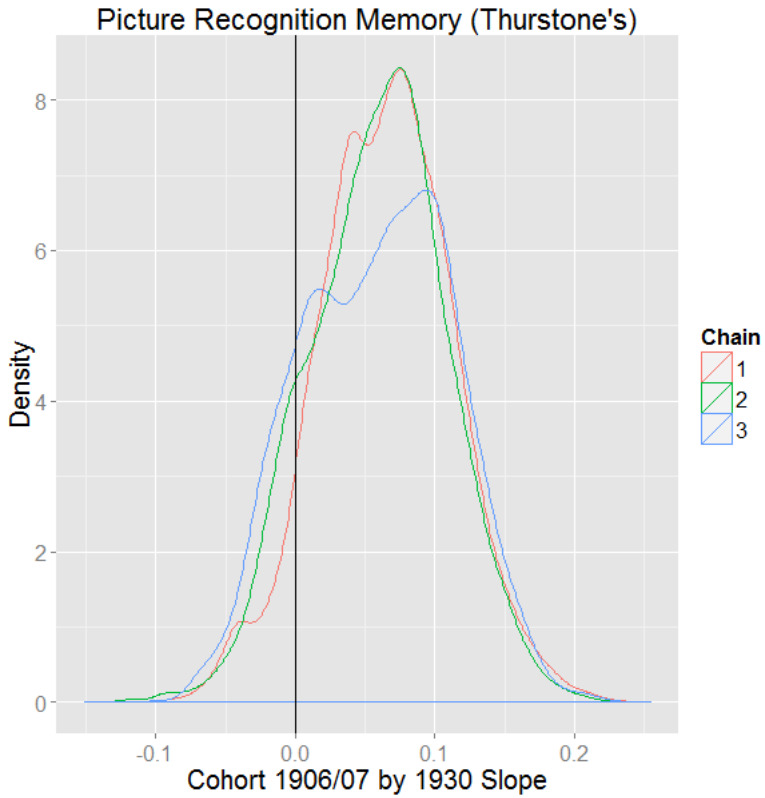



*Figure 7*. Marginal posterior density distribution of the cohort effects in level of cognitive performances at age 70.


Spatial Ability (Block Design)
Density
6
4
2
0
-0.4
-0.2
0.0
Cohort 1901/02 by 1930 Slope
Chain
1
2
3


Reasoning (Figure Logic)
Density
6
4
2
0
-0.4
-0.3
-0.2
-0.1
0.0
Cohort 1901/02 by 1930 Slope
Chain
1
2
3


Perceptual and Motor Speed (Figure Identification)
Density
5
4
3
2
1
0
-0.6
-0.4
-0.2
0.0
Cohort 1901/02 by 1930 Slope
Chain
1
2
3


Picture Recognition Memory (Thurstone's)
Density
8
6
4
2
0
-0.1
0.0
0.1
0.2
Cohort 1906/07 by 1930 Slope
Chain
1
2
3

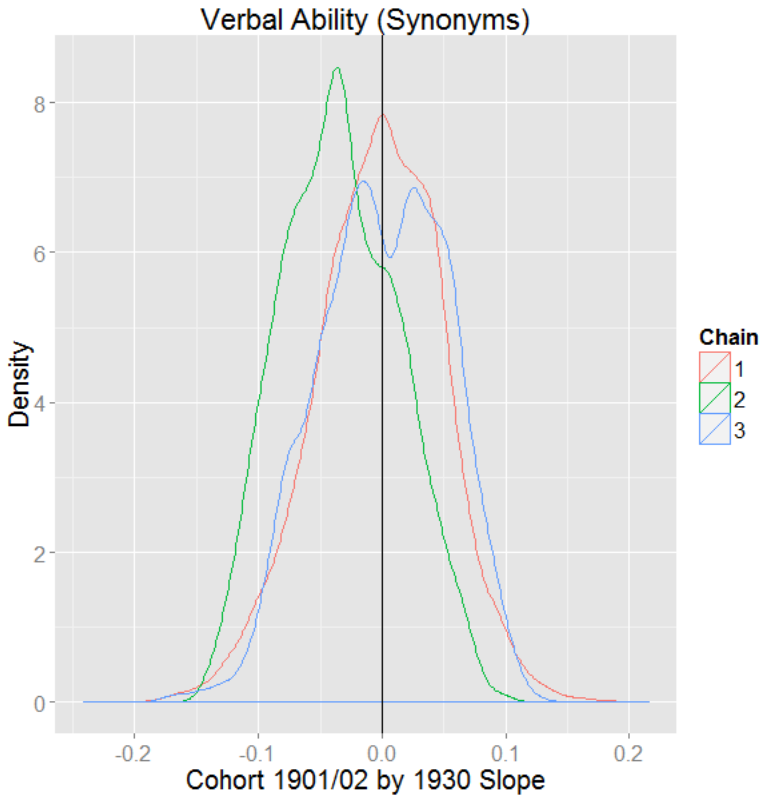



*Figure 8*. Marginal posterior density distribution of the cohort effects in linear rate of cognitive change between age 70 and 79.

**Study IV**

Descriptive statistics for the two cognitive outcomes variables analyzed in study IV, stratified by age at measurement and birth cohort, are presented in Table 8. Descriptive statistics concerning the cardiovascular risk factors, stratified by birth cohort, are presented in Table 9. There were significant cohort differences concerning the FRS ($F_{2, 1128} = 17.50$, $p < .001$), SBP ($F_{2, 1128} = 47.15$, $p < .001$), and BMI ($F_{2, 1128} = 7.29$, $p = .001$). Post hoc tests (Games-Howell) indicated that the 1930 cohort had lower mean FRS and SBP ($p$s < .001), but higher mean BMI ($p$s < .05), compared to the 1901-02 and 1906-07 cohorts. There were no significant differences between the 1901-02 and 1906-07 cohorts regarding these measures. There were also significant cohort differences regarding smoking status ($\chi^2_{2, N=1131} = 23.51$, $p < .001$), with a larger proportion of current smokers in the 1901-02 cohort compared to the later born cohorts. There were no significant cohort differences concerning gender distribution, diabetes status, or anti-hypertensive medication status.

