



Survival of very-low-birth-weight infants according to birth weight and gestational age in a public hospital

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Objectives. To determine the survival rates for infants weighing 500 - 1 499 g according to birth weight (BW) and gestational age (GA).

Design. This was a retrospective cohort study. Pregnancy and delivery data were collected soon after birth and neonatal data at discharge or at death.

Setting. Chris Hani Baragwanath Hospital (CHBH), a public-sector referral hospital, affiliated to the University of the Witwatersrand.

Subjects. Live births weighing between 500 g and 1 499 g delivered at or admitted to CHBH from January 2000 to December 2002.

Outcome measures. BW and GA-specific survival rates for all live infants born at CHBH and for those admitted for neonatal care.

Results. Seventy-two per cent of infants survived until discharge. The survival to discharge rate was 32% for infants

weighing < 1 000 g, and 84% for those weighing 1 000 - 1 499 g. Survival rates at 26, 27 and 28 weeks' gestation were 38%, 50% and 65% respectively. Survival rates for infants admitted to the neonatal unit were better than rates for all live births, especially among those weighing < 1 000 g or with a GA < 28 weeks. There was a marked increase in survival between the 900 - 999 g and 1 000 - 1 099 g weight groups. Provision of antenatal care, caesarean section, female gender and an Apgar score more than 5 at 1 or 5 minutes were associated with better survival to hospital discharge.

Conclusion. Survival among infants weighing less than 1 000 g is poor. In addition to severe prematurity, the poor survival among these infants (< 1 000 g) is most likely related to the fact that they were not offered mechanical ventilation. Mechanical ventilation should be offered to infants weighing < 1 000 g as it may improve their survival even in institutions with limited resources.

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The survival rates of very-low-birth-weight (VLBW) infants (birth weight < 1 500 g) to hospital discharge have been well documented in developed countries.^{1,7} Some of these studies have reported on improvement in outcome after the implementation of neonatal intensive care, use of mechanical ventilation and exogenous surfactant, especially for extremely low-birth-weight infants.^{1,3,5,7} The availability of neonatal intensive care beds/facilities and exogenous surfactant is limited in developing countries; this requires health providers in these countries to make decisions as to which infants should get access to or receive these limited facilities.

Chris Hani Baragwanath Hospital (CHBH) provides maternity and neonatal services for the population of Soweto and surrounding areas which form part of greater

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Johannesburg. It is also used as one of the referral centres for the southern part of Gauteng. From 2000 to 2002 there was an average of 19 000 hospital deliveries per year, and there were an additional 8 000 deliveries from midwife-run clinics for which CHBH is the referral hospital. The neonatal intensive care unit (NICU) is officially a 30-bed unit with 12 beds for mechanical ventilation. There are 2 other nurseries, one a 50-bed level II nursery and the other, previously a 40-bed level I nursery, which has been converted to a 24-hour kangaroo mother care (KMC) unit with 25 beds. On average, the bed occupancy rate is 95% for the beds used for mechanical ventilation and 180 - 200% for the rest of the NICU, and 130 - 180% in the level II nursery. Because of limited availability of beds for mechanical ventilation, infants weighing < 1 000 g are not offered mechanical ventilation. Furthermore, because of a limited budget, the unit is currently restricted to a quota of exogenous surfactant irrespective of the number of infants who may need it. Gestational age (GA) and birth weight (BW) are correlated with outcome, such that many proposals for deciding on management have focused on these measurements.^{2-4,6} Survival rates stratified by BW and GA have an important role to play in evaluating perinatal services and in counselling parents on prognosis. A threshold BW below which it is inadvisable to apply the technology of newborn intensive care will vary according to the number of patients requiring intensive care, relative survival rates and availability of



resources. Therefore it is vital that each unit has a continuing audit of survival rates for these infants, especially in areas with limited resources where there is competition for these resources. The objectives of this study were to determine the survival rates among VLBW infants admitted to CHBH according to BW and GA, and to determine perinatal factors or characteristics associated with better survival rate in our hospital.

