Journal Pre-proof

Outcomes in Early Adulthood for Very Preterm and Very Low Birth Weight Individuals: Evidence from Multi-National Cohorts

Dr Hanifa Pilvar, Catia Nicodemo, Prof., Stavros Petrou, Prof., Brian A. Darlow, Prof., Dr. Paula van Dommelen, Kari Anne I Evensen, Prof., Dr. Sarah Harris, John Horwood, Prof., Dr. Karen Mathewson, Saroj Saigal, Prof., Louis Schmidt, Prof., Dieter Wolke, Prof., Lianne J. Woodward, Prof., Dr. Sungwook Kim

PII: S2950-5410(25)00058-4

DOI: https://doi.org/10.1016/j.jpedcp.2025.200196

Reference: JPEDCP 200196

To appear in: The Journal of Pediatrics: Clinical Practice

Received Date: 28 July 2025

Revised Date: 17 November 2025 Accepted Date: 25 November 2025

Please cite this article as: Pilvar H, Nicodemo C, Petrou S, Darlow BA, van Dommelen P, Anne I Evensen K, Harris S, Horwood J, Mathewson K, Saigal S, Schmidt L, Wolke D, Woodward LJ, Kim S, Outcomes in Early Adulthood for Very Preterm and Very Low Birth Weight Individuals: Evidence from Multi-National Cohorts, *The Journal of Pediatrics: Clinical Practice* (2026), doi: https://doi.org/10.1016/j.jpedcp.2025.200196.

This is a PDF of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability. This version will undergo additional copyediting, typesetting and review before it is published in its final form. As such, this version is no longer the Accepted Manuscript, but it is not yet the definitive Version of Record; we are providing this early version to give early visibility of the article. Please note that Elsevier's sharing policy for the Published Journal Article applies to this version, see: https://www.elsevier.com/about/policies-and-standards/sharing#4-published-journal-article. Please also note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2025 Published by Elsevier Inc.



Outcomes in Early Adulthood for Very Preterm and Very Low Birth Weight Individuals: Evidence from Multi-National Cohorts

Running Title: Early adulthood Outcomes of Very Preterm Birth

Authors and Correspondence:

Dr. Hanifa Pilvar (corresponding author)

Email: hanifa.pilvar@phc.ox.ac.uk Telephone: +44 7752275269

Affiliation: Nuffield Department of Primary Care Health Sciences, University of Oxford, UK

Prof. Catia Nicodemo

Email: catia.nicodemo@economics.ox.ac.uk

University of Oxford, UK

- Prof. Stavros Petrou

Email: stavros.petrou@phc.ox.ac.uk

University of Oxford, UK

- Prof. Brian A. Darlow

Email: brian.darlow@otago.ac.nz University of Otago, New Zealand

- Dr. Paula van Dommelen

Email: paula.vandommelen@tno.nl

The Netherlands Organization for Applied Scientific Research (TNO), Netherlands

- Prof. Kari Anne I Evensen

Email: karianne.i.evensen@ntnu.no

Norwegian University of Science and Technology, Norway

- Dr. Sarah Harris

Email: sarah.harris@otago.ac.nz University of Otago, New Zealand

- Prof. John Horwood

Email: john.horwood@otago.ac.nz University of Otago, New Zealand

Dr. Karen Mathewson

Email: mathewkj@mcmaster.ca

McMaster University

- Prof. Saroj Saigal

Email: saigal@mcmaster.ca

McMaster University

Prof. Louis Schmidt
 Email: schmidtl@mcmaster.ca
 McMaster University

- Prof. Dieter Wolke

Email: D.Wolke@warwick.ac.uk University of Warwick, UK

- Prof. Lianne J. Woodward

Email: lianne.woodward@canterbury.ac.nz University of Canterbury, New Zealand

- Dr. Sungwook Kim

Email: sungwook.kim@phc.ox.ac.uk

University of Oxford, UK

Data Availability Statement: The data used in this study were provided confidentially for this project and are not publicly available due to privacy and ethical restrictions. However, data can be requested from the RECAP Preterm Consortium, subject to approval and compliance with the consortium's data access policies.

Funding Statement: This project is funded by Leverhulme Trust project grant (RPG-2022-319)

Conflict of Interest Disclosure: The authors declare no conflict of interest.

Credit Author Statement: Hanifa Pilvar led the formal analysis and was responsible for drafting the original manuscript. The study concept and methodology were jointly developed by Hanifa Pilvar and Sungwook Kim, who also secured the project's funding. Supervision was provided by Stavros Petrou, Sungwook Kim, and Catia Nicodemo. All other authors contributed to the interpretation of findings and critically reviewed the manuscript for important intellectual content, providing input during the writing and editing process.

Abstract

Background: Advances in neonatal care have improved survival rates for very preterm (VP) and very low birth weight (VLBW) infants, yet their long-term outcomes into adulthood remain understudied.

Objectives: To assess the impact of VP/VLBW status on mortality, educational attainment, and labour market outcomes in early adulthood using data from the RECAP Preterm Project.

Methods: We used harmonised data from five nationally representative cohort studies in high-income countries (Canada, Germany, the Netherlands, New Zealand, and Norway) participating in the RECAP Preterm Project. Our sample included 2,493 individuals born VP/VLBW and 496 term-born controls. We employed coarsened exact matching (CEM) to compare adult outcomes between VP/VLBW and term-born individuals, and an instrumental variable (IV) approach—using maternal nulliparity—to estimate the marginal effect of gestational age within the VP/VLBW group.

