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Intelligence in youth and all-cause-mortality: systematic review with meta-analysis

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3 **Intelligence in youth and all-cause-mortality: systematic review with meta-**
4 **analysis**
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Abstract

Background. A number of prospective cohort studies have examined the association between intelligence in childhood or youth and life expectancy in adulthood; however, the effect size of this association have yet to be quantified and previous reviews require updating.

Methods. The systematic review included an electronic search of EMBASE, MEDLINE and PSYCHINFO databases. This yielded 16 unrelated studies that met inclusion criteria, comprising 22,453 deaths among 1,107,022 participants.

Heterogeneity was assessed, and fixed effects models were applied to the aggregate data. Publication bias was evaluated, and sensitivity analyses were conducted.

Results. A one SD advantage in cognitive test scores was associated with a 24% (95% CI 23-25%) lower risk of death, during a 17 to 69 year follow-up. There was little evidence of publication bias (Egger's intercept = 0.10, $p = 0.81$), and the intelligence-mortality association was similar for men and women. Adjustment for childhood socioeconomic status (SES) in the nine studies containing these data had almost no impact on this relationship, suggesting that this is not a confounder of the intelligence-mortality association. Controlling for adult SES in five studies and for education in six studies attenuated the intelligence-mortality hazard ratios by 34% and 54%, respectively.

Conclusions. Future investigations should address the extent to which attenuation of the intelligence-mortality link by adult SES indicators is due to mediation, over-adjustment, and/or confounding. The explanation(s) for association between higher early life intelligence and lower risk of adult mortality require further elucidation.

Key words: *Intelligence, Mortality, Meta-analysis, Socioeconomic Factors,*

Systematic review.

Introduction

Individual differences in intelligence (cognitive ability, mental ability) test scores, as measured by standardised IQ-type tests in childhood, show an inverse association with risk of death from all causes throughout adulthood. That is, higher intelligence appears to confer protection. This finding is replicated in prospective cohorts from several Westernized countries¹, across different ranges of intelligence², and in follow-up periods from early through to late adulthood.²⁻⁴

Intelligence and somatic health may be inextricably linked throughout the life course. However, longitudinal studies help to establish causal pathway models of the effects of one upon the other. For example, morbidities such as diabetes, cancer, stroke and peripheral atherosclerosis, and/or their treatments, are reported to cause a decline in cognitive function after longitudinal follow-up.⁵⁻¹⁰ This illness-to-cognitive ability direction of association is a commonplace finding. The reverse direction of association is studied less often, and has only recently come to be recognized under the term 'cognitive epidemiology'.^{11, 12} That is, mental ability scores from early life associated with later adulthood morbidities, and before any somatic symptoms or risk factors of disease are manifest, provide evidence that cognitive abilities may be predictive of later health outcomes.

The association between pre-morbid intelligence and adult all-cause mortality was the subject of a systematic review¹, in which all nine studies that met the inclusion criteria demonstrated an inverse relationship between intelligence and risk of dying by follow-up. The review did not quantify the association. Furthermore, there were insufficient studies to address comprehensively a number of pertinent questions from this research domain. One issue is whether or not the association between intelligence and mortality is the same in women as in men. For example, it is possible

1
2
3 that sex differences in the incidence, age at onset of health behaviours, and the extent
4
5 to which these act as risk factors for disease^{13, 14}, could produce sex-specific
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7 intelligence-mortality gradients. Data from many more men than women have been
8
9 included in intelligence-mortality cohort studies to date, mainly due to some studies
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11
12
13 80 using military conscript databases. Moreover, when mixed-sex cohorts report
14
15 mortality risk as predicted by intelligence for men and women separately, they rarely
16
17 test for statistical difference but, rather, report the observed trend. With more studies
18
19 now reporting hazard ratios (HRs) for mortality by sex, there is an opportunity to
20
21 quantify the predictive effects of intelligence on mortality separately for men and
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23
24
25 85 women.

26
27 A second issue yet to be evaluated systematically is the extent to which
28
29 intelligence as a predictor of mortality is confounded by early life environmental
30
31 influences including socioeconomic factors. Socioeconomic status (SES) is
32
33 established as an important determinant of public health inequalities,¹⁵⁻¹⁸ including
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35
36 90 risk of mortality, and it can carry influence in childhood, via factors such as family
37
38 income and parental education, to predict individual differences in childhood
39
40 intelligence.^{19, 20} In this context, therefore, intelligence may be considered a mediating
41
42 variable on the pathway between early life influences and adult health outcomes. If
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44 early social factors substantially confound the link between intelligence and longevity,
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48 95 then adjusting for childhood SES would sizeably attenuate the effect size of the
49
50 association between intelligence and mortality. In their systematic review¹ Batty *et al*
51
52 identified three out of nine studies that adjusted for childhood SES: one of these
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54 showed no change from an unadjusted model, and two had modest attenuating effects,
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56
57 suggesting that intelligence has independent effects on risk of mortality from those of
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1
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3 100 early socioeconomic influences. Due to this small number of studies, the role of
4
5
6 childhood SES in the intelligence-mortality link requires further investigation.
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9
10 One explanation why intelligence may exert an influence on life expectancy is
11 its ability to predict educational outcomes²¹ and occupational class,²² which can both
12 affect health outcomes via a number of mechanisms, for example the knowledge and
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15 105 living conditions that contribute to better personal health risk assessment, behaviours
16
17 and management.²³ In population studies these adult SES factors are themselves
18
19 inversely associated with risk of mortality.²⁴⁻²⁶ Some prospective cohorts take account
20
21 of the attenuating effects of education and adult socioeconomic status in estimating
22
23 the risk of mortality according to intelligence; yet, to date, their influence has not been
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25
26
27 110 properly evaluated.

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29
30 Investigators are giving increasing attention to the issues raised here, with a
31
32 higher rate of publications reporting risk estimates for all-cause mortality according to
33
34 differences in intelligence since the first systematic review.¹ There is now an
35
36 opportunity to reevaluate this augmented literature, this time with a quantitative,
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38
39 115 meta-analytic approach. The systematic review by Batty *et al*¹ reported the overall
40
41 quality of the nine studies as 'moderate', which was in part related to the weak
42
43 validity of some measures of premorbid intelligence. Therefore, one important change
44
45 to the systematic process reported here is the inclusion of studies in which only valid
46
47 cognitive assessments were used. Kilgour *et al*²⁷ also raised a number of
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51 120 methodological considerations that should be addressed in intelligence-mortality
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53 studies, including taking account of ascertainment bias, age, sex, and education. In
54
55 this paper we address the influence of these factors using sub-group analyses.
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57
58 Accordingly, the aims of this report are to: (1) quantify the association
59
60 between pre-morbid intelligence and all-cause mortality; (2) determine whether there

1
2
3 125 are sex differences in the association; and (3) conduct sub-group analyses on studies
4
5 that adjust for early life SES, adult SES and education, to discover their magnitude of
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7 influence as potential confounders or mediators of the intelligence-mortality
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9 association.
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16 17 18 Methods

19 20 21 22 23 Systematic Review Process

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25 An electronic search was conducted of premorbid intelligence and all-cause mortality
26
27 135 in all published articles, letters, abstracts and reviews, using the electronic databases
28
29 MEDLINE, EMBASE and PSYCHINFO (via Ovid). Searches were limited to articles
30
31 on humans published in the English language. The databases were searched using a
32
33 cognitive ability-related term (*Aptitude or Cognition** or *Cognitive function** or
34
35 *Cognitive ability* or *Cognitive characteristics* or *Cognitive style* or *intellectual ability*
36
37 or *Intelligence measures* or *Intelligence quotient* or *Intelligence test** or *Intelligence**
38
39 140 or *IQ or Language test** or *Memory* or *Mental abilit** or *Mental capacity* or *problem-*
40
41 *solving* or *Problem solving* or *Psychological performance* or *Psychometrics*) AND a
42
43 mortality term (*Cause of Death** or *Cause of Death trends* or *Death** or *death rate* or
44
45 *Incidence* or *Morbidity* or *Morbidity trends* or *Mortality Rate* or *Mortality risk* or
46
47 145 *Mortality** or *Mortality trends*), an asterisk allowing the search term to precede a
48
49 longer word or phrase.
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56 The electronic search, conducted on 5th February 2010, yielded 19 236 articles.
57
58 Two authors (CC and NL) independently scanned each title and abstract, retrieving
59
60 articles on the basis of their relevance to intelligence and mortality. The inclusion

1
2
3 150 criteria listed below were applied to their respective shortlists of papers. The reference
4
5 lists of the selected articles were then examined, along with review papers on
6
7 intelligence and mortality, and our own personal files, for articles that the electronic
8
9 search might have missed. Among the final list of articles, when more than one paper
10
11 reported intelligence-mortality associations from the same cohort, thereby duplicating
12
13
14
15 155 data, three authors (CC, DB and ID) agreed upon those papers to be retained,
16
17 according to criteria of the following order: (1) the article reported HRs for mortality
18
19 per one standard deviation difference in IQ-type score; (2) the cohort size was larger;
20
21 (3) it was the original publication to report the data.
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27 160 **Inclusion Criteria**

