Survival, Hospitalization, and Acute-Care Costs of Very and Moderate Preterm Infants in the First 6 Years of Life: A Population-Based Study

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Objectives To investigate survival, hospitalization, and acute-care costs of very (28-31 weeks' gestation) and moderate preterm (32-33 weeks' gestation) infants in the first 6 years of life and compare outcomes with the more widely studied extremely preterm infants (24-27 weeks' gestation) and to full term (low risk) infants (39-40 weeks' gestation).

Study design Birth data from all women residing in New South Wales, Australia, with gestational ages between 24-33 and 39-40 weeks in 2001-2011 were linked probabilistically to hospitalization and mortality data. Study outcomes were evaluated with the use of descriptive and multivariable analyses at birth (N = 559 532), discharge (N = 540 240), and at 1 (N = 487 447) and 6 years of age (N = 230 498).

Results Mortality was greatest among extremely preterm infants (eg, 31.2% within 6 years) and decreased with increasing gestational age. Likewise, hospitalization within the first year of life increased with decreasing gestational age (aOR 5.5 [95% CI 4.7-6.4], 3.7 [3.4-4.0], and 2.6 [2.5-2.8] for birth at 24-27, 28-31, and 32-33 weeks' gestation, relative to 39-40 weeks' gestation). Hospitalization remained significantly increased with preterm birth at each year of age up to 6 years (aORs 1.3-1.6 at 6 years). Cumulative costs were significantly greater with preterm birth within the first year of life, and also between 1 and 6 years of age.

Conclusions The risks of adverse health outcomes were significantly greater in very and moderately preterm infants relative to full term infants but lower than extremely preterm infants. Crucially, preterm birth was associated with prolonged increased odds of hospitalization (up to age 6 years), contributing to greater resource use. *(J Pediatr 2016;169:61-8)*.

Fetal development is the single most important predictor of adverse infant health outcomes, with strong evidence linking early gestation to heightened morbidity and mortality, and other metrics such as birth hospitalization length of stay (LOS) and rehospitalization.[1-7] Preterm birth also is associated with increased resource use reflected by increased patient bed days and hospital costs, because of the greater requirement for follow-up medical care.[4,8,9] Most studies in which authors examine the association between preterm birth and infant health outcomes have based their outcomes on extremely low birth weight or extremely preterm neonates (eg, those born at <28 weeks' gestation),[6,10] or infants born at moderate/late preterm (>33 weeks' gestation).[2,11,12] Therefore, less is known about the risks of adverse health outcomes of neonates born at 28-33 weeks' gestation, which comprise a substantial proportion of neonates cared for in the neonatal intensive care unit (NICU) but who usually are not the focus of intensive developmental follow-up programs after discharge.[13]

To address this lack of information, we used population-based data collections from New South Wales (NSW), Australia, to assess survival, rates of hospitalization, and costs of hospital admissions in the first 6 years of life for preterm infants classified into 3 gestational age groups as defined by the World Health Organization[14]: extremely preterm (24-27 weeks), very preterm (28-31 weeks), and moderately preterm (32-33 weeks gestation), with comparison with infants born at full term (39-40 weeks' gestation). Our objectives were to define the risks of adverse health outcomes in neonates born at 28-33 weeks' gestation and relate these risks to infants born extremely preterm and to those born at full term, which have the lowest risk of adverse health outcomes.[15,16]

APDC	Admitted Patient Data Collection
ICD-10-AM	*International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification*
LOS	Length of stay
NAOI	Neonatal Adverse Outcome Indicator
NICU	Neonatal intensive care unit
NSW	New South Wales
PDC	Perinatal Data Collection
RBDM	Registry of Births, Deaths and Marriages
SCN	Special care nursery
USD	US dollars

