

Risk factors associated with the development of suspected moderate to severe language disorders in preterm infants: development of an early screening model

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Abstract

Background

Preterm children are at increased risk of neurodevelopmental impairments, including language disorders, which may adversely affect academic achievement and social functioning. Early identification of children at risk is essential to optimize intervention strategies. This study aimed to identify perinatal and environmental risk factors associated with language disorders at 4 years of age in preterm children and to develop an early predictive screening model, using the assessment of the communication section of the ASQ (Ages and Stages Questionnaire) at 24 months.

Methods

We conducted a retrospective observational study using data from the Loire Infant Follow-up Team (LIFT) cohort. Children born before 34 weeks' gestation between 2013 and 2021 who underwent language assessment at 4 years using the ERTL-4 screening tool were included. Language outcomes were classified as optimal (normal or mild impairment) or non-optimal (moderate or severe impairment). Potential neonatal, socioeconomic, and developmental predictors were analysed using multivariable logistic regression. Model performance was evaluated in independent training ($n = 1,292$) and validation ($n = 1,292$) samples using receiver operating characteristic (ROC) curves and calibration analyses.

Results

We included 2,584 preterm children. Independent risk factors for language disorders were male sex (adjusted OR for females: 0.69, 95% CI 0.54–0.90), unfavourable socioeconomic status (OR 3.08, 95% CI 1.89–5.02), low parental educational level (OR 2.93, 95% CI 1.62–5.32), neonatal hemodynamic instability (OR 1.84, 95% CI 1.09–3.09), abnormal communication score on the Ages and Stages Questionnaire (ASQ) at 24 months (OR 2.28, 95% CI 1.63–3.18), and speech therapy between 2 and 4 years of age (OR 3.76, 95% CI 2.52–5.63). The final predictive model demonstrated good discrimination with an AUC of 0.74 (95% CI 0.71–0.77) in the training cohort and 0.72 (95% CI 0.69–0.74) in the validation cohort.

Conclusions

Language disorders in preterm children are associated with both biological and socioeconomic factors. A predictive model combining neonatal characteristics, family environment, and ASQ communication screening at 24 months showed satisfactory performance and may help identify high-risk children who could benefit from early speech-language assessment and intervention.

What is Known

Premature infants are at risk for language disorders. The risk factors are still not well understood, and this can have a significant impact on children's social and educational lives if they are not addressed early.

What is New: Developing an early predictive model makes it possible to identify children at risk of developing a language disorder by age 4, to offer them early preventive or therapeutic intervention.

INTRODUCTION

Preterm birth represents a major global health challenge, affecting approximately one in ten children worldwide, corresponding to more than 13 million newborns annually, and about 6.9% of births in France [1, 2]. Advances in neonatal care over recent decades have substantially improved the survival of preterm infants. Consequently, clinical concerns have progressively shifted from survival to long-term neurodevelopmental outcomes.

Preterm children are at increased risk of psychomotor developmental delay compared with term-born peers [3–6]. Because brain development remains ongoing at birth, exposure to environmental, biological, and therapeutic factors associated with prematurity may disrupt neurodevelopmental processes and affect multiple cognitive and motor domains, particularly communication abilities [7–9]. These alterations may lead to language disorders, which are of major concern due to their impact on social functioning and academic achievement. The incidence of language disorders in preterm children is estimated at around 30%, compared with 5–8% in term-born populations. However, the preterm population remains highly heterogeneous in terms of gestational age and prematurity-related comorbidities, both of which strongly influence developmental outcomes.

Although the underlying pathophysiological mechanisms remain incompletely understood, recent studies suggest associations between cerebral white matter connectivity and language performance in extremely preterm children [10, 11], as well as delayed hemispheric lateralization of language networks [12, 13]. Nevertheless, knowledge of perinatal risk factors contributing to language disorders remains limited and heterogeneous.

Currently identified factors negatively associated with language development include lower parental or maternal educational level and economic status, male sex, and lower gestational age [14–25]. Additional associations have been reported with prolonged ventilation or bronchopulmonary dysplasia, retinopathy of prematurity [25], multilingual exposure [14, 21], gestational diabetes [24] and breastfeeding practices [26].

In this context, early identification of language disorders and timely targeted intervention are essential to improve developmental outcomes. Therefore, this study, based on the LIFT (Loire Infant Follow-up Team) cohort, aimed primarily to investigate perinatal risk factors associated with language disorders at 4

years of age screened using the ERTL-4 (Epreuve de Repérage des Troubles du Langage, Appendix 2) in preterm children. Secondary objectives were to assess the predictive value of the parental Ages and Stages Questionnaire (ASQ) in communication at 24 months (Appendix 1) and to develop a predictive model for language disorder occurrence.

MATERIALS AND METHODS

Study design and objectives

We conducted a retrospective observational analytical study aimed at identifying risk factors for language disorders in preterm children and at developing and validating a predictive model using separate training and validation samples. Data were extracted from the LIFT cohort.