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29 We included published cohort data which fulfilled criteria similar to that of the
30
31 previous systematic review on intelligence and all-cause mortality¹: (1) to minimise
32
33 risk of reverse causality, only cohorts where intelligence test score data were collected
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35 at a mean age of 24 years or younger were included (the period classified as childhood
36
37 and youth according to the World Health Organisation Study Group²⁸); (2) the
38
39 165 intelligence and mortality data were collected at the level of the individual; (3) the
40
41 relationship between intelligence and all-cause mortality was reported quantitatively.
42
43 We also stipulated that: (4) the premorbid test should demonstrate an acceptable
44
45 degree of validity as a measure of intelligence; and (5) the cohort was not selected
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50 170 from a clinical or unrepresentative population.
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55 **Statistical Analysis**

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57 The hazard ratio (HR) with 95% confidence intervals (CI) for all-cause mortality per
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59 SD advantage in intelligence test score was the principal outcome variable. For HRs
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3 175 expressed per one SD disadvantage in intelligence, the reciprocal was used. Reported
4 odds ratios (ORs) were treated as HRs, with the caveat that these effect estimates
5 approximate one another²⁹ when the incidence of an event (i.e. mortality) is low.³⁰ In
6 case-control studies reporting intelligence test means for living and deceased, we
7 converted the standardised mean difference to an OR using formulae by Chinn.³¹ We
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15 180 contacted authors if we were unable to derive an overall effect size from their
16 published data.
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20 Fixed effects models were assumed for the aggregation of HRs based on
21 evidence of a low degree of heterogeneity ($p < 0.10$)³² Sub-group analyses were
22 conducted by sex group, for those studies to adjust for SES variables, and by study
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27 185 characteristic groupings for the purposes of sensitivity analysis. MIX 1.5 software³³
28 was used for all analyses and production of plots. The inverse variance method was
29 used to weight studies' effect sizes.
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36 **Sensitivity analyses and publication bias**

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39 190 Sensitivity analyses aggregated effect sizes by the following study characteristics:
40 ascertainment rate at follow-up; age at intelligence testing; cohort size; duration of
41 follow-up; average birth year of the cohort; effect size measure (see Table 2 for group
42 parameters). Ascertainment rate may bias the intelligence-mortality effect size if those
43 who emigrate, and are therefore excluded from follow-up, differ on cognitive ability
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51 195 scores compared to those who remain within geographical regions for census. Follow-
52 up rates were estimated based on the proportion of participants from the original
53 cohort that were followed up and included in the final analyses, regardless of whether
54 or not intelligence test scores were available for them. Studies were grouped on the
55 basis of <80% or 80-100% ascertainment rates. We aggregated studies according to
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3 200 age at cognitive testing, firstly because the likelihood of an effect of bodily insults on
4 intellectual function increases with age and, with it, the risk of reverse causation bias
5 in the intelligence-mortality link. Conversely, the validity of cognitive testing may be
6 greater in older cohorts, and these may reflect more homogeneous results compared to
7 results of younger children at intelligence testing for whom there is more
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15 205 measurement error. For the duration of follow-up, we divided studies on the basis of a
16 median split of the years traced for mortality. Although there may be stronger
17 grounds for assuming causality as the time period between intelligence testing and
18 mortality increases, there is also evidence that, by older adulthood, the intelligence-
19 mortality association loses significance.³⁴ The reason for aggregating studies that
20 reported HRs or ORs was to ensure that our treatment of these measures of
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27 210 association did not inflate the overall effect size. We also grouped according to cohort
28 size and decade of birth, as these may also have influenced heterogeneity across the
29 studies. We did not aggregate for population representativeness as one of our criteria
30 ensured the exclusion of clinical samples. However, due to two study cohorts being
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39 215 less representative of the general population (twins and gifted children) than all
40 others, we have reported meta-analytic results with and without their effect sizes.^{35, 36}

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43 The funnel plot was used to assess publication bias with standard error on the
44 y-axis as recommended by Sterne and Egger.³⁷ Publication bias was further evaluated
45 with Egger's test of asymmetry, and trim-and-fill adjustment methods.
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52 53 54 Results

55 56 57 58 59 60 Systematic retrieval of studies

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4 The electronic search resulted in 19 236 publications and, of these, the two reviewers
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6 225 (CC, NL) extracted shortlists of 73 and 69 relevant articles, respectively (<0.4% of
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8 total publications), from which 90 non-duplicate publications were retrieved for closer
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10 inspection (see Figure 1 for review process). Among these, 64 failed to meet one or
11
12 more inclusion criteria. A further three studies that met inclusion criteria were
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14 identified from the reference lists of the remaining 26 papers, or from review articles
15
16
17 230 or our own records.³⁸⁻⁴⁰ Two out of 29 studies were excluded^{39, 40} because we were
18
19 unable to obtain sufficient data to calculate the intelligence-mortality effect sizes.
20
21 (Table 1 lists the characteristics of the final 27 studies). We excluded eleven articles
22
23 from the meta-analysis because they overlapped with cohort data of another report.^{34,}
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25
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27 38, 41-49 Justification for excluding these data were: (1) the overlapping reports of a
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29 235 sample were generally reported by the same research group resulting in consistent
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31 methods of sample selection and data linkage; (2) the majority of overlapping cohorts
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33 were of similar size and follow-up duration.
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40 [Figure 1 about here]
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46 **Study descriptions for meta-analysis**

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48 Sixteen prospective longitudinal cohort studies included 22 453 deaths among 1 107
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50 022 participants. These were from five countries: UK ($n = 7$), USA ($n = 5$), Sweden (n
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52 = 2), Australia ($n = 1$) and Denmark ($n = 1$), ranging in size from 862 to 994 262
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54 245 participants. Figure 2 illustrates these variables according to year of publication,
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56 showing a trend for larger cohorts accumulating in more recent years. Premorbid
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58 intelligence test scores were taken from school records ($n = 10$), military or national
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3 service conscription records ($n = 5$), or a research database ($n = 1$). The average age at
4 testing ranged from seven to 20 years, and length of follow-up ranged from 17 to 69
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8 250 years. Six cohorts were all-male (five from conscription databases), and the remainder
9
10 were mixed sex. A variety of cognitive assessments were used across studies, and we
11 identified evidence for each of them as having validity as standardized measures of
12 intelligence. The concurrent or predictive validity of five tests used across nine of the
13 study cohorts^{3, 4, 35, 50-55} have been described elsewhere.¹ Here we describe evidence
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20 255 for psychometric validity among the seven remaining cohorts.

21
22 The Binet and Stanford-Binet tests used in two studies^{36, 56} are well-
23 established, age-standardised intelligence tests for children. Scores on the original
24 Stanford-Binet test contain a single underlying factor of cognitive ability⁵⁷, and the
25 Binet scale has concurrent validity with version 12 of the Moray House intelligence
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30
31 260 test ($r \sim 0.80$).⁵⁶ Two studies included selected tests from the well-validated Moray
32 House series.⁵⁸ The first incorporated Moray House tests 57 and 58 in an eleven-plus
33 examination that also assessed language and arithmetic.⁵⁹ On this exam, total scores
34 have shown well-established associations with childhood height at ages nine and 13
35 years.⁶⁰ The second² used Moray House Picture Tests 1 and 2, which have also shown
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43 265 expected patterns of association with intrauterine and childhood growth.¹⁹ The
44 Hårnquist test used in the Danish Metropolit study⁶¹ has shown concurrent validity: a
45 general intelligence factor extracted from scores on the test at age 13 years strongly
46 positively correlated ($r = 0.78$) with a military classification intelligence test taken
47 five years later.⁶² The Armed Forces Qualification Test (AFQT) used in another
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55 270 study⁶³ strongly correlates with other well-validated IQ tests (median r with seven
56 tests = 0.81), and scores on the four subtests show high loadings on a single g factor,
57 from 0.81 to 0.87.⁶⁴ Finally, the Vietnam Experience Study⁶⁵ used the Army General
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3 Technical test, which strongly correlates with verbal reasoning ($r = 0.75$) and
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5
6 visuospatial ($r = 0.51$) scores from the Weschler Adult Intelligence Scale (WAIS), a
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8 275 standardised and well-validated cognitive ability test battery.
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12 [Figure 2 about here]
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18 Records of mortality were ascertained prospectively in seven studies, either by
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20 280 linkage of study members to national register databases^{4, 35, 51-52, 59} or by individual
21
22 follow-up with study participants or their families.^{36, 63} In the remaining studies,
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24 incidence of death was ascertained retrospectively by access to national death
25
26 registers—in Swedish cohorts record linkage used personal identification numbers
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28 rather than person names^{3, 50, 53}—with the exception of two studies that did not report
29
30 285 methods for extracting death records.^{54, 65}
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34 Ten papers estimated the intelligence-mortality effect size as a HR with CIs,^{2-4,}
35
36 36, 50, 53, 55, 56, 59, 65 two used ORs or logistic regression coefficients,^{51, 63} and two
37
38 reported means and standard deviations that we converted to ORs.^{35, 54} Authors of the
39
40 two remaining papers provided HRs^{52, 61} in response to email requests, which were
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42 290 unreported in their original publications.
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50 [Table 1 about here]
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55 **Intelligence-mortality meta-analysis: basic model**

