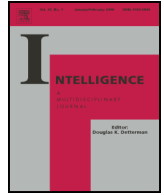




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Intelligence



Intelligence in young adulthood and cause-specific mortality in the Danish Conscription Database – A cohort study of 728,160 men

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ABSTRACT

An inverse association has been reported between early life intelligence and all-cause mortality. The aim of this study was to investigate whether this well-established association differed according to the underlying cause of death and across different birth cohorts. The associations between young adult intelligence and mortality from natural and external causes were investigated in the Danish Conscription Database (DCD), which is a cohort of more than 700,000 men born 1939–1959 and followed in Danish registers from young adulthood until late mid-life. Young adult intelligence was inversely related to all-cause mortality with a 28% higher risk of dying during the study period per 1 standard deviation (SD) decrease in intelligence test score (HR = 1.28 95% CI = 1.27–1.29). The strength of the observed inverse associations did not vary much across main groups of natural and external causes with the exception of the associations for mortality from respiratory diseases (HR = 1.61 95% CI = 1.55–1.67) and homicide (HR = 1.65 95% CI = 1.46–1.87) which were more pronounced compared to the rest. Moreover, for skin cancer mortality, each SD increase in intelligence test score was associated with a small increase in mortality risk (HR = 1.03 95% CI = 1.01–1.15). Furthermore, the association between intelligence and mortality was stronger for those born 1950–1959 compared to those born 1939–1949 for almost all natural and external causes of death.

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1. Introduction

Several studies have reported inverse associations between early life intelligence and all-cause mortality with age at end of follow-up ranging from 35 to as much as 85 years (Batty, Deary, & Gottfredson, 2007; Calvin et al., 2011; Whalley & Deary, 2001). Additionally, a number of studies have reported inverse associations between early life intelligence and mortality due to cardiovascular diseases (Batty, Shipley, Mortensen, Gale, & Deary, 2008; Batty, Wennerstad, et al., 2009; Hemmingsson, Melin, Allebeck, & Lundberg, 2006) and external causes (accidents (Batty, Gale, Tynelius, Deary, & Rasmussen, 2009; O'Toole,

1990), homicide (Batty, Mortensen, Gale, & Deary, 2008; Batty, Deary, Tengstrom, & Rasmussen, 2008), suicide (Batty, Wennerstad, et al., 2009; Sorberg, Allebeck, Melin, Gunnell, & Hemmingsson, 2013)), whereas the results on cancer mortality have been inconsistent (Batty, Wennerstad, et al., 2009; Batty, Mortensen, et al., 2009; Hemmingsson et al., 2006). However, these studies have generally been based on either small or relatively young study populations and the study populations were most often only followed until midlife resulting in a limited number of cases. Proposed mechanisms explaining the observed intelligence-mortality association include mediation by adult socioeconomic position and health-related behavior (Batty, Deary, & Gottfredson, 2007). In support of these mechanisms it is well established that early life intelligence is a valid predictor of later educational and occupational success (Neisser et al., 1996), and low intelligence test scores have been associated with smoking (Batty, Deary, & Macintyre, 2007; Batty, Deary, Schoon, & Gale, 2007b; Batty, Shipley, Mortensen, Boyle, et al., 2008), heavy alcohol consumption (Batty, Deary, & Macintyre, 2006, 2007; Batty, Shipley, Mortensen, Boyle, et al., 2008), physical inactivity (Batty, Deary, Schoon, & Gale, 2007a), and an unhealthy diet (Batty, Deary, Schoon, & Gale, 2007a). Furthermore, it has been proposed that people with high intelligence test scores are better at managing existing disease or injury (Gottfredson, 2004). Alternatively, the observed

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intelligence-mortality association could be a result of confounding by genetic factors and early life environmental factors. The influence of both genetic and environmental factors in explaining individual differences in young adult intelligence has been established in a number of twin and adoption studies (Deary, Johnson, & Houlihan, 2009; Nisbett et al., 2012). Additionally, lifespan has been shown to be modestly heritable (Hjelmborg et al., 2006) and the association between early life environment and risk of mid- and late-life mortality has been widely demonstrated (Galobardes, Lynch, & Davey Smith, 2004).

We consider the intelligence-mortality association to be the result of a complex interplay between the proposed mechanisms and not just a result of confounding by genetics and early life environment. Thus, we hypothesize that the association between intelligence and mortality will be stronger for deaths with a clear relation to health-related behavior (cardiovascular diseases, respiratory diseases, and lung cancer), compared to deaths with no such association (hormone-related cancer). Further, we hypothesize that the association between young adult intelligence and mortality could change over time as a consequence of changes in the social gradient in health-related behaviors. As an example, smoking used to be very common across all educational groups in Denmark, but since the 1950s a clear social gradient in smoking has appeared with a diminishing prevalence of smokers in the highly educated groups across time (Clemmensen, Lyng, & Clemmensen, 2012; Osler, 1992). We thus hypothesize that the associations between intelligence and smoking related deaths (respiratory disease and lung cancer) will be weaker for early birth cohorts compared to later birth cohorts.

