Developmental Delay in Moderately Preterm-Born Children at School Entry

Jorien M. Kerstjens, MD, Andrea F. de Winter, PhD, Inger F. Bocca-Tjeertes, MD, Elisabeth M. J. ten Vergert, MD, Sijmen A. Reijneveld, MD, PhD, and Arend F. Bos, MD, PhD

Objective To determine the prevalence and nature of developmental delay at preschool age in infants born moderately preterm compared with those born full-term and early preterm.

Study design Parents of 927 moderate preterm infants (32-35^{+6} weeks gestation), 512 early preterm infants (<32 weeks gestation) and 544 full-term infants (38-41^{+6} weeks gestation) completed the Ages and Stages Questionnaire (ASQ) when the child was aged 43-49 months. We analyzed rates of abnormal ASQ scores and odds ratios for abnormal ASQ scores in both preterm groups compared with the full-term group. We repeated the analyses after adjustment for socioeconomic status, sex, being part of a multiple birth, and small for gestational age status.

Results Abnormal (ie, >2 SDs below the mean) ASQ total scores were noted in 8.3% of moderate preterm infants, in 4.2% of full-term infants, and in 14.9% of early preterm infants. ORs of abnormal ASQ total scores were 2.1 (95% CI, 1.3-3.4) for moderate preterm infants and 4.0 (95% CI, 2.4-6.5) for early preterm infants. Both moderate and early preterm infants had more frequent problems with fine motor, communication, and personal-social functioning compared with full-term infants. Compared with full-term infants, moderate preterm infants did not have a greater prevalence of problems with gross motor functioning and problem solving, whereas early preterms did. Socioeconomic status, small for gestational age status, and sex were associated with abnormal ASQ scores in moderate preterm infants.

Conclusions At preschool age, the prevalence of developmental delay in moderate preterm infants was 2-fold of that in full-term infants and one-half of that in early preterm infants. *(J Pediatr 2011;159:92-8)*.

Moderately preterm infants, born after 32 weeks gestational age, have been considered at low risk for long-term developmental consequences of preterm birth. However, several recent epidemiologic studies have reported that compared with full-term–born children, moderately preterm-born children are more likely to have problems in kindergarten, show less school readiness, repeat grades more often in mainstream education, and receive more special education.[1-4] Moderate preterm infants as a group merit special attention given the increasing incidence of moderate preterm birth in the United States, from 7.4% of live births in 1983 to 10.4% of live births in 2003.[5,6] During the same period, the incidence of early preterm births (<32 weeks gestational age) remained constant at 1.8%-2.0% live births.[6] In Europe, the incidence of moderate preterm birth is 6%-9%.[6] The rising incidence and the possibility of long-term developmental impairments have triggered growing concerns about the economic consequences of moderate prematurity for society.[7,8]

The development of moderate preterm infants before school age has not been widely studied, whereas that of early preterm-born children (early preterm infants) has been studied extensively. Early preterm infants are at risk of developmental delay at an early age. Compared with full-term infants, they are more likely to have delays in fine and gross motor functioning, sensory integration, cognitive functioning, and communication and to have behavioral and socio-emotional problems.[9-12]

The extent to which the developmental risk profile of early preterm infants can be generalized to moderate preterm infants is unclear. The aim of the present study was to determine the prevalence and nature of developmental delay at preschool age in children born between 32 and 36 weeks gestation compared with both term-born and early preterm–born children. We hypothesized that the moderate preterm infants would have more developmental problems than the full-term infants, but fewer developmental problems than early preterm infants.

ASQ	Ages and Stages Questionnaire
Lollypop	Longitudinal Preterm Outcome Project
NICU	Neonatal intensive care unit
PCHC	Preventive child healthcare center
SES	Socioeconomic status
SGA	Small for gestational age

From the Division of Neonatology, Beatrix Children's Hospital (J.K., I.B.-T.,A.B.) and Department of Health Sciences (A.d.W., E.t.V., S.R.), University Medical Center Groningen, Groningen, The Netherlands

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This study is part of a larger cohort study on the development, growth, and health of preterm-born children known as the Lollypop Study (controlled-trials.com ISRCTN 80622320). It is part of the study program of the postgraduate School of Behavioral and Cognitive Neurosciences, University of Groningen. The Ages-and-Stages Questionnaire 48-month form was translated with permission from the author.

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Methods

Longitudinal Preterm Outcome Project (Lollypop) is a large prospective cohort study on the growth, development, and general health of preterm children.[13] The study's main focus is on moderate preterm infants, born between 32 and 35^{+6} weeks gestation. The Lollypop cohort comprises a community-based sample of early and moderate preterm (born before 36 weeks gestation) infants and a random sample of full-term infants seen at preventive child healthcare centers (PCHCs), enriched with a sample of early preterm infants from neonatal intensive care units (NICUs). Cohort size was based on estimates of data needed to compile growth charts for Dutch preterm children, leading to a planned inclusion of 1000 moderate preterm, 500 early preterm, and 500 full-term infants. Children were assessed at age 43-49 months. Prospective data on growth, development, and family characteristics were matched with retrospective data on pregnancy and birth from files maintained by PCHCs, pediatricians, and obstetricians. The Lollypop study was approved by the local institutional review boards. In this article, we present the results of the assessment of the children's development at age 4 years.