Estimates from the models fitted to the spatial ability and reasoning data are shown in Tables 10 and 11, respectively. In the analyses we fitted three types of models separately to each of the two cognitive measures. In all models we estimated average level of performance at age 70 and average linear rate of change from age 70 to 79 as unique parameters for each of the three birth cohorts. We included education and gender as main effects and interactions with the time component, but the effects of education and gender were constrained equal across the birth cohorts (in order to avoid overparameterization of the models).

In Model 1 we constrained the effects of FRS to zero on both the intercept and linear slope for all three cohorts (see estimates under Model 1 in Tables 10 and 11). In Model 2, we included the FRS effects on both level of performance at age 70 and rate of change from age 70 to 79, but in this model the FRS effects were constrained equal across the birth cohorts (estimates from these models are shown under Model 2, in Tables 10 and 11). This resulted in

a significant improvement in model fit for both cognitive measures (spatial ability: $\Delta\chi^2$ (2) = 11.14, $p$ = .004; logical reasoning: $\Delta\chi^2$ (2) = 6.17, $p$ = .046) compared to Model 1. As can be seen in Table 10 there was a significant effect of FRS on the linear slope for the spatial ability test, where higher risk score was related to steeper average decline. For each 10% increase in cardiovascular risk, there was an average increase in decline by 0.04 points per year on the raw scale (standardized = -0.01). There was no effect of cardiovascular risk on baseline performance on the spatial ability test.

For the reasoning test there was a significant negative effect of FRS on baseline performance, where each 10% increase in cardiovascular risk was related to an average decrease in baseline performance by 0.29 points on the raw scale (standardized estimate = -0.10). There was no effect of FRS on the linear slope on the reasoning test.

Next, in Model 3, we released the cohort constraints on the effects of FRS, and estimated the effects of FRS on both intercept and linear slope separately for each cohort. This enables the estimation of the cohort by FRS two-way interaction and the time by cohort by FRS three-way interaction. Estimates from these models are shown under Model 3 in Tables 10 and 11. Releasing the cohort constraints on FRS improved model fit significantly on the reasoning test ($\Delta\chi^2(2) = 7.72$ $p = 0.021$) but not the spatial ability test ($\Delta\chi^2(4) = 1.31$ $p = 0.86$). For the reasoning test there was a negative effect of FRS on baseline performance in the 1901-02 cohort, where a 10% increase in the risk for cardiovascular disease was associated with a decrease in expected baseline performance of 0.54 points (standardized estimate = -0.18). For the 1930 birth cohort there was a non-significant, positive, effect of FRS on baseline performance where a 10% increase in the risk for cardiovascular disease was associated with an increase in expected baseline performance of 0.05 points (standardized estimate = 0.02). The fixed effect estimates from Models 3 are plotted in Figure 9 and indicate

that the relative influence of the FRS index is somewhat stronger in the 1901-02 birth cohort in comparison to the 1930 cohort, particularly in the reasoning test.

Table 8. Sample characteristics in the H70 study stratified by birth cohort, gender, education, and measurement occasions

| Cognitive test | N | Gender | | Education | | Measurement occasions | | |
|---|---|---|---|---|---|---|---|---|
| | | Women (%) | Men (%) | Compulsory (%) | More than Compulsory (%) | Age 70 M (SD) | Age 75 M (SD) | Age 79 M (SD) |
| Spatial Ability | | | | | | | | |
| Cohort 1901 | 313 | 58.50 | 41.50 | 85.30 | 14.70 | 13.38 (6.64) | 12.87 (6.43) | 11.73 (7.28) |
| Cohort 1906 | 381 | 55.90 | 44.10 | 82.20 | 17.80 | 15.95 (6.91) | 14.61 (6.84) | 11.59 (7.45) |
| Cohort 1930 | 437 | 59.70 | 40.30 | 57.40 | 42.60 | 19.89 (6.82) | 17.23 (6.98) | 15.80 (6.86) |
| Total | 1131 | 58.10 | 41.90 | 73.50 | 26.50 | 16.45 (7.21) | 15.02 (7.00) | 13.26 (7.44) |
| Logical Reasoning[a] | | | | | | | | |
| Cohort 1901 | 371 | 58.20 | 41.80 | 85.70 | 14.30 | 12.61 (4.60) | 12.57 (5.15) | 12.41 (4.93) |
| Cohort 1930 | 454 | 58.60 | 41.40 | 58.60 | 41.40 | 16.82 (4.51) | 14.87 (5.13) | 14.66 (5.36) |
| Total | 825 | 58.40 | 41.60 | 70.80 | 29.20 | 14.17 (5.00) | 13.85 (5.26) | 13.76 (5.31) |

Note. [a] Data for cohort 1906 on the Logical Reasoning test was not collected at ages 75 and 79 and therefore omitted from the present analyses.

Table 9. Descriptives for the variables included in the computation of the Framingham Risk Score at baseline (age 70) as stratified by birth cohort.

| | Cohort | | |
|---|---|---|---|
| | 1901-02 | 1906-07 | 1930 |
| Framingham Risk score, M (SD) | 39.22 (16.41) | 38.21 (17.81) | 32.68 (15.89) |
| Systolic blood pressure, M (SD) | 168.47 (25.24) | 169.07 (22.16) | 155.16 (22.04) |
| Antihypertensive medication, n (%) | 76 (24.30) | 92 (24.10) | 120 (27.50) |
| Body mass index, M (SD) | 25.97 (3.81) | 25.89 (3.64) | 26.83 (4.17) |
| Diabetes, n (%) | 16 (5.10) | 25 (6.60) | 41 (9.40) |
| Current smoker, n (%) | 83 (26.50) | 60 (15.70) | 58 (13.30) |
| Gender, women n (%) | 183 (58.5) | 213 (55.9) | 261 (59.7) |