The aim of this large cohort study was to examine the hypothesis that the strength of the association between young adult intelligence and later mortality differed according to the underlying cause of death. Further, we aimed to explore the hypothesis that the strength of the intelligence-mortality association differed across time by examining the association between intelligence and cause-specific mortality in different birth cohorts.

2. Methods

2.1. Study population

The study was based on data from the Danish Conscript Database (DCD). The DCD is a database of 728,160 men born predominantly from 1939 through 1959 and examined at the Danish conscript board between 1957 and 1984. Examination details were digitized from conscript board register cards and the unique personal identification numbers were traced when necessary. A more detailed description of the DCD has been given in Christensen et al. (2015). A small proportion (0.2%) of cohort members was excluded from further analyses because of insufficient information on mortality status. Fig. 1 presents the number of cohort members who were excluded due to different types of missing information.

2.2. Measure of intelligence

Intelligence was assessed at the conscript board examination by an intelligence test called the Børge Prien Prøve (BPP) (Teasdale, 2009). This intelligence test comprises four subtests assessing logical, verbal, numerical and spatial abilities. The number of correct answers has been summed into a total score with a range of 0–78 and this total BPP-score has been shown to correlate substantially ($r = 0.82$) with the full-scale Wechsler Adult Intelligence Scale IQ-score (Mortensen, Reinisch, & Teasdale, 1989). Information on the BPP-score was missing for 57,828 (8.0%) cohort members. The missing observations were a result of missing registry information on 1) young men who volunteered for military service before appearing before the conscript board and 2) men who were exempted from appearing before the conscript board due to medical conditions rendering them unfit for military service.

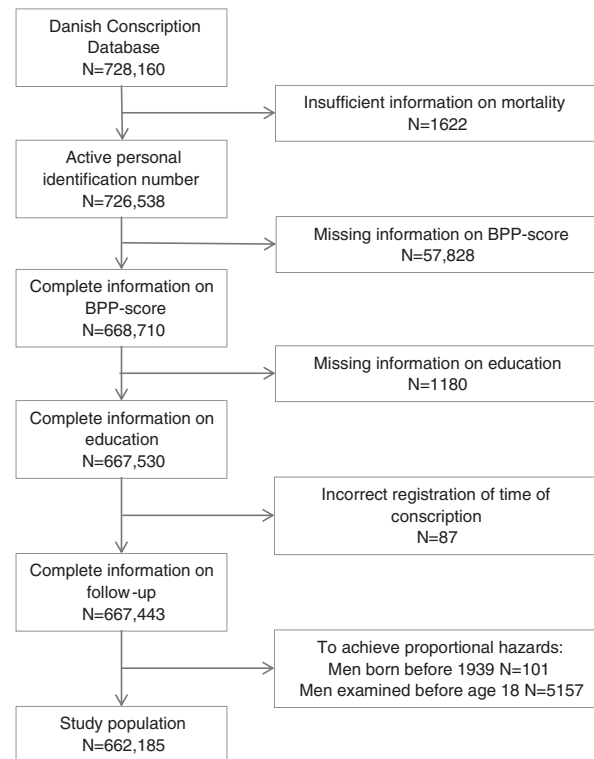


Fig. 1. Flow-chart presenting information on the number of cohort members excluded due to missing information and to achieve proportional hazards. Abbreviations: BPP-score: Børge Prien Prøve score (intelligence test score).

2.3. Ascertainment of all-cause and cause-specific mortality

The DCD was linked to the Danish Civil Registration System (Pedersen, 2011) for information on time of death or emigration for the period from April 2nd, 1968 until October 31st, 2013 and 117,868 deaths were identified. For information on the primary cause of death the DCD has been linked to the Danish Register of Cause of Death (DRCD) (Helweg-Larsen, 2011). In this study the main category (natural cause, accident, suicide, homicide) and primary cause of death were identified for 96,915 deaths occurring from January 1st, 1970 through October 31st, 2010. The identified deaths were categorized in natural and external causes according to the code for the main category of death and ICD-8 codes for the period from 1970 through 1993 and ICD-10 codes from 1994 through 2010. Deaths occurring in the period from April 2nd, 1968 until January 1st, 1970 were classified as unspecified. The categories and the corresponding ICD-8 and ICD-10 codes are presented in Table 1.

2.4. Measure of education

The young men reported their current educational level at the time of the conscript board examination. The educational level has been coded into three categories comprising low education (7–9th grade), a medium level of education (vocational training or 10–11th grade), and a high educational level (12th grade or more). In addition to the observations with missing information on the BPP-score, information on educational level was missing for 1180 (0.2%) cohort members.