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57 295 In the basic model, the HR from each of the 16 studies was either: unadjusted ($n = 2$),
58
59 adjusted for age ($n = 3$), sex ($n = 3$), age and sex ($n = 3$), or was unspecified ($n = 5$)
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3 (Table 1). However, there was a low degree of heterogeneity between the effect sizes
4
5 of these models ($Q = 17.7$, $I^2 = 15.5\%$, $p = 0.28$). In a fixed effects model, a one SD
6
7 advantage in intelligence was associated with the lower risk of all-cause mortality
8
9
10 300 (HR 0.76, 95% CI 0.75-0.77) (see Figure 3). The exclusion of two studies^{35,36} based
11
12 on selected samples (twins and gifted children) did not alter this estimate; neither did
13
14 the exclusion of two studies that reported ORs and where incidence of death was
15
16 between 20-40%^{35,54} (data not shown). The statistical weight of the largest study³ was
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18 70.5%; excluding this cohort from the model made a negligible change to the effect of
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21 305 intelligence on risk of mortality (HR 0.77, 95% CI 0.75-0.80).
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28 [Figure 3 about here]
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33 Sensitivity analyses results are presented in Table 2. Age at intelligence testing
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35 310 may have had a small effect in predicting the risk of mortality. Aggregation of studies
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37 in which premorbid intelligence was tested at an average age of between seven to 12
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39 years resulted in a small attenuation (16%) of the risk of mortality (HR 0.79, 95% CI
40
41 0.76-0.82) compared to that of 18 to 20 year olds (HR 0.75, 95% CI 0.74-0.77).
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43 Studies of longer follow-up (40 to 69 years) showed a 20% attenuation of the risk of
44
45 mortality as predicted by a one SD advantage in intelligence (HR 0.80, 95% CI 0.76-
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47 315 0.83), compared to those cohorts of shorter follow-up (HR 0.75, 95% CI 0.74-0.77).
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49
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51 Furthermore, there was a trend for cohorts born in the 1910s and 1920s to show an
52
53 attenuated effect size compared to those cohorts born in the 1930s to 1960s. However,
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55 these older age cohorts were also those with a longer duration of follow-up.
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59 320 Ascertainment bias was unlikely to have affected the total aggregate HR. That
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is, studies of low ascertainment (62-79%) showed a similar aggregate effect size (HR

0.76, 95% CI 0.75-0.78) to that of studies with 80-100% ascertainment (HR 0.77, 95% CI 0.74-0.80). There was also no observable effect of cohort size on the magnitude of the intelligence-mortality association.

325 The aggregate effect size for studies reporting ORs resulted in a higher risk of mortality as predicted by intelligence (0.71, 95% CI 0.64-0.79) compared to the aggregate effect size from studies reporting HRs (0.76, 95% CI 0.75-0.78). However, the four studies reporting ORs had among the lowest weightings of the 16 cohorts (0.42-1.08%), which may explain why their inclusion in the basic model was less likely to have incurred statistical bias.

Publication bias was first addressed by examination of the funnel plot, which revealed one study⁴ on the outside of 95% CI parameters (see Figure 4). Egger's test of asymmetry supported a low risk of publication bias (Intercept = 0.10, 95% CI -0.72-0.91, $p = 0.81$), as did application of trim and fill adjustments in which only one missing study was estimated, and its imputation made no difference to the magnitude of the risk estimate (HR 0.76, 95% CI 0.75-0.78).

[Figure 4 about here]

340 **Stratification by sex**

Seven studies reported intelligence-mortality effect sizes for men and women separately, and their follow up spanned 24 to 65 years.^{2, 51-53, 55, 59, 63} During this period the absolute risk of death was 5.6% for women and 8.2% for men. Four out of the seven studies reported negligible sex differences^{2, 51, 52, 63} (two of these formally tested intelligence × sex interaction effects), two reported a stronger effect for men

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3 (one reported a null effect in women with an intelligence \times sex interaction effect),^{53, 59}
4
5 and one reported a stronger effect in women.⁵⁵ However, fixed effects models were
6
7 applied to aggregate the sex-specific HRs, given the evidence for low heterogeneity
8
9 (Table 2). A one SD advantage in intelligence among women was associated with a
10
11 350 22% lower risk of all-cause mortality (HR 0.78, 95% CI 0.73-0.84), whereas among
12
13 men there was a 20% reduced risk of mortality per one SD advantage in intelligence
14
15 (HR 0.80, 95% CI 0.76-0.85). Nevertheless, there was a high degree of overlap in the
16
17 confidence intervals of these respective effect sizes. Egger's test of asymmetry
18
19 supported a lack of publication bias among sex-specific cohorts.
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[Table 2 about here]

Adjustment for childhood SES

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37 Nine studies that included 18 733 deaths, reported effect size models adjusted for
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39 360 childhood socioeconomic status, measured either by father's occupation or income^{2, 36,}
40
41 50, 51, 56, 59, 61, the highest socioeconomic index recorded for either parent³, or father's
42
43 education.⁵³ Heterogeneity was very low in unadjusted ($Q = 8.56$, $I^2 = 6.6\%$, $p = 0.38$)
44
45 and adjusted models ($Q = 7.49$, $I^2 = 0.0\%$, $p = 0.48$). In a fixed effects basic model the
46
47 HR for this sub-group of papers did not deviate from the HR for the 16 studies (HR
48
49 365 0.76, 95% CI 0.75-0.77). However, even after adjustment for childhood SES there
50
51 was a very small attenuation (by 4%) of the effect size (HR 0.77, 95% CI 0.75-0.79)
52
53 (see Figure 5). Excluding the large study of over one million Swedish men had no
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55 effect on the aggregate effect size of the childhood SES-adjusted model, except to
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57 slightly widen the 95% CI parameters (HR 0.77, 95% CI 0.74-0.80). Compared to the
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3 370 unadjusted model of this smaller group of studies in which there were 4608 deaths
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5 (HR 0.77, 95% CI 0.74-0.80), controlling for childhood SES had no effect on the
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7 intelligence-mortality gradient when the influence of this largest weighted study was
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9 removed.
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13 A tenth publication⁴⁶ from the systematic review, that could not be included in
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15 375 meta-analysis, reported data consistent with this finding: early life socioeconomic
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17 inequalities do little to explain the inverse association between intelligence and all-
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19 cause-mortality.
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22 23 24 25 26 **Controlling for adult SES and education**

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29 380 There was no evidence for publication bias among studies that controlled for adult
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31 SES or education. In five studies that adjusted for adult SES, there were 3070 deaths
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33 among 66 301 participants. Socioeconomic status was measured either by
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35 occupational social class^{4, 50, 51, 56}, or income.⁶⁵ The unadjusted effect size for this sub-
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37 group of studies (HR 0.76, 95% CI 0.72-0.79) matched that of all 16 studies. After
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39 adjustment for adulthood SES, the lower risk of mortality predicted by higher
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41 385 intelligence was attenuated by 33.5% from the basic model (HR 0.84, 95% CI 0.78-
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43 0.90) (see Figure 5).
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49 Among the six studies that adjusted for educational attainment there were 16
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51 023 deaths out of 1 026 742 participants.^{3, 51, 53, 56, 63, 65} Again, the aggregate effect size
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53 390 for this sub-group of studies in an unadjusted model (HR 0.76, 95% CI 0.74-0.77) was
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55 no different from that for all 16 studies. After adjustment for education (HR 0.89,
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57 95% CI 0.86-0.91), the effect of intelligence on mortality was reduced by 54.2% (see
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59 Figure 5). Exclusion of the large Swedish cohort³ from the model, as expected,
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3 widened the CI parameters (HR 0.87, 95% CI 0.81-0.93), but still reduced the
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6 395 intelligence-mortality gradient by 45.8% from the unadjusted model.
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9 Two further studies from the systematic review,^{45, 46} excluded from meta-
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11 analysis due to the type of statistics reported, are consistent with our result. They
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13 observed attenuation effects by education of over one third, of the intelligence-
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15 mortality association.
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21 [Figure 5 about here]
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23 24 **Multiple covariates**