Table 10. Parameter estimates from multiple-group latent growth curve models fitted to the spatial ability (Block Design test) data from three birth cohorts measured at ages 70, 75 and 79 as part of the H70 study (N=1131)

| | Model 1 | | Model 2 | | Model 3 | |
|---|---|---|---|---|---|---|
| Parameters | Estimates | *SE* | Estimates | *SE* | Estimates | *SE* |
| Intercept | | | | | | |
| Cohort 1901 | 12.60*** | 0.44 | 12.56*** | 0.45 | 12.61*** | 0.45 |
| Cohort 1906 | 14.73*** | 0.38 | 14.65*** | 0.39 | 14.65*** | 0.39 |
| Cohort 1930 | 17.31*** | 0.44 | 17.15*** | 0.47 | 17.19*** | 0.47 |
| Gender | 1.33*** | 0.41 | 1.55*** | 0.48 | 1.56*** | 0.48 |
| Education | 4.64*** | 0.49 | 4.65*** | 0.49 | 4.62*** | 0.49 |
| FRS | | | -0.12 | 0.14 | | |
| Cohort 1901 x FRS | | | | | -0.32 | 0.26 |
| Cohort 1906 x FRS | | | | | -0.13 | 0.20 |
| Cohort 1930 x FRS | | | | | 0.06 | 0.24 |
| Linear slope | | | | | | |
| Cohort 1901 | -0.27*** | 0.05 | -0.30*** | 0.05 | -0.30*** | 0.05 |
| Cohort 1906 | -0.46*** | 0.04 | -0.48*** | 0.05 | -0.48*** | 0.05 |
| Cohort 1930 | -0.52*** | 0.06 | -0.56*** | 0.06 | -0.56*** | 0.06 |
| Gender | -0.05 | 0.05 | 0.03 | 0.06 | 0.03 | 0.06 |
| Education | -0.11 | 0.06 | -0.11 | 0.06 | -0.11 | 0.06 |
| FRS | | | -0.04** | 0.02 | | |
| Cohort 1901 x FRS | | | | | -0.03 | 0.03 |
| Cohort 1906 x FRS | | | | | -0.04 | 0.02 |
| Cohort 1930 x FRS | | | | | -0.05 | 0.03 |
| Variability components | | | | | | |
| Intercept | 28.82 | 2.04 | 28.77 | 2.04 | 28.73 | 2.04 |
| Slope | 0.04 | 0.03 | 0.03 | 0.03 | 0.03 | 0.03 |
| Covariance | 0.11 | 0.19 | 0.12 | 0.19 | 0.12 | 0.19 |
| Residual | 12.05 | 0.72 | 12.08 | 0.72 | 12.08 | 0.72 |
| Model fit indices | | | | | | |
| $\chi^2(df)$ | 69.54(40) | | 58.41(38) | | 57.10(34) | |
| CFI | 0.98 | | 0.99 | | 0.98 | |
| RMSEA [90% *CI*] | 0.03(0.02-0.04) | | 0.02(0.01-0.03) | | 0.03(0.01-0.04) | |

Note. * p < .05. ** p < .01. *** p < .001.

Table 11. Parameter estimates from multiple-group latent growth curve models fitted to the reasoning ability (Figure Logic test) data from two birth cohorts measured at ages 70, 75 and 79 as part of in the H70 study (N=825)

| | Model 1 | | Model 2 | | Model 3 | |
|---|---|---|---|---|---|---|
| Parameters | Estimates | *SE* | Estimates | *SE* | Estimates | *SE* |
| Intercept | | | | | | |
| Cohort 1901 | 11.94*** | 0.28 | 11.84*** | 0.29 | 11.90*** | 0.29 |
| Cohort 1930 | 15.23*** | 0.36 | 15.00*** | 0.37 | 15.01*** | 0.37 |
| Gender | 1.06** | 0.36 | 1.53*** | 0.42 | 1.58*** | 0.41 |
| Education | 2.12*** | 0.43 | 2.12*** | 0.42 | 2.08*** | 0.42 |
| FRS | | | -0.29* | 0.13 | | |
| Cohort 1901 x FRS | | | | | -0.54*** | 0.15 |
| Cohort 1930 x FRS | | | | | 0.05 | 0.18 |
| Linear slope | | | | | | |
| Cohort 1901 | -0.08 | 0.05 | -0.08 | 0.05 | -0.08 | 0.05 |
| Cohort 1930 | -0.28*** | 0.06 | -0.28*** | 0.06 | -0.27*** | 0.06 |
| Gender | -0.05 | 0.06 | -0.07 | 0.07 | -0.07 | 0.07 |
| Education | -0.03 | 0.07 | -0.02 | 0.07 | -0.02 | 0.07 |
| FRS | | | 0.01 | 0.02 | | |
| Cohort 1901 x FRS | | | | | 0.03 | 0.03 |
| Cohort 1930 x FRS | | | | | -0.02 | 0.02 |
| Variability components | | | | | | |
| Intercept | 6.77 | 1.47 | 6.58 | 1.46 | 6.36 | 1.45 |
| Slope | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 |
| Covariance | 0.21 | 0.19 | 0.22 | 0.19 | 0.23 | 0.19 |
| Residual | 13.95 | 0.94 | 13.96 | 0.94 | 13.94 | 0.94 |
| Model fit indices | | | | | | |
| $\chi^2(df)$ | 74.03(24) | | 67.86(22) | | 60.14(20) | |
| CFI | 0.90 | | 0.91 | | 0.92 | |
| RMSEA [90% *CI*] | 0.05(0.04-0.06) | | 0.05(0.04-0.06) | | 0.05(0.03-0.06) | |

Note. * p < .05. ** p < .01. *** p < .001.

