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# Health-Related Quality of Life in Adults Born Extremely Preterm or Extremely Low Birthweight in the Post-Surfactant Era: A Longitudinal Cohort Study

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**Contributions:** JC, RM, LW, PA, AB, SG, GP, LP, GR, JW, KL conceived the study and CS wrote the first draft of the manuscript. JC, SG, JW acquired funding. JC was also involved with methodology, data curation, investigation, supervision/oversight and resources. RM, KL, and LW were also involved with methodology, data curation, investigation, formal analysis and supervision/oversight. GP, PA, JW, AB, SG, LP, GR provided supervision/oversight. All authors contributed to the revision of the manuscript, and take public responsibility for its content.

**Abbreviations:**

HRQoL - health-related quality of life.

HUI3 - Health Utilities Index Mark 3.

EP/ELBW - extremely preterm/extremely low birthweight.

NBW - normal birthweight.

IQ - intelligence quotient.

MD - median difference.

## Abstract

**Objectives:** To compare health-related quality of life (HRQoL) at 25 and 18 years in individuals born extremely preterm (EP; <28 weeks' gestation) or extremely low birthweight (ELBW; birthweight <1000 g) with term-born (≥37 weeks) controls. Within the EP/ELBW cohort, to determine whether HRQoL differed between those with lower and higher intelligent quotients (IQ).

**Methods:** HRQoL was self-reported using the Health Utilities Index-3 (HUI3) at 18 and 25 years by 297 EP/ELBW and 251 controls born in 1991-92 in Victoria, Australia. Median differences (MD) between groups were estimated using multiple imputation to handle missing data.

**Results:** Adults born EP/ELBW had lower HRQoL (median utility 0.89) at 25 years than controls (median utility 0.93; MD -0.040), but with substantial uncertainty in the estimate (95% confidence interval [CI] -0.088, 0.008), and a smaller reduction at 18 years (MD -0.016; 95% CI –0.061, 0.029). On individual HUI3 items , there was suboptimal performance on Speech (odds ratio (OR) 9.28; 95% CI 3.09, 27.9) and Dexterity (OR 5.44; 95% CI 1.04, 28.4) in the EP/ELBW cohort. Within the EP/ELBW cohort, individuals with lower IQ had lower HRQoL compared with those with higher IQ at 25 (MD -0.031; 95% CI -0.126, 0.064) and 18 years (MD -0.034; 95% CI -0.107, 0.040), but again with substantial uncertainty in the estimates.

**Conclusions:** Compared with term-born controls, young adults born EP/ELBW reported poorer HRQoL, as did those with lower IQ compared with those with higher IQ among the EP/ELBW cohort. Given the uncertainties, our findings need corroboration.

**What's already known on this subject**

The evidence for group differences in health-related quality of life (HRQoL) in adulthood between survivors born EP/ELBW and term-born controls, and how differences in HRQoL might alter with increasing age of survivors are unclear.

**What this study adds**

In our cohort of 25-year-olds born EP/ELBW in the surfactant era, HRQoL was lower than in term-born controls, and was a larger difference than when the cohorts were 18 years of age.

**How this study might affect research, practice, or policy**

This study suggests that there may be a reduction in HRQoL in survivors born EP/ELBW compared with term-born controls in the era since surfactant has been introduced into clinical practice. However, given the uncertainties in the estimates, the findings should be interpreted with caution until further research on this vulnerable population is completed. Whether the current findings persist into later adulthood remains to be determined.