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27 Eleven studies, including 15 148 deaths, reported effect sizes for the risk of mortality
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29 according to intelligence while adjusting for multiple variables^{2-4, 50-52, 54, 56, 61, 63, 65},
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31 (see Table 1 for covariates). Among these cohorts, four showed entire attenuation of
32 405 the intelligence-mortality effect size from unadjusted (or basic) models.^{51, 52, 63, 65}
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34 These studies tended to adjust for adult SES variables with the addition of other
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36 important covariates, including education⁶³ or smoking⁵² among other cardiovascular
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38 disease risk factors.^{51, 65} The remaining studies reported a smaller degree of
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43 410 attenuation from unadjusted models. Due to the varying number and nature of
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45 covariates across the studies it not appropriate to aggregate their effect sizes in meta-
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47 analyses.
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50 51 52 53 54 **Discussion**

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57 415 The present meta-analysis of 16 published prospective cohort studies, comprising over
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59 1.1 million participants and 22 453 deaths, demonstrates and quantifies the
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3 consistently-reported association between higher premorbid intelligence and lower
4 mortality risk. A one SD advantage in intelligence in childhood and youth was
5 associated with a 24% lower risk of mortality. The effect was similar in men and
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10 420 women, and was not explained by socioeconomic differences in early life, as
11 indicated by parental occupation or income. The association was attenuated by
12 approximately a third after adjusting for adult SES and by approximately a half after
13 adjusting for educational experience. Intelligence remained a predictor of mortality
14 after these attenuating effects, and removal of one study that carried by far the largest
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22 425 weighting in the models³ did little to change the magnitude of these effects.
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25 This is the first meta-analysis of studies examining the relationship between
26 premorbid intelligence and all-cause mortality. A recent systematic review, which was
27 based on nine identified at that time, reported the inverse association.¹ Since then the
28 number of publications of the intelligence-mortality association has grown, and the 16
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34 430 unrelated cohorts we identified represent more than four times as many deaths. We
35 found little evidence of publication bias, and so the estimated risk of mortality
36 according to one SD advantage in intelligence may be generalized to cohorts beyond
37 those included in this meta-analysis, at least to those of the five countries included in
38 the analyses. Our treatment of ORs as HRs in two studies where the absolute risk of
39 death was >5%, which could have incurred statistical error, was not found to inflate
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46 435 the aggregate effect size.
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51 Heterogeneity was not apparent across the studies despite most using different
52 assessments of premorbid intelligence. This may be because most omnibus
53 intelligence tests of the types used in the identified studies show strong loadings on
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58 440 general intelligence, *g*.⁷⁰ The intelligence-mortality association was however slightly
59 weaker among cohorts of younger ages at cognitive testing, and those of longer
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3 follow-up duration. As it was the same cohorts that were followed up beyond forty
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5 years who were the youngest at intelligence testing, it is difficult to establish which
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7 factor would make the larger contribution to attenuating the intelligence-mortality
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10 445 association. However, it seems less likely to have been due to differences in the
11
12 validity of intelligence tests taken at younger and older ages, given the equally low
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14 heterogeneity among these two cohort groupings. It may be that older cohorts at
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16 cognitive testing show a steeper intelligence-mortality gradient because of the
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18 increased likelihood of bodily insults, or, it is still possible that the association varies
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20 according to age at mortality, most likely due to cause of death.
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28 **Lack of confounding by sex and early life SES**

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30 Our observation of negligible differences between men and women in the relative risk
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32 of mortality as predicted by intelligence, may be surprising given well-documented
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34 455 sex differences in patterns of risk factors, onset and prevalence of specific diseases,
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36 and life expectancies.⁶⁷ However, there were exceptions in individual studies, with
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38 differences between men and women reported, although there seem to be cohort-
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40 specific explanations for these. In one study⁵⁵ the lower relative risk among men was
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42 probably due to the rise in deaths of higher intelligence servicemen during World War
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44 II.⁶⁸ In another, the lower relative risk among women could have resulted from a lack
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46 460 of statistical power due to the small number of female deaths.⁵⁹ The result from an
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48 older birth cohort study⁵³ of a null association among women, could have been
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50 influenced by a relatively higher incidence of smoking among well-educated women
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52 during an era before the health hazards of smoking were widely known. In general
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57 465 however, data from large post-war birth cohort studies show negligible sex
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59 differences in the effects of intelligence in relation to risk of mortality, and results
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3 from our meta-analyses support this. Equivalent effect sizes by sex still do not mean
4 that the mechanisms which explain the intelligence-mortality association act in equal
5 measure for men and women, and it continues to be of interest to study sex
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10 470 differences in cognitive epidemiology. Differences in health behaviours, risk patterns
11 and medical interventions should also be considered when comparing ethnic groups or
12 diverse countries. However, there is currently a lack of cohort data to evaluate how
13 such group differences influence the risk of all-cause mortality as predicted by
14 premonitory intelligence.

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22 475 Socioeconomic conditions in early life, determined by parental occupation or
23 income, were also unlikely confounders. Individual differences in cognitive ability
24 appear to act independently of childhood social inequalities in predicting all-cause
25 mortality. There may of course be alternative early life factors contributing to
26 confounding which were not covariates of the cohorts we reviewed. Among three
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34 480 studies that adjusted for birth weight in multivariate-adjusted models, one reported no
35 change from unadjusted models,² and two reported a risk attenuation of 1% and 4%
36 respectively compared to models that adjusted for childhood SES⁶¹ and education.⁵¹
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41 However, recent evidence suggests that birth weight may not be the ideal indicator for
42 exposures in the intrauterine environment, which carry their most critical influence on
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46 485 neurological and physiological development during the early prenatal period.⁶⁹ Other
47 qualitative characteristics in early childhood may further explain the relationship
48 between premonitory intelligence and longevity,²⁷ including style of parenting and
49 cognitive stimulation at home,⁷⁰ or the effects of diet. However, so far, the potential
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58 490 suggested variables are likely to be associated with parental intelligence.
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Attenuation of the intelligence-mortality association

Education and adult SES were found partially to attenuate the risk of mortality according to one SD advantage in intelligence. Premorbid cognitive ability may act via occupational status and wealth to reduce the risk of mortality, by providing a less hazardous work environment, a safer and more comfortable home environment, and the material means to access better and more immediate medical care. Furthermore, intelligence may be mediated by education to reduce the likelihood of death, perhaps by increasing a person's receptivity to health education messages (thereby reducing negative behaviours such as smoking and excess alcohol consumption, and promoting exercise and healthy eating), and by improving comprehension of medical terminology and instruction that impacts on disease management and prevention. Nevertheless, the results to date cannot tell us for certain whether education and adult SES are simply partial mediators of the association between intelligence and mortality; or whether the results reflect over-adjustments if both factors are partial surrogates for intelligence; or if these variables confound intelligence-mortality associations.⁷¹ Structural equation modelling can examine for statistical mediation, and one study to employ this technique reported that the effect of general intelligence factor on mortality was entirely mediated by income, education and poor physical health in adulthood.⁴⁹ However, in this study, with cognitive ability measured at age 20, the association between intelligence and mortality could also have been partially confounded by education. In our meta-analyses, two out of five studies that adjusted for adult SES,^{50, 65} and three out of six studies adjusting for education,^{3, 63, 65} had intelligence test scores measured in later youth (19-20 years of age) when most people have completed education. There is evidence for a causal association from childhood intelligence scores to later educational achievement in longitudinal studies, and it is

also likely educational experience can boost cognitive test scores to some extent.⁷²

Therefore reciprocal dynamic pathways between intelligence, education and adult SES need to be considered.

520 Few studies in the meta-analysis adjusted for both education and adult SES in
 11 the same model. It is suggested that both factors may overlap in their attenuation
 12 effects on the intelligence-mortality association,⁴⁰ but there is also evidence to show
 13 that they are not interchangeable, and have independent effects on health outcomes.^{73,}
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535 **Future directions**

50 The present meta-analysis was unable to consider cause of death in the intelligence-
 51 mortality association, but this would seem an important area for future systematic
 52 review, particularly as it was likely to have driven the stronger effect sizes of cohorts
 53 followed to younger ages in adulthood. For example, it may be that intelligence has a
 54 stronger relation to mortality caused by external events such as accidents,⁵⁴ more

