







Profiles of Functioning in 5.5-Year-Old Very Preterm Born Children in France: The EPIPAGE-2 Study

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Objective: Very preterm born children are at risk for impairments in multiple neurodevelopmental domains, but outcomes vary between individuals. The present study aimed to distinguish subgroups with distinct profiles of functioning across motor, cognitive, behavioral, and psychosocial domains. These profiles were related to neonatal and social/environmental factors.

Method: The sample included 1977 children born very preterm (<32 weeks' gestation) in 2011 from the French population-based EPIPAGE-2 cohort. Using latent profile analysis, subgroups of children were distinguished based on their functioning at 5.5 years. The relation between outcome profiles and neonatal and social/environmental factors was tested using multivariable multinomial logistic regression analysis.

Results: Four subgroups with distinct outcome profiles were distinguished: no deficit in any domain (45%); motor and cognitive deficits without behavioral/psychosocial deficits (31%); primarily behavioral and psychosocial deficits (16%); and deficits in multiple domains (8%). Male sex (odds ratio [OR] = 2.1-2.7), bronchopulmonary dysplasia (OR = 2.1-2.8), low parental education level (OR = 1.8-2.1), and parental non-European immigrant status (OR = 2.3-3.0) were independently associated with higher odds for all suboptimal outcome profiles compared to the favorable outcome profile.

Conclusion: Among 5.5-year-old very preterm born children, subgroups can be distinguished with distinct outcome profiles that vary in severity, type, and combinations of deficits. This information is important for the development of interventions that are tailored to the needs of large subgroups of children across multiple domains of functioning. General neonatal and social/environmental factors may be useful for early identification of very preterm born children at risk for general rather than domain-specific impairments.

Key words: infant, premature; motor skills; cognition; neurodevelopmental disorders; latent class analysis

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Very preterm birth (<32 weeks' gestation) is associated with poorer intelligence,¹ academic outcomes,² and motor skills,³ and an increased risk for behavioral and socioemotional problems⁴ compared to full-term birth. These neurodevelopmental outcomes have not improved over the last decades,^{1,5,6} and impairments do not ameliorate when children grow older.⁷⁻¹⁰ Moreover, there is currently little evidence in support of intervention programs that meaningfully improve long-term neurodevelopmental outcomes after very preterm birth.¹¹⁻¹³ However, most studies have evaluated outcomes or intervention effects at the group level, without addressing the large heterogeneity in the population. Consequently, there is lack of insight into the specific needs of subgroups of children, and it remains poorly understood which children have an increased risk for impairment and why. This limits early identification of high-risk infants who may benefit

from close monitoring and early support, as well as development of tailored prevention and intervention strategies.

Recently, studies have started examining the heterogeneity in outcomes after extremely/very preterm birth by identifying subgroups of children with different outcome profiles. Burnett *et al.*¹⁴ found 4 subgroups of extremely preterm born children with distinct profiles of behavioral and social-emotional problems. In a study on intelligence and executive function in extremely preterm born children, 4 subgroups were distinguished that differed mainly in terms of severity of deficits.¹⁵ However, the extent to which a child is able to successfully adapt to and function in daily life is not determined by functioning in 1 isolated domain but rather by functioning across multiple interrelated developmental domains. Therefore, identification of subgroups based on functioning in multiple domains would give a better reflection of the overall impact of very preterm

birth and the proportions of children with and without impairments. In a small sample of 85 very preterm and 40 full-term children, Lean *et al.*¹⁶ recently described 4 subgroups based on cognitive, language, and motor performance, and behavioral and socioemotional difficulties at 5 years of age. Of the very preterm born children, 27% had no impairments; 45% showed a profile with mild cognitive, language, and motor problems; 13% had moderate to severe parent-rated behavioral/psychosocial difficulties; and for 15% these difficulties were reported only by teachers. Although limited by the small sample size, these findings suggest that meaningful subgroups with distinct profiles of difficulties across multiple developmental domains may be identified in the very preterm population.

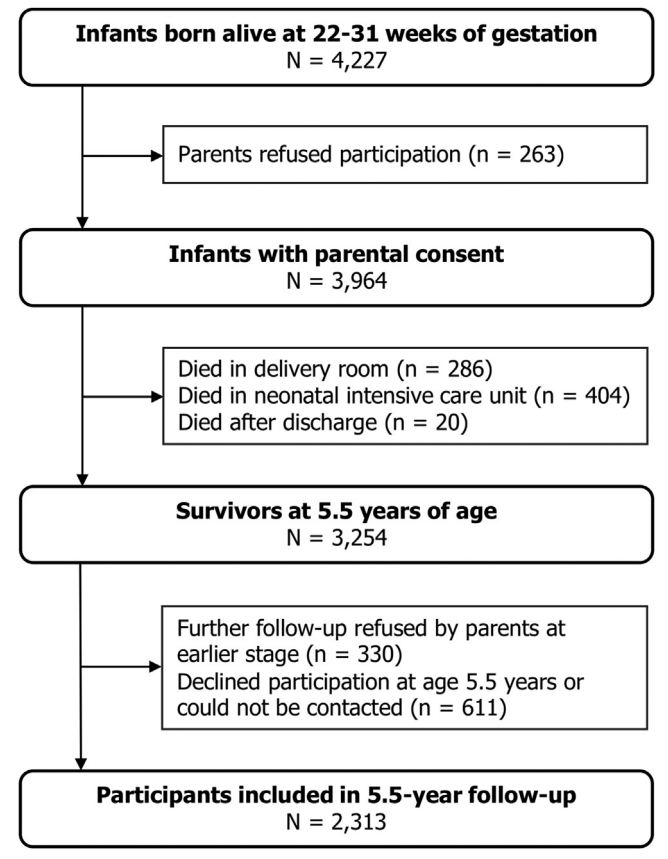
In addition to insight into distinct outcome profiles among very preterm born children, early identification of problems, support, and development of interventions will benefit from knowledge about which children are most likely to show which specific outcomes. Heeren *et al.*¹⁵ and Burnett *et al.*¹⁴ described differences in gestational age (GA), sex, social risk, and maternal mental health between profiles. Lean *et al.*¹⁶ found that family but not neonatal risk was associated with different outcome profiles. However, the lack of an association with neonatal factors could also be explained by the small number of very preterm born children included in that study. In moderately/late preterm born children, Johnson *et al.*¹⁷ found that GA, sex, preeclampsia, breastfeeding, and socioeconomic risk were associated with different cognitive and behavioral profiles at 5 years of age. The present study extends previous research by (1) identifying subgroups of children with distinct profiles of functioning across cognitive, motor, behavioral, and psychosocial domains in a large population-based cohort of very preterm born children in France (EPIPAGE-2) at 5.5 years of age, and (2) by studying the association between profiles and neonatal and social/environmental factors.