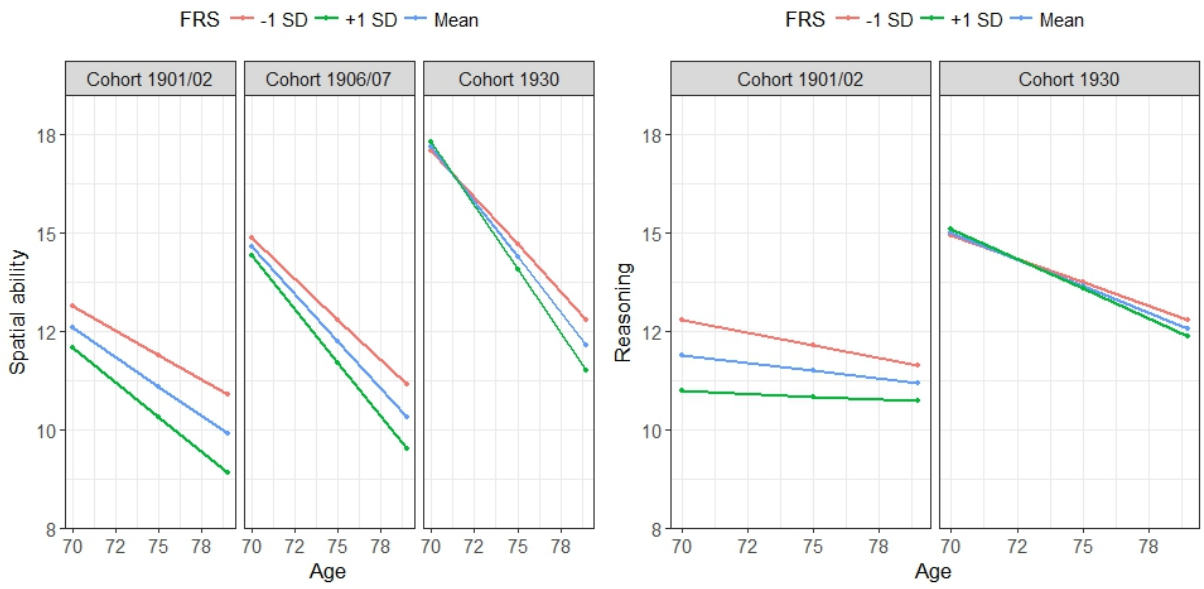



*Figure 9*. Estimated change trajectories from multiple-group LGCMs, conditioned on cardiovascular risk (FRS), and fitted to reasoning and spatial ability data from the H70. Groups are defined by birth cohorts.

## Discussion

The overarching aim of this thesis was to investigate birth cohort differences in cognitive functioning from ages 70 to 79 in three population-based representative Swedish samples. Overall, the results indicated substantial cohort differences in level of performance for all five cognitive outcomes studied (i.e., spatial ability, logical reasoning, verbal ability, perceptual-motor-speed, and long-term recognition memory), with later born cohorts outperforming earlier born. Interestingly, we found evidence for reliable cohort differences in rates of change regarding three cognitive outcomes (spatial ability, reasoning, and perceptual-motor-speed) on which later born cohorts declined at a faster rate than earlier born cohorts. Our results indicated little or no cohort differences in rates of cognitive change regarding recognition memory and verbal ability. We also found evidence of significant cohort differences in proportions of individuals showing cognitive decline, stability, and gain from age 70 to 79 on four cognitive outcomes (i.e. spatial ability, logical reasoning, verbal ability, and perceptual-motor-speed), where later born cohorts consisted of a smaller proportion showing cognitive gains, and a larger proportion showing decline, compared to earlier born cohorts. Finally, we found evidence of cohort differences in the association between cardiovascular risk, assessed through the FRS based on simple office-based non-laboratory predictors, and cognitive functioning and decline. Even though the effect sizes were small overall, they were even smaller for the 1930 cohort, particularly on the logical reasoning test.

### Cohort differences in cognitive performance

The finding that later born cohorts outperform earlier born cohorts on levels of performance is in line with our hypothesis and previous studies (e.g., Baxendale, 2010; Bowles et al., 2005; Christensen et al., 2013; Llewellyn & Matthews, 2009; Rönnlund &

Nilsson, 2008, 2009; Skirbekk et al., 2013) and further strengthen the notion that Flynn effects are evident also in old age.

The large cohort differences revealed in our studies , with effect sizes (i.e., Cohen's d) in study III ranging from 0.63 (for the verbal ability test) to 1.19 (for the perceptual-motor-speed test) when comparing the 1901-02 and 1930 cohorts at age 70 represent the "massive gains" Flynn alluded to in his seminal paper (Flynn, 1984). As there is hitherto no known genetic marker, or combination of genetic markers, with effect sizes comparable to those reported in this thesis (cf. Payton, 2009) our findings testify to the major importance of environmental influences in cognitive development over the lifespan. Our findings should therefore further strengthen the conviction in, and awareness of, the notion that changes in environmental factors, such as longer and better education, more complex work environments, and overall improvements in public health, including cardiovascular health, have significant long-term effects on cognitive functioning that extend into late life.

**Cohort differences and cognitive change**

The findings that later born cohorts consist of a larger proportion of individuals showing cognitive decline (Study I), and decline at a faster rate compared to earlier born cohorts on three cognitive measurements (i.e. spatial ability, reasoning, and perceptual-motor-speed; Studies II and III) were somewhat unexpected and not in line with our hypothesis nor the prediction by Schaie (2008) based on the co-constructionist model (i.e. that later born cohorts should decline at a slower rate than earlier born). Based on Schaie's (2008) prediction, that positive advancements regarding sociocultural influences and possibilities to control and counter negative neurobiological influences should lead to cohort differences in change trajectories, it would seem probable that later born cohorts should contain a smaller

proportion of decliners compared to earlier born cohorts, but our findings indicate the opposite.

Even though results from previous studies investigating cohort differences in trajectories of cognitive change have been inconsistent, we hypothesized that later born cohorts would decline at a slower rate compared to earlier born cohorts. Our results regarding cohort differences in rate of change are not in line with this hypothesis nor do they agree with the findings from Finkel et al. (2007), Schaie (2005), or Zelinski and Kennison (2007), but they partly agree with results from Gerstorf et al. (2011) and Hülür et al. (2013). Taken together, our results and the findings by Gerstorf et al. and Hülür et al. therefore suggest that secular trends may favor later born cohorts earlier in life, but that this effect may become reversed at the end of the lifespan.

The reasons for the observed cohort differences in rates of change and proportions of individuals showing cognitive decline, stability, and gain are unclear at the present. One possible explanation is related to cohort differences in selective survival into older ages. As life-expectancy has increased steadily in Sweden since the 19$^{th}$ century (Christensen, Doblhammer, Rau & Vaupel, 2009; de la Croix, Lindh & Malmberg, 2009; Statistics Sweden, 2013) the average remaining life expectancy, also at older ages, is slightly higher for later born cohorts compared with earlier born. This suggests that later born cohorts include a relatively larger proportion of frailer individuals who have survived to age 70 and are therefore more inclined to decline in cognition since comparatively frail individuals in the earlier born cohorts were less likely to survive even to age 70.