The primary objective of the study was to identify risk factors associated with the occurrence of language disorders at 4 years of age in a population of preterm children, screened using the ERTL4 tool. The secondary objectives were to determine whether the communication part ASQ administered at 24 months could predict suspected language disorders at 4 years, and to develop a multivariable model capable of estimating the risk of language disorders in preterm children.

Participants

We included children born between January 1, 2013 and June 30, 2021, with a gestational age below 34 weeks, who were enrolled in the LIFT network and for whom an ERTL4 assessment at 4 years of age was available. Among these children, 20 had no available ERTL4 score because their language impairment was too severe to allow test completion; these children were therefore included in the “non-optimal” outcome group.

Children were excluded if they were living outside the Pays de la Loire region or had discontinued follow-up due to relocation, loss to follow-up, or parental withdrawal. We also excluded children who had died, as well as those presenting comorbidities such as hearing impairment, genetic syndromes, or autism diagnosed at 18 months, 24 months, or 4 years. In addition, children with an abnormal screening result on the M-CHAT (Modified Checklist for Autism in Toddlers) at 18 or 24 months were excluded, as were children followed in specialized institutions for severe disabilities, those who did not undergo a pediatric assessment at 4 years, those without an ERTL4 assessment (except when severe language impairment prevented its completion), and those whose parents refused the use of their data.

Follow-up and language assessment

The LIFT cohort includes 23 maternity units in the Pays de la Loire region, including three level III centers, as well as all healthcare professionals involved in perinatal care. Follow-up within this perinatal network

is tailored according to each child's perinatal history and prematurity-related comorbidities, and it consists of specialized medical checkups every few years until 8 years old.

Language development was assessed at 24 months [27] using the parent-completed Ages and Stages Questionnaire (ASQ) composed of five areas, including communication with 6 items. For each item, three responses were possible : "yes" (10 points), "sometimes" (5 points), "not yet" (0 point). A score above 36.5 out of 60 was considered normal [28], whereas a score below this threshold was considered abnormal. At 4 years of age, language abilities were assessed by the physician in charge of the child's follow-up using the ERTL4 test. This test, divided into four subtests (words' repetition, sentences' repetition, prepositions well using and sentences' constructions), is validated for French-speaking countries to screen and classify children having normal language development, being at risk of moderate language disorder, or being at risk of severe language disorder [29–32].

Outcome and data collection

The primary outcome was defined based on the ERTL4 results, which were dichotomized into two categories. Children were classified as having an optimal outcome if they had normal results or a suspected mild language disorder (0 or 1 test failure), and as having a non-optimal outcome if they were suspected of having a moderate or severe language disorder (2 or more failed tests). The test was considered non-interpretable when certain items were missing and the children could not be classified into one of the two groups.

We analysed a wide range of variables, including perinatal, neonatal, and environmental factors. Maternal and pregnancy-related variables included maternal hypertension, maternal diabetes, singleton or multiple pregnancy, administration of antenatal corticosteroids, and mode of delivery. Neonatal variables included sex, gestational age, birth weight, head circumference at birth, Apgar score at 5 minutes, duration of enteral feeding, bronchopulmonary dysplasia (defined by the need for respiratory support after 36 weeks of gestation or a diagnosis made during hospitalization), retinopathy of prematurity, severe brain injury (intraventricular haemorrhage, periventricular leukomalacia), necrotizing enterocolitis, hemodynamic instability (defined by the need for at least two successive volume expansions or inotropic support), the presence and management of a patent ductus arteriosus (medical or surgical treatment), attainment of full oral feeding at term, and feeding practices at term.

Environmental and developmental variables included family socioeconomic status, parental educational level, the number and type of languages spoken at home, the ASQ communication score at 24 months, and the implementation of speech and language therapy between 2 and 4 years of age.

Statistical Analysis

Statistical analyses were performed using R version 4.5.2. A two-sided p-value < 0.05 was considered statistically significant. Continuous variables are presented as medians with interquartile ranges, and

categorical variables as counts and percentages.

The overall cohort was divided into a training sample and a validation sample. Comparisons between those two samples were performed using Pearson's Chi-squared test for categorical variables and the Wilcoxon rank-sum test for continuous variables, according to their distribution (or exact tests if needed).

A bivariate analysis was conducted to identify variables associated with the occurrence of language disorders in the training sample. Variables that were statistically significant in univariate analysis, as well as those considered clinically relevant, were included in a multivariable logistic regression model to identify independent risk factors. Results are reported as odds ratios (OR) with their 95% confidence intervals (CI). The model was developed in the training cohort and subsequently evaluated in the validation cohort. As a sensitivity analysis to control and prevent overfitting, a LASSO procedure was performed to explore variable selection and parsimony, using `glmmlasso` package (1.6.4). To account for twin clustering, a Generalized Estimating Equations (GEE) model with a binomial distribution, an exchangeable correlation structure, and robust standard errors (sandwich estimator) was fitted using the `geepack` package (1.3.13).

