Selection Bias and Outcomes for Preterm Neonates

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abstract

BACKGROUND: Reported survival and neurodevelopmental outcomes at 23 weeks' gestation are based on the infants admitted to NICUs. In this study, we aim to describe the association between clinical characteristics and admission to NICU at 23, 24 and 25 weeks' gestation.

METHODS: Cohort data from 2 national databases enabled comparison of the clinical characteristics all Australian births and all NICU admissions during 2010–2013 at 23, 24, and 25 weeks' gestation.

RESULTS: NICU admission occurred in 15% of all births at 23 weeks, in comparison with 49% at 24 weeks and 64% at 25 weeks. At 23 weeks, live-born infants were less likely to be admitted to NICU with birth weight <500 g compared with >500 g (13% vs 43%, $P < .0001$), and boys were admitted less compared with girls (33% vs 43%, $P < .018$). In contrast, birth weight (including birth weight <500 g) and sex had little or no impact on NICU admission at 24 and 25 weeks. Only 8% of live births were born by caesarean delivery at 23 weeks compared with 33% at 24 weeks and 48% at 25 weeks' gestation.

CONCLUSIONS: In the Australian population, admission to the NICU is more likely to be influenced by birth weight and sex at 23 weeks' gestation when compared with 24 and 25 weeks' gestation. Survival outcomes at 23 weeks may be affected by less active perinatal care. Uncertainty exists regarding the generalizability of current data regarding survival and developmental potential of live-born 23-week infants.

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WHAT'S KNOWN ON THIS SUBJECT: Levels of intervention and reported survival outcomes for preterm infants at 23 weeks' gestation vary around the world. In Australia, reported survival data at 23 weeks' gestation are based on the infants admitted to NICUs.

WHAT THIS STUDY ADDS: The survival of 23-week infants is influenced by active perinatal care of the fetus, including selection by birth weight and sex for admission to NICU. These effects are much less evident at 24 and 25 weeks.

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Diversity in practice and controversy exist in high-income countries worldwide regarding initiation of intensive care for preterm neonates born at 23 weeks' gestation.[1] Clinical guidelines vary from provision of palliative care at birth, care based on individual characteristics, to care directed by parental wishes.[2] At 24 and 25 weeks' gestation, initiation of intensive care is generally considered reasonable and in many centers is the default stance.[1]

The evidence base to support decision-making is complicated by a number of factors. Outcomes reported at 23 weeks' gestation vary around the world and are challenging to compare because of the varied denominator used to express these outcomes.[3] Survival per total birth, survival per live birth, or survival per admission to the NICU are all currently used.[3] In addition, the reporting of factors that indicate perinatal management with an active intent to optimize survival are variable, including antenatal steroid use, birth in a tertiary perinatal center, and caesarean delivery. Such perinatal factors may influence physiologic stability at birth, the capacity for effective resuscitation of infants, survival, and morbidity. Finally, ethical and cultural factors influence interpretation of reported outcomes.[1]

Variation in reported outcomes is illustrated by comparison of national prospective data from Sweden and France.[4,5] In Sweden, 52% of infants born live at 23 weeks survived between 2004 and 2007.[5] However, in France in 2011, intensive care was withheld or withdrawn for 91% of infants born at 23 weeks, and only 1 infant out of the 414 live-born infants survived to discharge.[4]

Currently, reports on prognosis for preterm birth in Australia are based on NICU admission data. In data published by the Australian and New Zealand Neonatal Network (ANZNN), it is shown that survival of infants admitted to the NICU was 55% at 23 weeks' gestation in 2013.[6] However, a large proportion of infants born at 23 weeks are not admitted to the NICU. Clinical characteristics associated with a decision to admit or not admit to the NICU have not been well described.

The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) of the United States reported that the survival of an extremely preterm infant improved by an amount similar to a 1-week increase in gestational age for each of the following factors: girl, antenatal steroid exposed, singleton, and for each 100 g increase in birth weight.[7] The selection of favorable prognostic characteristics based on such data may influence reports of survival outcomes. A greater understanding of the degree of selection bias and markers of active perinatal care are likely to be important in informing debate regarding management of infants at this gestation.