2.5. Statistical analysis

Associations between intelligence test scores and all-cause and cause-specific mortality were analyzed using Cox's proportional hazards models with age as the underlying time scale. Age at conscript

Table 1

Categories of specific causes of death, corresponding International Classification of Diseases (ICD) codes, and the number of deaths in each group in the period from April 2nd, 1968 to October 31st, 2013.

Cause of death	ICD-8 classification	ICD-10 classification	Number of deaths
Natural causes			74,850
All cancers	140–239	C00–C97, D00–D48	28,678
Lung cancer (lung and bronchi)	162 (excl. 162.09)	C34	6959
Gastro-intestinal cancers	150–159	C15–C26	8256
Hormone-related cancers	185–187	C60–C63	1664
Skin cancers	172–173	C43–C44	963
Cancer in other sites	Remaining cancer codes	Remaining cancer codes	8664
All cardiovascular diseases	390–458	I00–I52, I60–I99	18,505
Coronary heart disease	410–414	I20–I25	9311
Stroke	430–438	I60–I69	3685
Ischemic stroke	432–435	I63–I65, I66, I69.3	615
Hemorrhagic stroke	430–431	I60–I62, I69.0, I69.1, I69.2	2141
Respiratory diseases	460–519	J00–J99	3094
Infectious diseases, including tuberculosis	000–136	A00–A99, B00–B99	1584
Other natural causes of death	Remaining codes of natural causes	Remaining codes of natural causes	22,989
External causes			15,267
Accident	800–899, 900–949	V00–V99, W00–W99, X00–X58	7608
Suicide	950–959	X71–X83	7392
Homicide	960–970	X92–X99, Y00–Y09	267
Unspecified cause of death ^a			6798
Deaths occurring after 10.31.2010 ^b			20,953
Total number of deaths ^c			117,868

^a Deaths occurring from April 2nd, 1968 until January 1st, 1970 for which no cause of death is registered.

^b In this study information on cause of death was only available from January 1st, 1970 until October 31st, 2010.

^c Total number of deaths includes all deaths of DCD cohort members registered in the Danish Civil Registration System from April 2nd, 1968 and until October 31st, 2013.

board examination was used as entry time for all cohort members except for those examined before 1968, for which age at April 2nd, 1968, the date for the introduction of personal identification numbers, was used. Follow-up ended at age of death, emigration, or the 31st of October 2013 for all-cause mortality and 31st of October 2010 for cause-specific mortality. A small proportion of men (0.01%) were excluded because the time of conscription (registered as year and half-year of the examination) was incorrectly registered as happening after the cohort member died or emigrated. The mean BPP-score of the DCD-population has been shown to increase with increasing birth year (Christensen et al., 2015). Consequently, the models were stratified by birth year in order to control for the effect of calendar time. The proportional hazards assumption was tested graphically by plotting $\log(-\log)$ survival curves and the Schoenfeld residuals for the association between all-cause mortality and intelligence (nine groups), and education (three groups). To achieve proportional hazards cohort members born before 1939 ($n = 101$) or examined before they turned 18 ($n = 5157$) were excluded. When analyzing the association between intelligence and cause-specific mortality it is important to take into account the effect of subjects dying from other causes (competing risks). Competing risks was accounted for by using the Fine-Gray competing risks regression model as it is implemented in the `stcrreg` command in Stata. It specifies a model for the cumulative mortality and generates subdistribution hazard ratios (SHRs). In the present study, the SHRs were practically identical to the event specific hazard ratios (EHRs) for all outcomes except for homicide, for which the estimated SHR was only slightly lower than the EHR. This suggested that the observed EHRs were not affected to a high degree by the presence of competing risks. Consequently, we report the EHRs, which are easier to interpret and SHRs are only reported in the appendix (see Appendix A). All statistical analyses were conducted using STATA version 13.

Several analyses were performed. First, to examine the shape of the intelligence-mortality association we divided the BPP-score into nine groups of equal size, calculated the hazard ratios for mortality of each group compared to the group with the highest scores and performed a test for trend. Due to the limited number of cases of homicides, hemorrhagic and ischemic stroke in each BPP-score group these causes were omitted from these analyses. Second, we analyzed whether the intelligence-mortality association differed according to the underlying cause

of death by including the intelligence test score (the BPP-score) as a continuous variable in separate Cox's proportional hazard models for each cause of death. To express the hazard ratio per 1 standard deviation decrease in BPP-score, the BPP-score was divided by the standard deviation of the full population and the reciprocal value was taken. Finally, to investigate whether the association between intelligence and cause-specific mortality differed across time we did separate analyses for men born before 1950 and from 1950 and onwards. In these analyses cohort members were followed from age 29 (the age of the oldest members at April 2nd, 1968) until age 50 (the age of the youngest members in 2010) to distinguish a potential cohort effect from a potential difference in the intelligence-mortality association in different age groups. When applicable a Wald test was used to compare point estimates and the difference in the estimated associations for those born before and from 1950 was tested by including an interaction term between intelligence and a variable defining the two cohorts.