Model performance was assessed in terms of discrimination using the area under the receiver operating characteristic (ROC) curve (package `pROC` – 1.19.0.1) and internal validation via bootstrapping (500 replicates) for calibration (package `rms` – 8.1.0) and was compared with that of two other models. Model was then evaluated in the independent validation cohort using AUC and calibration plots.

RESULTS

We included 2,584 children born before 34 weeks' gestation, who were part of the LIFT cohort, had undergone a 4-year assessment with a valid ERTL-4 score, and whose parents had consented to the use of their data (Fig. 1).

The characteristics of patients in the training and validation samples of our cohort were comparable (Table 1).

Table 1
Patients characteristics

Characteristics	Overall N = 2,584 ¹	Training sample N = 1,292 ¹	Validation sample N = 1,292 ¹	p- value ²
Sex				0.11
Male	1,372 (53%)	706 (55%)	666 (52%)	
Female	1,212 (47%)	586 (45%)	626 (48%)	
Gestational age (weeks)				0.6
[31–33]	1,506 (58%)	737 (57%)	769 (60%)	
[29–30]	533 (21%)	277 (21%)	256 (20%)	
[26–28]	456 (18%)	234 (18%)	222 (17%)	
[22–25]	89 (3.4%)	44 (3.4%)	45 (3.5%)	
Birth weight (z-score)	-0.17 (-0.90, 0.46)	-0.15 (-0.89, 0.50)	-0.18 (-0.92, 0.45)	0.4
Unknown	3	0	3	
Socio-economic status				0.7
Favourable	707 (30%)	347 (29%)	360 (30%)	
Intermediate	1,364 (57%)	693 (57%)	671 (56%)	
Unfavourable	325 (14%)	166 (14%)	159 (13%)	
Unknown	188	86	102	
Parents education level				0.6
≥ 3 years after high school	1,018 (39%)	500 (39%)	518 (40%)	
≤ 2 years after high school	894 (35%)	463 (36%)	431 (33%)	
No high school graduation	172 (6.7%)	82 (6.3%)	90 (7.0%)	
Unknown	500 (19%)	247 (19%)	253 (20%)	
Apgar score				0.5
<7	254 (10%)	122 (9.9%)	132 (11%)	
≥ 7	2,209 (90%)	1,115 (90%)	1,094 (89%)	
Unknown	121	55	66	
Pregnancy				0.4

Characteristics	Overall N = 2,584¹	Training sample N = 1,292¹	Validation sample N = 1,292¹	p- value²
Single	1,705 (66%)	843 (66%)	862 (67%)	
Multiple	867 (34%)	443 (34%)	424 (33%)	
Unknown	12	6	6	
Delivery mode				0.7
Natural birth	1,024 (40%)	516 (40%)	508 (40%)	
Caesarean	1,546 (60%)	769 (60%)	777 (60%)	
Unknown	14	7	7	
Prenatal corticosteroid therapy				0.2
No	163 (7.2%)	74 (6.5%)	89 (7.8%)	
Yes	2,106 (93%)	1,058 (93%)	1,048 (92%)	
Unknown	315	160	155	
Speech therapy between 2 and 4 y.o.				> 0.9
No	2,257 (87%)	1,128 (87%)	1,129 (87%)	
Yes	327 (13%)	164 (13%)	163 (13%)	
¹ n (%); Median (Q1, Q3)				
² Pearson's Chi-squared test; Wilcoxon rank sum test				

The results of the bivariate analysis are presented in Table 2. In the training sample, factors associated with an increased risk of a suboptimal ERTL-4 score were male sex, unfavourable or intermediate socioeconomic status, parental education level of two years of post-secondary education or less, caesarean delivery, low gestational age (between 22 and 25 SA), low birth weight, presence of bronchopulmonary dysplasia, having received treatment for patent ductus arteriosus, episode of hemodynamic instability, pathological ASQ communication score at 24 months, and speech therapy initiated between 2 and 4 years of age.

Table 2
Factors associated with ERTL-4 results in bivariate analyses within the training sample

Characteristics	ERTL 4 test		Univariate logistic regression		
	Optimal (0 or 1 failure)	Non optimal (> 1 failure)	OR	95% CI	p-value
	N = 752 ¹	N = 540 ¹			
Sex					0.009
Male	388 (55%)	318 (45%)	—	—	
Female	364 (62%)	222 (38%)	0.74	0.59, 0.93	
Socio-economic status					< 0.001
Favourable	248 (71%)	99 (29%)	—	—	
Intermediate	406 (59%)	287 (41%)	1.77	1.34, 2.34	
Unfavourable	57 (34%)	109 (66%)	4.79	3.24, 7.16	
Unknown	41	45			
Parents education level					< 0.001
≥ 3 years after high school	349 (70%)	151 (30%)	—	—	
≤ 2 years after high school	267 (58%)	196 (42%)	1.70	1.30, 2.21	
No high school graduation	27 (33%)	55 (67%)	4.71	2.89, 7.85	
Inconnu	109 (44%)	138 (56%)	2.93	2.14, 4.02	
Spoken language					0.020
French	209 (65%)	114 (35%)	—	—	
Multilinguist or allophone	23 (52%)	21 (48%)	1.67	0.88, 3.16	
Unknown	520 (56%)	405 (44%)	1.43	1.10, 1.86	
Pregnancy					0.6
Single	494 (59%)	349 (41%)	—	—	

