



# Stability of Developmental Problems after School Entry of Moderately-Late Preterm and Early Preterm-Born Children

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**Objective** To assess the stability of developmental problems in moderately-late preterm-born children compared with early preterm and full term-born children before school entry at age 4 years and 1 year after school entry at age 5 years.

**Study design** We included 376 early preterm, 688 born moderately-late preterm, and 403 full term-born children from the Longitudinal Preterm Outcome Project (LOLLIPOP) cohort study. Developmental problems were assessed by the total score and the 5 domain scores of the Ages and Stages Questionnaire at ages 4 (ASQ-4) and 5 (ASQ-5). From the combinations of normal and abnormal ASQ-4 and ASQ-5 scores we constructed 4 categories: consistently normal, emerging, resolving, and persistent problems.

**Results** The ASQ-4 total score was abnormal more frequently in moderately-late preterm (7.9%,  $P = .016$ ) and early preterm-born children (13.0%,  $P < .001$ ) than in full term-born children (4.1%). Compared with the ASQ-5 total score, moderately-late preterm-born children had persistence and change comparable with full term-born children, and early preterm-born children had significantly greater rates than full term-born children of persistent (8.4% vs 2.2%,  $P < .001$ ) and emerging problems (7.8% vs 2.7%  $P = .001$ ). On the underlying domains, both early preterm and moderately-late preterm-born children had mainly emerging motor problems and resolving communication problems, but the changing rates of moderately-late preterm-born children were lower.

**Conclusions** After school entry, the overall development of moderately-late preterm-born children had stability patterns comparable with full term-born children, whereas early preterm-born children had greater rates of persistent and emerging problems. On the underlying domains, moderately-late preterm-born children had patterns comparable with early preterm-born children but at lower rates. (*J Pediatr* 2017;187:73-9).

**P**reterm birth (<36 weeks' gestational age [GA]) has important consequences for further short-term and long-term development. Worldwide, 11% of the children are born preterm.<sup>1</sup> At preschool age, 15%-24% of early preterm-born children (<32 weeks' GA), and 8%-25% of moderately-late preterm-born children (32<sup>0/7</sup>-35<sup>6/7</sup> weeks' GA) have developmental problems, in comparison with 4%-14% of full term-born children (38-41 weeks' gestational age).<sup>2,3</sup> After school entry, similar prevalence rates of developmental problems are reported among preterm-born children.<sup>4,5</sup> However, the preterm-born children with developmental problems at preschool age may not be the same children as those with developmental problems at early school age, as school entry stimulates development but also puts more demands on children's abilities.

Evidence on the stability of developmental problems of preterm-born children mainly concerns early preterm-born children and/or children with a low birth weight (<1500 g).<sup>6,7</sup> These early preterm-born children show, at age 4 years, greater rates of developmental problems on all domains,<sup>8</sup> which both emerge and resolve after school entry.<sup>9-11</sup> However, the evidence per developmental domain is inconsistent.<sup>6,12</sup> Moderately-late preterm-born children have at age 4 years problems with communication, fine motor function, and personal social skills.<sup>8</sup> After school entry, these preschool developmental problems of moderately-late preterm-born children are not good predictors for school problems and school readiness (predictive values 10.4%-17.1%).<sup>13,14</sup> However, studies that assess the association of developmental problems among moderately-late preterm-born children before and after school entry are lacking.

The aim of this study was to assess the stability patterns of developmental problems, overall and per domain, among moderately-late preterm-born children compared with early preterm-born children and full term-born children between the time before school entry and 1 year after school entry. We expected that

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ASQ	Ages and Stages Questionnaire
ASQ-4	Ages and Stages Questionnaire appropriate for age 4
ASQ-5	Ages and Stages Questionnaire appropriate for age 5
GA	Gestational age
LOLLIPOP	Longitudinal Preterm Outcome Project

developmental problems may both emerge and resolve after school entry, because this not only places greater demands on children's abilities but also provides them with more opportunities to practice these abilities by stimulating activities and by interacting with other children. In addition, we expected that problems might emerge more frequently in early preterm-born children and resolve more frequently in moderately-late preterm-born children, because moderately-late preterm-born children may have a less disrupted white matter maturation and more cortical plasticity than early preterm-born children.<sup>15,16</sup> These patterns may help to determine in advance of school entry which preterm-born children are likely to have the greatest risks of persistent and emerging problems after school entry and in which specific developmental domains. Such insight is important for the prevention and early identification of developmental problems in well-child care and neonatal follow-up and could facilitate early intervention, increasing the likelihood of normal development.

