Risk adjusted and population based studies of the outcome for high risk infants in Scotland and Australia

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Abstract

Objectives—To compare outcomes of care in selected neonatal intensive care units (NICUs) for very low birthweight (VLBW) or preterm infants in Scotland and Australia (study 1) and perinatal care for all VLBW infants in both countries (study 2).

Design—Study 1: risk adjusted cohort study; study 2: population based cohort study.

Subjects—Study 1: all 2621 infants of <1500 g birth weight or <31 weeks’ gestation admitted to a volunteer sample of hospitals comprising eight of all 17 Scottish NICUs and six of all 12 tertiary NICUs in New South Wales and Queensland in 1993–1994; study 2: all 5986 infants of 500–1499 g birth weight registered as live born in Scotland and Australia in 1993–1994.

Main outcomes—Study 1: (a) hospital death; (b) death or cerebral damage, each adjusted for gestation and CRIB (clinical risk index for babies); study 2: neonatal (28 day) mortality.

Results—Study 1. Data were obtained for 1628 admissions in six Australian NICUs, 775 in five Scottish tertiary NICUs, and 148 in three Scottish non-tertiary NICUs. Crude hospital death rates were 13%, 22%, and 22% respectively. Risk adjusted hospital mortality was about 50% higher in Scottish than in Australian NICUs (adjusted mortality ratio 1.46, 95% confidence interval (CI) 1.29 to 1.63, p < 0.001). There was no difference in risk adjusted outcomes between Scottish tertiary and non-tertiary NICUs. After risk adjustment, death or cerebral damage was more common in Scottish than Australian NICUs (odds ratio 1.9, 95% CI 1.5 to 2.5). Both these risk adjusted adverse outcomes remained more common in Scottish than Australian NICUs after excluding all infants <28 weeks’ gestation from the comparison. Study 2. Population based neonatal mortality in infants of 500–1499 g was higher in Scotland (20.3%) than Australia (16.6%) (relative risk 1.22, 95% CI 1.08 to 1.39, p = 0.002). In a post hoc analysis, neonatal mortality was also higher in England and Wales than in Australia.

Conclusions—Study 1: outcome was better in the Australian NICUs. Study 2: perinatal outcome was better in Australia. Both results may be consistent, at least in part, with differences in the organisation and implementation of neonatal care.

Keywords: neonatal intensive care units; mortality; very preterm infants; very low birthweight infants

Scotland and Australia have contrasting models of organisation for neonatal intensive care. In 1993 and 1994, nearly all infants who received neonatal intensive care were treated in 17 tertiary and non-tertiary centres in Scotland and in 23 tertiary centres in Australia. Average annual numbers of deliveries per neonatal intensive care unit (NICU) were therefore less than 4000 in Scotland1–7 and over 10 000 in Australia, assuming 65 000 and 250 000 annual births, respectively.1,8 In Australia a greater proportion of consultants who supervise NICUs are full time neonatologists, and neonatal specialist training for nurses is longer, typically requiring a year compared with six months in the United Kingdom. Official recommendations for nurse infant staffing ratios also differ: the British Association of Perinatal Medicine has recommended up to two ventilated infants per nurse each shift,9 whereas the Australian Health Ministers’ Advisory Council stipulates only one ventilated infant per nurse.10

STUDY 1
To investigate whether these models of organisation may be associated with differences in outcome, we prospectively compared risk adjusted hospital mortality in very low birthweight (VLBW; <1500 g) or very preterm (<31 weeks’ gestation) infants in selected NICUs in each country. The main aims were to compare outcomes between countries and types of NICU, adjusting for risk using gestation and CRIB (clinical risk index for babies) scores.9 CRIB is an index of clinical risk and illness severity in infants of <1500 g birth weight or <31 weeks’ gestation, which has been validated as more accurate than birth weight or gestation in assessing initial risk of hospital mortality among infants admitted for neonatal intensive care.10–15

Although the most valid measure of the outcome of care after admission to NICUs is hospital mortality, adjusted for clinical risk and initial illness severity, appropriate data for risk adjustment were not routinely collected when this study was planned. Risk adjusted mortality could only be measured in those units that accepted the invitation to participate in the project. This was therefore not a population based comparison and selection bias could not be excluded.
Table 1  Hospital organisation, clinical characteristics, and unadjusted outcomes for 2612 very low birthweight (VLBW) or preterm infants admitted to Scottish and Australian neonatal intensive care units in 1993 and 1994