3. Results

The study population consisted of 662,185 cohort members of which 117,868 died during follow-up (mean follow-up = 37.4 years (range = 0.01–42.8 years)). Table 2 presents the association between intelligence test scores (BPP-scores), mortality, and the included covariates. Cohort members in the highest scoring tertile of BPP-scores were generally older, had a higher educational level at conscription, and they were more often born in more recent birth years than those in the lowest scoring tertile. The mean BPP-score increased with increasing birth year and it was almost two standard deviations (23.2 points) lower in cohort members with low education compared to those with high education. The proportion of deaths was twice as high in the lowest scoring tertile of BPP-scores compared to the highest scoring tertile.

Fig. 2 presents the association between young adult intelligence, expressed as the BPP-score in nine groups of equal size, and cause-specific mortality in the period from conscription until late mid-life. We found a significant linear trend with decreasing risk of mortality the higher the intelligence test-score for all causes of death except for hormone-related cancer and skin cancer.

Table 3 presents the associations between young adult intelligence and all-cause and cause-specific mortality in the period from conscript

Table 2
Number of men, deaths of all causes, and distribution of covariates in relation to intelligence test scores (Børge Prien Prøve (BPP)-score) in tertiles for the 662,185 men.

	No., N	No. of deaths, N(%)	Intelligence test score (BPP-score)			Mean (SD)
			Low N(%)	Medium N(%)	High N(%)	
Study population	662,185	117,868 (17.8)	236,223 (35.7)	217,737 (32.9)	208,225 (31.4)	37.8 (12.0)
Age ^a , mean (SD)			19.1 (0.9)	19.5 (1.3)	20.6 (2.2)	
Birth year, N(%)						
1939–44	174,928	48,864 (41.5)	43.8%	30.1%	26.1%	35.6 (12.7)
1945–49	184,631	34,459 (29.2)	36.7%	32.1%	31.1%	37.7 (12.0)
1950–54	161,841	21,940 (18.6)	32.7%	34.2%	33.1%	38.6 (11.6)
1955–59	140,785	12,605 (10.7)	27.6%	35.8%	36.6%	37.4 (11.1)
Education, N(%)						
Low	169,761	40,881 (34.7)	70.1%	25.4%	4.5%	27.9 (9.9)
Medium	379,217	64,963 (55.1)	30.5%	41.5%	28.0%	38.3 (9.7)
High	113,207	12,024 (10.2)	1.5%	15.1%	83.4%	51.1 (7.4)
No of deaths, N(%)			55,778 (47.3)	36,004 (30.5)	26,086 (22.1)	

^a Age at conscript board examination.

board examination and until late mid-life (mean age at end of follow-up: 61.6 years). For all-cause mortality we found a 28% higher risk of dying during the study period for each standard deviation (SD) decrease in BPP-score (HR = 1.28 95% CI = 1.27–1.29). The association was somewhat attenuated when adjusting for educational level at time of conscription (HR = 1.21 95% CI = 1.20–1.21) but remained statistically significant. The association between intelligence and death due to natural causes was of a similar size (HR = 1.30 95% CI = 1.29–1.31) and was likewise somewhat attenuated when adjusting for education. The inverse association between intelligence and overall cancer mortality was relatively weak (HR = 1.18 95% CI = 1.17–1.20). Comparatively, the association between intelligence and lung cancer was stronger (HR = 1.37 95% CI = 1.34–1.40), but it was considerably attenuated after adjustment for education (HR = 1.22 95% CI = 1.19–1.25). We found relatively weak associations between intelligence and mortality due to gastro-intestinal (HR = 1.13 95% CI = 1.11–1.15) and

hormone-related cancers (HR = 1.04 95% CI = 1.04–1.14), respectively. For skin cancer we found a 7% lower risk of dying per 1 SD decrease in BPP-score (HR = 0.93 95% CI = 0.87–0.99). The association was only borderline significant and even though the estimate remained unchanged it was no longer statistically significant after adjustment for education. A relatively strong inverse association was found between intelligence and mortality due to all cardiovascular diseases (HR = 1.41 95% CI = 1.36–1.48). Furthermore, the association between intelligence and mortality due to coronary heart disease was more pronounced (HR = 1.47 95% CI = 1.41–1.54) compared to the association found for stroke (HR = 1.22 95% CI = 1.13–1.32). The association between intelligence and mortality due to respiratory diseases was particularly strong (HR = 1.61 95% CI = 1.55–1.67) compared to the other main categories of natural causes. However, as was the case for lung cancer, the association was considerably attenuated after adjustment for education (HR = 1.45 95% CI = 1.38–1.51). The association