Results: Mortality before adulthood was 16.7 percentage points higher among VP/VLBW individuals compared to term-born controls (95% CI: 13.2, 20.2). Among survivors, the likelihood of attaining less than secondary education was 4.3 percentage points higher (95% CI: -0.8, 9.4). Differences in economic activity and working hours were small and uncertain. Within the VP/VLBW group, each additional week of gestational age was associated with a 6.8 percentage point reduction in mortality (95% CI: -12.7, -1.0), with weaker associations for educational and labour market outcomes.

Conclusions: VP/VLBW birth is associated with elevated mortality and educational disadvantage in early adulthood. These findings highlight the importance of long-term support for this population beyond neonatal survival, particularly in education and development policy.

1 Introduction

The long-term consequences of preterm birth are becoming increasingly relevant as advances in neonatal care have significantly improved survival rates for preterm infants [1,2]. While the short-term health challenges associated with preterm birth are well documented, there is limited understanding of how early-life disadvantages shape outcomes in adulthood. Exploring associations between very preterm (VP) birth and very low birth weight (VLBW) with later-life indicators such as educational attainment and labour market participation can offer important insights for health and social policy.

A key challenge in studying long-term outcomes is the lack of data following preterm individuals into adulthood. Most studies focus on outcomes in childhood or adolescence, leaving a critical gap in our understanding of how early disadvantages evolve over the life course. This study addresses this limitation by using data from the RECAP Preterm Project [3,4,5,6], which harmonises multiple cohort studies of individuals born VP or VLBW across five high-income countries: Canada, Germany, the Netherlands, New Zealand, and Norway. These cohorts follow participants into early or mid-adulthood, enabling analysis of long-term educational and economic outcomes as well as mortality.

We adopt a two-pronged methodological approach. First, we use coarsened exact matching (CEM) to estimate differences in adulthood outcomes between VP/VLBW individuals and term-born controls, controlling for a range of covariates. Second, we assess how outcomes vary with each additional week of gestational age within the VP/VLBW group. To address potential endogeneity in gestational age, we employ an instrumental variable (IV) strategy, using nulliparity as an instrument—a variable shown in previous literature to be associated with gestational duration [7,8,9,10].

By combining harmonised data from multiple countries with rigorous empirical methods, this study seeks to deepen understanding of how early gestational disadvantages translate into adulthood outcomes and whether these effects vary incrementally with gestational age. The findings contribute to evidence on the life-course consequences of preterm birth and inform the design of policies aimed at supporting this vulnerable population.

2 Method

2.1 Study population

Our data comes from the RECAP Preterm Project [3,5,6], which is a consortium of longitudinal cohort studies of individuals born VP/VLBW in developed countries. Our analysis utilises data from five countries: the Netherlands (POPS¹), Germany (data from Bavaria, BLS²), New Zealand (NZ), Canada (CD) and Norway (NTNU³). We chose these countries since they have follow-up surveys in adulthood. Table 1 presents

¹ Project on Preterm and Small for Gestational Age Infants

² Bavaria Longitudinal Study Cohort

³ Norwegian University of Science and Technology

details of the birth year of each cohort, the number of adulthood follow-ups available, and the age of the cohorts at the time of these follow-ups. Additionally, the table outlines the inclusion criteria for each study and indicates whether a term-born control group is available for comparison.

All cohorts in our study were born in the 1980s, with the exception of the Canadian cohort, which is 1-8 years older than the median of other cohorts. For all five countries, we have follow-up data collected when the participants were in their mid-20s, which is the primary age range we focus on throughout this research. In terms of inclusion criteria, four countries included individuals based on very low birth weight (Birth Weight (BW) < 1500 grams) and/or very preterm birth (Gestation Age (GA) < 32 weeks). However, for Canada, the selection criteria are stricter, focusing on extremely low birth weight (BW<1000) and extreme preterm birth (GA<28), respectively.

We pooled data from all five countries to create a comprehensive dataset of 2493 individuals born very preterm and/or very low birth weight, referring to our combined sample as the VP/VLBW sample henceforth.

[Table 1 here]

2.2 Explanatory variables

To account for potential confounding factors, we selected control variables that were available across all five cohort studies, including birth outcomes (birth weight, Hadlock small for gestational age indicator [19], sex), parental characteristics (parental education), and neonatal outcomes (duration of assisted ventilation), all of which is measured at birth.

For parental characteristics, we used the education level of the least educated parent as a key variable⁴. To ensure consistency across all countries, we harmonised the years of education by constructing an indicator variable that equalled one if the least educated parent had lower secondary education (ISCED⁵ 0-2).

Regarding neonatal outcomes, we included the duration of assisted ventilation as a measure of neonatal health status.

2.3 Outcome measures

The outcomes of our study were measured when the participants were in their mid-20s. We selected variables that are consistently available across all datasets.

We began by examining the mortality rate prior to adulthood, as all individuals observed for educational or labour market outcomes are survivors. This means our analysis is inherently limited to those who represent the higher end of the distribution in terms of gestational length and/or birth weight, as individuals with poorer outcomes may not have survived to be observed.

2.4 Statistical analysis

Our analysis employs two approaches. First, we examined the differences in adult outcomes between the VP/VLBW sample and the term-born control group. Individuals in the control group were selected from infants born at term (GA≥37) in the same year. This approach focuses on comparing the levels of outcomes between

⁴ We also tried education level of the mother and the results were similar.