Methods

We evaluated survival rates until hospital discharge among infants weighing between 500 g and 1 499 g who were born alive or admitted to CHBH between January 2000 and December 2002. On admission to our neonatal unit the demographic, pregnancy and delivery data are collected routinely on all live-born infants including those who died before admission to the neonatal unit and on all outborn infants admitted to the unit. On discharge from the hospital or on the death of an infant while in hospital the above information, plus neonatal and outcome data, are extracted from the hospital charts and entered into a computerised database. This was a retrospective cohort study reviewing information from the computerised database, looking at the trends of survival according to BW, GA and growth, and presence or absence of certain perinatal factors or infant characteristics. There were 56 929 deliveries (54 510 live births) within the hospital over this 3-year period. Approximately 20% of total live births were low-birth-weight infants. The Soweto clinics that refer all their VLBW infants and those with medical problems to our hospital had approximately 8 000 deliveries per year over this period (accurate figures were not available). It was estimated that antenatal steroids were used in 30% of cases where they would have been recommended, because of late presentation of mothers in preterm labour (E Buchman – personal communication). Infants weighing < 1 000 g were not offered mechanical ventilation, but were otherwise managed like all other infants including resuscitation where appropriate, incubator care, monitored oxygen, antibiotics and intravenous fluids. The GA in completed weeks was determined from obstetric assessment (based on dates, clinical examination and occasionally ultrasound) or modified Ballard score.⁸ The GA recorded on the database was based on a combined assessment from antenatal and postnatal evaluation. However, since antenatal assessments were usually performed after 24 weeks and the Ballard scores were often done by relatively inexperienced doctors, it was recognised that GA as recorded in the database was subject to significant error. For this reason most of the analyses performed in this study are based on BW. VLBW infants were assessed to be small for GA using the Colorado intra-uterine growth chart.⁹ Infants who died before a diagnosis could be made were classified as having died as a result of immaturity. We did not have information on VLBW

live births who died at the clinics or referral hospitals. We therefore looked at survival rates among all live births delivered within CHBH, and then separately at all those admitted to our neonatal unit including referrals from clinics and other hospitals. This study was approved by the University of the Witwatersrand Human Research Ethics Committee.

Statistical methods

Data were analysed using Stata version 8 and SigmaStat version 2. Comparisons in BW and GA between survivors and non-survivors were performed using the Mann-Whitney rank sum test. Single and multiple logistical regression models were run to determine factors associated with survival. Variables entered into the model included antenatal clinic attendance, place of birth, mode of delivery, gender, small for GA, and Apgar score at 1 minute and 5 minutes. Separate models examined influence of different BW groups (in increments of 100 g) on survival using BW group 1 000 - 1 099 g as a reference point, and interaction of GA and being small for GA. Reported differences were considered to be significant when *p*-values were less than 0.05.

Results

There were 2 164 VLBW infants born alive or admitted to CHBH over this 3-year period. Their median BW and GA were 1 180 g (range 500 - 1 495 g) and 30 weeks (range 22 - 40 weeks) respectively. The majority of them (81%) were assessed to be less than 33 weeks. Only 31% of all the VLBW infants were assessed to be small for GA.

The VLBW infants represented 21% of total admissions to the neonatal unit. Among those infants delivered at CHBH, VLBW infants constituted 3% of total live births. Of the 2 164 VLBW infants, there were 587 deaths, 1 566 survivors, and in 11 the outcome was not recorded. Accepting a worst-case scenario, it was assumed for the purpose of analysis that these 11 infants had died. These 598 deaths constituted 55% of total deaths among all admissions to the neonatal unit. Eighty-five infants died in the labour ward nursery before admission to the neonatal unit. Among the infants who died in the labour ward nursery, 80% weighed less than 1 000 g. The overall survival rate for all VLBW infants born alive within CHBH was 72% (including deaths in the labour ward nursery). The overall survival rate was 74% among the VLBW infants admitted to the unit (excluding deaths in the labour ward nursery). The infants who survived and those who died differed significantly with regard to BW and GA. Survivors had a higher median BW (1 200 v. 980 g, *p* < 0.001) and median GA (30 v. 28 weeks, *p* < 0.001). Among the infants admitted to the NICU for ventilation, 452 were diagnosed with hyaline membrane disease, and of these 27% received exogenous surfactant.