## Introduction

Improvements in neonatal intensive care, especially the introduction of surfactant replacement therapy, have contributed to dramatic increases in the survival of infants born extremely preterm (EP, <28 weeks' gestation) or extremely low birthweight (ELBW, <1000 g) since the early 1990s.[1-3] However, survivors born EP/ELBW are more likely to develop motor, cognitive, educational and socio-emotional problems than their term-born (≥37 weeks) and normal birthweight (NBW; >2499 g) peers,[1 4-6] which might affect their health-related quality of life (HRQoL). The evidence for differences in HRQoL between individuals born EP/ELBW and at term in adulthood is less clear,[7-8] with most studies derived from cohorts born prior to the introduction of surfactant in the 1990s which did not include the most immature EP/ELBW infants due to lower survival rates in earlier eras. In addition, it is unclear whether HRQoL changes from adolescence to adulthood, when additional challenges may arise. Furthermore, individuals born EP/ELBW have lower intellectual quotients (IQs) than those born at term, which may affect their HRQoL.[9-11]

To address these gaps in the literature, this study aimed to (i) compare HRQoL in a geographic cohort of EP/ELBW individuals born in the era after surfactant was introduced into clinical care with term-born controls at 25 years, (ii) explore whether the differences in HRQoL between EP/ELBW and controls changed between late adolescence (18 years) and young adulthood (25 years), and (iii) determine whether individuals with a lower IQ within the EP/ELBW group reported different HRQoL at 18 and 25 years compared with those with a higher IQ. We hypothesised that adults born EP/ELBW would report worse HRQoL than controls, and, based on the literature,[12-14] the disparities in HRQoL between the groups would widen between 18 and 25 years of age. We also hypothesised that within the EP/ELBW group, those with lower IQ would report worse HRQoL than those with higher IQ.

## Methods

Participants comprised all survivors born EP/ELBW in the state of Victoria, Australia during 1991 and 1992 (*n*=297), and matched NBW and term-born controls (*n*=251) who survived to 25 years of age. Controls were randomly selected from births in the three tertiary maternity hospitals in Victoria and were matched for the expected date of birth of a survivor born EP/ELBW, the sex of the participant, whether English was the primary language spoken in the mother's country of birth, and the mother's health insurance status as a proxy for social class. Perinatal data were collected prospectively in the newborn period, as were outcome data from follow-up assessments of participants at 2, 5, 8, 18 and 25 years of age, corrected for prematurity.[5]

The Human Research Ethics Committees at the Royal Women's Hospital, Monash Medical Centre and Mercy Hospital for Women approved the initial and each of the follow-up studies (ethics approval for 25-year follow-up study is Project 08/06 (*ext*)). Participants gave written informed consent at ages 18 and 25 years.

Participants completed the Health Utilities Index Mark 3 (HUI3), a self-reported measure of HRQoL, at age 18 and 25 years. The HUI3 is a validated and reliable tool that can detect changes in quality of life over time,[15] and covers eight attributes: pain, cognition, emotion, dexterity, ambulation, speech, hearing, and vision. Each attribute is rated on a 5 or 6-point scale, with 1 representing normal function and 5 (or 6) indicative of severe impairment.[16] Each attribute is defined as sub-optimal if the level of function is reported as 2 or above.[17-18] The attribute scores are combined to an overall utility score that ranges from 0 to 1 (where 0 represents death and 1 represents perfect health), although values below 0 are possible, reflecting that some health states are identified as being worse than death. The HUI3 is an established tool that accurately measures HRQoL and is commonly used in population

health surveys.[19] Differences in utilities larger than 0.03 are deemed to be clinically important.[20-21]

Lower IQ was defined as having an IQ <-1 SD relative to the mean IQ of the term-born controls measured at age 18 years using the two-subtest version of the Wechsler Abbreviated Scale of Intelligence.[22]

Data were analysed using Stata Release 16.1.[25] The estimand of interest was the difference in median utilities between the birth groups, since the distribution of utilities was negatively skewed. Directed acyclic graphs (DAGs) were used to identify variables to control for confounding (see Supplementary Material Figure 1). Differences in median utilities at age 18 and 25 were estimated using quantile regression adjusted for the confounders of lower social class and lower maternal education. A similar approach was used to estimate the median differences in utilities between those with lower and higher IQ in the EP/ELBW group at age 18 and 25 years. Sub-optimal attributes at age 18 and 25 years were also compared between birth groups and between those with lower and higher IQ among the EP/ELBW participants using odds ratios [ORs] estimated using logistic regression, adjusted for lower social class and lower maternal education. A possible lack of independence of data from individuals arising from multiple births within the same family was accounted for by reporting all estimates with robust standard errors. In recognition of the increased potential for false positive findings that arise through the analysis of multiple outcomes, findings should be interpreted cautiously and in context with one another rather than in isolation.

