Peer reviewed article

Two years outcome of very pre-term and very low birthweight infants in Switzerland

H. U. Bucher, Y. Ochsner, J.-C. Fauchère, and the Swiss Neonatal Network

Summary

Background: There are only few reports worldwide on the outcome of very pre-term infants and very low birthweight infants for a whole country. In Switzerland official population statistics are based on birthweight only, gestational age not yet being documented.

Aim: The aim of the present study was to assess the outcome at two years of age for a geographically defined high-risk neonatal population based on both birthweight and gestational age.

Methods: All infants born in 1996 included in the Swiss Neonatal Network (a national anonymous registry established by the Swiss Society of Neonatology for liveborn infants before 32 completed gestational weeks or weighing less than 1500 g) were divided into three groups according to gestational age and birth weight: Group 1: born <32 completed gestational weeks and weighing ≥1500 g; group 2: born after 32 completed gestational weeks and weighing <1500 g; group 3: born <32 gestational weeks and weighing <1500 g.

Information at 24 months corrected age about growth, neurological outcome, frequency of respiratory infections, prescription of antibiotics and medical consultations during this period was obtained from the paediatricians caring for the infants. Fair outcome was defined as survival without serious neonatal complications or abnormal neurological findings at 24 months corrected for prematurity.

Results: 723 infants were born alive in Switzerland between 1.1. and 31.12.1996 before 32 completed weeks or weighing less than 1500 g at birth. Mortality was 4.3% for a total of 163 infants in group 1 (<32 weeks, ≥1500 g), 4.6% for 108 infants in group 2 (>32 weeks, <1500 g) and 18.6% for 452 infants in group 3 (<32 weeks, <1500 g). 6.5% of group 1 survivors followed up to 24 months corrected age had a poor neurological outcome as compared to 9.3% in group 2 and 10.9% in group 3. Infants in group 1 needed antibiotics less often after hospital discharge (interquartile range IQR: 0–2 courses) than infants in group 2 (0–3 courses) and 3 (0–3 courses). Infants in group 2 suffered from fewer airway infections (interquartile range 2–5 times) than in group 1 (2–6 times) and 3 (1–7 times). Infants in group 3 needed more medical consultations (IQR 12–21) than those in group 1 (10–16) and 2 (11–16).

The overall fair outcome at 24 months corrected age was 85.3% in group 1, 80.7% in group 2 and 59.6% in group 3. A close correlation between overall fair outcome and gestational age at birth on the one hand and with birthweight on the other can be observed.

Conclusions: This study gives estimates for mortality, poor and fair outcome at 24 months corrected age for very low birth weight infants (<1500 g) and for very pre-term infants (<32 completed gestational weeks). Gestational age is as important for predicting outcome as birthweight and should therefore be integrated into national statistics.

Key words: very low birthweight infants; very preterm infants; outcome; mortality; impairment

Introduction

The smallest newborn infants and those born much too early are of special interest for medical, economical, social and ethical reasons. In the second half of the 20th century, mortality for these infants has decreased continuously in industrialised countries, but morbidity and long-term cerebral outcome did not follow this trend. A study in Great Britain showed an increase of cerebral palsy in number and severity over the last 30 years [1]. Reports from the Netherlands and other industrialized countries confirmed the same trend [2, 3]. Long-term outcome studies from other countries such as Australia reported more optimistic results [4].

In Switzerland, neonatal mortality has been documented since 1971 by the Swiss federal statistical office but only for birth weight and not for gestational age [5]. As gestational age reflects maturity better than weight at birth, the Swiss Society of Neonatology decided in 1995 to document

gestational age, birth weight and other variables for all liveborn infants with a gestational age below 32 completed weeks or with a birth weight below 1500 g. For the cohort born between 1.1.1996 and 31.12.1996, mortality and morbidity during the first hospitalisation have already been published [6]. For the same cohort, the two years outcome of pre-term infants born before 32 completed weeks were compared with a control group born at term based on a questionnaire sent to the parents [7].

The aim of the present study was to compare on a national scale the outcome at 24 months corrected age between infants born very pre-term and infants with a very low birthweight. To this end, the original cohort was divided into three different groups: Group 1: infants born before 32 completed gestational weeks and weighing 1500 g or more at birth; Group 2: newborn infants born after 32 completed gestational weeks and weighing less than 1500 g at birth; group 3: infants born before 32 gestational weeks and weighing less than 1500 g at birth.

Information regarding growth, neurological impairment at 24 months after expected term of delivery, the frequency of respiratory infections during a 24-month period after discharge, the number of treatments with antibiotics and medical consultations was obtained from the paediatricians caring for the infants.

Fair outcome was defined as survival without serious neonatal complications or abnormal neurological findings at 24 months corrected age.