Table I. Perinatal information for very-low-birth-weight infants born at Chris Hani Baragwanath Hospital (CHBH) between 1 January 2000 and 31 December 2002

	Birth weight < 1 000 g		Birth weight ≥ 1 000 g			All
	500 - 799 g (N = 106)	800 - 999 g (N = 347)	1 000 - 1 199 g (N = 640)	1 200 - 1 399 g (N = 713)	1 400 - 1499 g (N = 358)	500 - 1 499 g (N = 2164)
Antenatal care (%)						
Yes	77 (73)*	261 (75)	513 (80)	549 (77)	300 (84)	1 700 (79)
No	19 (18)	64 (19)	110 (17)	129 (18)	49 (14)	371 (17)
Not recorded	10 (9)	22 (6)	17 (3)	35 (5)	9 (3)	93 (4)
Birthplace (%)						
CHBH	88 (83)	295 (85)	514 (81)	557 (78)	285 (80)	1 739 (80)
Other hospitals	4 (3)	4 (1)	27 (4)	41 (6)	12 (3)	88 (5)
Clinic/home	6 (6)	27 (8)	58 (9)	72 (10)	40 (11)	203 (9)
Not recorded	8 (8)	21 (6)	41 (6)	43 (6)	21 (6)	134 (6)
Mode of delivery (%)						
Vaginal	66 (62)	184 (53)	317 (50)	351 (49)	187 (52)	1 105 (51)
Caesarean	23 (22)	136 (39)	287 (44)	318 (45)	153 (43)	917 (42)
Not recorded	17 (16)	27 (8)	36 (6)	44 (6)	18 (5)	142 (7)
Apgar score (%)						
< 6 at 1 minute	35 (33)	88 (25)	134 (21)	109 (15)	46 (13)	412 (19)
Not recorded	27 (25)	47 (14)	82 (13)	111 (16)	47 (13)	314 (14)
< 6 at 5 minutes	21 (20)	35 (10)	34 (5)	29 (4)	8 (2)	127 (6)
Not recorded	31 (29)	70 (20)	121 (19)	140 (20)	58 (16)	420 (19)
Gender (%)						
Male	35 (33)	157 (45)	325 (51)	365 (51)	169 (47)	1 051 (49)
Female	71 (67)	186 (54)	307 (48)	342 (48)	186 (52)	1 092 (50)
Not recorded	-	4 (1)	8 (1)	6 (1)	3 (1)	21 (1)

Although only 2% of the mothers were rapid plasma reagin (RPR)-positive on routine testing for syphilis, a large number (20%) had no record of RPR results.

Perinatal factors or characteristics of VLBW infants admitted to CHBH (Table I)

Antenatal care

The mothers of 79% of these infants attended an antenatal clinic. Clinic attendance was defined as one or more clinic visits.

Place of birth

Eighty-five per cent of the infants were born in hospital, with the remainder in the Soweto clinics or at home, as shown in Table I. Only 5% of those referred postnatally had been born at other hospitals.

Mode of delivery

Forty-two per cent of these infants were delivered by caesarean section. The number of infants delivered by caesarean section

was lower among those weighing less than 1 000 g (39% v. 47%, $p < 0.004$), suggesting less intervention for the infants at lower BW or GA. Indications for caesarean section were not recorded in most cases.

Apgar scores and gender

Overall, 50% of all the VLBW infants were female, but there were fewer male infants in the group weighing less than 800 g (33% v. 50%, $p = 0.001$). A significant number of patients did not have Apgar scores recorded. Only 19% and 6% had Apgar scores less than 6 at 1 and 5 minutes respectively. The number of infants with Apgar scores less than 6 at 1 and at 5 minutes increased with decreasing BW.

Causes of death

Sixty-three per cent of the deaths were related to prematurity (Table II). The most common cause of death was classified as immaturity, mainly among infants weighing less than 1 000 g who were not offered mechanical ventilation. The second commonest cause of death was infection, clinically diagnosed in the majority and culture proven in 29%.



Table II. Causes of death among very-low-birth-weight infants born at or admitted to CHBH

Causes of death	Number (%)
Prematurity related	369 (63)
Immaturity	234 (63)
Hyaline membrane disease	60 (16)
Necrotising enterocolitis	49 (14)
Intraventricular haemorrhage	26 (7)
Sepsis	158 (27)
Culture proven	46 (29)
Presumed sepsis	112 (71)
Perinatal asphyxia	28 (5)
Congenital abnormalities	17 (3)
Unknown	15 (2)

Survival rates according to birth weight (Fig. 1)

The overall survival rate of infants weighing less than 1 000 g was 32%. There were no survivors among those weighing less than 600 g. Nineteen per cent of the infants weighing less than 1 000 g died in the labour ward nursery before they could be admitted. The survival rate improved when infants who died in the labour ward nursery before admission were excluded. This improvement was more noticeable among those weighing less than 1 000 g (Fig. 1), with overall survival rate increasing to 41%. Among those with BW > 999 g, the overall survival rate was 84%. It increased with increasing BW from 74% for those in the 1 000 - 1 099 g weight group to 91% for those weighing 1 400 - 1 499 g.