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3 prevalent among younger adults, than cause-specific mortalities more typical in later
4 life.⁴ Studies have already replicated the inverse association between premorbid
5 intelligence and cardiovascular disease (CVD)-related mortality, with increased effect
6 size magnitudes for coronary heart disease (CHD)-related deaths^{3, 75-78} compared to
7 stroke-related deaths.^{75, 77, 78} The relationship between childhood cognitive ability and
8 risk of cancer mortality is also likely to vary by type.⁴ For example, smoking-related
9 cancers might carry a stronger association with intelligence^{4, 79, 80} than other cancer
10 types.⁷⁹ Specific causes of death are therefore likely to be crucial in providing
11 545 explanations as to why intelligence predicts life expectancy, and larger cohorts with
12 increased numbers of cause-specific mortalities will help to clarify this issue.
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27 In the present study we found that education and social position in adulthood are
28 factors that may help to account for the intelligence-all-cause mortality association.
29 However, the extent to which these SES indicators act as partial surrogates for
30 intelligence, or mediators and/or confounders of the intelligence-mortality association
31 555 requires formal testing. Future longitudinal studies of mortality risk with repeated
32 measures of intelligence, education, and adult SES, spanning childhood to adulthood
33 could contribute to do this. Twin studies to determine the extent to which intelligence
34 shares genetic and environmental causes with health, education, and social class, in
35 predicting mortality, will also help to inform this issue. With evidence of associations
36 between cognitive performance and education showing substantial heritability,^{81, 82} it
37 is possible that these variables may share some genetic effects in predicting death.
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53 Although early life SES did not help to explain the intelligence-mortality
54 association and birthweight is another unlikely confounder, future studies could
55 explore alternative early life variables, in particular the intrauterine environment, and
56 565 how these might simultaneously determine neurological and physiological integrity,
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3 in interaction with genetic influences, leading to lifelong effects on cognition and
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For Review Only

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Key messages

- Higher intelligence test scores measured in youth are associated with the reduced risk of mortality by mid-to-late adulthood.
- The intelligence-mortality association does not appear to be confounded by gender or early life socioeconomic inequalities.
- Adult SES and education attenuate the intelligence-mortality association by a third and a half, respectively. Improved study design can contribute to a better understanding of the mechanisms involved in this effect, including: lifetime repeated measures of intelligence and SES indicators; detailed early life and adult covariate data, and specific causes of mortality; twin studies that estimate the environmental and genetic contributions to intelligence-SES-mortality associations.

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Table 1.

Characteristics of 27 Longitudinal Cohort Studies of Premorbid Intelligence and All-Cause Mortality

Study reference, [#]	Country, study name	Sex	Birth yr(s)	Age at cognitive test, yrs (M)	Years of survival follow-up (n yrs since cognitive test) ^a	Cohort Size, N	Deaths, n	Intelligence test, cohort type	Model adjustments
*O'Toole <i>et al</i> (1988), [54] b	Australia, Veterans Health Studies	M	1947-53 (incl. earlier periods)	≥18	1967-1982 (2 to 17)	2309	523	AGCT, conscription	Basic model: unspecified Multiple adjustments: post-school course, no of jobs; and during 2-year service history: AWOL offence, alcohol offence, duration of hospital stay, motor vehicle charge
*Whalley & Deary (2001), [55]	UK, SMS32 Aberdeen Cohort	M/F	1921	11	1932-1997 (1 to 65)	1153 (M) 1032 (F)	646 (M) 438 (F)	Moray House No. 12, school	Basic model: age
Deary <i>et al</i> (2003), [38]	UK, SMS32 Aberdeen Cohort	M/F	1921	11	1932-1997 (1 to 65)	1139 (M) 1032 (F)	633 (M) 438 (F)	Moray House No. 12, school	—
*Hart <i>et al</i> (2003), [4]	UK, SMS32 and Mid-span studies	M/F	1921	11	1970-2001 (38 to 69)	922	422	Moray House, school	Basic model: sex and age (HR= 0.85 [0.78 – 0.93]) Adult SES: basic model + adult social class (HR= 0.88 [0.79 – 0.98]) Multiple adjustments: Adult SES model + deprivation
*Osler <i>et al</i> (2003), [61]	Denmark, Metropolit2000	M	1953	12	1968-1998 (3 to 33)	7308	522	Harnquist, school	Basic model: unspecified Childhood SES: father's social class Multiple adjustments: childhood SES model + birth weight
Deary <i>et al</i> (2004), [44]	UK, SMS47 Six Day Sample	M/F	1936	11	1968-2000 (21 to 53)	908	125	Binet test, school	—

Kuh <i>et al</i> (2004), [46]	UK, National Survey of Health and Development (British 1946 birth cohort)	M/F	1946	8	1971-2000 (17 to 46)	2192 (M) 2057 (F)	133 (M) 96 (F)	NFER tests, school	—
Hart <i>et al</i> (2005), [34]	UK, SMS32 and Mid-span studies	M/F	1921	11	1970-2001 (38 to 69)	938	432	Moray House, school	—
*Martin & Kubzansky (2005), [36]	USA, Terman Life Cycle Study	M/F	1903-16	6-18 (11)	1922-1986 (1 to 64)	862	293	Stanford-Binet, school	Basic model: sex Childhood SES: poor health and father's occupation
*Hemmingson <i>et al</i> (2006), [50]	Sweden, Army Conscripts	M	1949-51	18-20 (19)	1971-2000 (1-31)	49 262	2022	SEB 1967, conscription	Basic model: unadjusted Childhood SES: father's occupation at age 9-11 Adult SES: adulthood socioeconomic position Multiple adjustments: all above models
Vagero <i>et al</i> (2006), [48]	Sweden, Army Conscripts (Stockholm Birth Cohort Study)	M	1953	(18)	1980-2002 (9 to 31)	6318	204	SEB, conscription	—
*Pearce <i>et al</i> (2006), [59]	UK, Newcastle Thousand Families	M/F	1947	11	1959-2003 (1 to 45)	357 (M) 360 (F)	30 (M) 19 (F)	Moray House Nos. 57 & 58, school	Basic model: unspecified Childhood SES: father's social class at birth (mother's if unavailable)
*Holsinger <i>et al</i> (2007), [35] c	USA, NAC-NRC Twin WWII Veterans	M	1917-27	17-21 (19)	1967-2004 (22 to 59)	984	385	AGCT / GCT, conscription	Basic model: unspecified
Batty, Gale <i>et al</i> (2008), [41]	USA, Vietnam Experience Study	M	1947	(19)	1985-2000 (18 to 33)	4157	231	Army General Technical, conscription	—

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*Batty, Shipley, Mortensen <i>et al</i> (2008), [65] d	USA, Vietnam Experience Study	M	1947	(20)	1985-2000 (18 to 33)	4316	241	Army General Technical, conscription	Basic model: age Education: educational level attained Adult SES: occupational prestige, educational grade & family income Multiple adjustments: basic model + adult SES model + rank, ethnicity, depression, BMI, pulse rate, posttraumatic stress disorder, somatic disease, martial status, alcohol consumption, blood pressure, blood glucose, generalised anxiety disorder, smoking, FEV1
*Deary <i>et al</i> (2008), [56]	UK, SMS47 Six Day Sample	M/F	1936	11	1968-2003 (21 to 56)	1181	193	Binet test, school	Basic model: with and without sex (no difference) Education: years of education Adult SES: occupational social class Multiple adjustments: sex and dependability
Starr <i>et al</i> (2008), [47]	UK, SMS32 Aberdeen Cohort	M/F	1921	11	1932-2007 (1 to 75)	202 (M) 152 (F)	102 (M) 56 (F)	Moray House No. 12, school	—
Batty, Mortensen <i>et al</i> (2008), [42]	USA, Vietnam Experience Study	M	1947	(20)	1985-2000 (18 to 33)	14 437	769	Army General Technical, conscription	—
Batty, Shipley, Gale <i>et al</i> (2008), [43]	USA, Vietnam Experience Study	M	1947	(20)	1985-2000 (18 to 33)	4166	233	Army General Technical, conscription	—
*Batty <i>et al</i> (2009), [3]	Sweden, Army Conscripts	M	1950-76	16-26 (18)	1971-2001 (1 to 30)	994 262	14 498	SEB, conscription	Basic model: age, year of birth, conscription testing centre Childhood SES: parental socioeconomic index (highest of either parent), height Education: educational level attained + multiple adjustments (see below) Multiple adjustments: basic model + childhood SES model + body mass index, blood pressure, psychiatric and somatic illness
*Jokela, Elovainio <i>et al</i> (2009), [63]	USA, National Longitudinal Study of Youth	M/F	1957-64	16-23 (19)	1980-2004 (0 to 24)	5682 (M) 5639 (F)	248 (M) 112 (F)	AFQT, research sample	Basic model: sex, birth year, ethnicity, health status Education: basic model + years of education and marital status Multiple adjustments: education model + household income