Figure 1 provides an overview of both sampling procedures. The community-based sample came from Dutch PCHCs, which monitor 90%-95% of all children at regular intervals from birth until age 4 years.[14] Thirteen PCHCs participated in the study. The PCHCs were randomly selected and stratified by region (north vs south), to balance differences in children's heights between these regions. Together the PCHCs monitored 45 446 children, representing 25% of the 4-year-olds in The Netherlands. Eight PCHCs checked the files of all children born between January 1 and December 31, 2002, and 5 PCHCs checked the files of all children born between June 1, 2002, and May 31, 2003. All children born before 36^{+0} weeks gestation without major congenital malformations, congenital infections, or syndromes were sampled. After each second preterm child sampled, the next term-born child (gestational age 38^{+0}-41^{+6} weeks) without the aforementioned exclusion criteria was drawn from the same files to serve as a control. The PCHCs sampled a total of 2758 children for the study.

Oversampling of early preterm infants was done by 5 tertiary NICUs covering a larger portion of The Netherlands. These NICUs sampled all early preterm infants born between January 1 and December 31, 2003, discharged alive from their unit, and not meeting the exclusion criteria. After removing all children that had been double-sampled, we tracked the local PCHCs of these children (32 additional centers), and asked them to join the study for the children involved. The NICUs sampled an additional 548 early preterm infants for the study.

Parents were invited to participate with their child in the study by mail at 4 weeks before the scheduled PCHC visit at age 43-49 months. The parents received an informational leaflet on the study, an informed consent form, and several questionnaires. They also received detailed instructions on

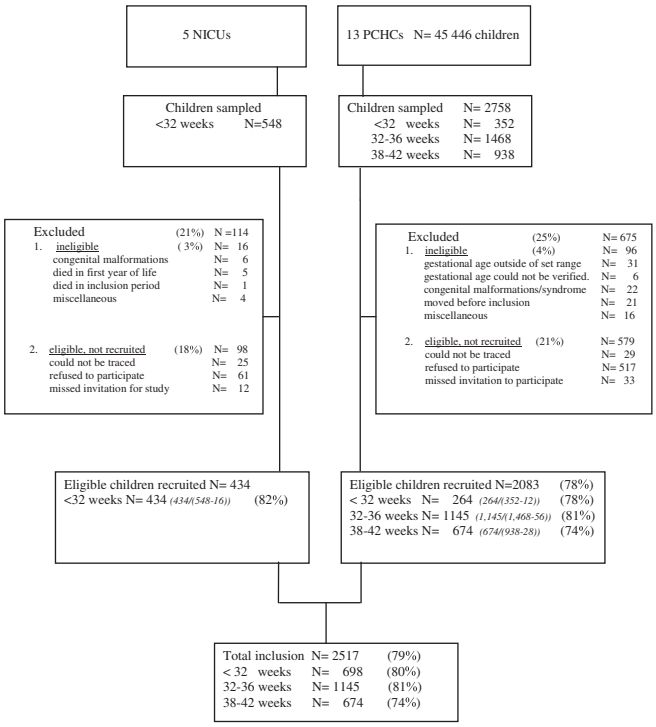

Figure 1. Overview of sampling procedures for the Lollypop study.

completing the Ages and Stages Questionairre (ASQ). The questionnaires were collected at the PCHC physician's visit. Parents of children who did not attend their regular visit were invited again and if necessary reminded by telephone or by a home visit (following routine PCHC procedures). Data were coded following standard practices for maintaining confidentiality.

Measures

Gestational age was confirmed by early ultrasound measurements in >95% of cases. In the remaining cases, only clinical estimates based on last menstrual date were available, and these were checked against clinical estimates of gestational age after birth. Children whose gestational age could not be confirmed were excluded from the analysis.

Development was assessed using the Dutch version of the age 48-month form of the ASQ, a validated parent-completed developmental screening tool.[13,15] The ASQ covers 5 developmental domains: communication, fine motor function, gross motor function, personal-social functioning, and problem solving.[15] Each domain has 6 questions on developmental milestones. Parents evaluate whether the child has achieved a milestone (yes, 10 points), has partly achieved the milestone (sometimes, 5 points), or has not yet achieved the milestone (no, 0 points). ASQ total score is calculated by adding all the domain scores and dividing the total by 5. The ASQ domain and ASQ total scores were dichotomized at 2 SD below the mean score of the Dutch