## Methods

This study was part of the Longitudinal Preterm Outcome Project (LOLLIPOP) cohort study, which has its main focus on the growth and development of moderately-late preterm-born children compared with both early preterm and full term-born children ([controlled-trials.com](http://controlled-trials.com) ISRCTN 80622320). The LOLLIPOP cohort is a community-based sample of early preterm and moderately-late preterm-born children and a random sample of full term-born children, born in 2002 and 2003 in the Netherlands. This community-based sample came from 13 preventive child health centers. These centers monitored a sample representative of 25% of the children born in 2002 and 2003 in The Netherlands. Children were included before their regular well-child visit at the age of 43-49 months. All children born before 36 weeks' GA without major congenital malformations, congenital infections, or syndromes were sampled. After each second preterm-born child which was sampled, the next full term-born child (38-41 weeks' GA), without the aforementioned exclusion criteria, was drawn from the same files to serve as a control. In addition, the early preterm-born sample was enriched with a sample of early preterm-born children, born in 2003, taken from 5 of the 10 neonatal intensive care units in The Netherlands. A detailed description of this study cohort can be found elsewhere.<sup>8</sup>

## Measures

**Developmental Problems: Ages and Stages Questionnaire (ASQ).** Developmental problems were measured with the ASQ, which is, worldwide, the most commonly used parent-completed developmental screener.<sup>17</sup> We used the validated Dutch versions appropriate for ages 4 (ASQ-4) and 5 years (ASQ-5).<sup>18-20</sup> The ASQ contains 5 domains: communication, gross motor, fine motor, problem solving, and personal-social skills. Each domain is assessed by the use of 6 questions about reaching milestones. The response format is "yes" (10 points), "sometimes" (5 points), or "not yet" (0 points). The scores of the questions were summed into a score for each

domain separately and overall, the ASQ total score. Subsequently, these scores were categorized into normal and abnormal scores, defined as abnormal if the score was more than 2 SDs below the mean of the Dutch reference population.<sup>19,20</sup>

We combined the dichotomous ASQ-4 and ASQ-5 outcomes on the 5 ASQ domains and the ASQ total score to form 4 stability categories for each ASQ outcome: stable normal, emerging problems, resolving problems, and persistent problems. The stable normal group had normal scores at both ages, the emerging problems group had a normal ASQ-4 score and an abnormal ASQ-5 score, the resolving problems group had an abnormal ASQ-4 and a normal ASQ-5, and the persistent problems group had 2 abnormal scores.

**Gestational Age.** The children in the preterm-born group were split into an early preterm-born category (25<sup>0/7</sup>-31<sup>6/7</sup> weeks' GA) and an moderately-late preterm-born category (32<sup>0/7</sup>-35<sup>6/7</sup> weeks' GA). GA was determined in completed weeks and was based on early ultrasound measurements in >95% of the cases. For the remaining cases, only clinical estimates based on last menstrual date were available; these were checked against clinical estimates of GA after birth.

**Covariates.** Covariates were selected based on previous studies of developmental problems in preterm-born children<sup>6,7,21,22</sup> and were divided into perinatal characteristics and family characteristics. Perinatal characteristics included sex, small for GA, and being part of a multiple pregnancy. Small for GA was determined as a birth weight below the 10th centile of the Dutch growth chart.<sup>23</sup> Family characteristics included low education of both mother and father, ethnicity (birth of parent and/or child outside the Netherlands), and single-parent family. Low education was defined as maximally primary education or low-level technical or vocational training.

## Procedure

One month before the children's well-child visit at age 43-49 months, parents received information about the LOLLIPOP study, an informed consent form, the ASQ-4, and a questionnaire about family and perinatal characteristics. These were returned by the parents at their child's scheduled well-child visit. Following parental informed consent, we retrospectively recorded perinatal characteristics from discharge letters of mother and child, well-child care records, and information from linked national birth registers. Approximately 4-6 weeks before the child's fifth birthday, parents received the ASQ-5. The ASQ-5 was returned by mail.

The ASQ-4 and ASQ-5 were completed within the determined time windows<sup>19,20</sup> (43-49 months and 57-63 months after birth, respectively) for 1467 children, including 376 early preterm, 688 moderately-late preterm, and 403 full term-born children (**Figure 1**). The children with only an ASQ-4 (within the time window) but not an ASQ-5 (no ASQ-5 n = 484, outside time window n = 25) had more frequently an abnormal ASQ-4 total score than the children with completed ASQ's at both ages (11.1% vs 8.1%,  $P = .048$ ), and their parents had more frequently a low education (28.6% vs 14.2%

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