Survival rates according to gestational age

The GA-specific survival rates of VLBW infants born alive at CHBH or admitted to the neonatal unit are presented in Fig. 2 and show a similar pattern to survival rates according to BW. Survival rate improved with increasing GA.

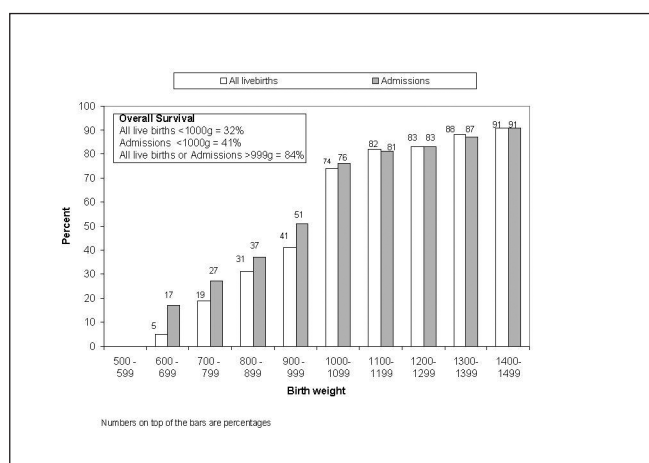


Fig. 1. Survival rates of very-low-birth-weight infants born (live births) or admitted (admissions) to Chris Hani Baragwanath Hospital according to birth weight (numbers at the top of the bars are percentages).

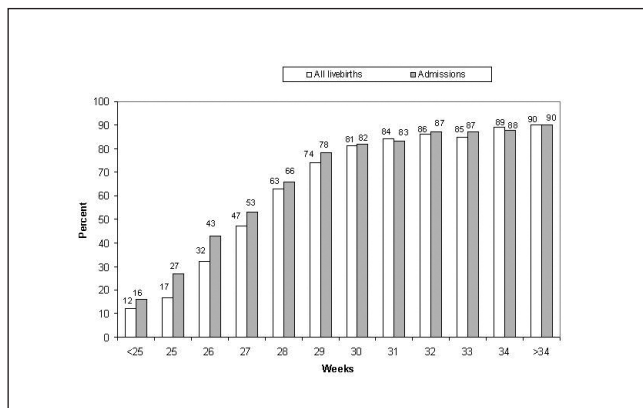


Fig. 2. Survival rates of very-low-birth-weight infants born (live births) or admitted (admissions) to Chris Hani Baragwanath Hospital according to gestational age (numbers at the top of the bars are percentages).

Factors associated with survival among VLBW infants

On logistical regression analysis the factors associated with better survival were antenatal clinic attendance and delivery by caesarean section. Male gender, Apgar score less than 6 at 1 and/or 5 minutes, and being small for GA were associated with poor survival (Table III). Fitting both GA and being small for GA together indicates that these are independently related to survival after adjusting for each other. The odds of survival to hospital discharge were much lower among infants weighing less than 1 000 g and increased with increasing BW, almost doubling with each increase of 100 g when compared with infants in the 1 000 - 1 099 g weight group (Table IV). There were no differences in odds of survival for infants in the 1 100 - 1 199 g and 1 000 - 1 099 g weight groups.

Discussion

This study determined the survival rates to hospital discharge for all VLBW infants born alive and/or admitted to a hospital setting where there are limited resources. This problem is compounded by a high low BW rate (LBWR), which is 20% in

Table III. Odds of surviving according to clinic attendance, place and mode of delivery, gender, Apgar scores and intrauterine growth

Characteristic	Adjusted odds ratio*	95% CI
Antenatal clinic attendance	1.50	1.15 - 1.97
Inborn	1.02	0.73 - 1.43
Caesarean section	1.44	1.14 - 1.82
Male	0.76	0.61 - 0.95
Apgar score < 6 at 1 minute	0.53	0.40 - 0.71
Apgar score < 6 at 5 minutes	0.37	0.23 - 0.58
Small for gestational age (SGA)	0.29	0.21 - 0.40

*For each model, the reported odds ratios are adjusted for all other variables shown.