METHOD

Study Population

EPIPAGE-2 is a prospective population-based cohort study designed to follow up preterm infants born at 22 to 34 weeks GA in France in 2011 until age 12 years.¹⁸ The present study is focused on outcomes of children born very preterm (<32 weeks' gestation) at 5.5 years of age. Participants were recruited at birth. From all live-born infants at 22 to 31 weeks GA, 3,254 children were alive and eligible for follow-up at age 5.5 years, of whom 2,313 children participated in assessments (71.1%). Participant flow from birth to follow-up at 5.5 years is presented in Figure 1. One infant born at 22 to 23 weeks' gestation survived, who was

FIGURE 1 Participant Flow From Birth to Follow-Up at 5.5 Years of Age



lost to follow-up at 5.5 years. Infants born at 22 to 26 weeks GA were recruited during an 8-month-period and infants born at 27 to 31 weeks GA during 6 months.

A sample of 592 full-term peers (singletons, 37-40 weeks GA, born between September 27 and December 5, 2011) was included as a reference sample. This sample was recruited from the population-based ELFE cohort (N = 18,040)¹⁹ to be assessed following the EPIPAGE-2 protocol. For financial and organizational reasons, 600 children could be assessed, which was sufficient to obtain estimates of main outcomes with good precision.²⁰ From all eligible children (N = 3,430), 2,846 parents agreed to participate, of whom 1,405 parents were contacted. Recruitment was terminated after inclusion of the desired number of 600 children.²⁰

Cognitive, Motor, Behavioral, and Psychosocial Functioning

The Wechsler Preschool and Primary Scale of Intelligence, Fourth Edition (WPPSI-IV), was used to assess cognitive abilities, using the indices verbal comprehension, visuospatial ability, fluid reasoning, working memory, and

processing speed. Index scores were derived using age-specific norms. Indices have adequate to good internal consistency ($r = 0.8-0.9$) and sufficient to good test–retest reliability ($r = 0.6-0.8$).²¹

The Movement Assessment Battery for Children, Second Edition (MABC-II)²² is a battery to test motor abilities in 3 domains: manual dexterity, aiming and catching, and balance. Subtests for the age band 3 to 6 years were administered. The test has age-standardized norms, and test–retest reliability was sufficient to good for all domains ($r = 0.7-0.8$).²²

Parents rated their child's behavior on the 25 items of the Strengths and Difficulties Questionnaire (SDQ) to assess the degree of emotional symptoms, conduct problems, hyperactivity/inattention, and peer relationship problems. Subscale scores were computed only if the number of missing items per subscale was <3 (see <http://www.sdqinfo.org>). Internal consistency was low to moderate for peer and conduct problems ($\alpha = 0.5-0.6$) and sufficient for emotional and hyperactivity/inattention problems ($\alpha = 0.7-0.8$).²³ Test–retest reliability was sufficient for all subscales ($r = 0.7$).²³

The Social Communication Questionnaire (SCQ) was filled out by parents to rate symptoms of autism spectrum disorders on 40 items across 3 domains: social interaction, communication, and repetitive behavior. In line with Johnson *et al.*,²⁴ subscale scores were computed only for cases with <3 missing items on the repetitive behavior subscale and <4 missing items on the communication and social interaction subscales. In these cases, missing values were replaced by the most frequent value (0 or 1) within each subscale. Internal consistency of the SCQ was found to be good ($\alpha = 0.8$).²⁵

Predictors of Outcome Profiles

Potential predictors of profiles of functioning were chosen based on previous studies,¹⁴⁻¹⁷ their known impact on brain function, and the incidence.¹ The following perinatal factors were included: sex, GA (weeks), small for gestational age (SGA; birthweight $<10^{\text{th}}$ percentile for GA and sex on French intrauterine growth curves²⁶), bronchopulmonary dysplasia (BPD; ≥ 28 days of $>21\%$ oxygen supply plus $<30\%$ oxygen (moderate) or $\geq 30\%$ oxygen and/or positive pressure (severe) at 36 weeks postmenstrual age²⁷), severe brain lesions (intraventricular hemorrhage grade 3/4, cystic periventricular leukomalacia), late-onset sepsis (positive blood culture and ≥ 5 days of antibiotics treatment), and receipt of breast milk at discharge (either partly or exclusively). Socioeconomic factors were measured at 5.5 years and included parental education level, as determined by the highest level of both

parents, or 1 parent in single-parent families (low: high school or lower; intermediate: post-secondary or short tertiary education; high: bachelor degree or higher), non-European country of birth of 1 or both parents (Maghreb, other African, other country), parent(s) without employment (one or both parents being unemployed or inactive), and single parenthood.

Procedure

The study was approved by the National Data Protection Authority (CNIL DR-2016-290), the Consultative Committee on Treatment of Information on Personal Health Data for Research Purposes (no. 16.263), and the Committee for Protection of People Participating in Biomedical Research (no. 2016-A00333-48). Written informed consent from both parents was required for participation in the 5.5-year follow-up. Participants were invited at one of the regional centers for assessments. The MABC-II was administered during medical assessment by a pediatrician. The WPPSI-IV was part of a battery of neuropsychological tests administered by trained psychologists. The SDQ and SCQ were completed by parents.

Statistical Analysis

Data Weighting. Data of the very preterm sample were weighted to account for differences in the recruitment duration between children born at <27 weeks GA and 27 to 31 weeks GA. Data of the ELFE cohort,¹⁹ from which the full-term sample was selected, were weighted to increase the representativeness of the sample for the general population of term-born children in France in 2011. More details are provided elsewhere.^{19,20}

Latent Profile Analysis. Mplus version 8 (Muthén and Muthén, 1998-2017) was used for all analyses. Mixture modeling, more specifically latent profile analysis (LPA), was performed to distinguish subgroups of very preterm born children based on 15 indicator variables, that is, subscale scores of the WPPSI-IV, MABC-II, SDQ, and SCQ. Data of the full-term sample were not included in the LPA, but weighted means and SDs were used to indicate the degree of impairments in the very preterm sample. The model was adjusted for clustering of children within families with multiples. Missing data on indicator variables were treated using full-information maximum likelihood estimation.²⁸ Models with an increasing number of profiles were tested. Bayesian information criterion (BIC), sample-size adjusted BIC (aBIC), and Lo–Mendell–Rubin (LMR) likelihood-ratio test were used to guide model selection.²⁹ Discrimination between profiles is indicated by the entropy. Classification probabilities describe the

probability that a case is assigned to a certain subgroup instead of the other subgroups. In addition, the decision on the number of profiles was informed by the meaningfulness and size of subgroups.³⁰ Subsequently, relations between latent profiles and potential risk factors were explored in a multivariable multinomial logistic regression model, adjusting for classification error introduced with profile assignment³¹ by using the R3STEP command implemented in Mplus. For GA, both linear and nonlinear relations with latent profiles were considered. Missing values in predictor variables were imputed using Bayesian estimation with 20 imputed datasets²⁸ based on available data on all indicators and predictors in the model.

RESULTS

Sample Characteristics and Missing Data

A total of 1,977 of the 2,313 very preterm born children who participated in the follow-up at 5.5 years (85.5%) completed at least 3 of the 4 tests. This sample was used for the LPA. Sample characteristics are shown in Table 1. The percentage of missing data for the 15 indicators was 12%, with 94.2% of the sample having ≤ 1 missing values. The percentage of missing values across the 11 predictors was 16.7%. The vast majority of cases (93.4%) had missing values for ≤ 1 predictor. The percentages per variable are presented in Table S1, available online. Missing data for indicators were associated with observed values on other indicators. The same was true for missing data for predictors (data available from author).