Missingness DAGs were used to depict missingness assumptions and guide the treatment of missing data (see Supplementary Material Figure 2).[26] Based on the missingness DAG, multiple imputation was used to handle missing data in the primary analysis, although we also report the results from a complete case analysis for comparison. Imputations were generated using chained equations with 50 imputations and 20 iterations between each

imputation. Imputation was performed separately for each aim (and for the first aim, separately within each birth group) and for each attribute comparison. Imputation models included HRQoL at age 18 and 25 years, IQ, social class, maternal education, and auxiliary variables that were predictors of missingness and associated with HRQoL (further details of the multiple imputation approach are provided in the Supplementary Material)[27]. Estimates of the median difference [MD] and OR were obtained using Rubin's rules,[28] and are reported with 95% confidence intervals (CIs) and *p*-values.

As missingness in HRQoL may be associated with HRQoL itself (see Supplementary Figure 2), a sensitivity analysis was conducted where we assumed individuals with missing data had a mean utility 0.01, 0.03, 0.05, 0.10 and 0.20 lower than the individuals with observed data based on potential differences informed by clinicians. This analysis was performed using a pattern-mixture approach[29] (see Supplementary Material for details).

## Results

HRQoL data at age 25 years were available for 56% (165/297) of individuals born EP/ELBW and 52% (131/251) of controls, and at age 18 years for 65% (194/297) of individuals born EP/ELBW and 59% (148/251) of controls. Compared with adults born EP/ELBW who did not report HRQoL data at 25 years, those with data had a higher mean IQ at 8 and 18 years, and less disability at 8 years, but had similar neonatal and demographic characteristics (Table 1). Adults from the control group who provided data at 25 years were less likely to have a mother with less education or be from a lower social class. HRQoL at 8 and 18 years was similar for both EP/ELBW and control groups between those with and without HRQoL data at 25 years.

Based on the primary analysis using multiple imputation, adults born EP/ELBW reported a median utility of 0.89 at 25 years, compared with a median utility of 0.93 reported

by controls. Overall, HRQoL was lower for individuals born EP/ELBW than controls at age 25 years (MD -0.040; 95% CI -0.088, 0.008; $p$=0.10). Although a clinically important difference, the width of the CI indicates large uncertainty in this estimate as it includes values in which both birth groups have similar HRQoL (). The difference was smaller and the evidence weaker in the complete-case (Table 2) and sensitivity analyses (Supplementary Table 1). There was a smaller difference in median utilities at 18 years between EP/ELBW (0.92) and control groups (0.94; MD at 18 years -0.016; 95% CI -0.061, 0.029; $p$=0.47) (Figure 1A).The EP/ELBW group were more likely to report sub-optimal function for speech (OR 5.44, 95% CI 1.04, 28.4) and dexterity (OR 9.28; 95% CI 3.09, 27.9) than the control group at 25 years of age. The disparities in these attributes between groups were less obvious at age 18 years (Table 3 and Supplementary Table 3).

Among the EP/ELBW cohort, individuals with lower IQ rated their HRQoL lower than those with higher IQ at age 25 years (median utilities 0.86 vs 0.90, respectively), but with considerable uncertainty around the estimate (MD -0.031; 95% CI -0.126, 0.064;) (Figure 1B). Similar results were obtained from the complete case (Table 2) and sensitivity analyses (Supplementary Table 1). Utilities were also lower in those with lower IQ groups at 18 years (median utilities 0.88 vs 0.93, respectively; MD -0.034; 95% CI -0.107, 0.040). In the EP/ELBW cohort, those with a lower IQ had similar odds of sub-optimal performance in all areas of the HUI3 than those with higher IQ, including in the complete-case analysis (Supplementary Table 3).