**Table IV. Odds of surviving according to weight group using 1 000 - 1 099 g as a reference weight**

Birth weight (g)	Odds ratio	95% CI
600 - 699	0.05	0.01 - 0.16
700 - 799	0.09	0.05 - 0.17
800 - 899	0.15	0.09 - 0.23
900 - 999	0.27	0.19 - 0.39
1 000 - 1 099	–	–
1 100 - 1 199	1.41	0.96 - 2.05
1 200 - 1 299	1.51	1.05 - 2.17
1 300 - 1 399	2.21	1.48 - 3.32
1 400 - 1 499	3.11	2.03 - 4.78

our hospital compared with the rate of < 10% in developed countries.^{4,10} Although VLBW infants accounted for a small number (3%) of our total live births, they accounted for 20% of our total admissions and a majority (55%) of all deaths in the unit. The combination of a high LBWR and high number of deliveries in the hospital puts a strain on the already limited resources.

Although as health care providers we would like to assist all infants delivered in our hospitals, because of limited resources we are often forced to restrict access to certain facilities, favouring those expected to have better short and long-term outcome. Because BW and GA have been shown to correlate with outcome,^{3,11,12} decisions on whether or not to offer neonatal intensive care can be based on these measurements at birth. Even after using these objective measures the outcomes might vary from hospital to hospital or from country to country as outcomes might be influenced by quality of antenatal, intrapartum and neonatal care.¹³ Therefore it is important that health workers working in obstetrics and neonatology know the outcomes of these infants in their own hospitals.

For over two decades we have been using a BW cutoff point of 1 000 g at CHBH when deciding whether or not to offer mechanical ventilation. This cutoff weight is also used by many other hospitals in the public sector in the country. Reports from developed countries have shown an improved outcome among infants weighing less than 1 000 g from the 1980s to the 1990s.^{3,5} Therefore among neonatologists within the country there is a debate as to whether it is appropriate to continue using a cutoff point of 1 000 g, and whether BW is an appropriate measurement to use in making decisions on which patients access ventilation.^{14,15} We are also concerned that providing mechanical ventilation for all infants when our NICU beds are limited may compromise the care and therefore the outcome not only for the infants weighing less than 1 000 g but for all ill newborn infants who share these resources.

The overall survival rates of 72 - 74% among VLBW infants born at or admitted to our hospital is an improvement compared with two decades ago,¹⁶ but lower than the survival rates of 83 - 90% from developed countries.^{2,7,11} The improved

survival rates among VLBW infants in developed countries in the 1990s has been associated with an improvement in perinatal care including use of antenatal steroids, use of exogenous surfactant, use of continuous positive airway pressure (CPAP) as a form of ventilation and increasing willingness and ability to manage these babies.¹⁷⁻¹⁹ The lower survival rates in our hospital can be explained by the lack or limited availability of these resources that have been shown to be associated with better survival. In our hospital the use of exogenous surfactant is restricted, and often delayed because of limited NICU beds and equipment, and as a result infants who need mechanical ventilation are often admitted to NICU late in the course of their illness. Most of the mothers present late in labour, resulting in inadequate time for antenatal steroids to be used or to have any effect. In addition infants weighing less than 1 000 g were not offered mechanical ventilation, which is not the case in developed countries.

The outcome of VLBW infants is related to maturity, so GA should be a better predictor than BW. In our setting use of GA is problematic because our mothers start attending antenatal clinics late, antenatal ultrasound is not offered routinely, and GA assessment using the Ballard score is often done by junior doctors who work under pressure owing to the patient load and rotate through our nursery for short periods. Because of these limitations and the known discrepancy between antenatal and postnatal assessment of GA,²⁰ we suggest that use of BW as a cutoff for access to mechanical ventilation is a more practical approach.