<table>
<thead>
<tr>
<th></th>
<th>Scottish tertiary centres</th>
<th>Scottish non-tertiary centres</th>
<th>Australian tertiary centres</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of centres</td>
<td>5</td>
<td>3</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Total VLBW/preterm infants admitted</td>
<td>827</td>
<td>156</td>
<td>1629</td>
<td>0.0001†</td>
</tr>
<tr>
<td>Number of intensive care cots*</td>
<td>10 (10, 20)</td>
<td>4 (4, 6)</td>
<td>20 (13, 20)</td>
<td>0.0001†</td>
</tr>
<tr>
<td>Annual volume of VLBW/preterm infants per centre*</td>
<td>104 (65, 121)</td>
<td>30 (30, 31)</td>
<td>297 (255, 422)</td>
<td>0.0001†</td>
</tr>
<tr>
<td>Gestation (weeks)*</td>
<td>29 (27, 31)</td>
<td>29 (27, 31)</td>
<td>29 (27, 30)</td>
<td>0.016†</td>
</tr>
<tr>
<td>Birth weight (g)*</td>
<td>1180 (900, 1400)</td>
<td>1171 (880, 1388)</td>
<td>1166 (908, 1375)</td>
<td>0.665‡</td>
</tr>
<tr>
<td>Five minute Apgar score*</td>
<td>9 (7, 9)</td>
<td>9 (7, 9)</td>
<td>8 (7, 9)</td>
<td>0.0001†</td>
</tr>
<tr>
<td>Worst base excess in first 12 hours (mmol/l)*</td>
<td>–5 (–8.45, –2)</td>
<td>–4 (–8.85, –2.6)</td>
<td>–4.05 (–6.7, –1.9)</td>
<td>0.0001†</td>
</tr>
<tr>
<td>Maximum Fio_2 in first 12 hours*</td>
<td>0.21 (0.21, 0.38)</td>
<td>0.25 (0.21, 0.4)</td>
<td>0.25 (0.21, 0.4)</td>
<td>0.0003†</td>
</tr>
<tr>
<td>CRIB score*</td>
<td>2 (1.6) (n = 761)</td>
<td>3 (1.7) (n = 136)</td>
<td>2 (1.6) (n = 1476)</td>
<td>0.410†</td>
</tr>
<tr>
<td>Hospital deaths (%)</td>
<td>172/775 (22%)†</td>
<td>33/148 (22%)</td>
<td>216/1628 (13%)</td>
<td>&lt; 0.0001†</td>
</tr>
<tr>
<td>Major brain damage in infants who had ultrasound scanning (%)</td>
<td>87/734 (12%)</td>
<td>12/151 (8%)</td>
<td>118/1480 (8%)</td>
<td>&lt; 0.0001†</td>
</tr>
</tbody>
</table>

*Median (interquartile range).
†From Kruskal-Wallis test for three independent samples.
‡If all missing cases in Scotland had survived, the hospital mortality for Scottish neonatal intensive care units would be 20.9%. If the missing case in Australia had died, the hospital mortality rate would be 13.3%. The difference between these rates remains statistically significant.

STUDY 2
Population based 28 day neonatal mortality statistics were available for all infants born alive and weighing between 500 and 1499 g, as they are a statutory requirement in Scotland and Australia. However, the neonatal death rate is a measure of perinatal rather than neonatal outcome, as it reflects both obstetric and neonatal care.16 17 Bearing in mind this caveat, we compared national neonatal death rates in liveborn infants of 500–1499 g during the same period. As neonatal care is an important component of perinatal care, we predicted that, provided that the sample of Scottish and Australian NICUs selected in study 1 were not atypical of each country, any difference in risk adjusted mortality between them would be reflected by a parallel difference in population based neonatal mortality.