⁵ International Standard Classification of Education

our sample of interest and individuals with normal birth characteristics. Next, we concentrated on the VP/VLBW sample alone, investigating the impact of one additional week of gestational age on adulthood outcomes. This method allowed us to assess the marginal effect of gestational age within the VP/VLBW sample.

2.4.1 Matching method

To achieve the first goal, we matched the observations using the coarsened exact matching (CEM) method [11], based on all baseline characteristics available in both the VP/VLBW sample and the term born control group, such as sex, family background, maternal age, nulliparity and country (see [12], for similar choice of baseline variables). As the Netherlands (POPS) cohort did not include a term-born control group, data from the Netherlands were excluded from the analysis in this section. In addition, New Zealand data does not have any information about mortality prior to adulthood in the control group. Hence, we have to exclude New Zealand from the mortality analysis in this subsection.

For family background, we relied on parental education level as a consistent variable available across all countries and in both the VP/VLBW and control groups. We present results using the CEM method as our baseline. We used the cem function from the cem package in R with automatic cut-points. For robustness, we also report results using propensity score matching [13]. We used the nearest neighbour method via the MatchIt package in R, with a logistic regression model (GLM) to estimate propensity scores. Both methods are effective in evaluating the average treatment effect on treated individuals [14]; however, some studies suggest that CEM may

perform better with smaller number of baseline covariates for matching [15,16,17].

More specifically, we regressed the outcome variable of individual i (Y_i) on a treatment indicator, which takes the value of 1 if the individual was VP/VLBW and 0 otherwise (treatment_i), along with country fixed effects (c_i) to control for country-specific differences in outcome levels. The regression model is specified as:

$$Y_i = \alpha \cdot \text{treatment}_i + c_i + \epsilon_i \tag{1}$$

In this equation, α represents the average treatment effect on the treated individuals, accounting for country-specific fixed effects (c_i). ϵ_i is the error term.

2.4.2 Instrumental variable method

Our second approach involved investigating the effects of one extra week of gestational age if the infant was born VP/VLBW. For this purpose, we limited our observations to the VP/VLBW sample and regressed the outcome variables we previously mentioned on gestational age, along with a set of control variables for birth outcomes, family background, and neonatal care received.

Specifically, in equation 2, we regressed the outcome variable for individual i (Y_i) on the duration of gestational age (GA_i), along with a set of control variables X_i and country fixed effects c_i . For the control variables, we chose those that are commonly controlled for in the literature (See for example [18]) and included parental education and maternal age to represent family background, sex, an indicator for Hadlock measure of small for gestational age (SGA) [19], birth weight (BW) for birth outcomes, and the duration of assisted ventilation as a measure of neonatal

health status. We used clustered standard errors at country level to account for within country correlations⁶ [20].

$$Y_i = \beta \cdot GA_i + X_i + c_i + \varepsilon_i \tag{2}$$

There is a potential bias in estimating equation (2) because not all relevant characteristics that influence both gestational age and later outcomes are observed in our data. Therefore, there may be omitted variables (for example household income) that are correlated with both GA and the outcome variable Y_i . To address this issue, we used an instrumental variable (IV) for GA that is correlated with GA but is independent of the error term in equations 2.

Our proposed IV is an indicator of whether the mother is nulliparous. Several studies have demonstrated that nulliparity is associated with lower gestational age and an increased risk of prematurity [7,8,9,10]. The Norwegian cohort was excluded from the IV analysis because information on maternal nulliparity was not available in this dataset.

3 Results

3.1 Testing model hypothesis

3.1.1 matching method

Table 2 shows the balance of baseline variables before and after performing coarsened exact matching (CEM). As shown, there were fewer girls and more low-educated parents in the VP/VLBW group compared to the control group. Additionally, mothers in the VP/VLBW group tended to be younger, and there were fewer nulliparous

-

⁶ We used R package Ife to run the IV regressions.

mothers. After performing the matching, the differences between the two groups became smaller, and for most variables, the difference was no longer statistically significant, except for maternal age. However, it is worth noting that the difference in mean maternal age between the groups after matching was reduced to just one year, which mitigated the potential bias from this imbalance.

[Table 2 here]

3.1.1 Instrumental variable method

The instrumental variable (IV) method relies on two key assumptions: relevance, meaning the instrument must be strongly correlated with the endogenous variable, and exclusion restriction, which requires that the instrument—here, an indicator for nulliparity—affects the outcome (e.g. educational attainment or labour market participation) only through gestational age (GA). To assess relevance, we regressed GA on nulliparity. Table 3, column 1, shows a strong correlation, with an F-statistic of 198, well above the threshold for weak instruments [21]. Including covariates in column 2 reduced the correlation slightly, but the F-statistic remained above 29⁷. We accounted for non-random attrition using inverse probability weighting (IPW); the first-stage regression with IPW (column 3) yielded an even higher F-statistic, further confirming instrument strength.

[Table 3 here]

⁷ For a single endogenous variable and a single instrument, a first-stage F-statistic above 25 indicates that the instrument is not considered weak [20].

The exclusion restriction cannot be directly tested, but we adopted two strategies to assess its plausibility. First, prior studies have shown seasonal variation in GA [22,23,24]. In the New Zealand cohort, we used season of birth as an additional instrument and conducted a Sargan test [24] to assess whether the instruments were valid. The test yielded a p-value of 0.22, suggesting no evidence that the instruments were invalid or that the model violated the required statistical assumptions. Second, we tested whether nulliparity correlated with maternal characteristics such as smoking, socioeconomic status (SES), marital status, and ethnicity, known to be associated with both neonatal outcomes and social determinants [26,27]. We found no significant associations, supporting the validity of the exclusion restriction.