The study sample ($N = 1,977$) was compared with very preterm born children who participated but had too many missing values on the indicator variables (ie, more than 1 of the 4 tests was not completed) ($n = 336$) and with children who were alive and eligible for follow-up but did not participate in the 5.5-year follow-up ($n = 941$) on neonatal and parental characteristics and presence of disabilities (Table 1). Percentage of parent(s) with a low education level, without employment, born outside of Europe, or single parenthood was lower among very preterm born children included in the analysis than among those not included. These groups did not differ on neonatal characteristics, except that a higher percentage of children in the study sample received breast milk at discharge. The percentage of children with cerebral palsy and moderate to severe cognitive impairment was significantly lower in the study sample compared to the group of children who did not complete more than 1 of the tests. The full-term reference sample was representative for the general population in terms of sex, single parenthood, maternal country of

birth, and maternal education level (see Table S2, available online).

Model Selection

Model fit statistics are presented in Table S3, available online. LMR pointed to a model with 4 latent profiles. BIC and aBIC continued to decrease, although to a lesser extent, when fitting a 5-profile model, but this resulted in 1 profile comprising a very small proportion of the sample (4%). In the 4-profile model, 1 of the profiles also represents a relatively small percentage of children (8%). However, this profile is also distinguished in the 3-profile model and describes an important subgroup of children, namely those children with the poorest outcomes. Considering both statistical information and qualitative differences between profiles, the 4-profile model was selected.

Profiles of Functioning

The 4 profiles are plotted in Figure 2. Two groups of profiles can be distinguished: 1 profile describing favorable outcomes across domains (45%) and 3 profiles describing suboptimal functioning (55%). The first is called the “favorable outcomes” profile, because functioning is highly similar to the full-term sample in all domains (within 0.5 SD), with significantly less symptoms of hyperactivity/inattention, conduct, and social problems. From the profiles describing suboptimal functioning, the “behavioral/psychosocial difficulties” profile was found in 16% of the children and characterized mainly by mild behavioral and psychosocial difficulties (~ 1 SD below full-term children). In contrast, 31% showed low-average to mildly impaired motor and cognitive functioning (~ 1 SD below full-term children) in the absence of behavioral and psychosocial difficulties (“motor/cognitive deficits” profile). Finally, a relatively small percentage of children (8%) showed a profile with mild to moderate difficulties in all domains (~ 1 to >2 SD below full-term children), except conduct and emotional problems. This profile is called “multi-domain impairments.”

Relation With Risk Factors

Figure 3 shows the results of the multivariable multinomial logistic regression model. For GA, a linear term was included in the model since bivariate regression analyses showed significant effects for the linear as opposed to quadratic ($p = .57-.76$) and cubic ($p = .23-.85$) terms. Male sex, BPD, low parental education level, parent(s) being born outside of Europe, and having parent(s) without employment were independently associated with increased odds of all 3 suboptimal outcome profiles in comparison to

TABLE 1 Characteristics of Very Preterm Born Children Included and Not Included in the Analysis

	Very preterm study sample (N = 1,977)	More than 1 in 4 tests not completed (n = 336)	No participation in 5-year follow-up (n = 941)	p
Neonatal characteristics				
Sex, % male	52.5	49.5	52.9	.44
Gestational age, wk, mean (SD)	28.9 (1.9)	29.1 (1.8)	29.0 (1.9)	.73
Birth weight, g, mean (SD)	1217.0 (345.0)	1256.4 (332.2)	1239.7 (342.7)	.89
Small for gestational age, %	36.5	32.5	34.8	.22
Multiple birth, %	33.0	36.2	29.8	.03 ^a
Breast milk at discharge, %	52.8	47.8	35.7	<.001
Moderate/severe bronchopulmonary dysplasia, %	12.1	11.1	9.9	.15
Severe brain lesions, %	5.0	4.5	5.8	.50
Late-onset sepsis, %	21.7	19.5	18.5	.07
Parental characteristics				
Parental education level at 5.5 y				
High school or lower	37.4	52.2	NA	<.001
Post-secondary or short tertiary education	26.0	20.8	NA	
Bachelor degree or higher	36.6	27.0	NA	
Maternal education level at birth				
Less than upper secondary education	45.3	56.3	68.4	<.001
Upper/post-secondary or short tertiary education	24.5	19.5	16.8	
Bachelor degree or higher	30.2	24.2	14.8	
Parent(s) without employment at birth, %	32.6	42.1	54.9	<.001
Parent(s) without employment at 5.5 y, %	41.1	53.6	NA	<.001
Parental place of birth				
Metropolitan France	70.1	65.4	56.3	<.001 ^b
French overseas territories	5.3	5.8	5.8	
Other European country	2.7	4.9	4.3	
Maghreb country	9.5	13.5	12.9	
Other African country	7.5	6.5	12.1	
Other country	4.8	4.0	8.7	
Single parenthood at birth	7.1	8.4	13.4	<.001 ^c
Single parenthood at 5.5 y	13.3	12.0	NA	.50
Disability at age 5.5 y				
Cerebral palsy, ^d %	5.3	8.1	NA	.02
Moderate/severe neurosensory impairment, ^e %	1.6	2.7	NA	.48
Motor impairment, ^f %	12.8	15.1	NA	.56
Cognitive impairment, ^g %	11.9	22.9	NA	.02

Note: Percentages, means, SD, and corresponding χ^2 and t tests were weighted according to sampling weights.

^aDifferences were not significant between the study sample and children who did not complete more than 1 of the 4 tests [$\chi^2(1) = 1.70, p = .19$] and between the study sample and children who were lost to follow-up [$\chi^2(1) = 3.79, p = .05$].

^bFor the difference between the study sample and children who did not complete more than 1 of the 4 tests, test statistics were $\chi^2(5) = 314.01, p = .02$.

^cDifferences were not significant between the study sample and children who did not complete more than 1 of the 4 tests [$\chi^2(1) = 0.84, p = .36$].

^dAny level of severity (Gross Motor Function Classification System level 1 or higher).

^eBinocular visual acuity <3.2/10 and/or uni- or bilateral hearing loss >40 dB not or partially corrected with hearing aids.

^fTotal score Movement Assessment Battery for Children II <5th percentile of the full-term sample.

^gFull Scale IQ >2 SD below the mean of the full-term sample.

the favorable outcome profile. For example, when all other risk factors in the model were taken into account, boys had 2.7 times higher odds than girls to show a profile of behavioral/psychosocial difficulties as opposed to a favorable outcome profile. When controlling for other factors, GA and SGA were negatively associated only with a profile of multi-domain impairments and not with behavioral/psychosocial or motor/cognitive deficits. Late-onset sepsis, receipt of breast milk, and single parenthood were not independently associated with any profile. Table S4, available online presents characteristics of the 4 subgroups according to outcome profile, classified based on the highest probability for 1 of the profiles.