The increase in survival rates by 100 g increments was marked between 600 and 1 000 g compared with between 1 000 and 1 499 g, reflecting severe organ immaturity at the limits of viability. The marked difference in survival rates between the 900 - 999 g and 1 000 - 1 099 g weight categories suggests the impact of providing mechanical ventilation. In countries where almost all VLBW infants are offered mechanical ventilation the survival rates are much better at 56 - 81% among those weighing 500 - 999 g, and 94 - 97% in the 1 000 - 1 499 g weight group.^{5,7,11}

Non-attendance at an antenatal clinic, vaginal delivery, an Apgar score < 6 at 1 minute and 5 minutes, and male gender were associated with lower survival rates. Antenatal clinic attendance helps in identifying patients at risk for delivering preterm, and this would allow better monitoring and early hospital admission of these patients. Failure to detect intrauterine growth retardation (IUGR) is associated with poor outcome.¹³ Better outcome among infants whose mothers attended an antenatal clinic highlights the importance of clinic attendance. The association of poor survival with vaginal delivery implies that caesarean section might be recommended for delivery of these infants. However this must be interpreted with caution because the presenting part and indication for



caesarean section were not recorded in this study. Survival rates of VLBW infants with breech presentation have been shown to be poorer after vaginal delivery. Female gender has continued to show its advantage over male gender, as has been reported previously.^{4,21}

As health workers working in limited resource areas we need to be aware of survival rates in our hospitals, our limitations, and areas that we can improve on. As we continue debating the cutoff points for mechanical ventilation of VLBW infants we also need to be aware of issues associated with taking care of these infants. These issues include the degree to which intensive care might prolong dying or extend suffering, including that of the parents, use of resources in the case of an infant who may eventually die, and the quality of life for survivors.^{22,23} Therefore the problems of resource allocation and justice need to be considered at all times. There needs to be ongoing assessment of these infants after hospital discharge, as they are still at risk of death or neurological impairment.²⁴

It is difficult to recommend a cutoff point for mechanical ventilation using GA because of unreliability of our GA assessment. However, if one were to choose a cutoff, based on our findings we would recommend 26 - 27 weeks. The observed improvement in outcome with increasing BW was marked between the 900 - 999 g and 1 000 - 1 099 g groups. This difference is most likely because of using 1 000 g as a cutoff point for ventilation. Among the groups that were not eligible for ventilation, the 900 - 999 g group had a better survival at 50%, compared with 37% for those weighing 800 - 899 g. Ventilating infants with a borderline survival rate without ventilation could improve their survival significantly. Therefore a change in policy to ventilate infants weighing less than 1 000 g needs to be considered. Implementation of this policy can be done in phases starting with the 900 - 999 g group first, reassessing its effects on survival of these infants and the impact on resource requirements. The suggested change in policy must accompany improvement in NICU facilities including bed space, equipment and staffing. Early use of CPAP and KMC in VLBW infants has been associated with good outcomes and less expense.^{25,26} Therefore their use must be encouraged in our hospitals.

References

1. Stewart AL, Reynolds EOR, Lipscomb AP. Outcome for infants of very low birth weight: survey of world literature. *Lancet* 1981; **1**: 1038-1041.