*Kuh <i>et al</i> (2009), [52]	UK, National Survey of Health and Development (British 1946 birth cohort)	M/F	1946	8, 11, 15	1971-2005 (10 to 51)	4128	195 (M) 137 (F)	NFER tests, school	Basic model: sex Multiple adjustments: basic model + father's social class, mother's & father's education, care of house & child, adult housing quality & tenure, adult social class, household income, smoking, education.
Weiss <i>et al</i> (2009), [49]	USA, Vietnam Experience Study	M	1947	(20)	1985-2000 (18 to 33)	4200	234	Army General Technical, conscription	—
Hemmingsson <i>et al</i> (2009), [45]	Sweden, Army Conscripts	M	1949-51	18-20 (19)	1990-2003 (19 to 36)	43 834	Not reported	SEB 1967, conscription	—
*Jokela, Batty <i>et al</i> (2009), [51] ^c	UK, National Child Development Survey (British 1958 birth cohort)	M/F	1958	11	1969-2004 (1 to 35)	14 132	213 (M) 116 (F)	NFER tests, school	Basic model: unspecified Childhood SES: father's occupational class Adult SES: occupational class Education: educational level attained Multiple adjustments: all previous models + child covariates (family difficulties, family size, problem behaviour, birth weight, height, mother's interest in child education, father's interest in child education), and adult covariates (marital status, psychosomatic symptoms, smoking, alcohol consumption, body mass index)
*Leon <i>et al</i> (2009), [2]	UK, ACONF	M/F	1955	7	1970-2007 (8 to 45)	11 603	426 (M) 235 (F)	Moray House Picture Tests Nos. 1 & 2, school	Basic model: age, sex Childhood SES: perinatal factors (which didn't alter the basic model), father's social class at birth, family size Multiple adjustments: all previous models + childhood height and weight
*Lager <i>et al</i> (2009), [53]	Sweden, Malmö Longitudinal Study	M/F	1927-28	10	1939-2003 (1 to 65)	832 (M) 698 (F)	363 (M) 176 (F)	Hallgren test, school	Basic model: unadjusted Childhood SES: father's education Education: educational level attained

Note. Studies appear in publication date order; those marked with an asterisk are included in the meta-analysis. ACONF = Aberdeen Children of the 1950s; AFQT = Armed Forces Qualification Test; AGCT = Army General Classification Test; GCT = General Classification Test; NFER = National Foundation for Educational Research; SMS32 = Scottish Mental Surveys of 1932; SMS47 = Scottish Mental Surveys of 1947; SEB = Swedish Enlistment Battery.

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^aIf years of follow-up and/or dates were not reported these were estimated according to the longest theoretical time period. ^bStudy included all deceased and a random sample of survivors from the original cohort, twice as large as the deceased group. ^cYears since cognitive testing is an estimate: in correspondence Holsinger *et al* reported that the vast majority of conscripts would have been 17-21 years old at testing. ^dYears since cognitive testing and birth year are approximations based on the mean age of participants at the beginning of follow-up in 1985-86. ^eModels for sex groups and those that adjusted for adult SES and multiple variables are based on a shorter follow-up period (23-46 years) and therefore a smaller sample size (n = 10 620).

For Review Only

Table 2.

Summary of HRs for all-cause mortality in relation to a one SD advantage in intelligence in 16 longitudinal cohort studies

Subgroups	Studies, <i>n</i>	Reference #s	Deaths, <i>n</i>	HR (95% CI)	Heterogeneity		risk attenuation from basic model
					<i>p</i>	<i>I</i> ² (%) ^a	
Basic model	16	2-4, 35, 36, 50-56, 59, 61, 63, 65	22 453	0.76 (0.75-0.77)	0.28	15.5	—
Mean age at cognitive testing							
	10	2, 4, 36, 51-53, 55, 56, 59, 61	4424	0.80 (0.77-0.83)	.61	0.0	—
7-12 yrs	6	3, 35, 50, 54, 63, 65	18 029	0.75 (0.74-0.77)	.54	0.0	—
18-20 yrs							
% ascertainment							
< 80%	7	3, 4, 52, 55, 59, 61, 65	17 148	0.76 (0.75-0.78)	.39	5.4	—
≥ 80%	7	2, 36, 50, 51, 53, 63	4397	0.77 (0.74-0.80)	.25	23.7	—
Invalid ^b	2	35, 54	908	—	—	—	—
Effect size							
HR	12	2-4, 36, 50, 52, 53, 55, 56, 59, 61, 65	20 856	0.76 (0.75-0.78)	.24	21.1	—

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OR	4	35, 51, 54, 63	1597	0.71 (0.64-0.79)	.57	0.0	—
Cohort size							
< 1,000	4	4, 35, 36, 59	1149	0.83 (0.76-0.91)	.26	25.3	—
1,000 – 10,000	7	52-56, 61, 65	3638	0.77 (0.74-0.81)	.30	17.4	—
> 10,000	5	2, 3, 50, 51, 63	17 870	0.76 (0.74-0.77)	.70	0.0	—
Follow-up duration							
< 40 years	7	3, 50, 51, 54, 61, 63, 65	18 495	0.75 (0.74-0.77)	.71	0.0	—
40-69 years	9	2, 4, 35, 36, 52, 53, 55, 56, 59	3958	0.80 (0.77-0.83)	.50	0.0	—
Cohort birth year							
1910s-20s	5	4, 35, 36, 53, 55	2723	0.82 (0.77-0.86)	.41	0.0	—
1930s-40s	4	52, 56, 59, 65	815	0.73 (0.65-0.80)	.80	0.0	—
1950s-60s	7	2, 3, 50, 51, 54, 61, 63	14 858	0.76 (0.74-0.77)	.56	0.0	—
<hr/>							
Sex ^c							
Female	7	2, 51-53, 55, 59, 63	1086	0.78 (0.73-0.84)	.17	33.4	—
Male	7	2, 51-53, 55, 59, 63	1771	0.80 (0.76-0.85)	.88	0.0	—

Adjusted for:

Childhood SES	9	2, 3, 36, 50, 51, 53, 56, 59, 61	18 733	0.77 (0.75-0.79)	.48	0.0	4.0% ^d
Adult SES	5	4, 50, 51, 56, 65	3070	0.84 (0.78-0.90)	.52	0.0	33.5%
Education	6	3, 51, 53, 56, 63, 65	16 023	0.89 (0.86-0.91)	.53	0.0	54.2% ^d

Note. All sub-analyses refer to fixed effects models.

^a I^2 (%) = percentage of variation across studies due to heterogeneity. ^bInsufficient data prevented estimation of ascertainment rate at follow-up. ^cNumber of deaths reported for men and women exclude data from Jokela *et al* [63] which were unreported. ^dRemoving the influence of by far the largest cohort by Batty *et al* [3] gave attenuation effects by childhood SES of 0.0% and by education of 45.8%.

Figure 1.

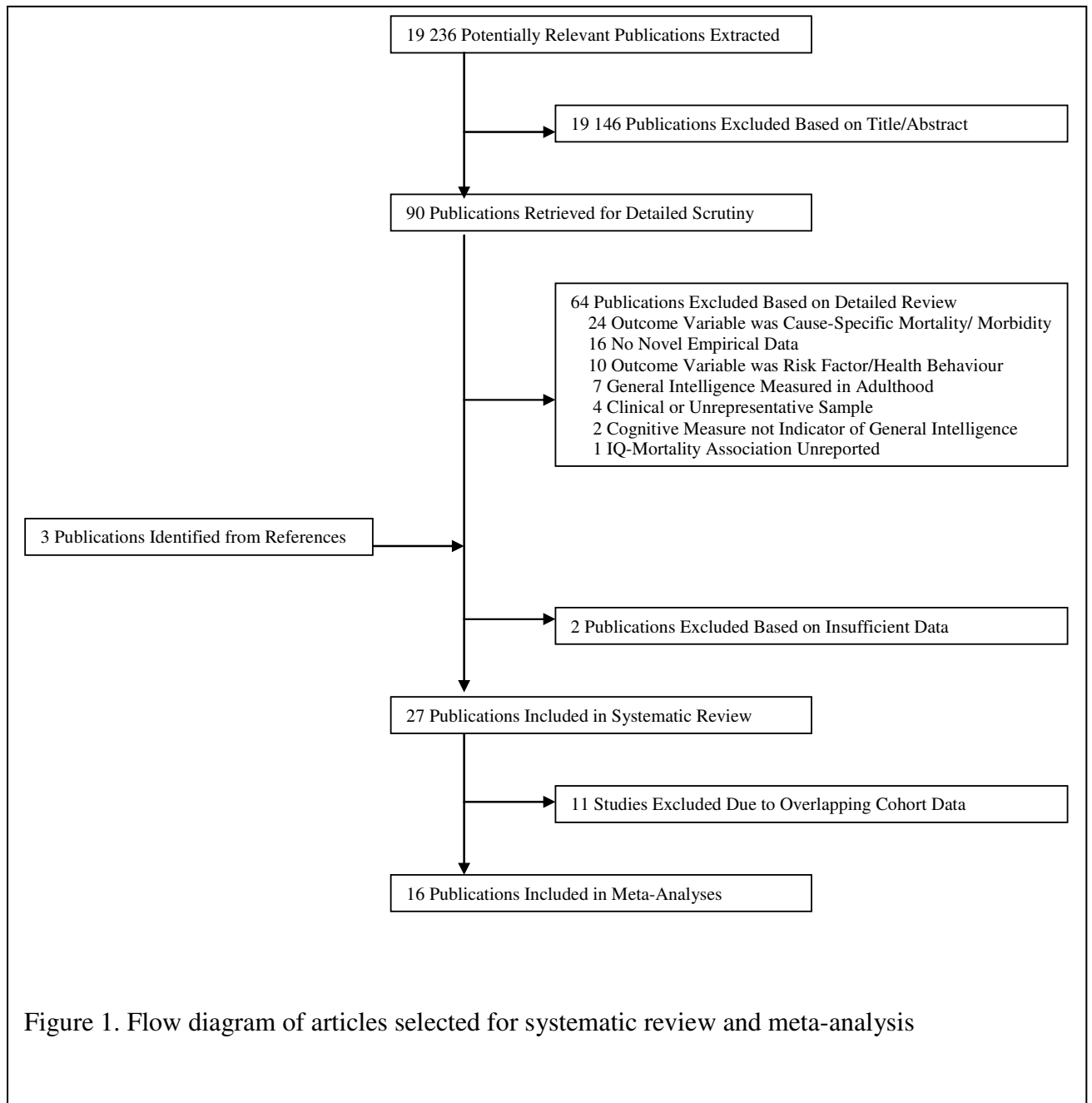


Figure 1. Flow diagram of articles selected for systematic review and meta-analysis

Figure 2.