A related explanation suggested by Gerstorf et al. (2011) and Hülür et al. (2013) concerns the consequences of manufactured survival (Carnes, Nakasato & Olshansky, 2005; Olshansky, Hayflick & Carnes, 2002). That is, advancements in life saving technologies and

medicine may have increased life expectancy of later born cohorts at all levels of functioning, but perhaps particularly in the lower functioning spectrum of the population (due to higher levels of survival regarding impairments and diseases that would have led to death in earlier cohorts). In line with this, Hülür et al. found not only steeper average decline in the later deceased cohort but also generally lower performance at age 80 compared with the earlier deceased cohort. Our results are not consistent with Hülür et al. since we found that the latest born cohort performed at a higher level than the earlier born cohorts at all measured ages and on all tests (see Figures 2 and 5).

Selective and manufactured survival are speculative explanations and would suggest a larger slope variability component (i.e., larger heterogeneity) in later born cohorts, especially the 1930 cohort, as compared with the earlier born cohorts. That was, however, not supported by our data (see Studies II and III). Also, other studies comparing the relevant cohorts indicate that the 1930 cohort is, on average, less frail than earlier born cohorts in terms of for instance sexual activity (Beckman, Waern, Gustafson & Skoog, 2008), lung functioning (Lak, Guo & Skoog, 2012), fitness and physical activity (Hörder, Skoog & Frändin, 2013) functional ability, and engagement in leisure activities (Falk et al., 2014).

The observed cohort differences in cognitive decline may also be related to differences in average age of onset of the cognitive decline. Due to less cognitive reserve and poorer overall health we might expect that a larger proportion of individuals in the earlier born cohorts would show an onset of cognitive decline prior to the baseline measurement at age 70 (i.e., left censuring). These individuals could therefore be expected to remain in the terminal decline phase over a longer period of time, than members of later born cohorts who are generally healthier and have greater cognitive reserve.

According to the hypothesis of cognitive reserve, there are individual differences regarding cognitive processes which allows people to cope differently well with brain pathology (see for instance Barulli & Stern, 2013; Richards & Deary, 2005; Stern, 2002, 2009). Individuals with higher cognitive reserve can make more efficient and flexible use of their cognitive processes (and the underlying neural substrates) and can therefore tolerate more pathology, without loss of performance, compared with individuals with less cognitive reserve (Alosco et al., 2012; Bartrés-Faz et al. , 2009; Ferreira et al., 2016; Franzmeier et al., 2017; Opdebeeck, Martyr, & Clare, 2016; Rentz et al., 2010; Tucker-Drob, Johnson, & Jones, 2009; Vemuri et al, 2011; Vuoksimaa et al., 2013). Several studies have reported brain pathology associated with normal aging, such as regional shrinkage/volume reduction (Head, Rodrigue, Kennedy & Raz, 2008; Raz et al., 2005), myelin degeneration, and loss of white matter nerve fibers (Peters, 2002), reduced activation of, and functional coupling between, regions (Podell et al., 2012), and thinning of the cortex (Salat et al., 2004; Thambisetty et al., 2010) in ages younger than 70.

Further, according to the hypothesis of cognitive reserve people with higher cognitive reserve are expected to show higher cognitive abilities (via for instance higher scores on cognitive tests) and to start declining, cognitively, later (i.e. after more severe pathology) than people with lower cognitive reserve (see for instance Barulli & Stern, 2013; Richards & Deary, 2005; Steffener & Stern, 2012; Stern, 2009; Tucker & Stern, 2011, Whalley, Deary, Appleton & Starr, 2004). This is supported by for example Brickman et al. (2011), Corral, Rodriguez, Amenedo, Sanchez and Diaz (2006), Roe et al. (2008), and Singh-Manoux et al. (2011). But, crucially, when people with higher cognitive reserve start to show decline, they are expected to decline more rapidly than people with lower cognitive reserve (Steffener & Stern, 2012; Stern, 2009; Tucker & Stern, 2011) due to the fact that people with higher

cognitive reserve will have sustained more severe pathology before showing any decline. This is supported by the systematic review, incorporating 133 studies and more than 400 000 subjects, by Meng and D'Arcy (2012), and also by Amieva et al. (2014), Hall et al. (2009), and Soldan et al. (2017). Thorvaldsson, Skoog and Johansson (2017) found partial support for this, using data from the 1901-02 cohort and IQ as a proxy for cognitive reserve. Higher IQ was related to delayed terminal decline on spatial ability, verbal ability and perceptual-motor-speed, and steeper decline on verbal ability and perceptual-motor-speed.

To the extent that later born cohorts in this study, on average, are evidencing higher cognitive reserve, as indicated by their higher level of performance, they should in accordance with the reserve hypothesis show an average onset of decline later in life (i.e. after more severe pathology) than earlier born cohorts and when they start to decline they should decline more rapidly. This implies that we should also find very different results concerning cohort differences in cognitive decline depending on the age ranges when measurements are taken. If later born cohorts on average have higher cognitive reserve, as indicated by the many studies finding evidence of Flynn effects in old age (e.g. Finkel et al., 2007; Gerstorf et al., 2011; Rönnlund & Nilsson, 2009), then later born cohorts should also, on average, start declining later in life compared to earlier born cohorts, but when they start to decline they should decline more rapidly. This might offer an explanation regarding the results in H70 as well as the discrepancy between those results and the results of previous studies.

Willis and Schaie (2006) had their baseline measurements taken when their participants were 60 years of age, Gerstorf et al. (2011) studied change from 50 to 80 years of age, and Finkel et al. (2007) measured performance from 62 to 78 years of age. Possibly it could be, then, that these studies, at least to some extent, studied their participants when mainly earlier born cohorts, supposedly with lower cognitive reserve on average, showed

decline. In the H70 study, baseline measurements were taken later, at 70 years of age. It is possible that baseline measurements in the H70 study were taken at a stage where also later born cohorts, supposedly evidencing higher average cognitive reserve, had started to decline. In accordance with the cognitive reserve hypothesis they should show more rapid decline than earlier born cohorts, supposedly evidencing lower average cognitive reserve. For the same reasons, later born cohorts would also consist of larger proportions of individuals showing cognitive decline which is in line with our findings.