Methods
STUDY 1
The risk adjusted cohort study included all 2612 infants of less than 31 weeks’ gestation or less than 1500 g birth weight admitted between 1 January 1993 and 31 December 1994 to 14 Australian or Scottish NICUs which agreed to provide a simple minimum dataset over this period. They comprised six of all 12 Australian NICUs in Queensland and New South Wales (Kirwan, Townsville; Mater and Royal Women’s, Brisbane; John Hunter, Newcastle; Westmead and King George V Hospitals, Sydney), the five designated tertiary Scottish NICUs (Aberdeen Maternity Hospital; Queen Mother’s Hospital for Sick Children, Yorkhill, Glasgow; Royal Maternity Hospital, Glasgow; Ninewells Hospital and Medical School, Dundee; Simpson Memorial Maternity Pavilion, Edinburgh), and three of the 12 non-tertiary Scottish NICUs (Southern General Hospital, Glasgow; Raigmore Hospital, Inverness; Forth Park Hospital, Kirkcaldy). The primary outcome was hospital mortality before hospital discharge. Infants admitted to neonatal units with inevitably lethal congenital malformations were excluded from all stages of the analysis. The severity of other congenital malformations were subsequently coded in three categories9 as acutely life threatening, not acutely life threatening, or absent or trivial, by a neonatologist unaware of the country of hospital. A secondary outcome was death or major cerebral damage on ultrasound, defined as cystic leucomalacia, porencephalic cyst, or parenchymal echodensities observed in either hemisphere.9 Measures of clinical risk and illness severity were abstracted from notes after discharge. CRIB includes three clinical components, birth weight, gestation, and severity of congenital malformation, and three measures of illness severity up to 12 hours from birth, maximum and minimum appropriate fraction of inspired oxygen, and worst base deficit.9 CRIB scores were calculated for every admission, from data up to 12 hours from birth or until death if sooner. Outcomes of transferred infants were attributed to the hospital providing the longer period of care between 12 and 72 hours from birth.

STUDY 2
National neonatal mortality statistics for all live births between 500 and 1499 g birth weight for 1993 and 1994 were obtained from statutory sources.1 4

STATISTICAL ANALYSES
Multiple logistic regression analysis was undertaken using hospital mortality and hospital mortality or survival with cerebral damage as outcomes. Goodness of fit was assessed by the Hosmer Lemeshow χ² statistic,18 for which p > 0.05 indicates satisfactory fit. Discriminatory power was assessed by receiver operator characteristic analysis.18 Differences in proportions were tested by χ² test, and differences between medians by the Kruskal-Wallis U test or Mann-Whitney test.
Results

STUDY 1
Table 1 describes hospital and clinical characteristics for the 2612 VLBW or preterm infants admitted to the study NICUs. Unadjusted hospital mortality was significantly higher in Scotland (22%) than in Australia (13%). Among all VLBW infants, the proportions of extremely low birthweight (500–999 g) infants were similar in the study cohort and each country (table 2). The average annual numbers of VLBW (500–1499 g) infants admitted per study NICU were 51 in Scotland and 121 in Australia. Both were more than the maximum possible average number admitted per NICU in all Scotland (n = 36) and Australia (n = 104), but the ratios were similar between countries (51:36 v 121:104; \( \chi^2 = 0.59, p = 0.441 \)).

A multiple logistic model was fitted by forward stepwise conditional regression, with hospital mortality as the dependent variable and CRIB, gestation, hospital type (Scottish tertiary NICU, Scottish non-tertiary NICU, or Australian NICU), and country of care as explanatory variables. All these variables except hospital type were independently associated with mortality, with no interactions between them and the model achieving satisfactory goodness of fit (table 3). The receiver operator characteristic curve area was 0.88. When CRIB was omitted, the model did not achieve satisfactory goodness of fit.

Australian NICUs were used as a reference by fitting models for hospital mortality using CRIB and gestation, and gestation alone, in Australian infants only. Adjusted hospital mortality was then calculated as the ratio of observed to predicted mortality using those models in all Scottish NICUs and in non-tertiary and tertiary Scottish NICUs separately. Mortality in Scottish NICUs was 46% higher than in Australian NICUs, adjusting for CRIB and gestation (table 3), and 69% higher adjusting for gestation alone (table 4). Adjusted mortality remained higher in Scottish NICUs after counting missing outcomes in Scotland as survivors and in Australia as deaths. Adjusted mortality was similar in Scottish tertiary and non-tertiary NICUs (tables 3 and 4). Compared with Australian NICUs, mortality in Scottish non-tertiary NICUs was not significantly higher after adjustment for CRIB and gestation (table 3), but was 61% higher after adjustment for gestation alone (table 4). The odds of hospital mortality in the whole cohort were twice as high in Scotland as in Australia (odds ratio 2.1, 95% confidence interval (CI) 1.6 to 2.8) and remained higher in Scotland in a cohort of 1803 infants which was obtained after excluding all those of less than 28 weeks’ gestation (odds ratio 1.9, 95% CI 1.2 to 2.9).