In this study, we hypothesize that live-born 23-week infants are selectively admitted to NICU on the basis of characteristics perceived to be of prognostic advantage and that this selection is greater at 23 weeks than with older gestations. Our aim in this study is to use Australian national perinatal and neonatal data sets to describe the association between clinical characteristics and admission to the NICU at 23, 24, and 25 weeks' gestation.

METHODS

Infants born in Australia at 23, 24, and 25 weeks' gestation in the 4-year cohort 2010–2013 were included. Birth details recorded via the national perinatal data collection (NPDC) of the Australian Institute of Health and Welfare (AIHW) were obtained. The NPDC records a broad range of demographic, obstetric, birth, and neonatal information on all live births and stillbirths in Australia of at least 20 weeks' gestation or 400 g birth weight.[8]

The NPDC does not have a reliable record of admission to NICU for all infants. To determine characteristics of NICU-admitted infants for the same gestations over the study epoch, a second national data set, the ANZNN, was used. All Australian NICUs submit detailed clinical and outcome data to the ANZNN. New Zealand NICU admissions were excluded from the ANZNN data because the NPDC does not include New Zealand birth data.

The definitions for common characteristics between the databases were identified and compared. The 2 databases are not designed with linkage by unique identifiers for individuals. The data within categories of matching definitions were transformed into deidentified aggregate summary numerical data. To maintain confidentiality, the minimum number of infants in a category was 5. Where necessary, categories were combined to increase numbers, prevent data suppression, and therefore allow derivation of the group of interest.

The number and proportion of stillborn and live-born infants were determined at 23, 24, and 25 weeks' gestation by using NPDC data. Stillbirths were considered as a whole group (including deaths due to congenital malformations) because cause-of-death data were not available for approximately half the stillborn cohort at each gestation. The contribution of medical termination of pregnancy to preterm birth and mortality is not recorded in either data set with sufficient quality because the report is voluntary and nonstandardized. Death due to congenital abnormality may be a proxy marker for palliative management of the fetus and infant. Similarly, induction of labor (IOL) may be unlikely at borderline gestations without palliative intent. These markers may have value in estimating the stillborn and live-born infants at each gestation who were not intended for intensive care admission. The NPDC data on death due to congenital abnormality were provided per year because contribution from different states within Australia was variable. To maintain the minimum of 5 per category each year, the 24- and 25-week gestations were combined.

The number of infants who were live born, but not admitted to NICU, was determined by the difference between aggregate numbers of live-born infants recorded by the NPDC and the infants admitted to NICU as registered with ANZNN. These data were used to test for association between NICU admission and clinical characteristics.

The databases had matching definitions and adequate data item completeness (defined as <5% missing data) in the following categories: maternal age, plurality, fetal presentation, onset of labor, caesarean delivery, birth weight, and sex. Terminology considered equivalent were NPDC's "spontaneous" with ANZNN's "preterm" labor and NPDC's "fetal death" and our use of "stillborn" for this study. The following dichotomous variables were analyzed: multiple pregnancy compared with singleton, breech (and other malpresentations: face, brow, shoulder, transverse, and compound) compared with vertex presentation, caesarean delivery compared with vaginal birth, and male sex compared with female. Multiple categories were compared in analysis of maternal age and birth weight to identify a threshold affecting admission to NICU.

Categories not recorded or incomplete in both databases were not included in the analysis. Onset-of-labor data were available for 2 categories in both databases: absence of labor and spontaneous labor. However, the third option, IOL, was only recorded by the NPDC (and may include cases in which IOL was attempted, but labor did not result), but this was not recorded by ANZNN. Maternal ethnicity was not stated in 25% of ANZNN data. Antenatal steroids and location of birth (relative to a tertiary neonatal center) were recorded in the ANZNN database but not the NPDC.