Characteristics	ERTL 4 test		Univariate logistic regression		
	Optimal (0 or 1 failure)	Non optimal (> 1 failure)	OR	95% CI	p-value
	N = 752 ¹	N = 540 ¹			
Multiple	253 (57%)	190 (43%)	1.06	0.84, 1.34	
Unknown	5	1			
Prenatal corticosteroid therapy					0.6
No	46 (62%)	28 (38%)	—	—	
Yes	623 (59%)	435 (41%)	1.15	0.71, 1.88	
Unknown	83	77			
Maternal hypertension					0.3
No	605 (59%)	421 (41%)	—	—	
Yes	147 (55%)	119 (45%)	1.16	0.89, 1.53	
Maternal diabetes					0.8
No	675 (58%)	488 (42%)	—	—	
Gestational diabetes	70 (60%)	46 (40%)	0.91	0.61, 1.34	
Pre-existing diabetes	7 (54%)	6 (46%)	1.19	0.38, 3.59	
Delivery mode					0.005
Natural birth	325 (63%)	191 (37%)	—	—	
Caesarean	424 (55%)	345 (45%)	1.38	1.10, 1.74	
Unknown	3	4			
Apgar score					0.2
< 7	65 (53%)	57 (47%)	—	—	
≥ 7	655 (59%)	460 (41%)	0.80	0.55, 1.17	
Unknown	32	23			

Characteristics	ERTL 4 test		Univariate logistic regression		
	Optimal (0 or 1 failure)	Non optimal (> 1 failure)	OR	95% CI	p-value
	N = 752 ¹	N = 540 ¹			
Gestational age					0.003
[31–33 SA]	440 (60%)	297 (40%)	—	—	
[29–30 SA]	171 (62%)	106 (38%)	0.92	0.69, 1.22	
[26–28 SA]	126 (54%)	108 (46%)	1.27	0.94, 1.71	
[22–25 SA]	15 (34%)	29 (66%)	2.86	1.53, 5.57	
Birth weight (z-score)	-0.10 (-0.82, 0.54)	-0.23 (-1.01, 0.41)	0.87	0.78, 0.97	0.011
Head circumference (z-score)	-0.16 (-0.81, 0.48)	-0.35 (-0.95, 0.35)	0.91	0.83, 1.00	0.060
Unknown	34	21			
Duration of feeding via a nasogastric tube	35 (23, 52)	35 (26, 51)	1.00	1.00, 1.01	0.2
Unknown	224	161			
Bronchopulmonary dysplasia					0.003
No	510 (62%)	317 (38%)	—	—	
Yes	118 (52%)	107 (48%)	1.46	1.08, 1.96	
Unknown	124 (52%)	116 (48%)	1.51	1.13, 2.01	
Retinopathy					0.048
No	127 (66%)	65 (34%)	—	—	
Yes	2 (67%)	1 (33%)	0.98	0.04, 10.4	
Unknown	623 (57%)	474 (43%)	1.49	1.08, 2.06	
Severe brain injuries					0.6
No	737 (58%)	527 (42%)	—	—	

Characteristics	ERTL 4 test		Univariate logistic regression		
	Optimal (0 or 1 failure)	Non optimal (> 1 failure)	OR	95% CI	p-value
	N = 752 ¹	N = 540 ¹			
Yes	15 (54%)	13 (46%)	1.21	0.56, 2.57	
Ductus arteriosus treatment					0.004
No treatment	678 (60%)	458 (40%)	—	—	
Yes (medical or surgical)	74 (47%)	82 (53%)	1.64	1.17, 2.30	
Hemodynamic instability					< 0.001
No	494 (63%)	286 (37%)	—	—	
Yes	43 (44%)	54 (56%)	2.17	1.42, 3.34	
Unknown	215 (52%)	200 (48%)	1.61	1.26, 2.05	
Necrotizing enterocolitis					0.6
No	742 (58%)	531 (42%)	—	—	
Yes	10 (53%)	9 (47%)	1.26	0.50, 3.14	
Feeding independence at term					0.4
Yes	568 (57%)	427 (43%)	—	—	
Incomplete	58 (62%)	35 (38%)	0.80	0.51, 1.24	
No	1 (100%)	0 (0%)	0.00		
Unknown	125	78			
Feeding methods at term					0.084
Exclusive breastfeeding or mixed	283 (60%)	186 (40%)	—	—	
Infant formula	82 (65%)	45 (35%)	0.83	0.55, 1.25	
Unknown	387 (56%)	309 (44%)	1.21	0.96, 1.54	