For both birth and IQ groups, there were minimal differences in attributes such as vision, hearing, pain, and emotion (Table 3).

## Discussion

In the era after the introduction of surfactant to clinical care, individuals born EP/ELBW in this geographical cohort study had lower overall HRQoL compared with term-born controls

at age 25 years. The median utilities indicate that there is a tendency for at least one attribute to be at a sub-optimal level in both groups, but that these may be either readily corrected or do not prevent any activities.[16] The median difference in utilities between the two groups at age 25 years represents a clinically important difference, and the disparity between EP/ELBW and controls increased from late adolescence, implying that a change in the management of HRQoL for adults born EP/ELBW may be necessary. However, there was substantial uncertainty in the estimates reflected in the width of the 95% CIs. Further, within the EP/ELBW group, those who had lower IQ reported lower HRQoL compared with those who had a higher IQ, again with uncertainty in the estimate, and the gap between these groups remained stable since late adolescence. Within individual areas of the HUI3, those born EP/ELBW reported more problems than controls in Speech and Dexterity at 25 years of age only, although there were minimal differences in attributes such as vision, hearing, pain and emotion.

Poorer performance between birth groups at age 25 years for speech and dexterity, but not at 18 years, might relate to the increasing demands associated with age, including needing more self-reliance for independent living. Technology and the internet have enabled individuals to become increasingly connected, allowing adults born EP/ELBW to compare their QoL with an ever-growing reference group of individuals who are similar to themselves rather than the whole population, which parents may use. Of note, several studies have shown that reports by parents and self-reports differ,[13,17-18] emphasising the importance of informant ratings when evaluating HRQoL in cohorts born preterm.[30]

There are conflicting reports on HRQoL of cohorts born preterm compared with term-born controls. In a systematic review of 18 studies reporting HRQoL outcomes in late adolescence to early adulthood of very preterm (<32 weeks' gestation) or very low birthweight (<1500 g birthweight) cohorts compared with term/NBW controls 11 studies

concluded there was little to no difference between groups, three were inconclusive, and four reported lower HRQoL in the preterm group compared with controls.[7] That study was not able to perform a meta-analysis due to the heterogeneity within the cohorts, and to the different measures used to assess HRQoL. All but two of the cohorts were born prior to the introduction of surfactant into clinical care; as noted above, these results may not be generalisable to cohorts born after the introduction of surfactant. Four studies in the systematic review used a version of the HUI to assess HRQoL; in 3 studies there was little evidence for group differences (one of which is the 18-year outcomes of the cohort of the present study),[12 14 23] while the other study reported poorer HRQoL in the preterm group than controls.[13] Since then, the EPICure study in the UK has reported poorer HRQoL at age 19 years in those born <26 weeks' gestation compared with term-born controls as rated by parents and participants themselves.[30]

Other studies have also explored differences in HRQoL in subgroups within the preterm population, especially those with disability.[7] The findings are also conflicting,[7] which may in part be explained by the different definitions of "disability", comprising varying combinations of cerebral palsy, developmental disorders, sensorineural problems involving vision and hearing, and intellectual impairment, although no study has explored mild cognitive differences using the HUI3. In the present study, we found on average that EP/ELBW individuals with lower IQ had lower HRQoL at 18 and 25 years than EP/ELBW individuals with a higher IQ, a difference that remained stable between adolescence and young adulthood, but at both ages there was uncertainty around the estimated differences.