To determine the association of a characteristic with NICU admission, the data were analyzed by comparing NICU admission with and without a characteristic. χ^2 statistical analysis was used with an α level of .05 and adjustment for multiple comparisons where appropriate. Relative risks (RRs) with 95% confidence intervals (CIs) were used to estimate the magnitude of risk for the outcomes.

Missing data were excluded, with these comprising <5% of the total for any variable reported (except death due to congenital abnormality). It was not possible to impute for "not stated" categories in aggregate data items.

The Southern Adelaide Clinical Human Research Ethics Committee and James Cook University Human Research Ethics Committees granted approval for this project.

RESULTS

The total number of births in Australia was similar at each gestation (Table 1). Mortality at 23 weeks was substantial in both the antenatal period (stillbirth) and the period between birth and admission to NICU (nonadmitted). Stillbirth at 23 weeks occurred in 61% of all births, declining to 40% at 24 weeks and 29% at 25 weeks' gestation (adjusted $P < .001$). The proportion of live births admitted to NICU increased with increasing gestation, from 38% at 23 weeks to 80% at 24 weeks and 90% at 25 weeks (adjusted $P < .001$).

Data were available on cause of death for 53% of stillbirths at 23, 24, and 25 weeks' gestation. Death due to congenital malformation in stillbirth was less at 23 weeks compared with 24 to 25 weeks (24% vs 34%, RR: 0.68, 95% CI: 0.55–0.85, $P < .001$). Less live-born infants died due to a congenital abnormality compared with stillbirths, and this decreased from 7% at 23 weeks to 2% at 24 to 25 weeks (RR: 3.78, 95% CI: 1.93–7.40, $P < .001$). Few (0.6%) infants admitted to NICU died of congenital abnormality. IOL was associated with 74% of all stillbirths at 23 weeks (Table 1). IOL was less common in live births and fell with advancing gestation (16% for 23 weeks, 9% for 24 weeks, and 4% for 25 weeks, $P < .001$ for all comparisons).

The proportion of live-born infants admitted to NICU at 23 weeks was lower for each characteristic analyzed when compared with 24 or 25 weeks' gestation ($P < .001$, comparing Tables 2, 3 and 4). In Table 2, we show the association of each defined characteristic with NICU admission at 23 weeks. The same analysis for 24 and 25 weeks' gestation is presented in Tables 3 and 4, respectively. Birth weight was associated with NICU admission of live births at 23 weeks, in contrast to 24 and 25 weeks in which no association with birth weight and admission was noted. At 23 weeks, 13% of live-born infants with birth weight <500 g were admitted to NICU compared with 43% of live-born infants with birth weight >500 g (RR: 0.30, 95% CI: 0.17–0.54, $P < .001$). The proportion of infants within each birth weight stratum admitted to NICU increased as weight increased at 23 weeks. In contrast, the proportion of live-born infants with birth weight <500 g admitted to NICU at 24 and 25 weeks (84% and 83%, respectively) was similar to the proportion of live births admitted in which birth weight was

TABLE 1 Survival Outcomes of Infants Born at 23, 24, and 25 Weeks' Gestation in Australia From 2010 to 2013, Derived From the AIHW NPDC and the ANZNN Database of Neonatal Intensive Care Admissions

Survival Outcomes	23 wk	24 wk	25 wk
Total births	1257	1155	1175
Stillborn, *n* (%)			
Total births	763 (61)	459 (40)	336 (29)
Congenital abnormality[a]	96 of 407 (24)	145 of 421 (34)[b]	145 of 421 (34)[b]
IOL	561 of 763 (74)	345 of 459 (75)	279 of 336 (83)
Live born			
n (% total births)	494 (39)	696 (60)	839 (71)
Congenital abnormality, *n* (%)[a]	18 of 273 (7)	15 of 860 (2)[b]	15 of 860 (2)[b]
IOL, *n* (%)	78 of 494 (16)	63 of 696 (9)	34 of 839 (4)
NICU admitted			
n (% of live born)	187 (38)	560 (80)	754 (90)
Congenital abnormality, *n* (%)[a]	7 of 1247 (0.6)[c]	7 of 1247 (0.6)[c]	7 of 1247 (0.6)[c]
Discharged from the hospital[d]			
n (% of NICU admitted)	98 (52)	361 (64)	578 (79)

[a] Percentage of total in which cause-of-death data were complete.