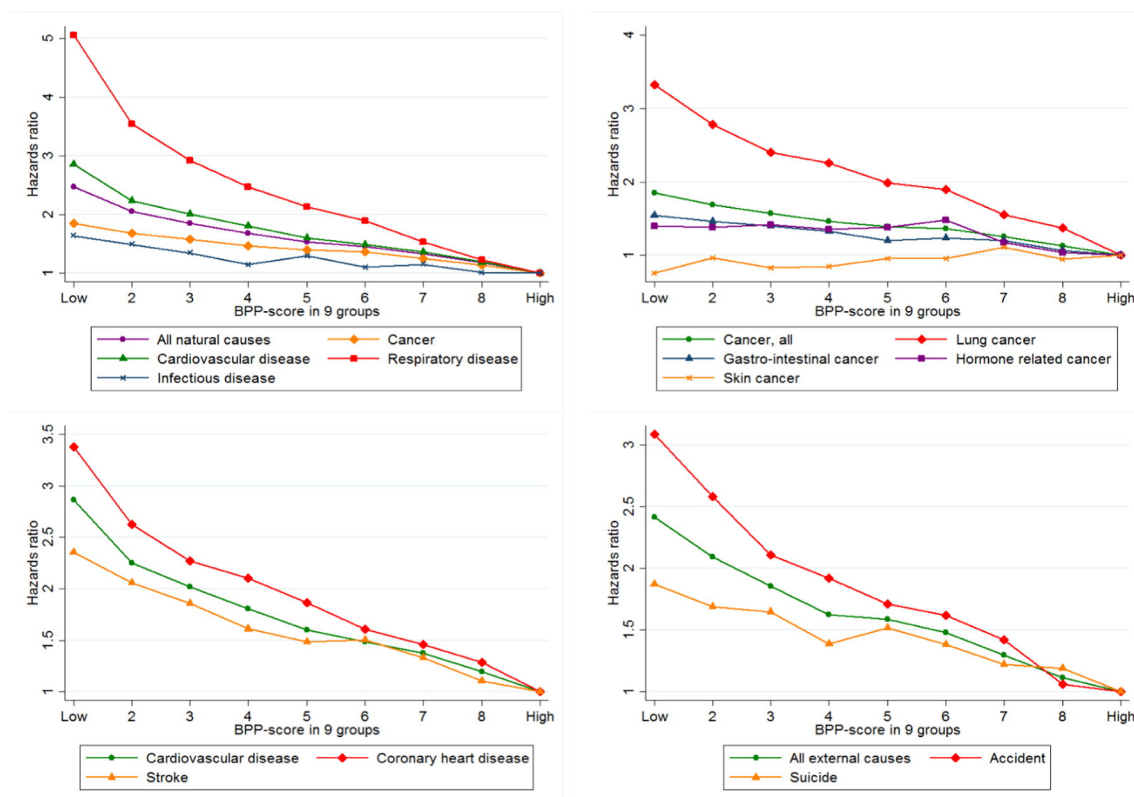


Fig. 2. Age-adjusted hazard ratios for the associations between intelligence test score (Børge Prien Prøve (BPP)-score) in nine equal sized groups and cause-specific mortality in 662,185 men.

Table 3

Age-adjusted hazard ratios (HR) per 1 standard deviation decrease in intelligence test score (Børge Prien Prøve (BPP)-score) for all-cause and cause-specific mortality in 662,185 men.

	Number of deaths	Model 1 ^c		Model 2 ^d	
		HR	CI ^e	HR	CI ^e
All-cause mortality ^a	117,868	1.28	1.27,1.29	1.21	1.20,1.21
Cause-specific mortality ^b					
All natural causes	74,850	1.30	1.29,1.31	1.22	1.21,1.24
Cancer, all	28,678	1.18	1.17,1.20	1.13	1.11,1.15
Lung cancer (lung and bronchi)	6959	1.37	1.34,1.40	1.22	1.19,1.25
Gastro-intestinal cancer	8256	1.13	1.11,1.15	1.10	1.07,1.12
Hormone-related cancer	1664	1.09	1.04,1.14	1.09	1.03,1.16
Skin cancer	963	0.93	0.87,0.99	0.93	0.86,1.01
Cancer in other sites	8664	1.16	1.14,1.18	1.12	1.10,1.15
Cardiovascular disease, all	18,505	1.36	1.34,1.38	1.28	1.26,1.30
Coronary heart disease	9311	1.41	1.38,1.44	1.31	1.28,1.34
Stroke, all	3685	1.29	1.25,1.33	1.22	1.17,1.27
Ischemic stroke	615	1.33	1.23,1.44	1.30	1.18,1.43
Hemorrhagic stroke	2141	1.20	1.15,1.25	1.16	1.10,1.22
Respiratory disease	3094	1.61	1.55,1.67	1.45	1.38,1.51
Infectious diseases, including tuberculosis	1584	1.18	1.13,1.24	1.19	1.12,1.27
Other natural causes of death	23,185	1.37	1.35,1.39	1.28	1.26,1.30
All external causes	15,267	1.29	1.27,1.31	1.16	1.14,1.19
Accident	7608	1.40	1.37,1.43	1.19	1.16,1.22
Suicide	7392	1.18	1.16,1.21	1.13	1.10,1.16
Homicide	267	1.65	1.46,1.87	1.31	1.13,1.53