A separate multiple regression model was then fitted, relating the composite variable of hospital death or survival with major cerebral damage to gestation, CRIB, and country. This had satisfactory goodness of fit (Hosmer-Lemeshow \( \chi^2 = 4.21, 8 \) df, \( p = 0.84 \)), with no interaction between explanatory variables. After adjustment for CRIB and gestation, the odds of death or survival with major cerebral damage were twice as high in Scottish as in Australian NICUs (odds ratio 1.9, 95% CI 1.5 to 2.5). The odds of death or survival with major brain damage remained higher in Scotland in the cohort of 1803 infants obtained after excluding those of less than 28 weeks’ gestation (odds ratio 2.0, 95% CI 1.4 to 2.8).

STUDY 2
Table 5 shows that neonatal mortality was higher in Scotland (20.3%) than Australia (16.6%) among all 5986 infants 500–1499 g birth weight (relative risk 1.22, 95% CI 1.08 to 1.38).
Organisation and implementation of neonatal care

In England and Wales neonatal mortality statistics for very low birthweight infants included live born infants < 500 g birth weight. However, their case mix, as the average numbers of VLBW infants for both randomly selected and they admitted more than their patients’ mortality risk was similar soon after birth, having accounted for prior risk and treatment, such as antenatal steroids, neonatal resuscitation, early surfactant treatment, and neonatal care after 12 hours after birth. Therefore the lower risk adjusted mortality in Australia is consistent with more effective neonatal care after 12 hours after birth.

Our study was designed to impose as little extra work as possible by collecting only a minimum of data. We did not therefore request information about transfers between hospitals before or after birth or the number of liveborn infants after 20 weeks’ gestation who died without admission to neonatal units, or who were admitted to neonatal units for comfort measures by birth weight, was nationally representative (table 2) and they accounted for about 75% of all high risk infants admitted in Scotland, over 95% in Queensland, and nearly 50% in New South Wales during the study period. Compared with that in Scottish and Australian tertiary NICUs, adjusted mortality was not significantly different in Scottish non-tertiary NICUs, but this may reflect small sample size and wide confidence intervals (tables 3 and 4). Scottish tertiary NICUs showed a trend to higher risk adjusted mortality than Scottish non-tertiary NICUs after adjustment for CRIB and gestation, but this was not statistically significant. However, a true excess mortality in tertiary hospitals is not inconceivable. Larger nationally representative studies of hospital outcome in relation to volume, staffing policy, and workload are needed. Furthermore, birthweight specific and gestation specific hospital death rates are less valid indicators of NICU performance, as they are more influenced by events before birth. We addressed these issues by adjusting hospital mortality for gestation and CRIB.

Caution is required in interpreting the results because these NICUs were not randomly selected and they admitted more than the average numbers of VLBW infants for both countries. However, their case mix, as measured by birth weight, was nationally representative (table 2) and they accounted for about 75% of all high risk infants admitted in Scotland, over 95% in Queensland, and nearly 50% in New South Wales during the study period. Compared with that in Scottish and Australian tertiary NICUs, adjusted mortality was not significantly different in Scottish non-tertiary NICUs, but this may reflect small sample size and wide confidence intervals (tables 3 and 4). Scottish tertiary NICUs showed a trend to higher risk adjusted mortality than Scottish non-tertiary NICUs after adjustment for CRIB and gestation, but this was not statistically significant. However, a true excess mortality in tertiary hospitals is not inconceivable. Larger nationally representative studies of hospital outcome in relation to volume, staffing policy, and workload are needed. Furthermore, birthweight specific and gestation specific hospital death rates are less valid indicators of NICU performance, as they are more influenced by events before birth.
care only. Previous work showed no difference in outcome between postnatally transferred and inborn infants after adjusting for clinical risk and initial severity of illness. However, as variations in admission policy for very immature infants may lead to selection bias, we compared risk adjusted hospital mortality and the composite outcome of mortality or cerebral damage after excluding infants of less than 28 weeks’ gestation. Both risk adjusted adverse outcomes remained more common in Scottish than Australian NICUs.