Characteristics	ERTL 4 test		Univariate logistic regression		
	Optimal (0 or 1 failure)	Non optimal (> 1 failure)	OR	95% CI	p-value
	N = 752 ¹	N = 540 ¹			
ASQ communication score (24 months)					< 0.001
Normal	572 (67%)	276 (33%)	—	—	
Pathological	95 (37%)	165 (63%)	3.60	2.70, 4.83	
Unknown	85 (46%)	99 (54%)	2.41	1.75, 3.34	
Speech therapy between 2 and 4 y.o.					< 0.001
No	713 (63%)	415 (37%)	—	—	
Yes	39 (24%)	125 (76%)	5.51	3.80, 8.14	
Unknown	0	0			
¹ n (%); Median (Q1, Q3)					
Abbreviations : CI = Confidence Interval, OR = Odds Ratio					

Table 3 shows the results of the multivariate regression analysis. The adjusted results indicated a higher risk of having a pathological language score at age 4 in cases of unfavourable socioeconomic status, parental education level of two years of post-secondary education or less, male sex, history of hemodynamic instability during the neonatal period, pathological ASQ score, or the initiation of speech therapy between 2 and 4 years of age.

Table 3
Regression table from a multivariate analysis of risk factors associated with language disorders at age 4 identified by ERTL4

Characteristics	OR	95% CI	p-value
Sex			0.005
Male	—	—	
Female	0.69	0.54, 0.90	
Socio-economic status			< 0.001
Favourable	—	—	
Intermediate	1.40	0.96, 2.02	
Unfavourable	3.08	1.89, 5.02	
Parents education level			0.003
≥ 3 years after high school	—	—	
≤ 2 years after high school	1.49	1.06, 2.09	
No high school graduation	2.93	1.62, 5.32	
Inconnu	1.57	1.01, 2.42	
Gestational age (weeks)			0.4
[31–33]	—	—	
[29–30]	1.03	0.72, 1.48	
[26–28]	1.22	0.77, 1.93	
[22–25]	2.11	0.86, 5.18	
Birth weight (z-score)			0.8
]–Inf,–1]	—	—	
]–1,0]	0.90	0.63, 1.27	
]0,1]	0.85	0.59, 1.23	
]1,Inf[	0.82	0.50, 1.36	
Delivery mode			0.064
Natural birth	—	—	
Caesarean	1.32	0.98, 1.76	
Bronchopulmonary dysplasia			0.055

Characteristics	OR	95% CI	p-value
Sex			0.005
No	—	—	
Yes	0.69	0.46, 1.05	
Unknown	1.48	0.93, 2.37	
Severe brain injuries			0.9
No	—	—	
Yes	1.07	0.39, 2.94	
Ductus arteriosus treatment			0.4
No treatment	—	—	
Yes (medical or surgical)	1.22	0.76, 1.97	
Hemodynamic instability			0.030
No	—	—	
Yes	1.84	1.09, 3.09	
Unknown	1.42	0.96, 2.09	
Feeding methods at term			0.3
Exclusive breastfeeding or mixed	—	—	
Infant formula	0.69	0.43, 1.11	
Unknown	0.95	0.71, 1.26	
ASQ communication score (24 months)			< 0.001
Normal	—	—	
Pathological	2.28	1.63, 3.18	
Unknown	2.07	1.43, 3.00	
Speech therapy between 2 et 4 y.o.			< 0.001
No	—	—	
Yes	3.76	2.52, 5.63	
Abbreviations : CI = Confidence Interval, OR = Odds Ratio			

To assess the performance of the final model, built with the variables used in the multivariate analysis, we generated an ROC curve on the construction (or training sample), which yielded an AUC of 0.74 (95%

CI : 0.71–0.77) [Figure 2]. To validate the reliability of this model, we applied it to the validation sample. It achieved an AUC of 0.72 (95% CI : 0.69–0.74), demonstrating good reproducibility and robust performance.

For comparison, we generated ROC curves for different models: “ASQ 24 months alone” and “Neonatal and socioeconomic factors” [Figure 3]. These yielded AUCs of 0.66 (95% IC : 0.63–0.70) and 0.67 (95% IC : 0.64–0.70), respectively. These two isolated models are therefore less discriminative than our final model selected to predict the onset of language disorders at 4 years.

Neonatal and socioeconomic factors do not appear to carry more weight in the prediction than the results of the ASQ test at 24 months. The sensitivity of the ASQ test alone was 0.52, the specificity was 0.73, the positive predictive value was 0.59, and the negative predictive value was 0.67.