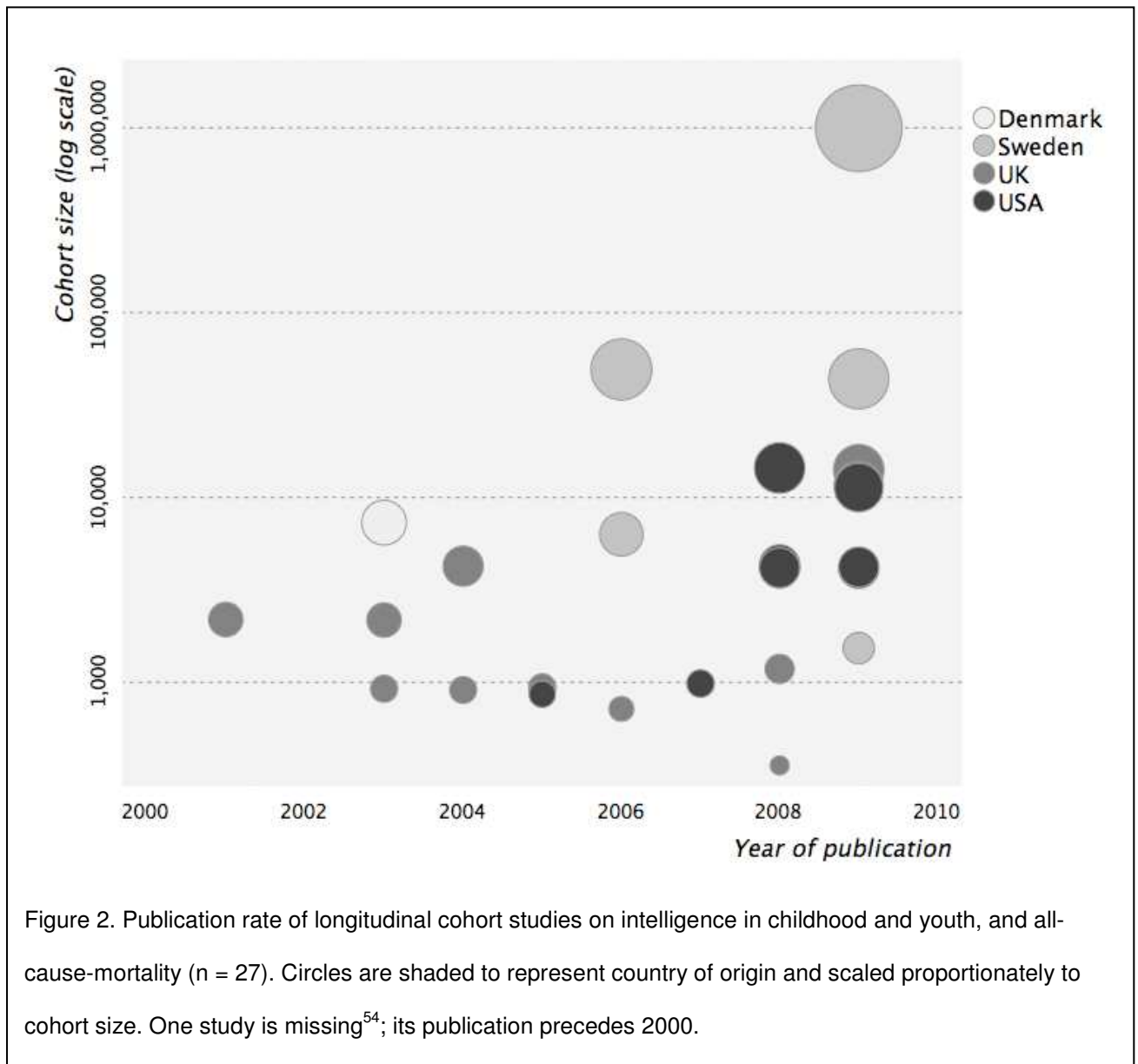


Figure 2. Publication rate of longitudinal cohort studies on intelligence in childhood and youth, and all-cause-mortality (n = 27). Circles are shaded to represent country of origin and scaled proportionately to cohort size. One study is missing⁵⁴; its publication precedes 2000.

Figure 3.

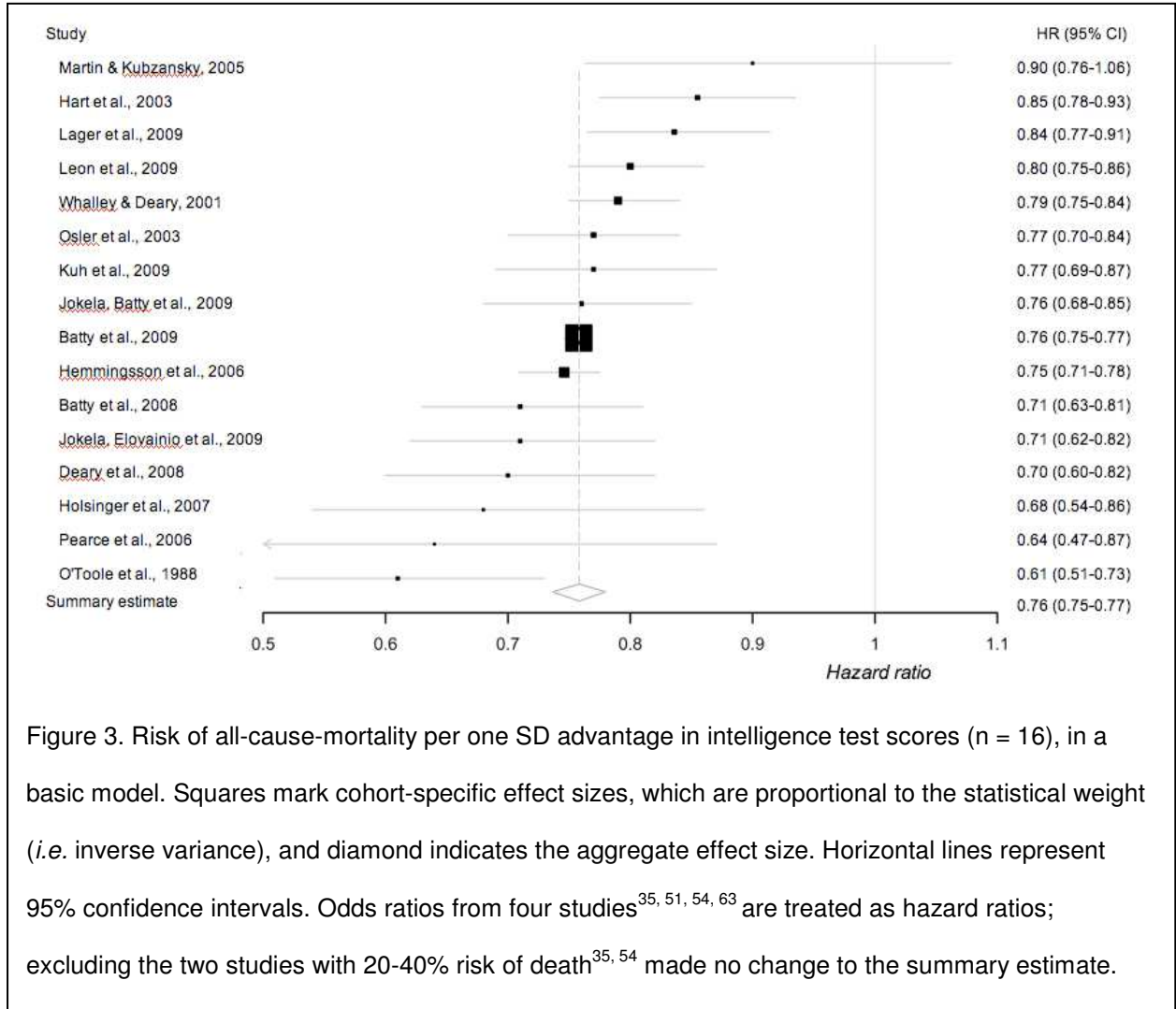


Figure 3. Risk of all-cause-mortality per one SD advantage in intelligence test scores ($n = 16$), in a basic model. Squares mark cohort-specific effect sizes, which are proportional to the statistical weight (*i.e.* inverse variance), and diamond indicates the aggregate effect size. Horizontal lines represent 95% confidence intervals. Odds ratios from four studies^{35, 51, 54, 63} are treated as hazard ratios; excluding the two studies with 20-40% risk of death^{35, 54} made no change to the summary estimate.