[b] Gestation categories were combined to maintain deidentification because of low numbers of live-born infants with death due to congenital abnormality at 24 and 25 wk reported within individual years by AIHW.

[c] Gestation categories were combined to maintain deidentification because of low numbers of live-born NICU-admitted infants with death due to congenital abnormality at 23, 24, and 25 wk reported within individual years by AIHW.

[d] Total of data published by the ANZNN for the years 2010,[9] 2011,[10] 2012,[11] and 2013.[6]

TABLE 2 Proportion of Infants With Selected Perinatal Characteristics Admitted to the NICU at 23 Weeks

Characteristic Present	NICU Admitted Out of Total With Characteristic, *n* (%)	Comparative Characteristic	NICU Admitted Out of Total With Comparative Characteristic, *n* (%)	RR	RR 95% CI	*P*
Live birth	187 of 494 (38)	Stillbirth	0 of 763 (0)			
Maternal age, y		Maternal age, y				
<20	19 of 43 (44)	>20	168 of 451 (37)	1.19	0.83–1.69	.37
20–34	132 of 350 (38)	<20 or >34	55 of 144 (38)	0.99	0.77–1.26	.92
≥35	36 of 101 (36)	<35	151 of 393 (38)	0.93	0.69–1.24	.61
Multiple pregnancy	52 of 117 (44)	Singleton	135 of 377 (36)	1.24	0.97–1.58	.09
Breech or other	87 of 210 (41)	Vertex	100 of 284 (35)	1.18	0.94–1.47	.16
Onset of labor		Onset of labor				
Spontaneous	158 of 393 (40)	Nonspontaneous	29 of 101 (29)	1.40	1.01–1.95	.03
No labor	18 of 22 (82)	With labor	169 of 472 (36)	2.29	1.81–2.88	<.001
Cesarean delivery	27 of 39 (69)	Vaginal delivery	160 of 455 (35)	1.97	1.54–2.51	<.001
Birth wt, g		Birth wt, g				
<500	10 of 78 (13)	>500	177 of 416 (43)	0.30	0.17–0.54	<.001
500–599	72 of 206 (35)	<500 or ≥600	115 of 288 (40)	0.88	0.69–1.11	.26
600–699	85 of 172 (49)	<600 or ≥700	102 of 322 (32)	1.56	1.25–1.94	.001
≥700	20 of 38 (53)	<700	167 of 456 (37)	1.44	1.04–1.99	.05
Boy	88 of 266 (33)	Girl	99 of 228 (43)	0.76	0.61–0.96	.02

Denominators are total numbers of live-born infants with the indicated characteristics (from the AIHW NPDC). Numerators indicate NICU admission with the characteristic (using data from all Australian NICUs from the ANZNN data set). RR indicates the likelihood of NICU admission with a characteristic present compared with the likelihood of admission with the comparative characteristic.

>500 g and also similar within birth weight strata.

A lower proportion of boys were admitted to NICU at 23 weeks (Table 2). At 23 weeks, 33% of live-born boys were admitted, compared with 43% of live-born girls (RR: 0.76, 95% CI: 0.61–0.96, $P = .018$). There was less association between sex and NICU admission at 24 weeks and none by 25 weeks.