This proposed explanation, however, is speculative and a test of this hypothesis would require a longer follow-up period starting at younger ages as well as information about time of death for the study participants. Information about age of death is, however, not completely available in the presented studies as a substantial proportion of the 1930 birth cohort is still alive.

Another alternative explanation for the observed steeper rate of decline for the later born cohorts may relate to reduction in cognitive stimulation as a consequence of retirement. Some studies have found evidence of an acceleration in cognitive decline after retirement (e.g. Bonsang, Adam & Perelman, 2012; Mazzonna & Peracchi, 2012; Rohwedder & Willis, 2010; but see also Coe, Von Gaudecker, Lindeboom & Maurer, 2012), which may interact with ability levels, where reduced stimulation has larger effects among the more able as compared with the less able. Individuals in the later born cohorts are not only proportionally more cognitively able, as reflected by their higher average performances, but they are also better educated and more likely to have had cognitively stimulating professions than those in earlier cohorts. Related to this notion are findings from a study by Coe et al. (2012) suggesting that retirement has different effects on cognitive functioning between white-collar

and blue-collar workers. They found no effect of retirement on cognition for white-collar workers but, possibly, a positive effect for blue-collar workers.

Finkel, Andel, Gatz and Pedersen (2009) studied the association between three aspects of work complexity (complexity with data, people, and things) and cognitive decline after retirement (on measures of verbal ability, memory, spatial ability, and processing speed) in a Swedish sample of twins. They found a significant association between complexity with people and rate of decline on spatial ability, where high complexity was related to faster decline. Apart from this, there were no significant associations.

Taken together, the results of Finkel et al. (2009) and Coe et al. (2012) indicate that the association between retirement and cognition later in life may be moderated by type of occupation and cognitive demands in work life. This may partly explain our findings, but further evaluation is needed in the form of analyses that include more detailed information concerning type of occupation, work complexity, and post-retirement cognitive stimulation.

One final possible explanation for the observed cohort differences in rates of change could be related to the psychometric properties of the cognitive measures used in our studies. First, the tests could vary in sensitivity to detect within-person change depending on level of performance. For example, it may be relatively easier to detect within-person change over several years in high performing individuals compared to low performing individuals. This explanation cannot be excluded given the observed cohort difference in level of performance observed in our studies. In line with this reasoning, Proust-Lima, Amieva, Dartigues and Jacqmin-Gadda (2007) evaluated several psychometric tests and concluded that the tests differed in the sensitivity to detect change conditioned on level of performance. Some tests are superior in detecting change among high performing participants, others better at detecting change among the low performing.

Second, our findings may also be biased by differential practice effects conditioned on birth cohort. Practice effects may always be a potential source of bias regarding results in longitudinal studies (e.g. Lövdén, Ghisletta & Lindenberger, 2004; Salthouse, 2016; Thorvaldsson, 2016). Substantial practice effects have been found even when repeated measures are distributed over several years (e.g. Rönnlund, Lövdén & Nilsson, 2007; Rönnlund, Nyberg, Bäckman & Nilsson, 2005; Salthouse, Schroeder & Ferrer, 2004). Further, it has also been reported that practice effects vary due to an interaction between the participant's level of ability and the difficulty of the task in question (Rabbitt, Diggle, Holland & Mc Innes, 2004). On easy tasks, the benefits of repeated testing are greater for the less able, while the more able benefit more on difficult tasks. To the extent that the cognitive tests analyzed in this study could be considered easy, this could provide yet another possible explanation for our findings. That is, if the tests used in the H70 could be considered easy then the lower performing earlier born cohorts should experience greater practice effects. These effects, in turn, could at least partly mask the true extent of their cognitive decline making it appear that they had declined to a lesser extent than the later born cohorts. When Thorvaldsson, Hofer, Berg, and Johansson (2006) evaluated practice effects in the 1901-02 cohort from the H70 study, they found evidence of relatively limited practice effects on levels of performance regarding verbal and spatial ability, but no practice effects for perceptual-and motor-speed, short-term memory or working memory.

**Gender, education, and cognitive aging**

In study II we investigated whether gender and education could account for the cohort differences in levels of functioning and rates of change on two measures of fluid abilities (i.e.

spatial ability and logical reasoning). We also investigated possible cohort trends in the effects of gender and education on level of functioning and rate of change.

Based on findings from previous studies (e.g. de Frias et al., 2006; Maitland et al., 2000; Meinz & Salthouse, 1998; Munro et al., 2012) we hypothesized that men would, on average, perform at a higher level than women on the two fluid measures. This hypothesis was supported in the 1906-07 and 1930 cohorts, but not in the 1901-02 cohort where we found no gender differences. These results also contradicted our hypothesis of a cohort trend in the gender effect, where we expected gender to become less important in later born cohorts because of the fact that gender was a more important determinant regarding educational, occupational, and social opportunities in the earlier born cohorts. The reasons for these findings are unclear at present. It could possibly reflect the labor conditions in the earlier born cohorts where most men were blue-collar workers and most women were housewives. Surprisingly, the average estimates from the 1906-07 cohort were more similar to those from the 1930 cohort than from the 1901-02 cohort. The reasons for this are unclear. Gender was not significantly associated with rate of change in either the spatial ability or the reasoning test.

In line with our hypothesis we did find that the more highly educated performed, on average, at a higher cognitive level as compared with those with lower education. This trend was evident in all three cohorts, but, for unknown reasons, the association was strongest in the 1906-07 cohort. We did not, therefore, find a clear birth cohort trend regarding the effect of education. We further hypothesized that higher education would be related to less cognitive decline. This was, however, not supported by the data. On the contrary, we found that longer education was associated with steeper decline on the spatial ability test, though not

on the reasoning test. Once again, for unknown reasons, this effect was strongest for the 1906-07 cohort.

Education is commonly used as a proxy for cognitive reserve (with higher educational attainment indicating higher cognitive reserve). Above I have suggested that birth cohort differences in cognitive reserve might account for our findings of steeper decline in later born cohorts. In line with this reasoning, and to the extent that education is a valid proxy for cognitive reserve, we would expect higher educational attainment to be associated with steeper cognitive decline. This was, however, only partly supported by our data. It should be noted, though, that in the H70 study there is less variance in educational attainment compared to many other studies, which imposes constraints (i.e. due to restriction of range) on the estimates of the association between education and cognitive functioning and change.