Figure 4.

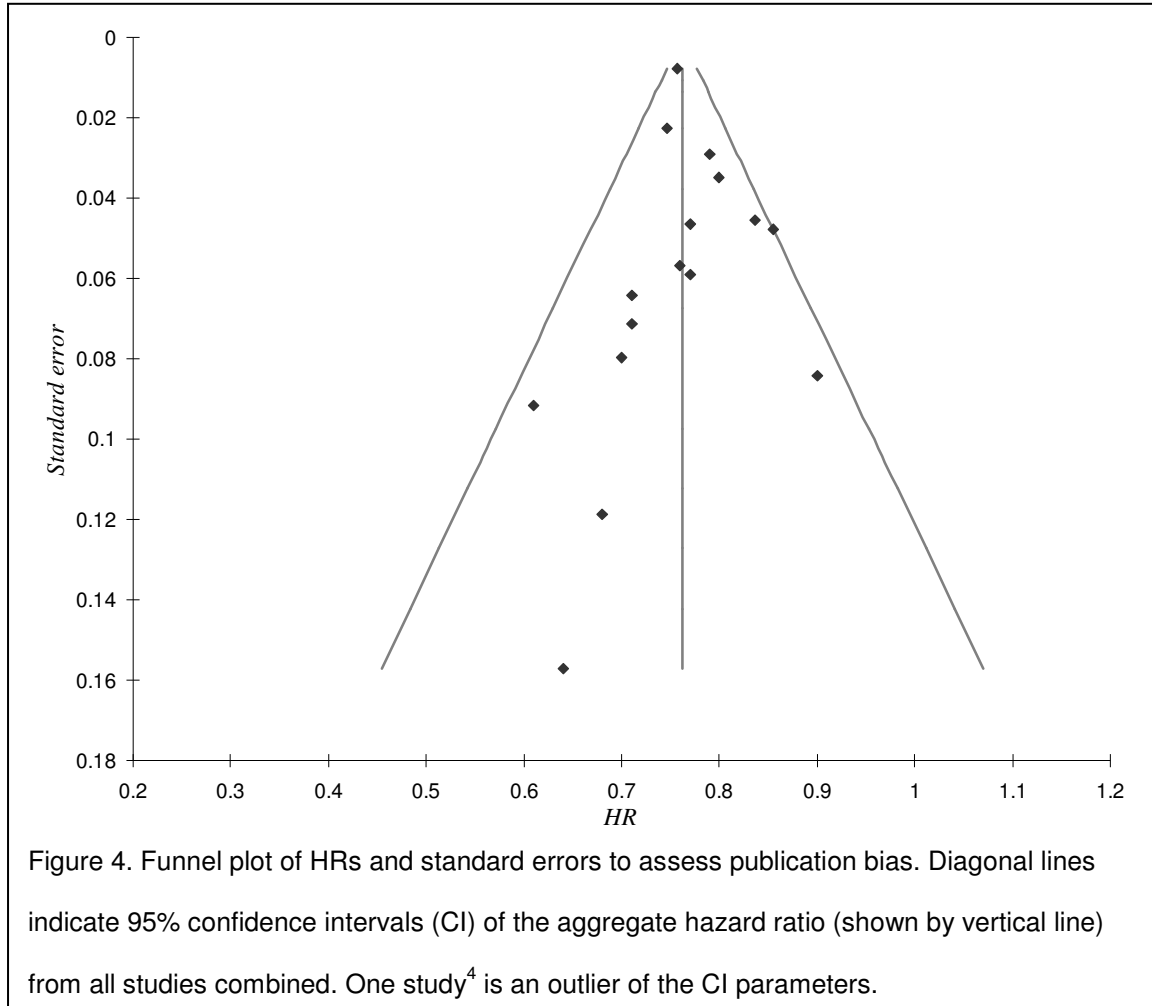


Figure 5.

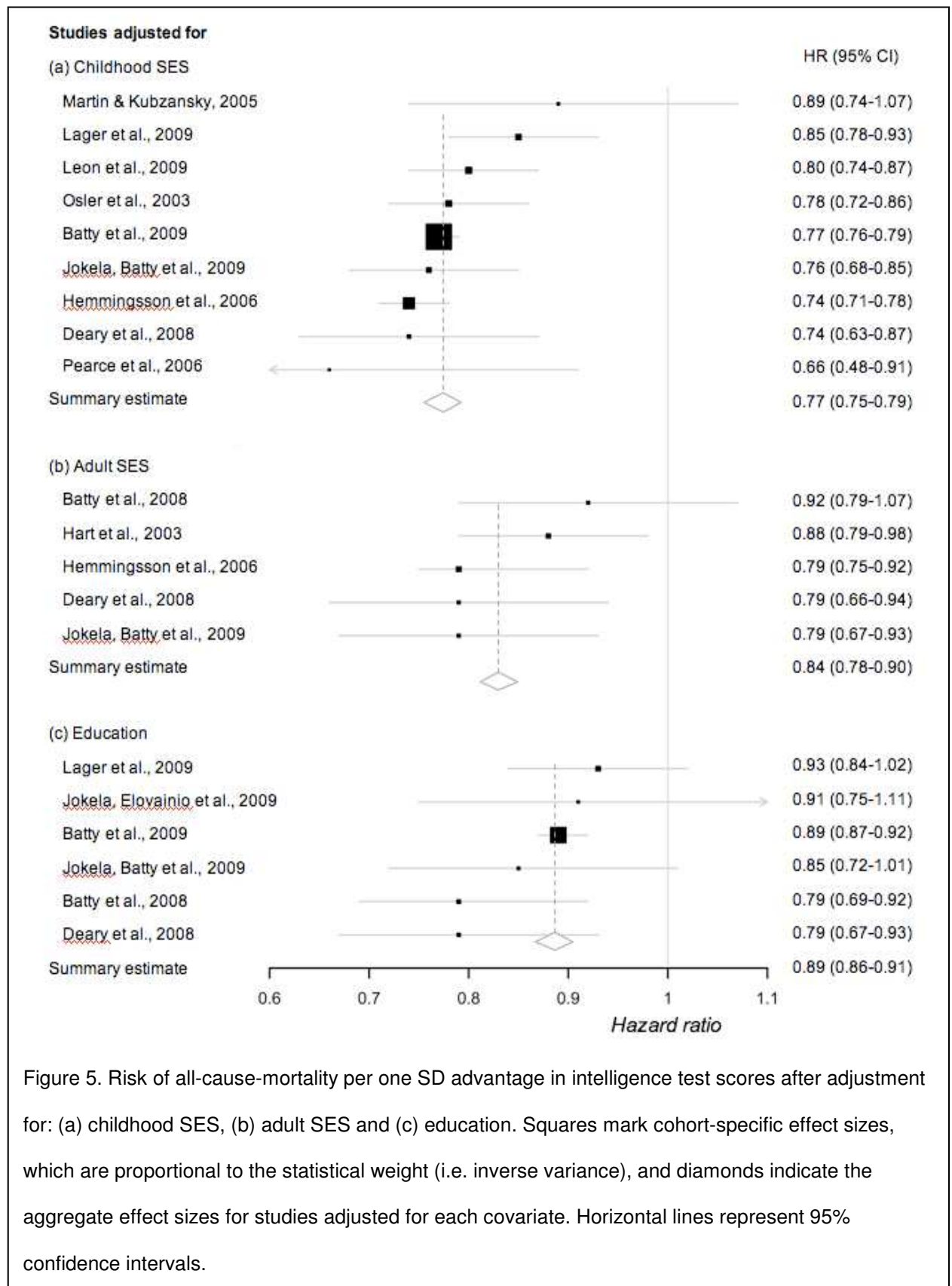


Figure 5. Risk of all-cause-mortality per one SD advantage in intelligence test scores after adjustment for: (a) childhood SES, (b) adult SES and (c) education. Squares mark cohort-specific effect sizes, which are proportional to the statistical weight (i.e. inverse variance), and diamonds indicate the aggregate effect sizes for studies adjusted for each covariate. Horizontal lines represent 95% confidence intervals.