2. Hack M, Wright LL, Shankaran S, Tyson JE, Horbar JD, Bauer CR, Younes N for the National Institute of Child Health and Human Development Neonatal Research Network. Very-low-birth-weight outcomes of the National Institute of Child Health and Human Development Neonatal Network, November 1989 to October 1990. *Am J Obstet Gynecol* 1995; **172**: 457-464.
3. Hack M, Friedman H, Fanaroff AA. Outcomes of extremely low birth weight infants. *Pediatrics* 1996; **98**: 931-937.
4. Cartledge PHT, Stewart JH. Survival of very low birthweight and very preterm infants in a geographically defined population. *Acta Paediatr* 1997; **86**: 105-110.
5. The Victorian Infant Collaborative Study Group. Improved outcome into the 1990s for infants weighing 500 - 999 g at birth. *Arch Dis Child* 1997; **77**: F91-F94.
6. Draper ES, Manktelow B, Field DJ, James D. Prediction of survival for preterm births by weight and gestational age: retrospective population based study. *BMJ* 1999; **319**: 1093-1097.
7. Darlow BA, Cust AE, Donoghue DA, on behalf of the Australian and New Zealand Neonatal Network (ANZNN). Improved outcomes for very low birthweight infants: evidence from New Zealand national population based data. *Arch Dis Child Fetal Neonatal Ed* 2003; **88**: F23-F28.
8. Ballard JL, Khoury JC, Wedig K, Wang L, Eilers-Walsman BL, Lipp R. New Ballard score, expanded to include extremely premature infants. *J Pediatr* 1991; **119**: 417-423.
9. Lubchenco LO, Hansman C, Boyd E. Intrauterine growth in length and head circumference as estimated from live births at gestational ages from 26 to 42 weeks. *Pediatrics* 1966; **37**: 403-408.
10. Arias E, MacDorman MF, Strobino DM, Guyer B. Annual summary of vital statistics-2002. *Pediatrics* 2003; **112**: 1215-1230.
11. Stevenson DK, Wright LL, Lemons JA, Oh W, Korones SB, Papile L-A, Bauer CR, Stoll BJ, Tyson JE, Shankaran S, Fanaroff AA, Donovan EF, Ehrenkranz RA, Verter J, for the National Institute of Child Health and Human Development Neonatal Research Network. Very low birth weight outcomes of the National Institute of Child Health and Human Development Neonatal Research Network, January 1993 through December 1994. *Am J Obstet Gynecol* 1998; **179**: 1632-1639.
12. El-Metwally D, Vohr B, Tucker R. Survival and neonatal morbidity at the limits of viability in the mid 1990s: 22 to 25 weeks. *J Pediatr* 2000; **137**: 616-622.
13. Richardus JH, Graafmans WC, Verloove-Vanhorick SP, Mackenbach JP, The EuroNatal International Audit Panel, The EuroNatal Working Group. Differences in perinatal mortality and suboptimal care between 10 European regions: results of an international audit. *Br J Obstet Gynecol* 2003; **110**: 97-105.
14. Smith J, Pieper CH, Kirsten GF. Born too soon, too small, to die - a plea for a fair innings. *S Afr Med J* 1999; **99**: 1148-1151.
15. Rothberg AD, Cooper PA. Rationing versus equity - the South African dilemma. *S Afr Med J* 1999; **99**: 1151-1153.
16. Cooper PA, Saloojee H, Bolton KD, Mokhachane M. Survival of low-birth-weight infants at Baragwanath Hospital - 1950 - 1996. *S Afr Med J* 1999; **99**: 1179-1181.
17. De Klerk AM, De Klerk RK. Nasal continuous positive airway pressure and outcomes of preterm infants. *J Paediatr Child Health* 2001; **37**: 161-167.
18. Crowley P. Prophylactic corticosteroids for preterm birth. *Cochrane Database Syst Rev* 2000; **2**: CD00065.
19. Kresch MJ, Clive JM. Meta-analyses of surfactant replacement therapy of infants with birth weights less than 2 000 grams. *J Perinatol* 1998; **18**: 276-283.
20. Hack M, Horbar JD, Malloy MH, Tyson JE, Wright L, Wright E. Very low birthweight outcomes of the NICHD. Neonatal network. *Pediatrics* 1991; **87**: 587-597.
21. Stevenson DK, Verter J, Fanaroff AA, Oh W, Ehrenkranz RA, Shankran S, Donovan EF, Wright LL, Lemons, Tyson JE, Korones SB, Bauer CR, Stoll BJ, Papile L-A for the National Institute of Child Health and Human Development Neonatal Research Network. Sex differences in outcomes of very low birthweight infants: the newborn male disadvantage. *Arch Dis Child Fetal Neonatal Ed* 2000; **83**: F182-F185.
22. Paris JJ, Crone RK, Reardon R. Physician's refusal of requested treatment. The case of Baby L. *N Engl J Med* 1990; **322**: 1012-1015.
23. Boyle MH, Torrance GW, Sinclair JC, Horwood SP. Economic evaluation of neonatal intensive care of very low birth weight infants. *N Engl J Med* 1983; **308**: 1330-1336.
24. Cooper PA, Sandler DL. Outcome of very low birth weight infants at 12 to 18 months of age in Soweto, South Africa. *Pediatrics* 1997; **99**: 537-544.
25. Holt AW, Bersten AD, Fuller S, Piper RK, Worthley LI, Vedig AE. Intensive care costing methodology: cost benefit analysis of nasal continuous positive airway pressure for severe cardiogenic pulmonary oedema. *Anaesth Intensive Care* 1994; **22**: 170-174.
26. Charpak N, Ruiz-Pelaez JG, Figueroa de Calume Z. Current knowledge of Kangaroo Mother Intervention. *Curr Opin Pediatr* 1996; **8**: 108-112.

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