^a All-cause mortality for the period from 2nd of April 1968 through 31st of October 2013.

^b Cause-specific mortality for the period from 2nd of April 1968 through 31st of October 2010.

^c Stratified by birth year.

^d Stratified by birth year and adjusted for educational level at time of conscript board examination.

^e CI: 95% confidence intervals presented in brackets.

between intelligence and mortality due to infectious diseases was relatively weak (HR = 1.18 95% CI = 1.13–1.24), and adjusting for education did not change the estimate. A clear inverse association was found for mortality due to external causes (HR = 1.29 95% CI = 1.27–1.31), with the strongest associations observed for accidents and homicide (HR = 1.40 95% CI = 1.37–1.43; HR = 1.65 95% CI = 1.46–1.87).

Table 4

Age-adjusted hazard ratios (HR) per 1 standard deviation decrease in intelligence test score (Børge Prien Prøve (BPP)-score) for all-cause and cause-specific mortality from age 29 to age 50 presented separately for cohort members born before 1950 and from 1950 and onwards.

	Number of deaths	Born before 1950		Number of deaths	Born from 1950		P value ^b
		HR	CI ^a		HR	CI ^a	
All-cause mortality	16,960	1.25	1.23,1.27	14,170	1.43	1.41,1.45	<0.001
Cause-specific mortality							
All natural causes	10,579	1.25	1.24,1.26	9084	1.41	1.38,1.43	<0.001
Cancer, all	3519	1.14	1.11,1.18	2593	1.26	1.21,1.31	<0.001
Lung cancer (lung and bronchi)	622	1.38	1.28,1.49	460	1.47	1.34,1.62	0.27
Gastro-intestinal cancer	890	1.14	1.07,1.21	688	1.30	1.20,1.40	<0.05
Hormone-related cancer	125	1.13	0.96,1.34	103	1.24	1.01,1.51	0.51
Skin cancer	221	0.87	0.77,0.99	148	0.87	0.73,1.04	0.97
Cancer in other sites	1661	1.11	1.06,1.16	1194	1.22	1.15,1.30	<0.05
Cardiovascular disease, all	3075	1.41	1.36,1.46	1954	1.51	1.44,1.58	<0.05
Coronary heart disease	1930	1.47	1.41,1.54	924	1.58	1.48,1.69	0.07
Stroke, all	552	1.22	1.13,1.32	437	1.39	1.26,1.53	<0.05
Ischemic stroke	82	1.52	1.23,1.88	54	1.34	1.02,1.77	0.48
Hemorrhagic stroke	441	1.18	1.08,1.30	344	1.37	1.23,1.53	<0.05
Respiratory disease	260	1.43	1.27,1.61	266	1.97	1.74,2.23	<0.001
Infectious diseases, including tuberculosis	350	0.93	0.84,1.04	539	1.22	1.12,1.33	<0.001
Other natural causes of death	3375	1.38	1.33,1.43	3732	1.56	1.51,1.61	<0.001
All external causes	4868	1.22	1.19,1.26	3729	1.41	1.37,1.46	<0.001
Accident	2015	1.31	1.26,1.35	1821	1.53	1.47,1.60	<0.001
Suicide	2788	1.12	1.09,1.16	1817	1.24	1.18,1.29	<0.001
Homicide	65	1.70	1.41,2.05	91	1.68	1.39,2.03	0.48

^a CI: 95% confidence intervals presented in brackets.

^b P for interaction between intelligence and cohort (born before and from 1950 and onwards).

After adjustment for education both estimates were considerably attenuated (HR = 1.19 95% CI = 1.16–1.22; HR = 1.31 95% CI = 1.13–1.53).