Rates of cerebral damage or disability may not reflect the quality of NICU care, as the timing of cerebral damage leading to disability is often unclear. For example, by salvaging infants whose brains are damaged before birth, effective neonatal care may push up, not reduce, the prevalence of disability. In previous studies, CRIB has been associated with cerebral haemorrhage before discharge and with death or disability in survivors at 18 months. If we assume that the proportion of preterm infants sustaining postnatally determined brain damage was similar in each country, then the lower rate of cerebral damage in Australian NICUs after adjustment for CRIB and gestation is further evidence of better NICU performance.

STUDY 2
If NICUs were generally less effective in Scotland than Australia, we predicted that population based neonatal mortality for all infants of 500–1499 g birth weight would also be higher in Scotland. Table 5 supports that prediction. An alternative explanation for the difference in neonatal mortality may be differences in accuracy of ascertainment and completeness of registration, particularly for extremely immature infants at the edge of viability. However, definitions of live births and statutory requirements for registration are similar in both countries and a trend to greater survival in Australia was also seen in infants of 1000–1499 g birth weight, in whom failure to be registered as live born is less likely.

In further analyses, population based neonatal mortality in infants of less than 1500 g birth weight was also lower in Australia than in England and Wales during the study period 1993–1994. The same was true for Australia compared with Scotland and England and Wales in 1995 and 1996, and for all four years combined (table 5). These differences in neonatal outcome were therefore not transient. The inclusion of infants of less than 500 g may have disadvantaged England and Wales somewhat in these comparisons, but the same pattern of difference in mortality between the three populations was also seen for infants of 1000–1499 g birth weight.

How else could the overall findings be explained? An ideal system for risk adjustment would reliably assess total risk and illness severity at birth or NICU admission. As this is not practicable, illness severity is measured from data soon afterwards, reflecting the infant’s intrinsic condition and prior treatment, hence the possibility of “lead time bias” or “early treatment bias”. Units that increase their infants’ illness severity by poor early treatment may decrease their risk adjusted mortality compared with those that improve early illness severity. If Australian NICUs made their infants more ill or Scottish NICUs did the opposite, this lead time or early treatment bias may explain the increased risk adjusted mortality in Scottish NICUs. However, that explanation is unlikely, as hospital mortality remained higher in Scottish NICUs when adjusted for gestation alone (table 4).

Another improbable explanation is that the NICUs in this study are unrepresentative of all Australian NICUs, whose true level of performance is equal to or worse than that of Scottish NICUs. If this were so, the excess 28 day neonatal mortality reported in Scotland would need to be attributed to less effective obstetric and early neonatal care in Scotland than Australia.

Can the better outcomes in Australia be attributed entirely to genetic, social, or environmental factors? This is also unlikely. Between 1985 and 1994, stillbirths and deaths in the first month in Australia fell from 11.8 to 8.0 per 1000 births, while stillbirths and deaths in the first week in Scotland fell from 9.8 to 7.4 per 1000 births. These trends are more likely to reflect rapid advances in obstetric and neonatal care rather than genetic, socioeconomic, or environmental improvement. Furthermore, although the risk of being of very low birth weight may increase with lower social class, it is not clear that, within the lower social class group, mortality is related to social class independently of birth weight, gestation, or illness severity. The findings are also unlikely to reflect differences in the scoring of congenital malformations, as these were coded in ignorance of each infant’s nationality.

We conclude that neonatal intensive care was more effective in this sample of Australian NICUs, echoing a recent international comparison of paediatric intensive care, and that neonatal mortality was lower in Australia. These findings may be consistent, at least in part, with differences in the organisation of neonatal services, such as greater specialisation of medical and nursing staff, or higher nurse/patient ratios, or with differences in speed of implementation of effective treatment. If substantial increases in the daily volume of patients are associated with more effective care, the markedly greater numbers of patients treated by Australian NICUs may also be important.

Although these findings may focus attention on perinatal and neonatal services in Scotland and England and Wales, there is no room for inertia in Australia, or elsewhere. Few countries collect national data on mortality and disability after neonatal intensive care. Given the potential burden on families and high costs to society, this seems illogical. We suggest that neonatal and postneonatal deaths in infants admitted to NICUs should be linked with measures of early illness severity, so that population based risk adjusted rates of NICU mortality can be monitored. Effective systems for
monitoring the rate of major disability in survivors is also needed and may be feasible at relatively little cost. These initiatives could help health planners in future demand for paediatric services and in building a framework for large randomised trials to track outcomes and test promising strategies for prevention.

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