Risk of Mortality into Adulthood According to Gestational Age at Birth

Ravisha Srinivasjois, FRACP[1,2], Wendy Nembhard, PhD[3,4], Kingsley Wong, MSc[4], Jenny Bourke, PhD[4], Gavin Pereira, PhD[5], and Helen Leonard, MPH[2,4]

Objectives To quantify the independent risks of neonatal (0-28 days), postneonatal (29-364 days), 1- to 5- and 6- to 30-year mortality by gestational age and investigate changes in survival over time in an Australian birth cohort.

Study design Maternal and birth related Western Australian population data (1980-2010) were linked to the state mortality data using a retrospective cohort study design involving 722 399 live-born singletons infants.

Results When compared with 39- to 41-week born infants, the adjusted risk ratio for neonatal mortality was 124.8 (95% CI 102.9-151.3) for 24-31 weeks of gestation, 3.4 (95% CI 2.4-4.7) for 35-36 weeks of gestation, and 1.4 (95% CI 1.1-1.8) for 37-38 weeks of gestation. For 24-31 weeks of gestation infants, the adjusted hazard ratio for postneonatal mortality (29-364 days) was 13.9 (95% CI 10.9-17.6), for 1- to 5-year mortality 1.4 (95% CI 0.7-3.0) and for 6- to 30-year mortality 1.3 (95% CI 0.8-2.3). The risk of neonatal and postneonatal mortality for those born preterm decreased over time.

Conclusions In Western Australia, late preterm and early term infants experienced higher risk of neonatal and postneonatal mortality when compared with their full-term peers. There was insufficient evidence to show that gestational length was independently associated with mortality beyond 1 year of age. Neonatal and postneonatal mortality improved with each decade of the study period. *(J Pediatr 2017;190:185-91).*

Improvements in maternal and neonatal care over recent years such as the advent of surfactant in the 1990s, more optimal antenatal steroid administration, and advances in neonatal surgery have contributed to better survival of preterm infants.[1-3] Despite this progress, extreme preterm infants born at gestational ages of less than 32 weeks experience higher risk of neonatal and postneonatal mortality when compared with infants born at full term.[4]

Although many sociodemographic characteristics such as maternal age, education, socioeconomic status, infant sex, and birthweight[5-8]contribute to increased risk of mortality, clinical risk factors such as mode of delivery, and type of cesarean delivery (emergency vs elective) have also been shown to modify this risk.[5,9-11] Despite these modifying factors, gestational age continues to be a strong determinant of morbidity and mortality in early childhood. We previously demonstrated that, compared with term births born at 39-41 weeks of gestation, rehospitalization rates were higher up to 18 years for all preterm infants born <37 weeks of gestation and early term infants born at 37-38 weeks of gestation.[12] The effect was highest during the first year of life and declined by adolescence. Children born preterm specifically had increased risk of admissions for infections at all ages and for injury-related admissions between 5 and 18 years.[13] Recent reports have also indicated that even late preterm infants born at 35-36 weeks of gestation and early term infants born at 37-38 weeks of gestation experience higher mortality in the neonatal period compared with full term infants.[14] However, there is still a paucity of specific information on the gestational-age-specific risk of late childhood and adult mortality for each gestational age category.[15]

Given the importance of understanding the risk of short- and long-term mortality for children born at various gestational ages, born preterm, we aimed to examine the risk of neonatal (0-28 days), postneonatal (29-364 days), 1- to 5-year and 6- to 30-year mortality by gestational age in an Australian birth cohort. We also investigated temporal changes in risk of neonatal and postneonatal mortality for births between 24 and 28 weeks of gestation.

Methods

We carried out a retrospective cohort study using data from the Midwives' Notification System. All live births in Western Australia between January 1, 1980 and December 31, 2010 were included. Gestational age at birth was the exposure variable and mortality from 0 to 30 years was the outcome variable. The Midwives'

AHR	Adjusted hazard ratio
ARIA	Accessibility/Remoteness Index of Australia
ARR	Adjusted risk ratio
IRSD	Index of Relative Socio-Economic Disadvantage

From the [1]Department of Neonatology and Paediatrics, Joondalup Health Campus, Perth, Western Australia; [2]School of Paediatrics and Child Health, University of Western Australia, Perth, Australia; [3]Department of Epidemiology, University of Arkansas for Medical Sciences and Arkansas Children's Research Institute, Little Rock, AR; [4]Telethon Kids Institute; and [5]School of Public Health, Curtin University, Perth, Australia

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Notification System was established in 1975 and receives information from midwives and other healthcare professionals about all births they attend in Western Australia. All births for infants of at least 20 weeks of gestation, or with a birthweight of at least 400 g if the gestational age is unknown, are included. Maternal information is reported from conception to 24 hours following birth, death, discharge, or transfer from the delivery site, whichever occurs first. History of previous pregnancy outcomes and medical conditions diagnosed before conception and present during the index pregnancy is also recorded.