Further specification of results according to parental place of birth is shown in Table S5, available online. For children from parent(s) born in Maghreb or other African countries, the odds for all 3 suboptimal profiles were increased compared to children of whom both parents were born in Metropolitan France/Europe. For children from parent(s) born in other non-European countries or in French overseas territories, odds were higher for behavioral/psychosocial and multi-domain impairments but not motor/cognitive deficits. Results for the latter group may be driven mainly by the large proportion of these children who were born in the overseas territories themselves (70%), which was associated with increased odds for multi-domain

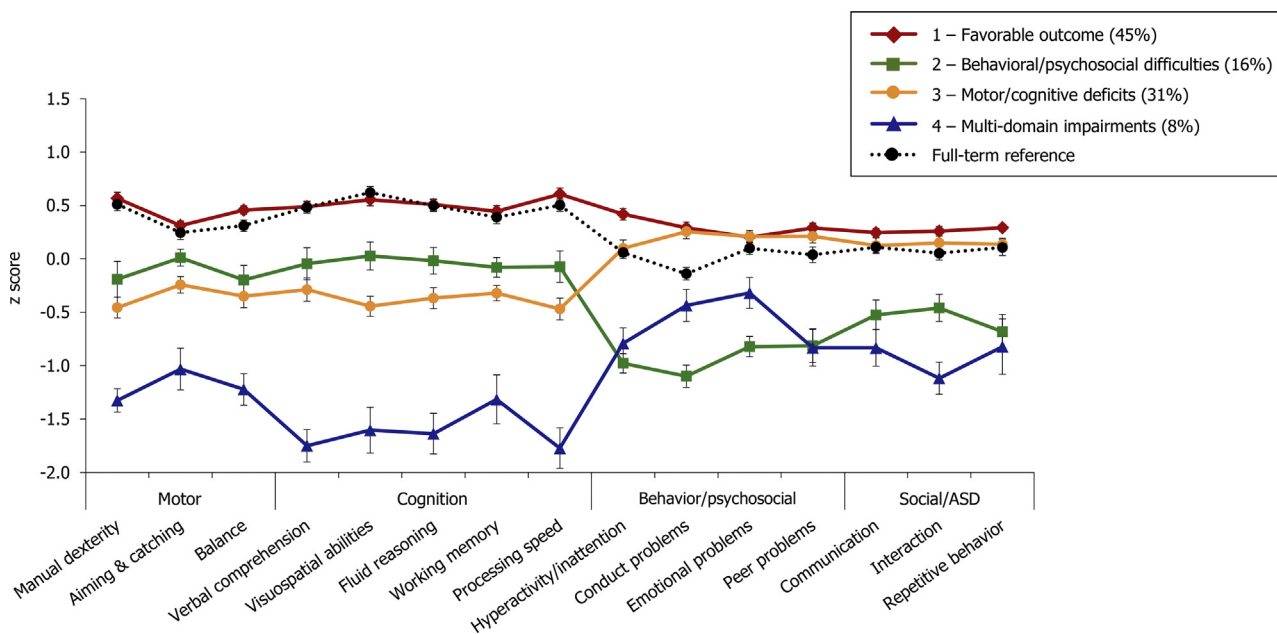
(odds ratio [OR] = 5.06, 95% CI = 2.75-9.31) and behavioral/psychosocial difficulties (OR = 2.44, 95% CI = 1.29-4.62). It should be noted that confidence intervals for all these results are wide (see Table S5, available online), requiring cautious interpretation.

A few predictors were associated with differences in odds between the multi-domain impairments profile and the other 2 suboptimal outcome profiles. Parental non-European immigrant status (OR = 1.72, 95% CI = 1.11-2.66) and unemployment/inactivity (OR = 2.35, 95% CI = 1.46-3.78) were associated with increased odds for multi-domain impairments as opposed to mild motor/cognitive deficits. Lower GA (weeks; OR = 1.20, 95% CI = 1.05-1.37), severe brain lesions (OR = 3.40, 95% CI = 1.12-10.34), and unemployed/inactive parents (OR = 2.63, 95% CI = 1.57-4.43) were associated with higher odds for multi-domain impairments than a profile with mainly behavioral/psychosocial difficulties. None of the predictors were associated with differences in odds between the behavioral/psychosocial and motor/cognitive difficulties profiles.

DISCUSSION

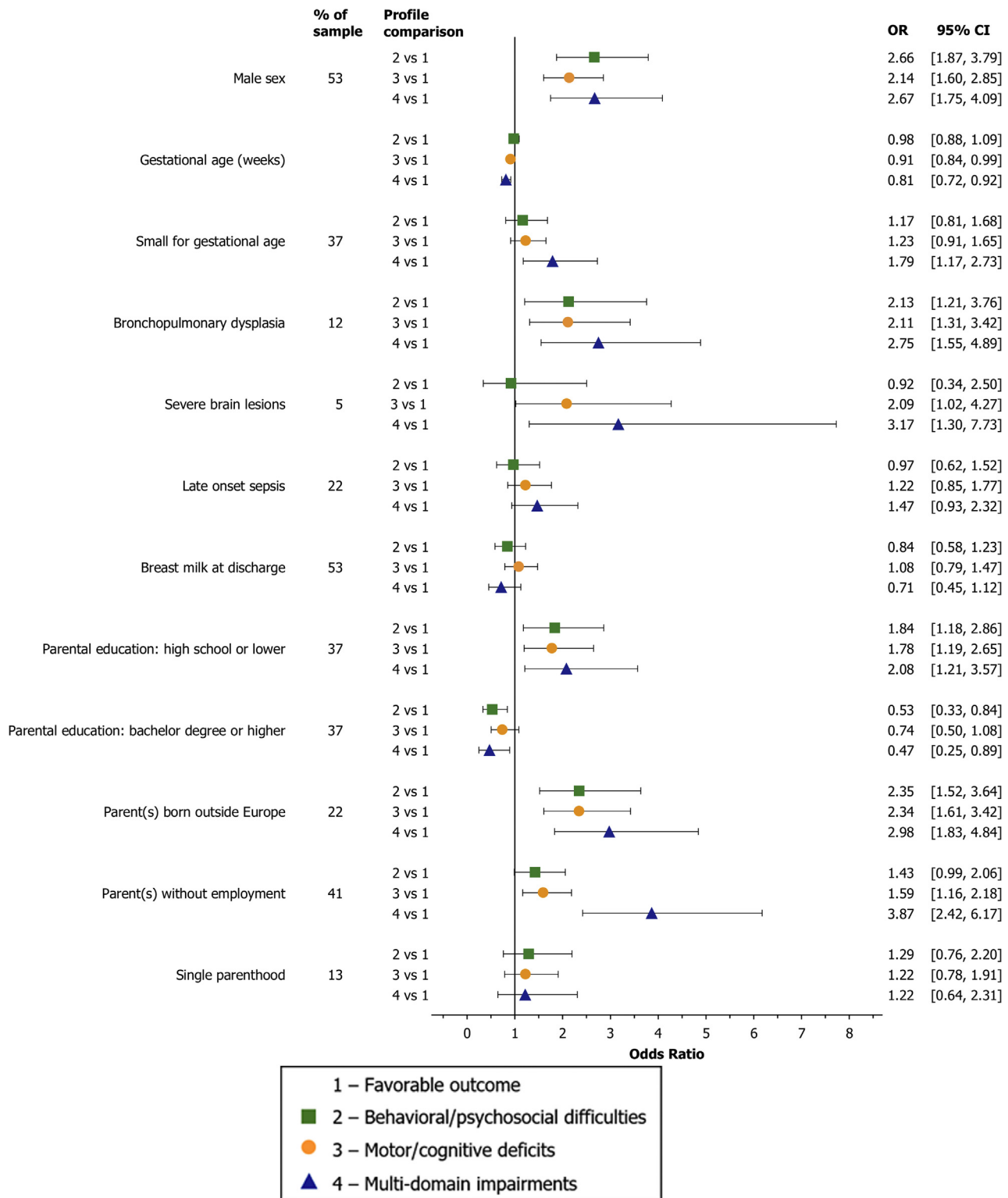
The present study is the first large-scale study to identify subgroups of very preterm born children according to their