3.2 Summary statistics

Table 4 presents the summary statistics for four groups of variables for the VP/VLBW and control groups⁸. In our VP/VLBW cohort, the average gestational age was 30 weeks, and the average birth weight was 1,179 grams, which was approximately 10 weeks and 2200 grams lower than control group, respectively. There were fewer females in our VP/VLBW sample. Additionally, 43% of the VP/VLBW sample were SGA, which was a substantially higher proportion compared to the control cohort, where only 4.6% were SGA. Furthermore, half of the VP/VLBW individuals represented the first pregnancy of their mothers in both groups.

_

⁸ Please note that some variables are not available for some countries. For example, in the control group of Canada, we do not have information about maternal age. In, Norway, we do not have information about nulliparity neither in VP/VLBW nor in control group. This table only includes observations that have all birth outcome and parental characteristics measures in both VP/VLBW and control group.

In terms of parental education, In our VP/VLBW sample, 27% of infants have low educated parents which was significantly higher than the control sample by a 19 percentage point difference. Average maternal age was 27 years at the time of giving birth in the VP/VLBW sample which was two years lower than in the control group. On average, infants in the VP/VLBW cohort received 13 days of assisted ventilation following birth.

In terms of outcomes, Table 4 shows that approximately 28.3% of the VP/VLBW sample died before reaching adulthood. This is 35 times higher than the mortality rate for term-born children. We then consider four types of outcomes that are recorded in most of the cohorts. It is important to note that the number of observations decreases when analysing follow-up surveys due to attrition across all cohorts. Strategies to account for this attrition are discussed in the Methodology section.

We assessed the probability of being low educated, defined as having less than secondary education (ISCED 0-2 levels), with around 25% of respondents classified as low educated in the VP/VLBW sample, which was 8 percentage points higher than for the controls. Additionally, 80% of the VP/VLBW sample was economically active, meaning they were engaged in paid employment. Among those who were employed, the average working hours were 33 hours per week. This working hour information was available for all countries except Norway. We did not observe any significant difference in the mean of these two adulthood outcomes between the VP/VLBW and control groups.

[Table 4 here]

3.3 Comparing Outcomes Between VP/VLBW and Term-Borns

In this subsection, we compare the differences in the adulthood outcomes between the VP/VLBW sample and the control term-born group. It should be noted that for this analysis we included all countries except Netherlands which did not have a control group. The point estimate of the coefficient α of equation 1 is reported in Table 5.

The probability that an individual born VP/VLBW died before adulthood was 16.7 (95% CI: [13.2, 20.2]) percentage points higher compared to term-born controls. This considerable difference suggests that those who survive are a particularly select group within the VP/VLBW sample. Despite this, survivors still experience worse outcomes in adulthood in comparison to the control group. Specifically, they had a 4.3 (95% CI: [-0.8, 9.4]) percentage point higher probability of being low educated. We did not observe any statistically significant differences in terms of economic activity (95% CI: [-9, 2] percentage point) and working hours (95% CI [-2.092, 2.952] hours); however, the signs of the point estimates are consistent with the scenario of worse adulthood outcomes for individuals born VP/VLBW.

We have also used propensity score matching and compared results. Point estimates are similar in terms of the sign of the coefficient but they are different in size. For example, using the PSM method, the probability that an individual born VP/VLBW

died before adulthood was 9.8 (95% CI [5.7, 13.9]) percentage points higher compared to term-born controls and the probability of having low educated was 8 (95% CI [1.9, 14.1]) percentage point higher.

[Table 5 here]

3.4 The Value of Extra Gestational Weeks for VP/VLBW

In the previous subsection, we found evidence of lower educational attainment among VP/VLBW individuals in adulthood, although this association was only significant at 10% confidence interval. In this sub- section, we focus on investigating how gestational age influences adulthood outcomes within the VP/VLBW sample.

Table 6, panel A, displays the Ordinary Least Squares (OLS) estimates from equation 2. The findings show that each additional week of gestational age decreases the probability of death before reaching adulthood by 1.8 (95% CI [-2.8, -0.8]) percentage points. We do not observe any statistically significant effect in terms of other adulthood outcomes.

Panel B of Table 6 presents the results of the instrumental variable analysis, where maternal nulliparity was used as an instrument for gestational age. Compared with the ordinary least squares (OLS) results, the estimated effect of gestational age became stronger after accounting for potential bias from unobserved factors. This suggests that infants born at lower gestational ages may also be more likely to have other unmeasured disadvantages, such as neonatal complications or less favourable socioeconomic conditions, which influence later outcomes. We found that higher GA at birth significantly reduced the probability of mortality before adulthood by 6.8 (95% CI [-12.7, -1.0])

percentage points, underscoring the role of additional gestational time in enhancing survival rates. However, we did not observe any statistically significant effects of GA on other adulthood outcomes, such as low educational attainment (95% CI [-37.2, 3.6] percentage point), economic activity (95% CI [-29.4, 12.2] percentage point), or working hours (95% CI [-1.912, 3.411] hours).

One potential concern is that the duration of assisted ventilation may be censored for infants who died shortly after birth, which could bias the estimated effect of gestational age on later outcomes. However, our 2SLS results remain robust when we exclude all control variables or omit only the assisted ventilation variable (see Table A1). SGA might also be multicollinear with birthweight and gestation age. We omitted SGA from the list of covariates and the results remained stable (see Table A1). Another concern is the non-linearity in mortality with respect to GA. We tried probit and Logit model for the mortality and marginal effects are quite similar to the linear probability model.