Caesarean delivery was less frequent in live births at 23 weeks compared with 24 weeks (8% vs 33%, RR: 0.72, 95% CI: 0.58–0.89, $P < .001$) and was 48% at 25 weeks (24 vs 25 weeks, RR: 1.07, 95% CI: 1.03–1.12, $P = .045$). Caesarean delivery was associated with but not completely predictive of NICU admission at 23 weeks, with 69% of live births born by caesarean admitted to the NICU in contrast to 35% of vaginal births (RR: 1.97, 95% CI: 1.54–2.51, $P < .001$). At 24 and 25 weeks, 96% and 90%, respectively, of infants born by caesarean delivery were admitted to the NICU. These data are paralleled by the category of "no labor," which

TABLE 3 Proportion of Infants With Selected Perinatal Characteristics Admitted to the NICU at 24 Weeks

Characteristic Present	NICU Admitted Out of Total With Characteristic, *n* (%)	Comparative Characteristic	NICU Admitted Out of Total With Comparative Characteristic, *n* (%)	RR	RR 95% CI	*P*
Live birth	560 of 696 (80)	Stillbirth	0 of 459 (0)			
Maternal age, y		Maternal age, y				
<20	41 of 46 (89)	>20	519 of 650 (80)	1.12	1.00–1.24	.13
20–34	387 of 492 (79)	<20 or >34	173 of 204 (85)	0.93	0.86–1.00	.07
≥35	132 of 161 (82)	<35	428 of 535 (80)	1.02	0.94–1.11	.58
Multiple pregnancy	140 of 175 (80)	Singleton	420 of 521 (81)	0.99	0.91–1.08	.86
Breech or other	272 of 332 (82)	Vertex	288 of 364 (79)	1.04	0.96–1.11	.35
Onset of labor		Onset of labor				
Spontaneous	459 of 531 (86)	Nonspontaneous	101 of 165 (61)	1.41	1.24–1.60	<.001
No labor	105 of 110 (95)	With labor	455 of 586 (78)	1.23	1.16–1.30	<.001
Cesarean delivery	222 of 231 (96)	Vaginal delivery	338 of 465 (73)	1.32	1.24–1.41	<.001
Birth wt, g		Birth wt, g				
<500	27 of 32 (84)	>500	533 of 664 (80)	1.05	0.90–1.23	.57
500–599	83 of 108 (77)	<500 or ≥600	477 of 588 (81)	0.95	0.85–1.06	.30
600–699	233 of 293 (80)	<600 or ≥700	327 of 403 (81)	0.98	0.91–1.06	.60
700–799	151 of 181 (83)	<700 or ≥800	409 of 515 (79)	1.05	0.97–1.14	.24
≥800	66 of 78 (85)	<800	494 of 618 (80)	1.06	0.96–1.17	.33
Boy	297 of 382 (78)	Girl	263 of 314 (84)	0.93	0.86–1.00	.05

Denominators are total numbers of live-born infants with the indicated characteristics (from the AIHW NPDC). Numerators indicate NICU admission with the characteristic (using data from all Australian NICUs from the ANZNN data set). RR indicates the likelihood of NICU admission with a characteristic present compared with the likelihood of admission with the comparative characteristic.

TABLE 4 Proportion of Infants With Selected Perinatal Characteristics Admitted to NICU at 25 Weeks

Characteristic Present	NICU Admitted Out of Total With Characteristic, *n* (%)	Comparative Characteristic	NICU Admitted Out of Total With Comparative Characteristic, *n* (%)	RR	RR 95% CI	*P*
Live birth	754 of 839 (90)	Stillbirth	0 of 336 (0)			
Maternal age, y		Maternal age, y				
<20	45 of 51 (88)	>20	709 of 788 (90)	0.98	0.88–1.09	.70
20–34	531 of 570 (93)	<20 or >34	223 of 269 (83)	1.12	1.06–1.19	<.001
≥35	178 of 217 (82)	<35	576 of 622 (93)	0.89	0.83–0.95	<.001
Multiple pregnancy	155 of 166 (93)	Singleton	599 of 673 (89)	1.05	1.00–1.10	.10
Breech or other	289 of 322 (90)	Vertex	465 of 517 (90)	1.00	0.95–1.05	.93
Onset of labor		Onset of labor				
Spontaneous	538 of 576 (93)	Nonspontaneous	216 of 263 (82)	1.14	1.07–1.21	<.001
No labor	213 of 228 (93)	With labor	541 of 611 (89)	1.06	1.01–1.10	.04
Cesarean delivery	360 of 401 (90)	Vaginal delivery	394 of 438 (90)	1.00	0.95–1.04	.93
Birth wt, g		Birth wt, g				
<500	35 of 42 (83)	>500	719 of 797 (90)	0.92	0.81–1.06	.15
500–599	58 of 68 (85)	<500 or ≥600	696 of 771 (90)	0.94	0.85–1.05	.19
600–699	126 of 140 (90)	<600 or ≥700	628 of 699 (90)	1.00	0.94–1.06	.96
700–799	211 of 233 (91)	<700 or ≥800	543 of 606 (90)	1.01	0.96–1.06	.68
≥800	324 of 352 (92)	<800	430 of 487 (88)	1.04	1.00–1.09	.08
Boy	409 of 456 (90)	Girl	345 of 383 (90)	1.00	0.95–1.04	.85