There are few reports of trajectories of HRQoL. Saigal et al reported trajectories of HRQoL across 3 time points, 12-16 years, 22-26 years and 29-36 years, in a Canadian cohort of ELBW participants born in the late 1970s.[14] ELBW participants with neurosensory impairment had poorer HRQoL than ELBW participants without neurosensory impairment,

and both of these subgroups had lower HRQoL than NBW controls at all 3 time points. There was a similar rate of decline with increasing age for all three groups. The EPICure cohort also provided evidence of a decline in parent-reported HRQoL between age 11 and 19 years.[30]

Strengths of our study include the geographic cohort of all infants born EP/ELBW and contemporaneously recruited term-born controls in Victoria, with follow-up to 25 years of age. Limitations relate to the attrition rate with increasing age of follow-up. Given the length of follow-up, study complexity, and considering that many families had left the state of Victoria, these follow-up rates were comparable to similar studies spanning decades.[31-33] The missing data in HRQoL at age 18 and 25 years were accounted for by using multiple imputation and we performed a comprehensive sensitivity analysis a range of assumptions about the missing data in these variables. Although our study is as large or larger than most others, there is still uncertainty in whether there is a clinically important difference in HRQoL between groups, reflected in the width of the 95% CI.

In an era with high survival outcomes, individuals born EP/ELBW are rating their HRQoL lower than term-born controls at age 25 years, which is a larger difference than at age 18 years. However, given the uncertainties in the estimated differences, our findings need corroboration. Longer-term surveillance is imperative, as life's challenges increase through adulthood, so that we can gain a holistic understanding of how HRQoL in survivors born EP/ELBW might change later in life.

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**Table 1:** Comparison of participants with and without HRQoL data at age 25 years

| | **EP/ELBW** | | **Term-Born Controls** | |
|---|---|---|---|---|
| | **HRQoL Data at age 25 *n* = 165** | **No HRQoL data at age 25 *n* = 132** | **HRQoL Data at age 25 *n* = 131** | **No HRQoL data at age 25 *n* = 120** |
| ***Baseline - neonatal*** | | | | |
| Male - *n* (%) | 74 (45%) | 63 (48%) | 53 (41%) | 68 (57%) |
| Gestational age (weeks) - mean (SD) | 26.6 (2.0) | 26.8 (1.8) | 39.3 (1.3) | 39.3 (1.3) |
| Birthweight (g) - mean (SD) | 884 (159) | 894 (163) | 3394 (462) | 3411 (409) |
| Cystic PVL - *n* (%)* | 7 (4%) | 11 (8%) | - | - |
| Intraventricular hemorrhage - *n* (%)* | 7 (4%) | 11 (8%) | - | - |
| Surgery in the newborn period - *n* (%) | 39 (24%) | 38 (29%) | 0 (0%) | 0 (0%) |
| Postnatal corticosteroids - *n* (%)* | 56 (34%) | 41 (31%) | - | - |
| Supplemental oxygen at 36 weeks - *n* (%)* | 65 (39%) | 56 (42%) | - | - |
| ***8-year outcomes*** | | | | |
| IQ - mean (SD) | 97.8 (16.1) – *N* = 158 | 91.8 (15.3) – *N* = 100 | 108.0 (11.4) – *N* = 127 | 99.7 (16.3) – *N* = 84 |
| HUI-2 - median (IQR) | 0.95 (0.87 – 1.00) – *N* = 153 | 0.93 (0.84 – 1.00) – *N* = 104 | 1.00 (0.95 – 1.00) – *N* = 127 | 0.97 (0.88 – 1.00) – *N* = 85 |
| Lower maternal education – *n* (%) | 81 (51%) – *N* = 160 | 59 (55%) – *N* = 108 | 34 (27%) – *N* = 127 | 44 (52%) – *N* = 85 |
| Lower social class - *n* (%) | 44 (28%) – *N* = 158 | 39 (35%) – *N* = 110 | 18 (14%) – *N* = 128 | 24 (28%) – *N* = 86 |
| No disability - *n* (%) | 106 (66%) – *N* = 161 | 51 (42%) – *N* = 122 | 119 (93%) – *N* = 128 | 67 (75%) – *N* = 89 |
| ***18-year outcomes*** | | | | |
| HUI3 - median (IQR) | 0.92 (0.82 - 1.00) – *N* = 134 | 0.96 (0.87 - 1.00) – *N* = 52 | 0.95 (0.88 - 1.00) – *N* = 101 | 0.94 (0.82 - 1.00) – *N* = 32 |
| *Sub-optimal attributes – n* (%): | | | | |
| Vision | 35 (26%) – *N = 136* | 6 (12%) – *N* = 52 | 23 (22%) – *N* = 106 | 5 (15%) – *N* = 33 |
| Hearing | 4 (3%) – *N =137* | 2 (4%) – *N* = 52 | 1 (1%) – *N* = 106 | 1 (3%) – *N* = 33 |
| Speech | 27 (20%) – *N* = 137 | 7 (13%) – *N* =52 | 13 (12%) – *N* = 105 | 5 (15%) – *N* = 33 |
| Ambulation | 4 (3%) – *N* = 137 | 4 (8%) – *N* = 52 | 0 (0%) – *N* = 105 | 3 (9%) – *N =33* |
| Dexterity | 8 (6%) – *N* = 135 | 3 (6%) – *N* = 52 | 1 (1%) – *N* = 105 | 0 (0%) – *N* = 33 |