In summary, gender and education accounted only partially for the observed birth cohort differences in levels of performance and rates of change. To better understand the observed cohort differences, future analyses need to consider additional factors such as engagement in cognitively stimulating activities, work complexity, engagement in social activities/social networks, and health-related behaviors such as exercise.

**Cardiovascular health, cohort differences, and cognitive functioning**

Our main findings in Study IV indicate relatively weak associations between the cardiovascular risk, assessed with the FRS based on non-laboratory predictors, and both level of cognitive functioning and rate of change. These associations were, however, somewhat larger in the first birth cohort, providing at least partial support for our hypothesis of moderating effects of birth cohort.

Our findings that elevated cardiovascular risk was associated with lower cognitive performance and a steeper rate of decline is in line with findings from several previous studies (e.g. Elias et al., 2004; Kaffashian et al., 2011). Overall, the effects of cardiovascular risk on levels of performance and rates of change in Study IV were small and in line with the small overall effect size reported in the meta-analysis by DeRight et al. (2015).

Our results also indicate that the associations between cardiovascular risk and cognitive functioning and change are somewhat reduced in later born cohorts. Thus, cardiovascular risk is a less important factor for cognition in later born cohorts, which may not be that surprising considering that, in line with previous research (e.g. Harmsen, Wilhelmsen & Jacobsson, 2009; Rosengren et al., 2009, Zhi et al., 2013) we found that overall cardiovascular risk was significantly lower in the 1930 cohort compared to the earlier born cohorts, reflecting their improved overall cardiovascular health.

A possible explanation for the relatively weak effect sizes found in Study IV could be that the FRS index based on non-laboratory predictors is less valid for quantification of cardiovascular burden when assessed at age 70 and beyond. This could be due to that the beta weights, as generated from the original Framingham cohort and used in the computation of the FRS, are not completely generalizable to the observed sample at this age. The FRS was developed using a sample ranging in age from 30 to 74 (D'Agostino et al., 2008), which only partly overlaps with the age range studied in this thesis.

A further, possible, problem with the cardiovascular risk model used in this study relates to the fact that there are indications of non-linear associations between some of the predictors used in the FRS and cognitive performance and risk for dementia. The FRS is based on assumed linear associations, and therefore does not account for non-linear associations. There are indications of a U-shaped association between blood pressure and

cognitive functioning (Glynn et al., 1999; Kennelly & Collins, 2012; Kennelly, Lawlor & Kenny, 2009b; Qiu et al., 2005; Skoog et al., 1996; Thorvaldsson et al., 2012; Waldstein, 2003). That is, both low and high blood pressure are associated with worse cognitive functioning and increased risk of developing dementia. The implication of this is that low blood pressure should also be taken into account in order to predict cognitive decline, especially in an older population, which is not the case with the FRS.

A large body of research indicates a negative association between cognitive functioning and weight in midlife and younger ages, but the association in older ages is less clear (Dahl & Hassing, 2012; Smith, Hay, Campbell & Trollor, 2011). Sabia, Kivimaki, Shipley, Marmot and Singh-Manoux (2008), however, found that both underweight and obesity in late midlife (mean age 61 years) were related to poorer cognitive functioning compared to normal weight, indicating another possible U-shaped association, now between cognitive functioning and weight. Smith et al. (2011) also suggest this possible U-shaped association. According to their review, results indicate that up to the age of 72 years the association between weight and cognition is negative (in that overweight is related to worse cognitive functioning compared to normal weight), but that over the age of 72 overweight participants perform, on average, better than normal weight. It has been suggested that underweight, and loss of weight, in older ages may be a marker of worse general health, which in turn is likely associated with worse cognitive functioning (Nilsson & Nilsson, 2009). Low weight and weight loss may also be a preclinical sign of dementia (Gustafson, 2006) or a consequence of cognitive decline and neurodegeneration (Smith et al., 2011). Thus, low BMI should perhaps also be considered a risk factor for cognitive decline, but this is not taken into account in the FRS.

In the FRS model employed in our studies, smoking status is dichotomized (as non-smoker or current smoker). This is likely to constitute an over-simplification of the relationship between smoking status and cognitive functioning. Some studies have reported differences between former smokers and never smokers, where former smokers evince larger cognitive declines compared to never smokers (e.g. Anstey et al., 2007; Sabia et al., 2012). Thus, being a former smoker may also constitute a risk factor for cognitive decline, but this information is not incorporated in the FRS.

In sum, and despite the potential problems concerning the use of FRS addressed, it should be noted that our effect sizes are comparable to the overall effect size of r = -.16 reported in the meta-analysis by DeRight et al. (2015).

**Methodological reflections**

A major strength of the studies presented in this thesis is that we could use data from three representative population-based samples, born up to 30 years apart, measured over 9 years at the same chronological ages (i.e., 70, 75, and 79) on the same cognitive measures. A further unique strength is the age homogeneity of the birth cohorts in that participants in each cohort were born at most 12 months apart.

There are, however, also some limitations that need to be addressed. One limitation is that we only have three measurements at most per cohort and test, as more measurement occasions and longer follow-ups would be preferred to more thoroughly capture change and actual trajectories. Another limitation is that a shorter version of the perceptual-motor-speed measure was used at age 75 for the 1930 cohort. This could have led to underestimation of the cohort effects (due to ceiling effects) at age 75 and possibly overestimation of the decline in the 1930 cohort. Finally, the baseline participation rate for the 1930 cohort (i.e. 66%) was

lower compared to the earlier born cohorts which may have produced a somewhat more selective sample for this cohort.

**Contributions of the separate studies**

As mentioned above, there are few studies that have incorporated large, multi-birth cohorts, population-based representative samples followed longitudinally and measured on comparable cognitive measurements over long time. In this sense the H70 provides unique opportunities regarding studies of cohort differences in cognitive aging. In the papers that this thesis is based on we wanted to take advantage of these possibilities and study in detail several aspects of cohort differences in cognitive aging. It is our belief that, although there is a clear common thread linking the studies in this thesis, each study makes independent and important contributions in its own right.