DISCUSSION

Our findings regarding the risk factors for language disorders in preterm children are consistent with some factors previously reported in the literature. As described in several studies, we identified a strong association between low parental socioeconomic status and the risk of language disorders in our cohort [19–21]. Indeed, children from socioeconomically disadvantaged backgrounds are exposed to a lower quantity of words compared to those from higher socioeconomic groups, and exposure to a limited vocabulary has been shown to increase the risk of language delay [33, 34]. Moreover, other factors related to disadvantaged socioeconomic conditions may negatively impact language development, such as increased exposure and vulnerability to environmental toxins, including lead [35, 36], as well as poorer adherence and access to follow-up care and early intervention programs. The findings from our cohort and the literature regarding parental education level [15–17, 20, 22, 25] are likely linked to socioeconomic factors.

We also identified male sex as a risk factor for language disorders. This association, frequently reported in the literature [15, 23] although sometimes debated, has been observed across different languages [37] and may be explained by a combination of biological and environmental factors [38].

In addition, we found that experiencing at least one episode of hemodynamic instability during the neonatal period was associated with language disorders. Although this specific association is rarely described as such in the literature, close findings have been reported in the context of neonatal sepsis or neonatal stress [39]. Given the immaturity of cerebral autoregulation in preterm infants and the vulnerability of the developing brain, fluctuations in cerebral blood flow and oxygenation may lead to brain injury [40], potentially resulting in adverse neurodevelopmental outcomes.

Furthermore, an abnormal communication score on the ASQ at 24 months was a strong predictor of subsequent language disorders in our cohort. This finding is consistent with previous studies showing that early communication difficulties are predictive of later language impairment [18, 22].

Some factors identified in the bivariate analysis were not found to be significant in the multivariate model, including caesarean delivery, low gestational age and low birth weight, bronchopulmonary dysplasia, and patent ductus arteriosus treatment. This may reflect residual confounding given the complexity of factors associated with prematurity [41], the absence of an independent association as suggested in other studies [18], or insufficient statistical power.

Moreover, we chose in this study to identify risk factors for moderate to severe language disorders, rather than mild ones, which explains how we interpreted the ERLT4 test results.

Some of our results should be interpreted with caution due to a relatively high proportion of missing data, particularly regarding breastfeeding, retinopathy and multilinguist. In addition, approximately 28% of eligible children did not undergo assessment at 4 years of age, and 13% of those assessed did not have interpretable ERTL-4 test results.

Furthermore, our study did not identify any association between the presence of severe brain injuries and language disorders. This is likely due to the fact that most children with severe brain injuries who survived are treated at specialized institutions and were not included in our cohort because they do not receive standard follow-up.

Data regarding speech therapy between 2 and 4 years of age should also be interpreted cautiously, as it is unclear whether therapy was actually initiated or only prescribed, and whether it targeted language disorders or feeding and oral-motor difficulties.

In addition, as the definition of bronchopulmonary dysplasia continues to evolve, data may have been heterogeneous or imprecise across the inclusion period. Similarly, the study population is highly heterogeneous when considering oxygen requirement, given the wide variability in pulmonary disease severity among preterm infants depending on gestational age and perinatal conditions. Furthermore, data to examine feeding methods (long-term nasogastric tube feeding, gastrostomy) as a risk factor for developing a language disorder were missing [42].

Nevertheless, the model we developed demonstrated good screening performance. The contribution of the ASQ is particularly important, as its performance was nearly equivalent to that of a model incorporating neonatal and socioeconomic factors, highlighting its relevance for routine follow-up of preterm children. Considering evidence from studies showing an association between structural brain abnormalities on MRI and language disorders [22, 43], future models could be improved by incorporating neuroimaging data to increase their discriminative ability.

In order to improve neurodevelopmental outcomes in preterm children, particularly their communication abilities, the implementation of a secondary prevention strategy would be of interest : children identified at risk at 24 months using our model—combining neonatal, socioeconomic, and ASQ communication data— could benefit from an early speech-language evaluation to diagnose an emerging language

disorder and begin follow-up care promptly [44], thereby maximizing communication outcomes during the preschool years.

Finally, language disorders in preterm children are often part of broader neurodevelopmental and cognitive impairments [45, 46], requiring a multidisciplinary approach involving various professionals in the field of neurodevelopmental support, such as physical therapists, occupational therapists, psychologists and neuropsychologists, paediatricians and neuropaediatricians, ENT specialists and ophthalmologists, in addition to the speech-language pathologist.

Abbreviations

LIFT

Loire Infant Follow-up Team

ERTL 4

Epreuve de Repérage des Troubles du Langage

ASQ

Age and Stage Questionnaire

M-CHAT

Modified Checklist for Autism in Toddlers

GEE

Generalized Estimating Equations

ROC

Receiver Operating Characteristic

AUC

Area Under Curve

MRI

Magnetic Resonance Imaging

Declarations

Competing interests :

The authors have no relevant financial or non-financial interests to disclose.

Ethics approval :

This study protocol was reviewed and approved by Medic Ethic Review Committee (METC) Amsterdam UMC location AMC W20_533. This research has been conducted in accordance with the Declaration of Helsinki.