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Methods

The study population included all births to women residing in NSW, Australia, with a gestational age between 24-33 and 39-40 weeks, during the period January 1, 2001, to December 31, 2011. Data were obtained from the NSW Perinatal Data Collection (PDC), the NSW Admitted Patient Data Collection (APDC), and the NSW Registry of Births, Deaths and Marriages (RBDM) deaths data and have been described previously.[15] In summary, the PDC is a population-based surveillance system that records all births in NSW that are ≥20 weeks' gestation or ≥400 g birth weight and includes information on maternal medical conditions, maternal and infant characteristics, and obstetric data. The APDC is a census of all hospital separations from public and private hospitals in NSW and is based on information collected at discharge. Separate records of hospital admission for both mothers and infants are created at the time of birth, and relevant diagnoses associated with each admission are coded according to the *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification* (ICD-10-AM).[17] The NSW RBDM is a register of vital statistics for NSW residents that includes information on all deaths. PDC records were linked to maternal and infant hospital records (APDC), and RBDM death records by the Centre for Health Record Linkage, which uses ChoiceMaker software (http://oscmt.sourceforge.net) to probabilistically link records, with probable matches that fall below the "true match" threshold reviewed clerically. Strict quality assurance procedures are followed to ensure that both false-positive and false-negative results are each less than 5 in 1000. Infant APDC hospital records were available up to the age of 6 years. The linkage rate between the PDC and infant and mother's APDC was high (~97%), and the proportion of missing data was small.[18] This study was approved by the NSW Population and Health Services Research Ethics Committee.

Study Outcomes

Study outcomes in the neonatal period were stillbirth, neonatal death up to 28 days postbirth, death before neonatal discharge, admission to special care nursery (SCN) or NICU, birth admission LOS and median costs, postmenstrual age at discharge, and readmission to hospital within 30 days of discharge from the birth admission. Postmenstrual age at discharge was defined as the sum of gestational age at birth and the number of completed weeks subsequently spent in hospital between birth and discharge. Longer term outcomes assessed were mortality up to 6 years of age, admission to hospital (and primary diagnosis) by age, mean acute care costs per hospital admission up to 6 years of age (excluding birth admission), and cumulative acute care costs within the first year of life (excluding birth admission) and between 1 and 6 years of age. Estimates of acute care costs for each hospital stay were derived according to the NSW Cost of Care Standards 2009/10,[19] as previously described.[15] Costs in Australian dollars were converted to US dollars (USD) via a mean exchange rate of 0.9033 (for the year 2014). The most common health conditions associated with hospitalization were identified from the APDC based on primary ICD-10-AM diagnosis codes.

Predictive Factors

The covariates used in the study reflect known risk factors identified in the literature.[5,20-24] The main predictive factor was gestational age group divided into 3 preterm categories: 24-27, 28-31, 32-33, with infants born at 39-40 weeks' gestation used as the full-term comparator. Severe neonatal morbidity was defined by a modified Neonatal Adverse Outcome Indicator (NAOI).[25] The NAOI uses information on diagnosis and procedure codes from the APDC and data from the PDC to generate a composite metric that covers a range of conditions commonly observed in severely ill infants. The indicator was developed through a comprehensive process involving literature review, validation studies, and expert consultation, culminating in the identification of a suite of reliably reported conditions, diagnoses, and procedures that are indicative of serious neonatal morbidity.

The indicator showed strong associations with readmission to hospital and mortality, providing face validity, and facilitates the reliable identification of infants with severe neonatal morbidity from population-based, administrative data collections. The composite indicator helps compensate for the underascertainment associated with the use of individual diagnosis and procedure codes to identify infants born with severe neonatal morbidity.[25] Diagnoses of gestational age <32 weeks and birth weight <1500 g were not included in the modified NAOI. Procedures pertaining to the use of central venous or arterial catheters and the administration of any intravenous fluids, which is common at <32 weeks' gestational age, also were excluded from the definition of the NAOI to better identify seriously ill extremely and very preterm infants.

Information on gestational age, parity, maternal age, public or private hospital status, labor onset (spontaneous or planned), plurality (singleton or multiple birth), admission to SCN or NICU, and smoking during pregnancy were obtained from the PDC. The infant APDC provided data on intensive care unit admission, hospital discharge and transfer information, and congenital anomalies (ICD-10-AM codes Q00-Q99). Patent ductus arteriosus and minor congenital anomalies diagnosed at birth such as tongue-tie, undescended testicle, and glandular (mild) or unspecified hypospadias were excluded from the definition of major congenital anomalies. Parental marital status around the time of birth was obtained from maternal APDC records. The Australian Bureau of Statistics Index of Relative Socio-economic Disadvantage, 2006, was used to assign socioeconomic status.[26] The index was allocated to each PDC record by matching on postcode of residence and infants were classified into either "disadvantaged" (1-20th percentile), "average" (21st-80th percentile), or "advantaged" (81st-100th percentile) categories. Postcode