Denominators are total numbers of live-born infants with the indicated characteristics (from the AIHW NPDC). Numerators indicate NICU admission with the characteristic (using data from all Australian NICUs from the ANZNN data set). RR indicates the likelihood of NICU admission with a characteristic present compared with the likelihood of admission with the comparative characteristic.

was strongly associated with NICU admission and reflect caesarean birth without labor.

Maternal age was associated with NICU admission at 25 weeks, but there were no other significant differences at any gestation in maternal age, plurality, or presentation (Tables 2–4).

DISCUSSION

Current survival outcomes of infants born at 23 weeks' gestation in Australia are based on the 15% of all infants and 38% of live-born infants at this gestation who are admitted to the NICU. In contrast, the corresponding proportions admitted to NICU at 24 and 25 weeks are 49% and 64% of all births and 80% and

90% of live births, respectively. As survival reports are based on live-born NICU-admitted infants, there is the greatest potential for selection bias at 23 weeks, and accuracy of prognosis for a fetus or live-born infant will increase with increasing gestation.

Those admitted to NICU at 23 weeks' gestation in our cohort had more favorable prognostic characteristics. Birth weight >500 g and female sex favored provision of intensive care after live birth at 23 weeks. At 24 and 25 weeks, in contrast, gestation alone is the dominant factor influencing NICU admission, with little effect of birth weight or sex. This may indicate either a more nuanced approach to clinical management at 23 weeks based on perception of prognosis relating to birth weight and sex or greater intrinsic physiologic instability for weight <500 g and male sex at this gestation. However, the abrupt change in influence of weight and sex on NICU admission between 23 and 24 weeks suggests clinical bias against admission at 23 weeks rather than a graduated physiologic influence.

Measures that may indicate active perinatal care in this study include the rates of stillbirth, admission of live-born infants to the NICU, and birth by caesarean delivery. These were all different at 23 weeks compared with 24 and 25 weeks. Stillbirth and nonadmission of live-born infants to the NICU were important influences on survival at 23 weeks' gestation, more so than at 24 and 25 weeks. Willingness to perform a caesarean delivery at 23 weeks was also lower at 23 weeks than at 24 and 25 weeks. These data are consistent with a more conservative attitude to management of the fetus at 23 weeks, which may include less intrapartum monitoring and active intervention to optimize survival.

In previous studies, authors reporting outcomes after prematurity have excluded infants with lethal congenital abnormality or birth after termination of pregnancy.[4,5,7,12,13] Notably, the reasons for higher stillbirth and non-NICU admission after live birth at 23 weeks are not explained by inclusion in this data set of infants unintended for NICU admission as indicated by death attributed to congenital abnormality. Some caution is required with this interpretation, however, because of incomplete data on cause of death, and this is a limitation of our study. Likewise, rates of IOL were only slightly higher in live-born infants at 23 weeks compared with 24 weeks and were similarly high at each gestation for stillborn infants. IOL is an imperfect indicator of lack of intent for NICU admission because reasons for IOL may include termination of pregnancy, in utero fetal death, chorioamnionitis, and avoidance of caesarean delivery for maternal health reasons.