Consent to participate :

Only children whose parents consented to the use of their data were included.

Fundings :

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Author Contribution

All authors contributed to the study conception and methodology. Data collection and analysis were performed by Ghislain Leduc, Jean-Cristophe Rozé, Valérie Rouger. Writing : Marion Flamant, Laura Buzzegoli. Review and editing: Cyril Flamant. Resources: Laura Buzzegoli. All authors read and approved the final manuscript.

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Figures

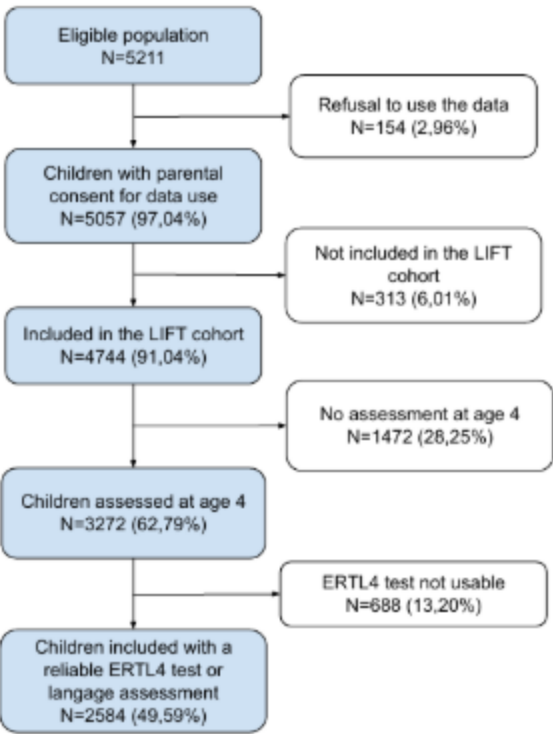


Figure 1

Flowchart

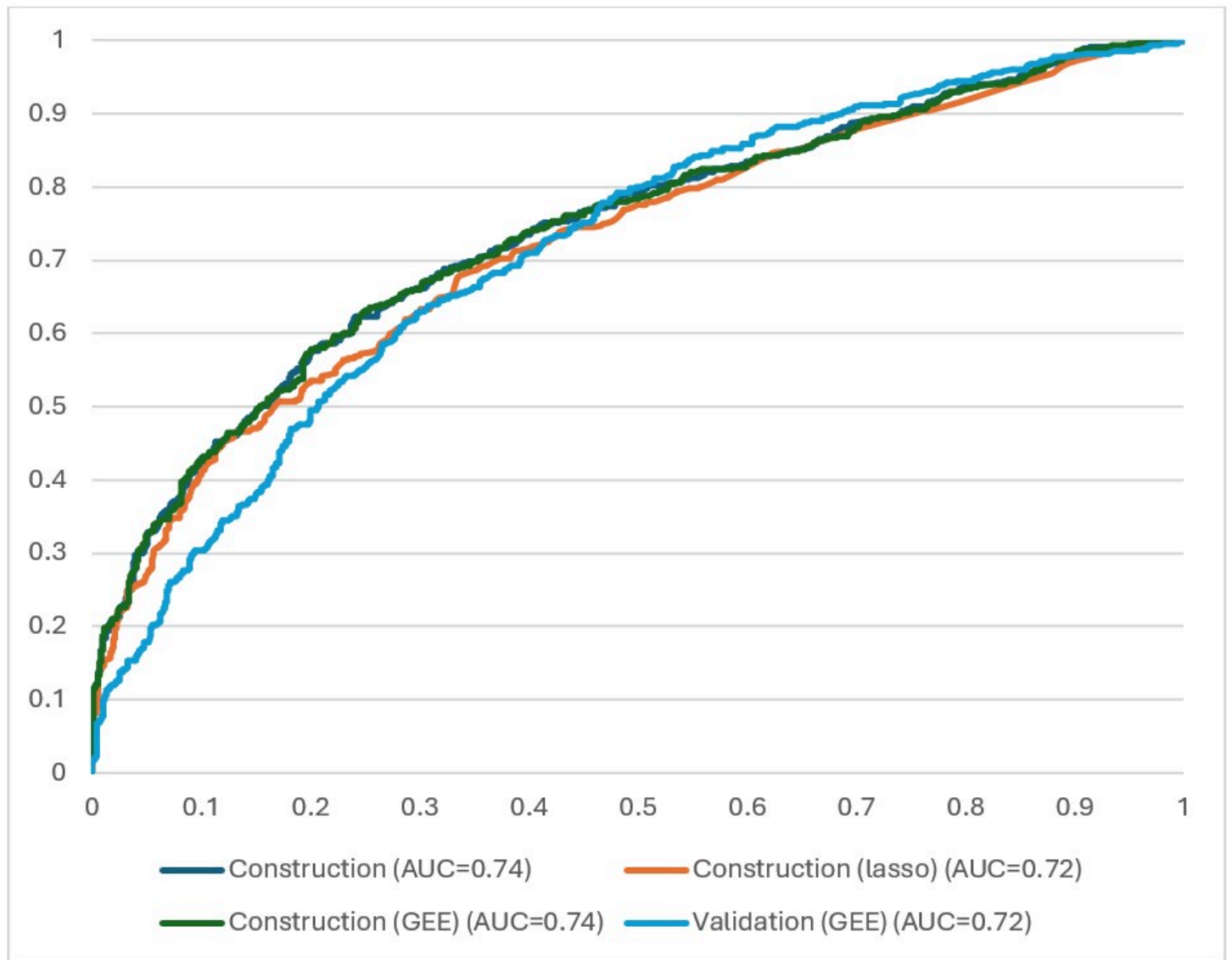


Figure 2

ROC curve and AUC of the final model

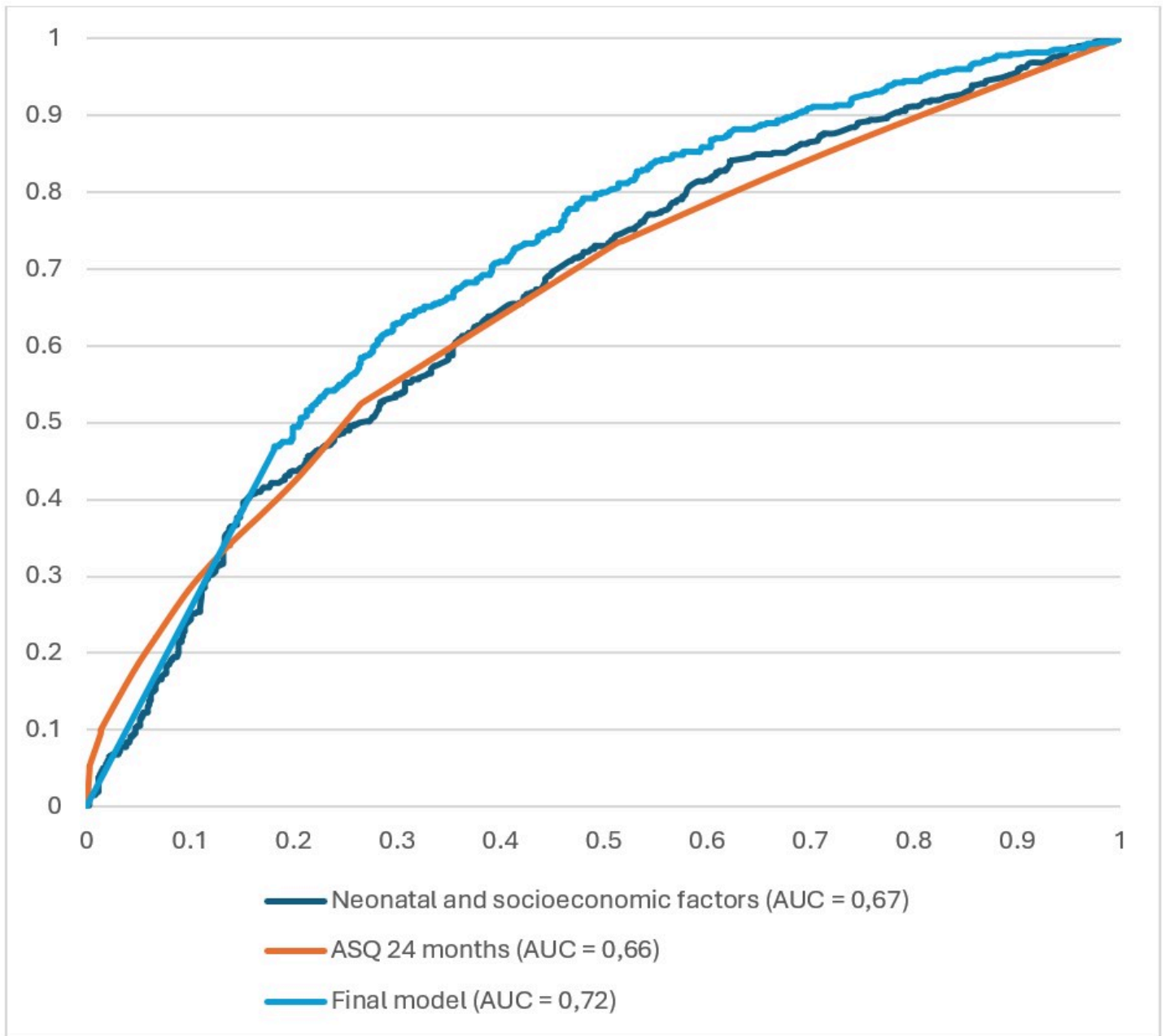


Figure 3

Comparison between the final model, the neonatal and socioeconomic model, and the ASQ model alone