[Table 6 here]

4 Discussion

This study contributes to the growing body of research on the life-course implications of very preterm birth and very low birth weight, highlighting substantial disparities in outcomes between individuals born VP/VLBW and their term-born counterparts. The observed mortality risk before adulthood was notably higher among the VP/VLBW group, even when limiting the sample to individuals discharged after birth. Among survivors, there was a greater likelihood of lower educational attainment. While estimates for labour market

participation and working hours did not show large effects, the direction of associations suggests potential long-term disadvantages in economic engagement.

Within the VP/VLBW group, we found that each additional week of gestation was associated with a marked reduction in the probability of mortality before adulthood, although the effect on educational and economic outcomes was less pronounced. These results are consistent with a gradient in vulnerability linked to gestational age, particularly with regard to survival, and point to the importance of early gestational development as a determinant of later outcomes.

Our findings are in line with earlier research from various European countries showing negative associations between preterm birth and educational achievement of school aged children [28,29,30,31,32]. Several studies emphasise that the effects are strongest for individuals born extremely preterm (<28 weeks) [32,33]. Additional birth-related indicators—such as being small for gestational age or having low Apgar scores—have also been linked to educational disadvantage in studies from Sweden and Denmark [28,35]. However, there is less evidence on the persistence of these disadvantages into adulthood, largely due to limitations in available data.

Our study builds on emerging research tracking preterm individuals into adulthood [36,37].

A meta-analysis, for example, found that VP/VLBW adults were less likely to complete secondary education or be employed and more likely to receive welfare benefits compared to term-born adults [34]. Our findings are broadly consistent with this pattern and strengthen the case for early developmental disadvantage persisting into adult life. While

we did not observe differences in all adulthood outcomes, this may reflect limited statistical power in later-life measures or delayed emergence of effects.

4.1 Strengths and Limitations

Key strengths of this study include the use of harmonised, nationally representative cohort data from multiple high-income countries and the application of rigorous methods, including coarsened exact matching and an instrumental variable approach. The availability of a term-born comparison group in four cohorts enhances interpretability.

However, the study is not without limitations. First, longitudinal follow-up into adulthood resulted in some attrition, which may introduce bias. Second, the Dutch POPS cohort did not include a term-born control group, reducing comparability. Third, heterogeneity in data collection and definitions across cohorts constrained our ability to harmonise variables and limited the scope for alternative instruments in the IV analysis. Fourth, findings may not generalise to lower-income settings with different healthcare systems. Fifth, the absence of strong associations with labour market outcomes may reflect low statistical power, as the number of VP/VLBW individuals who have reached adulthood remains modest. Sixth, the definition of adulthood in this study is limited to the mid-20s, whereas key transitions in education and employment may continue well into the 30s in contemporary contexts [38,39].

Please note that our adulthood outcomes are measured in early adulthood, and as mentioned earlier, many individuals in the control group are not low educated — that is,

they are still in higher education. Therefore, finding no statistically significant effects on labour market outcomes is expected. These effects may become more pronounced in later adulthood. Finally, as the participants in the cohorts in this study were born in the 1980s, the results reflect obstetrical and neonatal care practices of that era. Consequently, these findings may not fully represent outcomes for contemporary cohorts of extremely preterm infants, who have benefited from substantial advances in perinatal and neonatal medicine.

4.2 Implications for Policy and Practice

Our results underscore the need to address not only survival but also long-term developmental trajectories in individuals born very preterm. While mortality in high-income settings has decreased due to advances in neonatal care [40], many VP/VLBW individuals continue to face enduring cognitive, educational, and psychosocial challenges [41]. Structured early intervention programmes, including parental support, developmental therapy, and tailored educational services, could help mitigate these challenges. Schools may also play a critical role in supporting preterm-born children through individualised learning plans and better awareness of neurodevelopmental differences.

4.3 Directions for Future Research

Further research should explore the mechanisms through which gestational age affects long-term outcomes and how these are shaped by postnatal interventions, family environment, and socioeconomic status. Longitudinal studies extending into later adulthood

would help clarify whether the disadvantages seen in the mid-20s widen or diminish over time.

References

- Santhakumaran S, Statnikov Y, Gray D, Battersby C, Ashby D, Modi N. Survival of very preterm infants admitted to neonatal care in England 2008–2014: time trends and regional variation. Arch Dis Child Fetal Neonatal Ed. 2018;103(3).
- Butler V, Gaulard L, Sartorius V, Ancel PY, Goffinet F, Fresson J, Zeitlin J, Torchin H.
 Trends in the survival of very preterm infants between 2011 and 2020 in France. Arch
 Dis Child Fetal Neonatal Ed. 2024.
- 3. Bamber D, Collins HE, Powell C, Gonçalves GC, Johnson S, Manktelow B, Ornelas JP, Lopes JC, Rocha A, Draper ES. Development of a data classification system for preterm birth cohort studies: the RECAP Preterm Project. BMC Med Res Methodol. 2022;22(1):8.
- 4. Darlow BA, Horwood LJ, Woodward LJ, Elliott JM, Troughton RW, Elder MJ, Epton MJ, et al. The New Zealand 1986 very low birth weight cohort as young adults: mapping the road ahead. BMC Pediatr. 2015;15:1–8.
- 5. Teixeira R, Queiroga AC, Freitas AI, Lorthe E, Santos AC, Moreira C, Barros H. Completeness of retention data and determinants of attrition in birth cohorts of very preterm infants: a systematic review. Front Pediatr. 2021;9:529733.
- 6. Teixeira R, Doetsch J, Freitas AI, Lorthe E, Santos AC, Barros H, RECAP Preterm Consortium. Survey of data collection methods and retention strategies in European birth cohorts of children and adults born very preterm. Paediatr Perinat Epidemiol. 2022;36(5):706–14.