In our study, we report similar factors to the NICHD: gestation, sex, plurality, and birth weight.[7] Our findings differ in that weight <500 g and male sex were only negatively predictive of NICU admission at 23 weeks' gestation. Furthermore, multiple pregnancy had no association with NICU admission at any gestation. In the NICHD study, non-NICU–admitted infants had less intervention and worse prognostic characteristics to those admitted, but the authors of the study did not differentiate those stillborn.[7] Also, in the NICHD study, authors describe a select population of births in tertiary referral centers in an era (1998–2003) when few 23-week infants were admitted.[13]

There are few other studies in which researchers tested for selection bias of extremely preterm infants relative to admission to NICU. In France, infants were infrequently admitted to NICU at 23 weeks, but factors associated with admission between 24 and 26 weeks' gestation are well described and similar to those reported in our study: older gestational age, greater birth weight, multiple pregnancy, and additionally, in vitro fertilization. There was no effect of sex, maternal age, or ethnicity.[4]

In several other studies, authors suggest that active perinatal management in extreme prematurity is the main determinant of survival and neurodevelopmental outcomes, rather than admission of infants with the most favorable prognostic characteristics. Comparison between regions in Sweden reveals marked variation in stillbirth, NICU admission, and survival of extremely premature infants, with few differences in demographic or clinical characteristics.[14] Within the NICHD, the centers with highest intervention rates appear to have the best outcomes.[15] In European[14] and Canadian[16] centers, better outcomes were significantly associated with more active perinatal management, although determining effect of individual components of active perinatal management is challenging from these cohort studies.

The strength of our study is the use of contemporary population cohort data from 2 national databases maintained by organizations that lead in collaboration, data collation, cleaning, and validation.[6,8] The numbers of infants included per annum approximate those of the largest outcome studies to date.[4,7,12,17] Future linkage studies between these databases in which researchers use unique identifiers for individuals could allow a multivariate analysis to determine the influence of individual characteristics of all infants on outcomes through the perinatal period to long-term follow-up.

Limitations of the study include an assumption that both the databases cover exactly the same population and that correct information is provided to AIHW and ANZNN. Lack of data availability or completeness precluded comparison variables relating to ethnicity, antenatal steroid use, and outborn or inborn status relative to a tertiary institution. Antenatal steroid administration may be an important indicator of active management of the pregnancy because intent to optimize survival of the fetus is not directly recorded. This information may be used to help determine the significant contribution of physiologic and technical limitations to outcomes in prematurity when active management is provided. Also, outborn status has previously been found to be important in the Australian context.[18] The data sets were also unable to quantify other factors important in counseling that may influence the decision to admit to NICU, including the clinician and family's beliefs and values, because this may lead to a rational decision to choose palliative care.[1,19]

Provision of active perinatal management both reflects and determines survival and neurodevelopmental outcomes. A self-perpetuating feedback loop exists: perception of prognosis determines if active perinatal management is provided and thus influences the outcomes achieved, and the outcomes achieved inform the perception of prognosis. On a population level, professionals involved in communication of outcomes and policy makers should be mindful that the decision to provide active perinatal care and admit to NICU may be a major factor in determining survival and outcome rates measured and subsequently quoted.

CONCLUSIONS

In the Australian population, admission to NICU is more likely to be influenced by birth weight and sex at 23 weeks' gestation, when compared with 24 and 25 weeks' gestation. Survival outcomes at 23 weeks may be affected by less active perinatal care. Uncertainty exists regarding the generalizability of current data regarding the survival and developmental potential of live-born 23-week infants.

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ABBREVIATIONS

AIHW: Australian Institute of Health and Welfare
ANZNN: Australian and New Zealand Neonatal Network
CI: confidence interval
IOL: induction of labor
NICHD: National Institute of Child Health and Human Development
NPDC: national perinatal data collection
RR: relative risk

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