FIGURE 2 Estimates of Functioning Across Domains for the 4 Latent Profiles



Note: Functioning of full-term children is plotted as a reference (dotted line). Scores for both the very preterm and full-term sample were standardized according to the very preterm sample (ie, z = 0 corresponds to the weighted mean of the very preterm sample) and scaled so that a lower z score reflects poorer performance or an increase in difficulties for all indicators. Please note color figures are available online.

FIGURE 3 Odds Ratios for the Relation Between Predictors and Suboptimal Outcome Profiles Relative to the Favorable Outcome Profile



Note: Please note color figures are available online.

motor, cognitive, behavioral, and psychosocial functioning at 5.5 years of age in a population-based cohort of 1,977 children. Four subgroups were distinguished, each showing a different profile of outcomes. A large minority of children (45%) showed no difficulties in any of the developmental domains. The majority (55%) of 5.5-year-old very preterm born children showed 1 of 3 suboptimal outcome profiles that differed in severity, type, and combination of difficulties: 31% of the children showed low-average to mildly impaired motor and cognitive functioning in absence of behavioral and psychosocial difficulties; 16% had mild behavioral and psychosocial symptoms with low-average motor and cognitive functioning, and 8% showed moderate motor and cognitive deficits, in combination with mild hyperactivity/inattention and social/autism spectrum disorder (ASD) symptoms. Male sex, bronchopulmonary dysplasia (BPD), low parental education level, and parental non-European immigrant status were the most important predictors of suboptimal outcome, increasing the odds for all 3 suboptimal outcome profiles. In contrast, few factors could distinguish between these suboptimal profiles.

The findings indicate clearly distinct profiles of functioning in subgroups of very preterm born children, in which children differ with respect to both the severity and the type of deficits that are predominant. Motor and cognitive performance differed between the profiles mainly in terms of severity of deficits. Within subgroups, motor and cognitive difficulties co-occurred with similar levels of severity. In a review, Diamond³² pointed to the close interrelationship between motor and cognitive development, given the co-occurrence of motor and cognitive difficulties in a variety of developmental disorders, similar time scales of development, and overlap in brain regions activated during cognitive and motor tasks. Executive processes that rely on large-scale brain networks have been identified as an important underlying mechanism of the relation between motor and cognitive development.³³ Deficits in these processes and underlying brain networks have been widely reported in very preterm born children and in a range of developmental psychopathologies,^{34,35} which may explain the co-occurrence of motor and cognitive deficits across clinical populations.

The 2 profiles with behavioral and psychosocial difficulties, the “behavioral/psychosocial difficulties” and “multi-domain impairments” profiles, described similar levels of hyperactivity/impulsivity and peer problems. However, the “multi-domain impairments” profile showed generally increased ASD symptomatology, whereas in the “behavioral/psychosocial difficulties” profile, hyperactivity/impulsivity and peer problems co-occurred particularly with

conduct and emotional problems. This suggests that the similar levels of peer relationship problems in both profiles may have different underlying mechanisms. The co-occurrence of peer, conduct, and emotional problems has been described by Van Lier *et al.*,³⁶ who found some evidence that externalizing problems in early childhood hamper peer relationships, resulting in internalizing problems. Moreover, peer problems, more specifically victimization by peers, worsened externalizing problems. Meta-analytic findings indeed showed that peer victimization can both precede and result from externalizing problems.³⁷ Extremely and very preterm born children are vulnerable for peer victimization, which predicted later emotional problems.³⁸ Although conduct problems have not frequently been reported after very preterm birth at the group level, the present study and findings from Burnett *et al.*¹⁴ show that there is a significant proportion of children with conduct problems that may affect peer relationships and emotional development.^{36,38} However, Burnett *et al.*¹⁴ showed that these problems do not necessarily co-occur. Further research on the co-occurrence of these symptoms is of interest to understand their potential interaction. The SDQ does not distinguish between hyperactivity and inattention, but these symptoms may also differ between profiles, with primarily hyperactivity in the “behavioral/psychosocial difficulties” profile and inattention in the “multi-domain impairments” profile.³⁹ In sum, similar symptoms of behavioral and psychosocial problems in very preterm born children may have different underlying mechanisms and co-occurring problems in different subgroups of children, and may thus require different approaches for treatment.

To facilitate early detection of problems in high-risk infants and to provide targeted prevention and intervention, it is important to understand which children are most at risk for which problems. We found a number of factors that were independently associated with suboptimal outcomes after very preterm birth, albeit with small nonsignificant differences in the strengths of the associations between the suboptimal outcome profiles. The odds for any of the 3 suboptimal profiles compared to an optimal outcome was on average 2.5 times higher for boys, 2.4 times higher for children with BPD, 1.9 times higher when parents had a low education level, and 2.5 times higher when parent(s) were non-European immigrants. In a Swedish population-based study,⁴⁰ extremely preterm born girls outperformed boys at 2.5 years of age, whereas there were no sex differences for neonatal and socioeconomic factors. These factors had generally similar effects on outcomes in both sexes, with only a few sex-specific effects.⁴⁰ The present study also showed increased impairments in boys

independent of neonatal morbidities and socioeconomic factors. These findings thus suggest a specific vulnerability in boys for difficulties across developmental domains. In the general population, male individuals have an increased risk of early-onset disorders, whereas female individuals are overrepresented in adolescent-onset disorders.⁴¹ Most research after very preterm birth has been conducted in (early) childhood. More research in adolescence and adulthood is needed to understand whether impairments after very preterm birth are characterized by an overall male preponderance, or whether this is age dependent.