The associations between young adult intelligence and all-cause and cause-specific mortality from age 29 to age 50 are presented separately for cohort members born before 1950 (1939–1949) and from 1950 and onwards (1950–1959) in Table 4. When excluding cohort members who died before they turned 29 years old, the cohort included 354,681 men born from 1939 through 1949 and 296,647 men born from 1950 through 1959. The observed associations were inverse for all causes of death except for skin cancer and they were generally stronger for cohort members born from 1950 and onwards compared to those observed for the cohort members born before 1950. In contrast to these general findings the associations between intelligence and mortality from skin cancer and homicide did not differ according to birth cohort. For ischemic stroke the intelligence-mortality association was stronger, though not significantly, for cohort members born before 1950 compared to those born from 1950 and onwards. For the associations for which a stronger association was found for the more recent born birth cohort, the estimates were significantly stronger for those born from 1950 and onwards compared to those born in the preceding decade for all causes except for lung and hormone-related cancer, and coronary heart disease. The largest difference was seen for mortality due to respiratory diseases, where an almost two-fold increase in mortality risk (HR = 1.97 95% CI = 1.74–2.23) was observed per 1 SD decrease in intelligence test score among the cohort members born from 1950 and onwards compared to an around 40% higher risk for cohort members born before 1950 (HR = 1.43 95% CI = 1.27–1.61).

4. Discussion

4.1. Main findings

In the present study of 662,185 men followed for a mean of 37.4 years from young adulthood until late mid-life we found an inverse association between young adult intelligence and all-cause mortality, and all groups of natural and external causes of death except for skin cancer. Further, a clear gradient with a lower risk of mortality the higher the intelligence test score was found for all causes of death except for hormone-related cancer and skin cancer. Generally, the strength of the

associations was relatively similar across many causes of death. However, the associations between intelligence and mortality due to respiratory diseases and homicide were particularly strong compared to the rest of the natural and external causes, and comparing specific types of cancer, revealed a strong association between intelligence and lung cancer relative to the rest of the cancer types. Comparing the strength of the observed intelligence–mortality associations of cohort members born before 1950 and from 1950 onwards, we generally found stronger intelligence–mortality associations for the more recently born cohort members compared to those born before 1950 for all causes except for skin cancer and homicide for which no cohort differences were identified.

4.2. Comparison with previous findings

4.2.1. All-cause mortality

The hazard ratio of 1.28 per 1 SD decrease in intelligence test score found in this study converts to a hazard ratio of 0.78 per 1 SD increase in intelligence test score. This result corresponds to the hazard ratio of 0.76 per 1 SD increase in intelligence test score obtained in a recent meta-analysis of 16 prospective cohort studies with more than 1 million participants and 22,000 deaths (Calvin et al., 2011).

4.2.2. Cancer

The findings from previous studies on the association between early life intelligence and cancer mortality have been inconsistent (Batty, Wennerstad, et al., 2009; Batty, Mortensen, et al., 2009; Hemmingsson et al., 2006). Two of the previous studies found no association between young adult intelligence and cancer mortality (Batty, Wennerstad, et al., 2009; Hemmingsson et al., 2006), whereas the third study, a study of 14,491 Vietnam Veterans followed until a mean age of 53 years, revealed a strong association between young adult intelligence and mortality due to smoking related cancers and no association with other cancers (Batty, Mortensen, et al., 2009). Our results contribute to this limited number of studies and suggest that the somewhat weak association between intelligence and overall cancer-mortality could reflect differences in the strength of the associations between intelligence and specific cancer types with smoking related cancers having the strongest association. For skin cancer we found a slightly lower risk of mortality the lower the intelligence test score, which can be converted to a hazard ratio of 1.03 (95% CI: 1.01–1.15) per 1 SD increase in intelligence test score. This finding is in accordance with previous findings of a higher incidence of malignant melanomas in individuals with a high socioeconomic status (SES). In a recent review of the relation between SES and malignant melanoma in Northern Europe the authors found that a high socioeconomic status (SES) was associated with taking sun holidays, and with a higher incidence and mortality of malignant melanomas in the period from the 1950s through the 1980s. From the 1990s the incidence of malignant melanomas remained high in high SES individuals, but the mortality risk was now lower in high compared to low SES individuals (Idorn & Wulf, 2014). The very weak association found between intelligence and skin cancer mortality in the present study might reflect a transition in the association between intelligence and skin cancer mortality going from a higher risk among those with high intelligence test scores in previous years to a higher risk among those with low scores in more recent years.

4.2.3. Cardiovascular disease (CVD)

A few studies have reported inverse associations between early life intelligence and mortality from CVD and coronary heart disease (CHD) (Batty, Deary, Benzeval, & Der, 2010; Batty, Shipley, Mortensen, et al., 2008; Batty, Wennerstad, et al., 2009; Hemmingsson et al., 2006). In a study of young Swedish men (Hemmingsson, Essen, Melin, Allebeck, & Lundberg, 2007) the authors found a stronger association between intelligence and the risk of developing CHD than CVD between the age of 40 and 54 years. This corresponds to the pattern observed in the

present study of a stronger association between intelligence and CHD mortality compared to CVD mortality and between intelligence and ischemic stroke compared to hemorrhagic stroke.