| | | | | |
|---|---|---|---|---|
| Emotion | 41 (30%) – *N* = 135 | 13 (25%) – *N* = 52 | 28 (27%) – *N* = 103 | 9 (27%) – *N* = 33 |
| Cognition | 46 (34%) – *N* = 134 | 15 (29%) – *N* = 52 | 24 (23%) – *N* = 105 | 11 (35%) – *N* = 31 |
| Pain | 29 (21%) – *N* = 135 | 9 (17%) – *N* = 52 | 31 (30%) – *N* = 105 | 10 (31%) – *N* = 32 |
| IQ - mean (SD) | 98.0 (16.2) – *N* = 149 | 89.9 (15.3) – *N* = 75 | 108.6 (12.5) – *N* = 112 | 100.2 (14.6) – *N* = 43 |
| IQ <-1 SD – *n* (%) | 57 (38%) – *N* = 149 | 45 (60%) – *N* = 75 | 12 (11%) – *N* = 112 | 14 (33%) – *N* = 43 |
| ***25-year outcomes*** | | | | |
| HUI3 – median (IQR) | 0.91 (0.74 – 1.00) | - | 0.95 (0.85 – 1.00) | - |
| *Sub-optimal attributes – n* (%): | | | | |
| Vision | 55 (33%) – *N* = 165 | - | 42 (32%) – *N* = 131 | - |
| Hearing | 6 (4%) – *N* =165 | - | 2 (2%) – *N* =131 | - |
| Speech | 28 (17%) – *N* = 165 | - | 3 (2%) – *N* =131 | - |
| Ambulation | 8 (5%) – *N* =165 | - | 2 (2%) – *N* = 131 | - |
| Dexterity | 11 (7%) – *N* = 165 | - | 0 (0%) – *N* = 131 | - |
| Emotion | 60 (36%) – *N* = 165 | - | 44 (34%) – *N* = 131 | - |
| Cognition | 59 (36%) – *N* = 165 | - | 29 (22%) – *N* = 131 | - |
| Pain | 57 (35%) – *N* = 165 | - | 40 (31%) – *N* = 131 | - |

Notes: *Perinatal characteristics specific to EP/ELBW born infants (not measured for controls); IQR = interquartile range; SD = standard deviation. CHQ = child health questionnaire, WRAT-4 = Wide Range Achievement Test, Edition 4; PVL = periventricular leukomalacia; M-ABC = Movement Assessment Battery for Children; HUI = Health Utilities Index; SD = standard deviation. No Disability = no cerebral palsy, blindness, or deafness, and an IQ >=-1SD relative to controls . Sample sizes for outcomes at age 8 and 18 years listed (N) as not all individuals were assessed at those ages.