- 7. James S, Gil KM, Myers NA, Stewart J. Effect of parity on gestational age at delivery in multiple gestation pregnancies. J Perinatol. 2009;29(1):13–19.
- 8. Koullali B, Van Zijl MD, Kazemier BM, Oudijk MA, Mol BWJ, Pajkrt E, Ravelli ACJ. The association between parity and spontaneous preterm birth: a population based study. BMC Pregnancy Childbirth. 2020;20:1–8.
- 9. Lin L, Lu C, Chen W, Li C, Guo VY. Parity and the risks of adverse birth outcomes: a retrospective study among Chinese. BMC Pregnancy Childbirth. 2021;21(1):1–11.
- 10. Szyszka M, Rzońca E, Rychlewicz S, Baczek G, Ślezak D, Rzońca P. Association between parity and preterm birth—retrospective analysis from a single centre in Poland. Healthcare. 2023;11:1763.
- 11. lacus SM, King G, Porro G. Multivariate matching methods that are monotonic imbalance bounding. J Am Stat Assoc. 2011;106(493):345–61.
- 12. Van Beek PE, Leemhuis AG, Abu-Hanna A, Pajkrt E, Aarnoudse-Moens CSH, Van Baar AL, Andriessen P, Ravelli ACJ. Preterm birth is associated with lower academic attainment at age 12 years: a matched cohort study by linkage of population-based datasets. J Pediatr. 2022;251:60–66.
- 13. Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. Multivariate Behav Res. 2011;46(3):399–424.
- 14. Fullerton B, Pöhlmann B, Krohn R, Adams JL, Gerlach FM, Erler A. The comparison of matching methods using different measures of balance: Benefits and risks exemplified within a study to evaluate the effects of German disease management programs on

- long-term outcomes of patients with type 2 diabetes. Health Serv Res. 2016;51(5):1960–80.
- 15. Guy D, Karp I, Wilk P, Chin J, Rodrigues G. Propensity score matching versus coarsened exact matching in observational comparative effectiveness research. J Comp Eff Res. 2021;10(11):939–51.
- 16. King G, Nielsen R. Why propensity scores should not be used for matching. Polit Anal. 2019;27(4):435–54.
- 17. Ripollone JE, Huybrechts KF, Rothman KJ, Ferguson RE, Franklin JM. Evaluating the utility of coarsened exact matching for pharmacoepidemiology using real and simulated claims data. Am J Epidemiol. 2020;189(6):613–22.
- 18. Medlock S, Ravelli ACJ, Tamminga P, Mol BWM, Abu-Hanna A. Prediction of mortality in very premature infants: a systematic review of prediction models. PLoS One. 2011;6(9):e23441.
- 19. Hadlock FP, Harrist RB, Martinez-Poyer J. In utero analysis of fetal growth: a sonographic weight standard. Radiology. 1991 Oct;181(1):129-33.
- 20. Cameron AC, Miller DL. A practitioner's guide to cluster-robust inference. J Hum Resour. 2015;50(2):317–72.
- 21. Stock JH, Yogo M. Testing for weak instruments in linear IV regression. 2002.
- 22. Bodnar LM, Simhan HN. The prevalence of preterm birth and season of conception.

 Paediatr Perinat Epidemiol. 2008;22(6):538–45.

- 23. Darrow LA, Strickland MJ, Klein M, Waller LA, Flanders WD, Correa A, Marcus M, Tolbert PE. Seasonality of birth and implications for temporal studies of preterm birth. Epidemiology. 2009;20(5):699–706.
- 24. Hviid A, Laksafoss A, Hedley P, Lausten-Thomsen U, Hjalgrim H, Christiansen M, Olsen SF. Assessment of seasonality and extremely preterm birth in Denmark. JAMA Netw Open. 2022;5(2):e2145800.
- 25. Sargan JD. The estimation of economic relationships using instrumental variables. Econometrica. 1958;26(3):393–415.
- 26. Ion R, López Bernal A. Smoking and preterm birth. Reprod Sci. 2015;22(8):918–26.
- 27. Roustaei Z, Räisänen S, Gissler M, Heinonen S. Associations between maternal age and socioeconomic status with smoking during the second and third trimesters of pregnancy: a register-based study of 932,671 women in Finland from 2000 to 2015. BMJ Open. 2020;10(8):e034839.
- 28. Abel K, Heuvelman H, Wicks S, Rai D, Emsley R, Gardner R, Dalman C. Gestational age at birth and academic performance: population-based cohort study. Int J Epidemiol. 2017;46(1):324–35.
- 29. Berbis J, Einaudi MA, Simeoni MC, Brévaut-Malaty V, Auquier P, d'Ercole C, Gire C.

 Quality of life of early school-age French children born preterm: a cohort study. Eur J

 Obstet Gynecol Reprod Biol. 2012;162(1):38–44.
- 30. Bhutta AT, Cleves MA, Casey PH, Cradock MM, Anand KJS. Cognitive and behavioral outcomes of school-aged children who were born preterm: a meta-analysis. JAMA. 2002;288(6):728–37.