4.2.4. Respiratory diseases

We found a strong association between intelligence and mortality due to respiratory diseases, for which there are no previous studies. However, chronic obstructive pulmonary disease (COPD) has been shown to be underreported as cause of death (Jensen, Godtfredsen, Lange, & Vestbo, 2006). If COPD is only reported as the primary cause of death for people with very severe COPD, a group which is characterized by a high proportion of people with low education (Gershon, Dolmage, Stephenson, & Jackson, 2012; Lange, Marott, Vestbo, Ingebrigtsen, & Nordestgaard, 2014), then the association between intelligence and mortality from respiratory diseases could be overestimated.

All together, the findings for natural causes of the present and previous studies reveal a pattern, which suggests that smoking could be an important mediating factor in the observed intelligence–mortality association.

4.2.5. External causes

The inverse associations between intelligence and external causes of death are in accordance with findings from previous studies (Allebeck, Allgulander, & Fisher, 1988; Batty, Mortensen, et al., 2008; Batty, Wennerstad, et al., 2009; Batty, Gale, et al., 2009; Gunnell, Magnusson, & Rasmussen, 2005).

4.3. Adjustment for educational level at conscription

It has been hypothesized that the intelligence–mortality association could be explained by mediation through SEP in adulthood. However, findings from previous studies investigating mediation by adult education or other SEP measures have been inconsistent in studies of the association between young adult intelligence and mortality from different types of CVD (Batty, Wennerstad, et al., 2009; Hemmingsson et al., 2006; Modig Wennerstad, Silventoinen, Tynelius, Bergman, & Rasmussen, 2010) and of external causes (accidents and suicide (Batty, Wennerstad, et al., 2009; Hemmingsson et al., 2006)). In the present study adjusting for young adult education significantly attenuated the association between intelligence and mortality from CHD, accidents, and homicide. For cancer mortality previous studies have reported either no or a very limited effect of adjusting for adult education or other measures of adult SEP (Batty, Wennerstad, et al., 2007; Batty, Mortensen, et al., 2009; Hemmingsson et al., 2006). In our study adjusting for young adult education significantly attenuated the association between intelligence and mortality from lung cancer, but not the other types of cancer. Furthermore, the association between intelligence and mortality from respiratory diseases was also significantly attenuated when adjusting for education in our study. Due to the rather late onset of life-style related diseases the limited effect of adjusting for education found in some studies could be related to the relatively young age at end of follow-up in the previous studies (mean age at end of follow-up: 40–53 years) (Batty, Wennerstad, et al., 2009; Batty, Mortensen, et al., 2009; Hemmingsson et al., 2006; Modig Wennerstad et al., 2010) compared to our study (mean age at end of follow-up: 62 years).

4.4. Difference in effect across birth cohorts

To our knowledge, no other study has explored the strength of the intelligence–mortality association across birth cohorts. We were surprised to find a consistent pattern of significantly stronger associations for cohort members born 1950 and onwards compared to those born before 1950 for almost all natural and external causes. This pattern was observed for all causes except for mortality from skin cancer and

homicide, for which there was no difference, and for mortality from ischemic stroke, for which a stronger association was found for those born before 1950, but the difference between the two cohorts was not significant. For the associations for which the pattern was observed, the estimates were significantly stronger for those born from 1950 and onwards for all causes except for lung and hormone-related cancer, and coronary heart disease. If health-related behaviors have become more socially patterned over the years, creating a greater divide between individuals with high and low intelligence test scores, this could be part of the explanation. However, we do not have data to support this hypothesis.

4.5. Strengths and limitations

The strengths of this study lie in the combination of the large study population and the long follow-up period ensuring a large number of cases, which has allowed detailed categorization of specific causes of death while maintaining sufficient statistical power. The risk of selection bias is limited given the population based nature of the cohort, stemming from the legal requirement of all young Danish men to appear before the conscript board. Finally, the lack of information on potential confounding or mediating factors, such as childhood socioeconomic position, disease or injury and adult health-related behaviors, is a limitation of the present study.

4.6. Conclusion

In conclusion, in this study of a large cohort of young men followed for a mean of 37.4 years we found inverse associations between young adult intelligence and all natural and external causes of death except for skin cancer. The strength of the intelligence-mortality association varied between specific types of cancer and particularly strong associations were found for mortality due to respiratory diseases and homicide. Comparing the strength of associations for cohort members born before 1950 and from 1950 and onwards a consistent pattern of stronger intelligence-mortality associations in the later born cohort was found across almost all natural and external causes.

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.intell.2016.08.001>.

Conflict of interest

The authors declare that they have no conflict of interest.

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