When looking at birth characteristics and neonatal morbidities, BPD was the most important risk factor, being associated with all suboptimal outcome profiles. This is in line with findings from a multivariable meta-regression analysis of cognitive outcomes¹ and bivariate analysis of motor, academic, and behavioral/psychosocial outcomes.^{42,43} Given the relatively high incidence in current populations of extremely preterm born infants,⁴⁴ the present findings indicate that BPD is an important factor for the identification of children with an increased risk of long-term impairments, and may be a key target for prevention and interventions to improve outcomes, although the exact mechanisms underlying this association remains to be elucidated. Gestational age, small for gestational age, and severe brain lesions increased the odds for “multi-domain impairments” but not for milder domain-specific problem profiles. Receipt of breast milk at discharge did not decrease the odds for any suboptimal profile compared to a favorable outcome profile. Generally, evidence supports the beneficial effects of breast milk on neurodevelopmental outcomes after very preterm birth.^{17,45-47} However, studies in preterm and full-term children showed diminished or nonsignificant effects of breast milk after controlling for socioeconomic factors and parental IQ.^{45,48} This was also seen in the present study. When socioeconomic and sociodemographic factors were taken into account, receipt of breast milk could not distinguish very preterm born children with favorable and suboptimal outcome profiles. Another explanation for this finding may be that 47% of very preterm born infants in France received breast milk at discharge,⁴⁹ of whom only 36% received breast milk at 6 months,⁵⁰ whereas associations with long-term neurodevelopmental outcomes are most pronounced with prolonged breastfeeding.^{51,52}

Low parental education level was independently associated with increased odds for any suboptimal outcome profile compared to a favorable outcome. Parental education level may affect preterm birth outcomes in multiple ways through parenting, health-related behavior before, during, and after pregnancy, access to high-quality healthcare and education, and better socioeconomic position of the family

and neighborhood.⁵³ Independent of education level of parents, their country of birth (ie, non-European country) was one of the most important predictors of suboptimal outcomes. Possible mechanisms include the worse position of non-European minorities on the French labor market irrespective of education,^{54,55} increased maternal mental health problems among first-generation immigrant mothers in France⁵⁶ that may be further increased in mothers of preterm children⁵⁷ and affect children’s development,⁵⁸ and increased rates of unmet health care needs among minorities in France,⁵⁹ which have all been associated with perceived discrimination.⁵⁹⁻⁶¹ Other potential mechanisms include lower attendance in preschool education programs⁶² and multi-lingualism, which has been associated with poorer cognitive outcomes after very preterm birth.⁶³ Our findings remain largely inconclusive regarding more specific differences based on parental place of birth due to unprecise estimates, although outcomes were poorer in all specified minority groups. Moreover, place of birth is a proxy of ethnicity/race that may not capture diversity as covered by this broader concept. The findings nevertheless call for insight into factors contributing to the poorer outcomes of children from non-European immigrants and disadvantaged socioeconomic backgrounds, the needs of these families, and how to improve their access to services.

The findings should be interpreted in light of the study’s limitations. The study sample, derived from a large representative population-based cohort, was representative of the very preterm population in terms of neonatal characteristics, but seemed selective in terms of social characteristics and disabilities. Given the importance of social factors for long-term outcomes, the proportions of children with suboptimal outcome profiles likely underestimate proportions and severity of impairments at the population level. However, severity was implicated by performance of a full-term reference sample, in which we also found evidence for similar forms of selection bias. This could imply that performance in both the very preterm and full-term reference sample was better than in the population. In contrast, behavioral/psychosocial symptoms were increased in our full-term reference sample compared to the total ELFE cohort,²⁰ to a French SDQ validation study,⁶⁴ and to the very preterm subgroup with a favorable outcome profile. This may affect the interpretation of the severity of behavioral/psychosocial symptoms specifically, but does not affect our conclusions on which symptoms are predominant in which subgroups of very preterm born children. Another limitation is the use of a single-informant instead of multi-informant approach to assess behavioral/psychosocial functioning. Moreover, diagnostic instruments are preferable over screening tools, albeit less feasible in large-scale

national studies. Finally, outcome profiles were associated with important perinatal and social/environmental characteristics, but did not include parental mental health problems, which are increased in the preterm population⁵⁷ and are known to be associated with suboptimal child development.⁵⁸

The present findings make an important contribution to our understanding of the core deficits and co-occurrence of problems in subgroups of very preterm born children. More than half of the 5.5-year-old children (55%) had motor and cognitive problems that co-occurred with similar levels of severity. A quarter of the very preterm born children showed additional behavioral/psychosocial problems: those with mild motor and cognitive deficits experienced mainly hyperactivity/inattention, conduct, emotional, and peer problems, whereas more severe motor and cognitive deficits co-occurred mainly with symptoms of hyperactivity/inattention and ASD. These findings imply that similar problems may have a different etiology in different subgroups of children and may require a different approach of intervention and support. Although the findings need replication, the information is useful for the development of targeted interventions and support that is tailored to the needs of large subgroups of children across multiple domains of functioning. Moreover, the findings suggest that general demographic, neonatal, and social/environmental factors that are available at the time of discharge may be useful for the identification of very preterm born children with an increased risk of impairments. However, these factors were associated with a general rather than domain-specific vulnerability. Further research is necessary to determine how accurately such factors can predict the risk for impairments in individual infants.

REFERENCES

1. Twilhaar ES, Wade RM, De Kieviet JF, Van Goudoever JB, Van Elburg RM, Oosterlaan J. Cognitive outcomes of children born extremely or very preterm since the 1990s and associated risk factors: a meta-analysis and meta-regression. *JAMA Pediatr.* 2018;172:361-367. <https://doi.org/10.1001/jamapediatrics.2017.5323>.
2. Twilhaar ES, De Kieviet JF, Aarnoudse-Moens CSH, Van Elburg RM, Oosterlaan J. Academic performance of children born preterm: a meta-analysis and meta-regression. *Arch Dis Child Fetal Neonatal Ed.* 2018;103:F322-F330. [10.1136/archdischild-2017-312916](https://doi.org/10.1136/archdischild-2017-312916).
3. De Kieviet JF, Piek JP, Aarnoudse-Moens CS, Oosterlaan J. Motor development in very preterm and very low-birth-weight children from birth to adolescence: a meta-analysis. *JAMA.* 2009;302:2235-2242. <https://doi.org/10.1001/jama.2009.1708>.
4. Johnson S, Marlow N. Preterm birth and childhood psychiatric disorders. *Pediatr Res.* 2011;69:11-18. <https://doi.org/10.1203/PDR.0b013e318212faa0>.
5. Cheong JL, Anderson PJ, Burnett AC, *et al.* Changing neurodevelopment at 8 years in children born extremely preterm since the 1990s. *Pediatrics.* 2017;139:e20164086. <https://doi.org/10.1542/peds.2016-4086>.
6. Moore T, Hennessy EM, Myles J, *et al.* Neurological and developmental outcome in extremely preterm children born in England in 1995 and 2006: the EPICure studies. *BMJ.* 2012;345:e7961. <https://doi.org/10.1136/bmj.e7961>.
7. Linsell L, Johnson S, Wolke D, Morris J, Kurinczuk JJ, Marlow N. Trajectories of behavior, attention, social and emotional problems from childhood to early adulthood