- 31. Eves R, Mendonça M, Baumann N, Ni Y, Darlow BA, Horwood J, Woodward LJ, et al.

 Association of very preterm birth or very low birth weight with intelligence in adulthood: an individual participant data meta-analysis. JAMA Pediatr. 2021;175(8):e211058.
- 32. Ream MA, Lehwald L. Neurologic consequences of preterm birth. Curr Neurol Neurosci Rep. 2018;18:1–10.
- 33. Ahlsson F, Kaijser M, Adami J, Lundgren M, Palme M. School performance after preterm birth. Epidemiology. 2015;26(1):106–11.
- 34. Baranowska-Rataj A, Barclay K, Costa-Font J, Myrskylä M, Özcan B. Preterm birth and educational disadvantage: heterogeneous effects. Popul Stud. 2023;77(3):459–74.
- 35. Ladelund AK, Bruun FJ, Slavensky JA, Ladelund S, Kesmodel US. Association of Apgar score at 5 minutes with academic performance and intelligence in youth: a cohort study. Acta Obstet Gynecol Scand. 2022;101(3):303–12.
- 36. Johnson RC, Schoeni RF. The influence of early-life events on human capital, health status, and labour market outcomes over the life course. BE J Econ Anal Policy. 2011;11(3).
- 37. Bilgin A, Mendonça M, Wolke D. Preterm birth/low birth weight and markers reflective of wealth in adulthood: a meta-analysis. Pediatrics. 2018;142(1).
- 38. Arnett JJ. Emerging adulthood: A theory of development from the late teens through the twenties. Am Psychol. 2000;55(5):469.

- 39. Saigal S, Day KL, Van Lieshout RJ, Schmidt LA, Morrison KM, Boyle MH. Health, wealth, social integration, and sexuality of extremely low-birth-weight prematurely born adults in the fourth decade of life. JAMA Pediatr. 2016;170(7):678–86.
- 40. Johnson S, Marlow N. Early and long-term outcome of infants born extremely preterm.

 Arch Dis Child. 2017;102(1):97–102.
- 41. Wolke D, Johnson S, Mendonça M. The life course consequences of very preterm birth.

 Annu Rev Dev Psychol. 2019;1(1):69–92.

A Appendix

A.1 Inverse probability weighting

In our analysis, we created Inverse Probability Weights (IPWs) to adjust for non-random attrition in outcome variables in adulthood surveys, which is related to the education level of parents. We first generated a binary indicator (responded) to capture whether a respondent has missing data on the outcome variables. Then, we estimated the probability of response using a logistic regression, where the outcome is the responded variable, and the predictor is the education level of the parents. This model provides predicted probabilities (predict) of response for each observation. Finally, we calculated the IPWs by taking the inverse of the predicted probability, with the formula: $weight = \frac{1+\exp(predict)}{\exp(predict)}$, which accounts for the likelihood of response based on the predictor variable. These weights will be used in subsequent regression models to correct for bias due to the non-random attrition.

A.2 Extra tables

Table A1: Two SLS effect of one extra gestational week on the outcomes for VP/VLBW (without any control variable and without assisted ventilation)

		Mortality	Low	Economically	Number of Working
		iviortanty	education	active	hours.
				(3)	(4)
Panel A: Tv	vo SL			. ,	
GA		-0.043***	-0.033	-0.026	0.903
		(0.014)	(0.025)	(0.053)	(1.002)
Observations		2,176	932	970	800
Controls		No	No	No	No
Country FE		Yes	Yes	Yes	Yes
Panel B: T	wo SI	LS without	assisted ve	ntilation in the	covariates
GA		-0.064**	-0.147	-0.060	1.209
		(0.031)	(0.112)	(0.107)	(1.518)
				,Q,	
Observations		1,701	905	940	779
Controls		Yes	Yes	Yes	Yes
Country FE		Yes	Yes	Yes	Yes
Panel C: Tv	vo SLS	S without S	GA in the d	ovariates	
GA		-0.049**	-0.081	-0.032	0.315
		(0.015)	(0.062)	(0.056)	(0.878)
Observations		1,636	887	918	761
Controls		Yes	Yes	Yes	Yes
Country FE		Yes	Yes	Yes	Yes
Mean of dep.	var.	0.11	0.27	0.79	33.3

Note: Standard errors are clustered at country level. Norway is excluded from the analysis as it does not have any information about nulliparity. Control variables are: maternal age, parental low education indicator, sex, SGA, birth weight. *p<0.1; **p<0.05; ***p<0.01

Tables

Table 1: Specification of data sets

Geographic region	Birth year	Number of adulthood follow-ups	Age at follow up	Selection criteria	Control group
Netherlands (POPS)	1983	3	19, 28, 35	GA< 32 or BW<1500 g	Not available
Bavaria, Germany (BLS)	1985-86	1	26-28	GA< 32 or BW<1500 g	Term born
New Zealand (NZ)	1986	2	22-23, 26-30	BW<1500 g	Term born
Canada (CD)	1977-82	2	24, 35	BW<1000 g	Term born
Norway (NTNU)	1986-88	1	26	BW<1500 g	Term born

Table 2: Balance of baseline Variables Before and After Matching

			VP/VL	C	ontrol			_
			BW					
Variable	Mean	SD	Ν	Mean	SD	Ν	Diff	p-value
Before								_
matching	0.47	0.50	1157	0.54	0.50	595	-0.07	0.01
Female								
Low Education	0.13	0.33	1157	0.08	0.28	595	0.04	0.01
Parent								
Mother Age	27.10	5.45	1157	28.90	4.63	595	-1.80	< 0.01
Nulliparous	0.47	0.50	1157	0.53	0.50	595	-0.07	0.04
After matching	3							
Female	0.50	0.50	758	0.49	0.50	510	0.02	0.57
Low Education	0.07	0.25	758	0.06	0.24	510	0.00	0.73
Parent								
Mother Age	27.70	4.83	758	28.80	4.55	510	-1.18	< 0.01
Nulliparous	0.50	0.50	758	0.54	0.50	510	-0.03	0.32

Note: The reported p-values reflect the results of two-sample t-tests comparing the VP/VLBW and control groups.