Midwives' Notification System data were linked to the Western Australian Death Registrations Database from January 1, 1980 through December 31, 2010. Children were considered deceased if so noted in the database. Children not recorded as deceased were censored on December 31, 2010, the end of the study period. All data files were linked by the Data Linkage Unit of the Western Australian Department of Health, Data Linkage Branch.

Gestational age was categorized into very preterm (24-31 completed weeks), moderate preterm (32-34 completed weeks), late preterm (35-36 completed weeks), early term (37-38 completed weeks), full term (39-41 completed weeks), and post-term (≥42 weeks) based on dating ultrasound and last menstrual period where dating ultrasound was not available.[16] Other variables included maternal age group (<20, 20-34, ≥35 years), maternal race (Aboriginal, White, other), maternal marital status (married [including de facto], never married, former/unknown), infant sex (female, male), birth decade (1980-1989, 1990-1999, 2000-2010), infant birthweight (400-1499, 1500-2499, ≥2500 g), parity (0, 1, 2, 3, 4, ≥5), onset of labor (spontaneous, induced, no labor [elective cesarean delivery]), mode of delivery (vaginal/vacuum/forceps, elective cesarean delivery, emergency cesarean delivery), and smoking status during pregnancy (yes, no).

We obtained community-level socioeconomic status information for each mother by linking the Midwives' Notification System data to the Socio-Economic Indexes for Areas Collection District level data from the Australian Bureau of Statistics based on maternal address reported in Census. A collection district is the smallest area unit for which socioeconomic data is provided and is roughly equivalent to a small group of suburban blocks in urban areas.[17] We used the Socio-Economic Indexes for Areas Index of Relative Socio-Economic Disadvantage (IRSD) for Census years 1996, 2001, and 2006 to indicate general socioeconomic status with low and high index scores representing relatively greater or lack of disadvantage respectively.[17,18] In our analysis, the continuous score was categorized into 6 percentile groups: 0-10, 11-25, 26-50, 51-75, 76-90 and >90. We used the Accessibility/Remoteness Index of Australia (ARIA) classification (major city, inner regional, outer regional, remote, very remote) to indicate geographic remoteness.

Statistical Analyses

Descriptive statistics were used to summarize maternal and birth characteristics of the study population. Infants with structural or chromosomal birth defects were excluded from the analyses. Mortality risks were estimated using Cox proportional hazards regression models for each gestational age group during the overall (birth-30 years) and 4 separate periods: neonatal (0-28 days), infant (29-364 days), 1-5 years, and 6-30 years, conditional on survival to the beginning of the period. In the analysis, follow-up time was censored at death or the end of the period (eg, neonatal: 28 days). Log binomial regression was used if investigation of the Schoenfield residuals indicated that the proportional hazards assumption was violated. Adjusted models included all study covariates and potential confounders of infant sex, maternal race, maternal age, maternal marital status, parity, mode of delivery, onset of labor, birth decade, ARIA classification, and IRSD. Birth decade was included in multivariate models to adjust for time trend effects. Smoking status was excluded from the models as the data were only available from September 1997 onward. The models that investigated the association between mortality (neonatal, infant, 1-5 years, and 6-30 years) and individual gestational age (24-34 weeks) after accounting for potential confounders were fitted using log binomial regression. Estimates, as well as its 95% CIs, were reported. The postestimation "margins" command in Stata was used to estimate the average adjusted predicted risk of mortality for individual gestational age. In total, 83 591 (11.6%) of records had missing data that was distributed as follows: onset of labor (N = 1), method of delivery (N = 2), maternal age (N = 16), parity (N = 1688, 0.23%), ARIA (N = 79 525, 11.01%), and IRSD (N = 81 933, 11.34%). For all models, missing data were mainly related to ARIA classification and IRSD scores because some addresses were not able to be geocoded to within a radius that fits within a single CD and, therefore, were unable to have an area-based statistic assigned to them. The software package Stata (StataCorp. 2015 Stata Statistical Software: Release 14; StataCorp LP, College Station, Texas) was used for all analyses.

The study was reviewed and approved by the Government of Western Australia Department of Health, Human Ethics Review Committee and the Western Australian Aboriginal Health Ethics Committee.

Results

Between January 1, 1980 and December 31, 2010 inclusive, there were 792 373 births in Western Australia. We excluded 42 869 children with structural or chromosomal anomalies and excluded 27 105 births because of indeterminate sex, multiple fetuses (ie, twin, triplet, etc), birthweight less than 400 g and stillbirths/terminations of pregnancies. Two infants were also excluded for death dates that preceded their date of birth. The final study population consisted of 722 399 singleton births. The maternal and birth characteristics of the children are shown in **Table I** and **Table II**, respectively. Of the total births, 65% were full term, 27% were early term, and extreme prematurity accounted for less than 1%. The majority of mothers were white (86%), married (90%), primiparous or para 1 (74%), and less than 35 years of age at the birth of their child (87%). Almost three-quarters (72%) lived in major cities, 10% each in inner and outer regional areas, and a smaller proportion lived