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- following extremely preterm birth: a prospective cohort study. *Eur Child Adolesc Psychiatry.* 2019;28:531-542. <https://doi.org/10.1007/s00787-018-1219-8>.
8. Linsell L, Johnson S, Wolke D, *et al.* Cognitive trajectories from infancy to early adulthood following birth before 26 weeks of gestation: a prospective, population-based cohort study. *Arch Dis Child.* 2018;103:363-370. <https://doi.org/10.1136/archdischild-2017-313414>.
9. Mangin KS, Horwood L, Woodward LJ. Cognitive development trajectories of very preterm and typically developing children. *Child Dev.* 2017;88:282-298. <https://doi.org/10.1111/cdev.12585>.
10. Twilhaar ES, de Kieviet JF, van Elburg RM, Oosterlaan J. Academic trajectories of very preterm born children at school age. *Arch Dis Child Fetal Neonatal Ed.* 2019;104:F419-F423. <https://doi.org/10.1136/archdischild-2018-315028>.
11. Spittle A, Orton J, Anderson P, Boyd R, Doyle LW. Early developmental intervention programmes post-hospital discharge to prevent motor and cognitive impairments in preterm infants. *Cochrane Database Syst Rev.* 2012;24:CD005495. <https://doi.org/10.1002/14651858.CD005495.pub3>.
12. Anderson PJ, Lee KJ, Roberts G, *et al.* Long-term academic functioning following cogmed working memory training for children born extremely preterm: a randomized controlled trial. *J Pediatr.* 2018;202:92-97. <https://doi.org/10.1016/j.jpeds.2018.07.003>.
13. Ohlsson A, Jacobs SE. NIDCAP: a systematic review and meta-analyses of randomized controlled trials. *Pediatrics.* 2013;131:e881-e893. <https://doi.org/10.1542/peds.2012-2121>.