**Table 2:** Median differences (95% confidence intervals [CI]) in Health-Related Quality of Life compared between birth groups at age 18 and 25 years, and between those with lower and higher IQ among participants born EP/ELBW

| | ***Age 18 Years*** | | ***Age 25 Years*** | |
|---|---|---|---|---|
| **Method of Analysis** | **Median Difference (95% CI)** | ***p*-value** | **Median Difference (95% CI)** | ***p*-value** |
| **A. ELBW/EP vs controls** | | | | |
| Primary analysis: multiple imputation | -0.016 (-0.061, 0.029) | 0.47 | -0.040 (-0.088, 0.008) | 0.10 |
| Complete case analysis | -0.014 (-0.050, 0.023) | 0.46 | -0.026 (-0.065, 0.013) | 0.20 |
| **B. Lower intellectual quotient vs higher intellectual quotient measured at 18 years among EP/ELBW cohort** | | | | |
| Primary analysis: multiple imputation | -0.034 (-0.107, 0.040) | 0.36 | -0.031 (-0.126, 0.064) | 0.51 |
| Complete case analysis | -0.055 (-0.120, 0.011) | 0.10 | -0.063 (-0.170, 0.044) | 0.25 |

EP/ELBW = extremely preterm/extremely low birthweight.

**Table 3:** Odds ratios (95% confidence intervals [CI]) of sub-optimal function for each sub-scale attribute compared between birth groups at age 18 and 25 years, and between those with lower and higher IQ among participants born EP/ELBW, using multiple imputation to handle missing data, and adjusting for lower social class and lower maternal education

| | ***Age 18 Years*** | ***Age 25 Years*** |
|---|---|---|
| **Method of Analysis** | **Odds Ratio (95% CI)** | **Odds Ratio (95% CI)** |
| **A. ELBW/EP vs controls** | | |
| Vision | 1.14 (0.68, 1.89) | 1.08 (0.67, 1.76) |
| Hearing* | 1.48 (0.31, 7.09) | 2.71 (0.62, 11.8) |
| Speech* | 1.46 (0.83, 2.55) | 9.28 (3.09, 27.9) |
| Ambulation | 1.50 (0.41, 5.54) | 4.17 (0.89, 19.7) |
| Dexterity | 3.42 (0.82, 14.2) | 5.44 (1.04, 28.4) |
| Emotion | 0.79 (0.44, 1.43) | 1.01 (0.62, 1.63) |
| Cognition | 1.24 (0.67, 2.31) | 1.55 (0.95, 2.51) |
| Pain | 0.66 (0.37, 1.17) | 1.23 (0.76, 2.01) |
| **B. Lower intellectual quotient vs higher intellectual quotient measured at 18 years among EP/ELBW cohort** | | |
| Vision | 1.02 (0.50, 2.06) | 1.08 (0.55, 2.12) |
| Hearing* | 2.30 (0.44, 12.0) | 2.10 (0.42, 10.6) |
| Speech | 1.85 (0.75, 4.52) | 1.48 (0.64, 3.45) |
| Ambulation* | 1.26 (0.27, 5.82) | 3.41 (0.78, 14.9) |
| Dexterity | 1.04 (0.20, 5.38) | 1.94 (0.56, 6.71) |
| Emotion | 1.00 (0.46, 2.20) | 0.77 (0.39, 1.52) |
| Cognition | 1.37 (0.63, 2.94) | 1.56 (0.82, 3.00) |
| Pain | 1.26 (0.64, 2.50) | 1.69 (0.90, 3.17) |

EP/ELBW = extremely preterm/extremely low birthweight. Results from a logistic regression models adjusted for lower social class and maternal education.

*Lower social class omitted as *mi estimate* would not converge using logistic regression (likely due to social class being a perfect predictor).