Table3: First stage regression of GA on nulliparity

	Dependent variable:					
	GA					
	(1)	(2)	(3)			
Nulliparous	0.719***	0.361**	0.360**			
	(0.051)	(0.066)	(0.063)			
Observations	1,636	1,636	1,636			
Adjusted R ²	0.184	0.694	0.692			
Country FE	Yes	Yes	Yes			
Controls	No	Yes	Yes			
IPW	No	No	Yes			
F-stat of excluded var.	198.75	29.91	32.65			

Note: Table shows the first stage regression of equation 2. In column 1 no control variable is added. In column 2, we add all sets of control

variables. In column 3 we use IPW. Standard errors are clustered at country level. Norway is excluded from the analysis as it does not have any information about nulliparity. Control variables are: maternal age, parental low education indicator, sex, SGA, birth weight, duration of assisted ventilation. *p<0.1; **p<0.05; ***p<0.01

Table 4: Summary statistics of variables of the study

	VP/VLBW				ontrol			
Variable:	Mean	SD	N	Mean	SD	N	Diff	p-value
Birth outcomes:								
Gestation age (weeks)	29.60	2.93	2493	39.80	1.01	496	-10.20	< 0.01
Female (%)	47.10	49.90	2489	53.80	49.90	595	-6.69	< 0.01
Birth weight (grams)	1179.0	323	2493	3450	481	496	-2270	< 0.01
Small for GA (%)	43.40	49.60	2489	4.64	21.00	496	38.76	< 0.01
Nulliparous (%)	49.90	50.00	2176	53.30	50.00	330	-3.47	0.24
Parental characteristics:								
Low educated parent (%)	27.10	44.50	1845	8.29	27.60	591	18.81	< 0.01
Mother's age (years)	27.20	5.15	2416	28.90	4.63	445	-1.72	<0.01
Neonatal outcomes:								
Duration of assisted vent. (d	ays) 12.70	28.00	2336	NA	NA	-	-	-
Adulthood outcomes:								
Mortality rate (%)	28.30	45.10	2493	0.81	8.95	496	27.49	< 0.01
Low education (%)	24.90	43.30	987	16.90	37.50	539	8.00	< 0.01
Number of working hours	33.40	14.80	802	34.20	13.90	344	-0.80	0.40
Economically active (%)	78.70	40.90	1025	79.30	40.50	542	-0.60	0.78

• Note: Mortality rate shows mortality at any time before 28 year survey which means 28.3% of 2493 live births died before reaching 28 years-old. The number of observations differs between outcomes in the control cohort because not all countries provided mortality data for the control group (New Zealand lacked such data), whereas educational data were available for all cohorts in control group. Consequently, the number of observations for the education variable (n = 539) is slightly higher than for mortality (n = 496). POPS does not have any control group. Mean shows the average, SD shows the standard deviation and N shows the number of observations. The reported p-values reflect the results of two-sample t-tests comparing the VP/VLBW and control groups. For binary variables (coded 0 and 100), the mean represents the percentage of individuals with the value 100, and the standard deviation is calculated from this binary coding.

Table 5: Coarsened exact matching between VP/VLBW and term born infants

Outcome var.:	Mortality	Low Economically		Number of Working
		Education	Active	Hours
Treated	0.167***	0.043*	-0.035	0.43
	(0.018)	(0.026)	(0.028)	(1.287)
Observations	1268	1268	1268	986
Country FE	yes	yes	yes	yes

Note: Netherlands is excluded from the analysis as it does not have a control cohort. New Zealand does not have mortality data for control cohorts and is omitted from the first

Journal Pre-proof

column. FE stands for fixed effects. Standard errors are reported in the parenthesis. *p<0.1; **p<0.05; ***p<0.01

Table 6: OLS and Two SLS effect of one extra gestational week on the outcomes for VP/VLBW

	Mortality	Low education	Economically active	Number of Working hours.
	(1)	(2)	(3)	(4)
Panel A: OLS				
GA	-0.018**	0.011	-0.005	0.292
	(0.005)	(0.011)	(0.006)	(0.265)
Panel B: Two SI	LS			
GA	-0.0682**	-0.168	-0.0862	0.749
	(0.0299)	(0.104)	(0.106)	(1.357)
Observations	1,636	887	918	761
Controls	Yes	Yes	Yes	Yes
Country FE	Yes	Yes	Yes	Yes
Mean of dep. var.	0.11	0.27	0.79	33.3

Note: Standard errors are clustered at country level. Norway is excluded from the analysis as it does not have any information about nulliparity. Control variables are: maternal age, parental low education indicator, sex, SGA, birth weight, duration of assisted ventilation. *p<0.1; **p<0.05; ***p<0.01

Journal Pre-proof

Declaration of interests		

 \Box The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☑ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Hanifa Pilvar reports financial support was provided by Leverhulme Trust. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.