14. Burnett AC, Youssef G, Anderson PJ, *et al.* Exploring the “preterm behavioral phenotype” in children born extremely preterm. *J Dev Behav Pediatr.* 2019;40:200-207. <https://doi.org/10.1097/DBP.0000000000000646>.
15. Heeren T, Joseph RM, Allred EN, O’Shea TM, Leviton A, Kuban KC. Cognitive functioning at the age of 10 years among children born extremely preterm: a latent profile approach. *Pediatr Res.* 2017;82:614-619. <https://doi.org/10.1038/pr.2017.82>.
16. Lean RE, Lessov-Shlaggar CN, Gerstein ED, *et al.* Maternal and family factors differentiate profiles of psychiatric impairments in very preterm children at age 5 years. *J Child Psychol Psychiatry.* 2020;61:157-166. <https://doi.org/10.1111/jcpp.13116>.
17. Johnson S, Waheed G, Manktelow BN, *et al.* Differentiating the preterm phenotype: distinct profiles of cognitive and behavioral development following late and moderately preterm birth. *J Pediatr.* 2018;193:85-92. <https://doi.org/10.1016/j.jpeds.2017.10.002>.
18. Ancel P-Y, Goffinet F. EPIPAGE 2: a preterm birth cohort in France in 2011. *BMC Pediatr.* 2014;14:97. <https://doi.org/10.1186/1471-2431-14-97>.
19. Charles M-A, Thierry X, Lanoe J-L, *et al.* Cohort profile: the French national cohort of children ELFE: birth to 5 years. *Int J Epidemiol.* 2020;49:368-369. <https://doi.org/10.1093/ije/dy227>.
20. Pierrat V, Marchand-Martin L, Marret S, *et al.* Neurodevelopmental outcomes at 5 years among children born preterm: the EPIPAGE-2 cohort study 2021;373:n741. <https://doi.org/10.1136/bmj.n741>.
21. Wechsler D. Technical and Interpretative Manual: WPPSI-IV. New York: Pearson; 2012.
22. Henderson SE, Sugden D, Barnett AL. Movement Assessment Battery for Children—2. (MABC-2). Examiner’s Manual. London: Pearson Education Ltd; 2007.
23. Stone LL, Otten R, Engels RC, Vermulst AA, Janssens JM. Psychometric properties of the parent and teacher versions of the strengths and difficulties questionnaire for 4- to 12-year-olds: a review. *Clin Child Fam Psychol Rev.* 2010;13:254-274. <https://doi.org/10.1007/s10567-010-0071-2>.
24. Johnson S, Hollis C, Hennessy E, Kochhar P, Wolke D, Marlow N. Screening for autism in preterm children: diagnostic utility of the Social Communication Questionnaire. *Arch Dis Child.* 2011;96:73-77. doi: 10.1136/adc.2010.194795.
25. Kruck J, Baduel S, Rogé B. SCQ Manual (French version). Paris: Hogrefe France; 2017.
26. Ego A, Prunet C, Lebreton E, *et al.* Customized and non-customized French intrauterine growth curves. I—Methodology. *J Gynecol Obstet Biol Reprod.* 2016;45:155. <https://doi.org/10.1016/j.jgyn.2015.08.009>.
27. Jobe AH, Bancalari E. Bronchopulmonary dysplasia. *Am J Respir Crit Care Med.* 2001; 163:1723-1729. <https://doi.org/10.1164/ajrccm.163.7.2011060>.
28. Enders CK. Applied Missing Data Analysis. New York: Guilford Press; 2010.
29. Nylund KL, Asparouhov T, Muthén BO. Deciding on the number of classes in latent class analysis and growth mixture modeling: a Monte Carlo simulation study. *Struct Equat Model.* 2007;14:535-569. <https://doi.org/10.1080/1070510701575396>.
30. Nylund-Gibson K, Choi AY. Ten frequently asked questions about latent class analysis. *Transl Issues Psychol Sci.* 2018;4:440. <https://doi.org/10.1037/tps0000176>.
31. Vermlut JK. Latent class modeling with covariates: two improved three-step approaches. *Polit Anal.* 2010;18:450-469. <https://doi.org/10.1093/pan/mpq025>.
32. Diamond A. Close interrelation of motor development and cognitive development and of the cerebellum and prefrontal cortex. *Child Dev.* 2000;71:44-56. <https://doi.org/10.1111/1467-8624.00117>.
33. Roebbers CM, Röthlisberger M, Neuenschwander R, Cimeli P, Michel E, Jäger K. The relation between cognitive and motor performance and their relevance for children’s transition to school: a latent variable approach. *Hum Mov Sci.* 2014;33:284-297. <https://doi.org/10.1016/j.humov.2013.08.011>.
34. Snyder HR, Miyake A, Hankin BL. Advancing understanding of executive function impairments and psychopathology: bridging the gap between clinical and cognitive approaches. *Front Psychol.* 2015;6:328. <https://doi.org/10.3389/fpsyg.2015.00328>.
35. Menon V. Large-scale brain networks and psychopathology: a unifying triple network model. *Trends Cogn Sci.* 2011;15:483-506. <https://doi.org/10.1016/j.tics.2011.08.003>.
36. Van Lier PA, Vitaro F, Barker ED, Brendgen M, Tremblay RE, Boivin M. Peer victimization, poor academic achievement, and the link between childhood externalizing and internalizing problems. *Child Dev.* 2012;83:1775-1788. <https://doi.org/10.1111/j.1467-8624.2012.01802.x>.
37. Reijntjes A, Kamphuis JH, Prinzie P, Boelen PA, Van der Schoot M, Telch MJ. Prospective linkages between peer victimization and externalizing problems in children: a meta-analysis. *Aggress Behav.* 2011;37:215-222. <https://doi.org/10.1002/ab.20374>.
38. Wolke D, Baumann N, Strauss V, Johnson S, Marlow N. Bullying of preterm children and emotional problems at school age: cross-culturally invariant effects. *J Pediatr.* 2015; 166:1417-1422. <https://doi.org/10.1016/j.jpeds.2015.02.055>.
39. Johnson S, Kochhar P, Hennessy E, Marlow N, Wolke D, Hollis C. Antecedents of attention-deficit/hyperactivity disorder symptoms in children born extremely preterm. *J Dev Behav Pediatr.* 2016;37:285. <https://doi.org/10.1097/DBP.0000000000000298>.
40. Månsson J, Fellman V, Stjernqvist K, Group ES. Extremely preterm birth affects boys more and socioeconomic and neonatal variables pose sex-specific risks. *Acta Paediatr.* 2015;104:514-521. <https://doi.org/10.1111/apa.12937>.
41. Zahn-Waxler C, Shirtcliff EA, Marceau K. Disorders of childhood and adolescence: gender and psychopathology. *Annu Rev Clin Psychol.* 2008;4:275-303. <https://doi.org/10.1146/annurev.clinpsy.3.022806.091358>.
42. Anderson PJ, Doyle LW. Neurodevelopmental outcome of bronchopulmonary dysplasia. *Semin Perinatol.* 2006;30:227-232. <https://doi.org/10.1053/j.semperi.2006.05.010>.
43. Cheong JL, Doyle LW. An update on pulmonary and neurodevelopmental outcomes of bronchopulmonary dysplasia. *Semin Perinatol.* 2018;42:478-484. <https://doi.org/10.1053/j.semperi.2018.09.013>.
44. Siffel C, Kistler KD, Lewis JF, Sarda SP. Global incidence of bronchopulmonary dysplasia among extremely preterm infants: a systematic literature review. *J Matern Fetal Neonatal Med.* 2021;34:1721-1731. <https://doi.org/10.1080/14767058.2019.1646240>.
45. Lechner BE, Vohr BR. Neurodevelopmental outcomes of preterm infants fed human milk: a systematic review. *Clin Perinatol.* 2017;44:69-83. <https://doi.org/10.1016/j.clp.2016.11.004>.
46. Johnson S, Hollis C, Kochhar P, Hennessy E, Wolke D, Marlow N. Autism spectrum disorders in extremely preterm children. *J Pediatr.* 2010;156:525-531. <https://doi.org/10.1016/j.jpeds.2009.10.041>.
47. Belfort MB, Anderson PJ, Nowak VA, *et al.* Breast milk feeding, brain development, and neurocognitive outcomes: a 7-year longitudinal study in infants born at less than 30 weeks’ gestation. *J Pediatr.* 2016;177:133-139. <https://doi.org/10.1016/j.jpeds.2016.06.045>.
48. Walfisch A, Sermer C, Cressman A, Koren G. Breast milk and cognitive development—the role of confounders: a systematic review. *BMJ Open.* 2013;3:e003259. <https://doi.org/10.1136/bmjopen-2013-003259>.
49. Mitha A, Piedvache A, Glorieux I, *et al.* Unit policies and breast milk feeding at discharge of very preterm infants: the EPIPAGE-2 cohort study. *Paediatr Perinat Epidemiol.* 2019; 33:59-69. <https://doi.org/10.1111/ppe.12536>.
50. Bonnet C, Blondel B, Piedvache A, *et al.* Low breastfeeding continuation to 6 months for very preterm infants: a European multiregional cohort study. *Matern Child Nutr.* 2019; 15:e12657. <https://doi.org/10.1111/mcn.12657>.
51. Boucher O, Julvez J, Guxens M, *et al.* Association between breastfeeding duration and cognitive development, autistic traits and ADHD symptoms: a multicenter study in Spain. *Pediatr Res.* 2017;81:434-442. <https://doi.org/10.1038/pr.2016.238>.
52. Mortensen EL, Michaelsen KF, Sanders SA, Reinisch JM. The association between duration of breastfeeding and adult intelligence. *JAMA.* 2002;287:2365-2371. <https://doi.org/10.1001/jama.287.18.2365>.
53. Wolke D. Is social inequality in cognitive outcomes increased by preterm birth-related complications? *JAMA Netw Open.* 2019;2. e192902-e192902. <https://doi.org/10.1001/jamanetworkopen.2019.2902>.
54. Langevin G, Mascler D, Moizeau F, Peterle E. Ethnic gaps in educational attainment and labor-market outcomes: evidence from France. *Educ Econ.* 2017;25:84-111. <https://doi.org/10.1080/09645292.2016.1183591>.
55. Meurs D, Pailhé A, Simon P. The persistence of intergenerational inequalities linked to immigration: labour market outcomes for immigrants and their descendants in France. *Population.* 2006;61:645-682. <https://doi.org/10.3917/POPE.605.0645>.
56. El-Khoury F, Sutter-Dallay A-L, Panico L, *et al.* Women’s mental health in the perinatal period according to migrant status: the French representative ELFE birth cohort. *Eur J Public Health.* 2018;28:458-463. <https://doi.org/10.1093/eurpub/cky008>.
57. Yaari M, Treyvaud K, Lee KJ, Doyle LW, Anderson PJ. Preterm birth and maternal mental health: longitudinal trajectories and predictors. *J Pediatr Psychol.* 2019;44: 736-747. <https://doi.org/10.1093/jpepsy/jsz019>.
58. Kingston D, Tough S. Prenatal and postnatal maternal mental health and school-age child development: a systematic review. *Matern Child Health J.* 2014;18:1728-1741. <https://doi.org/10.1007/s10995-013-1418-3>.
59. Rivenbark JG, Ichou M. Discrimination in healthcare as a barrier to care: experiences of socially disadvantaged populations in France from a nationally representative survey. *BMC Public Health.* 2020;20:1. <https://doi.org/10.1186/s12889-019-8124-z>.
60. Meurs D. Employment and Wages of Immigrants and Descendants of Immigrants: Measures of Inequality and Perceived Discrimination. Trajectories and Origins: Survey on the Diversity of the French Population. New York: Springer; 2018. https://doi.org/10.1007/978-3-319-76638-6_4.
61. Missinne S, Bracke P. Depressive symptoms among immigrants and ethnic minorities: a population based study in 23 European countries. *Soc Psychiatry Psychiatr Epidemiol.* 2012;47:97-109. <https://doi.org/10.1007/s00127-010-0321-0>.
62. Organisation for Economic Co-operation and Development. Immigrant Students at School: Easing the Journey Towards Integration. OECD Publishing; 2015. <https://doi.org/10.1787/20776829>.
63. Van Veen S, Remmers S, Aarnoudse-Moens C, Oosterlaan J, van Kaam A, van Wassenae-Leemhuis A. Multilingualism was associated with lower cognitive outcomes in children who were born very and extremely preterm. *Acta Paediatr.* 2019;108:479-485. <https://doi.org/10.1111/apa.14516>.
64. Shojaei T, Wazana A, Pitrou I, Kovess V. The Strengths and Difficulties Questionnaire: validation study in French school-aged children and cross-cultural comparisons. *Soc Psychiatry Psychiatr Epidemiol.* 2009;44:740-747. <https://doi.org/10.1007/s00127-008-0489-8>.