In study I we took a somewhat more, to the general public, easily accessible approach compared to the other studies and investigated cohort differences in proportions of participants evincing cognitive gain, stability or decline from age 70 to 79.

In Study II we used multiple-groups latent growth curve modelling to investigate cohort differences in levels of cognitive performance and trajectories of change, which were not investigated in Study I, using two measures of fluid ability, while also incorporating education and gender as moderators of the birth cohort effects.

In Study III we extended the analyses from study II by incorporating five cognitive measures and also presented the evidence in the form of conditioned probability distributions using a Bayesian analytical framework.

In Study IV we focused on possible cohort differences in the association between cardiovascular risk and cognitive aging, rather than on cohort differences in cognitive aging

*per se*. Cardiovascular risk has been advanced as an important modifiable factor related to cognitive functioning and change in aging. Further, research has indicated secular decreases in cardiovascular risk. It is therefore important to study both the strength of the association between cardiovascular risk and cognitive aging and the possible cohort differences in this association.

**Conclusions and implications**

The results presented in this thesis provide evidence of moderate to large birth cohort differences in levels of cognitive performance at ages 70 to 79 in a population-based sample. Further, we found reliable evidence for birth cohort differences in trajectories of change for three out of five cognitive measures (i.e., reasoning, perceptual-motor-speed, and spatial ability) but not regarding verbal ability or long-term picture recognition memory. We also found indications of moderating effects of birth cohort on the association between cardiovascular risk and cognitive functioning and decline.

In light of the worldwide phenomenon of population aging, and the fact that aging unfortunately is accompanied by cognitive decline and an increased risk of dementia, it is of great importance to identify modifiable risk factors. As cardiovascular risk factors are modifiable, through medical treatments, specific preventions, and overall lifestyle changes (such as diet, exercise, smoking cessation), these factors are increasingly recognized as important targets in this respect (Arntzen et al., 2011; Gunstad et al., 2006; Stephan & Brayne, 2008). Our findings, however, indicate that the relative importance of cardiovascular risk factors has decreased in later born cohorts. Improved health awareness in the general population and directed public health efforts to prevent compromised health have paved the way for more healthy aging in this respect.

Findings indicative of secular trends in cognitive functioning and modifiable rates of decline in the general aging population are also important from a life-span perspective, as developmental psychology must be able to account for these significant cohort differences.

The co-constructive model of adult development proposed by Schaie (2008) and Willis and Schaie (2006) is capable of accounting for the observed cohort differences in levels of functioning. It is less obvious how, and to what extent, the model can account for the observed cohort differences in rates of change reported in this thesis as the co-constructive model proposes that later born cohorts should decline less steeply which is in direct opposition to our results.

According to Baltes and colleagues (e.g. Baltes, 1997; Li, 2003) improvements in human cognitive functioning are dependent on further advancements regarding cultural resources (in line with the second principle of the model). Further, the effectiveness of these cultural resources, in terms of enhancing development and staving off decline, diminishes with advancing age (in line with the third principle). The observed cohort differences in level of performance are in line with the second principle; as cultural resources such as education, knowledge, technology, health care, etc. improve, average cognitive functioning can be expected to increase. But why, then, should later born cohorts decline at a faster rate? That enhanced cultural resources cannot stave off decline indefinitely is in line with the third principle postulated by Baltes and colleagues, but why later born cohorts, who have enjoyed more evolved cultural resources compared to earlier born cohorts, should decline at a faster rate is seemingly left unanswered by the co-constructionist model.

The cognitive reserve hypothesis seems more capable of explaining the observed cohort differences in both levels of performance and rates of change. An individual's level of cognitive reserve is influenced by interactions among genetic factors and environmental

influences, like experiences and life-style factors such as education, social and material environment, work complexity, engagement in cognitively stimulating activities, dietary habits, and health and health-related behaviors (e.g., Foubert-Samier et al., 2012; Le Carret et al., 2003; Richards & Deary, 2005; Scarmeas & Stern, 2010; Stern, 2002; Tucker & Stern, 2011; Whalley et al., 2004). To a large extent these are the same factors that have been suggested as driving the Flynn effect. Therefore, because these factors evolve over time, there will be birth cohort differences in cognitive functioning as well as cognitive reserve. Further, as described above, we can expect that individuals with higher cognitive reserve will demonstrate decline later in life compared to those lower in cognitive reserve. Unfortunately, when they start decline they will experience a faster decline.

The reported findings of substantial cohort differences in cognitive functioning are also very important to practitioners and researchers using cognitive testing to assist in evaluations concerning for instance work capability, dementia status, and disability. According to Trahan et al. (2014) the Flynn effect is not well-known and rarely addressed in many behavioral sciences, but because of the prevalent use of IQ- and cognitive tests in research and clinical practice, it ought to be acknowledged. Practices such as standardization of cognitive tests, interpretation of test scores, establishment of cut-off values, and decision-making based on cognitive evaluations need to account for these secular trends (Hiscock, 2007; Trahan et al., 2014).

Skirbekk et al. (2013) projected that if Flynn effects continue increases in cognitive functioning will counterbalance the increase in population age. That is, even though the proportion of older people in the population increases, the observed Flynn effects are projected to lead to an improvement in cognitive functioning at the population level. This may very well be the case, but to the extent that the results from the studies in this thesis,

indicating that later born cohorts show steeper cognitive decline than earlier born, generalize to the entire population and are replicated in other studies, the projected improvement in cognitive functioning at the population level will most likely be attenuated in older ages.

Worldwide populations are aging (Alwin & Hofer, 2008; Christensen et al., 2009). One strategy to deal with the possible economic strain posed by this population aging is to raise the age of retirement. Many governments are considering implementing, or have already implemented, this strategy (Christensen et al., 2009). In light of the fact that several studies, including the studies presented in this thesis, have found that later born cohorts tend to outperform earlier born regarding level of cognitive functioning this seems reasonable. However, it is also important to recognize that the presented evidence of steeper cognitive decline suggests that we cannot expect that later born cohorts are protected from subsequent cognitive decline. In this respect our results are important in the debate regarding postponing retirement and for future definitions of old age, now often associated with age of retirement.

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