Methods

The original cohort consisted of 723 infants born alive in Switzerland between 1.1. and 31.12.1996 before 32 completed weeks or weighing less than 1500 g at birth. Selected variables on birth and neonatal course were collected in a central anonymous registry. 627 infants were discharged from hospital alive. 156 were allocated to group 1 (<32 completed weeks, ≥1500 g), 103 to group 2 (≥32 weeks, <1500 g) and 361 to group 3 (<32 weeks, <1500 g). The parents of 350 infants (56%) gave permission to obtain information about the first two years after hospital discharge from the paediatrician taking care of their infant. 98% of the paediatricians answered the specific questions about growth, neurological examination, respiratory infections, antibiotics prescribed and number of consultations.

Weight, length and head circumference at 24 months corrected for prematurity were calculated as z-scores (standard deviation score). This method enables compensation for gender differences and for variation in time.

To assess the overall outcome, a combined variable for "poor outcome" was defined including serious neonatal sequelae (severe intracranial haemorrhage, periventricular leucomalacia, retinopathy grade 3 or more, chronic lung disease at 36 weeks) and neurological impairment including hearing and visual abnormalities at 24 months.

Comparisons between the three groups were analysed using the Chi-square test for proportions and the Wilkoxon rank sum test for continuous variables.

Results

Figure 1 represents birthweight in relation to gestational age for the whole cohort of 723 infants divided in the three groups. A total of 96 (13.3%) infants died with 7 infants (4.3%) in group 1, 5 (4.6%) in group 2, and 84 (18.6%) in group 3.

The neonatal characteristics of all 627 surviving infants divided in the three groups are given in table 1. Poor neonatal outcome consisting of severe intracranial haemorrhage, periventricular leucomalacia, retinopathy grade 3 or 4 or oxygen dependency at 36 weeks was found in 13 of 156 surviving infants (8.3%) in group 1, in 13 of 103 infants (12.6%) in group 2 and in 84 of 368 infants (22.8%) in group 3. For the infants without any available follow-up information from the paediatricians, the corresponding percentages are lower for all three groups: 7.8%, 10.2% and 19.9% respectively.

All three groups were significantly below the mean with respect to weight, length and head circumference at 24 months after expected term of birth (fig. 2). The difference was largest in group 2 for all three measures.

Neurological examination at 24 months corrected age for prematurity was normal in 54 of 92 infants (58.7%) in group 1, in 25 of 54 infants (53.4%) in group 2 and in 104 of 220 infants (47.3%) in group 3. Hearing or visual problems were most frequent in group 3 with 7.9% as compared to 3.3% in group 1, and to 3.9% in group 2 (table 2).

Infants in group 1 needed antibiotics less often after hospital discharge (interquartile range: 0–2 courses) than infants in group 2 (IQR 0–3 courses) and 3 (IQR 0–3 courses) (fig. 3). Group 2 infants were less frequently reported to have airway infections (IQR 2–5 times) than group 1 (IQR 2–6 times) or group 3 infants (IQR 1–7 times). Infants in group 3 needed more medical consultations (IQR 12–21) than those in group 1 (IQR 10–16) and 2 (IQR 11–16).

85.3% of infants in group 1 had a "fair" or impairment-free outcome at 24 months corrected age. The corresponding percentage was 80.7% for group 2 and 59.6% for group 3 infants. When the infants were classified according to gestational age

Figure 1

Birth weight and gestational age.

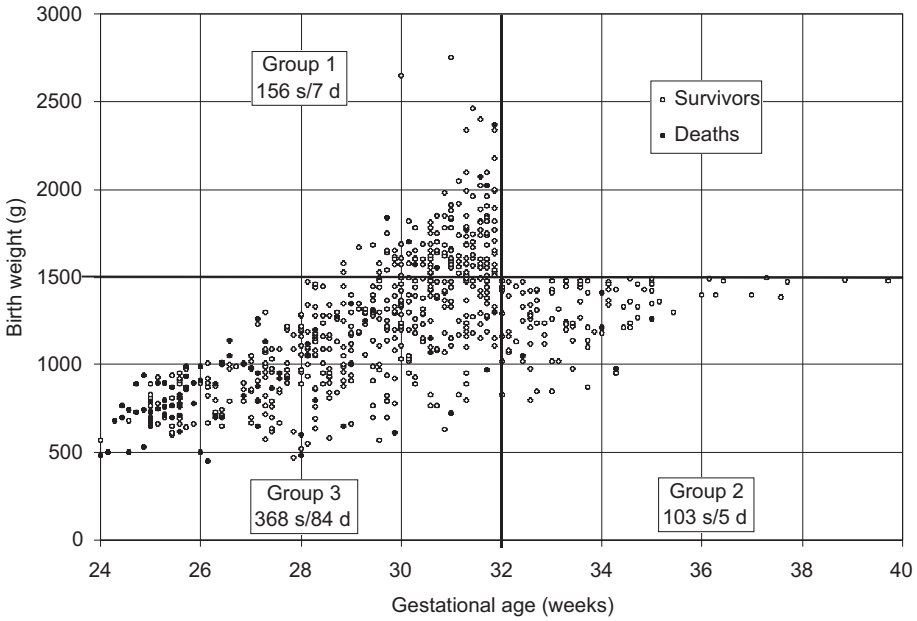
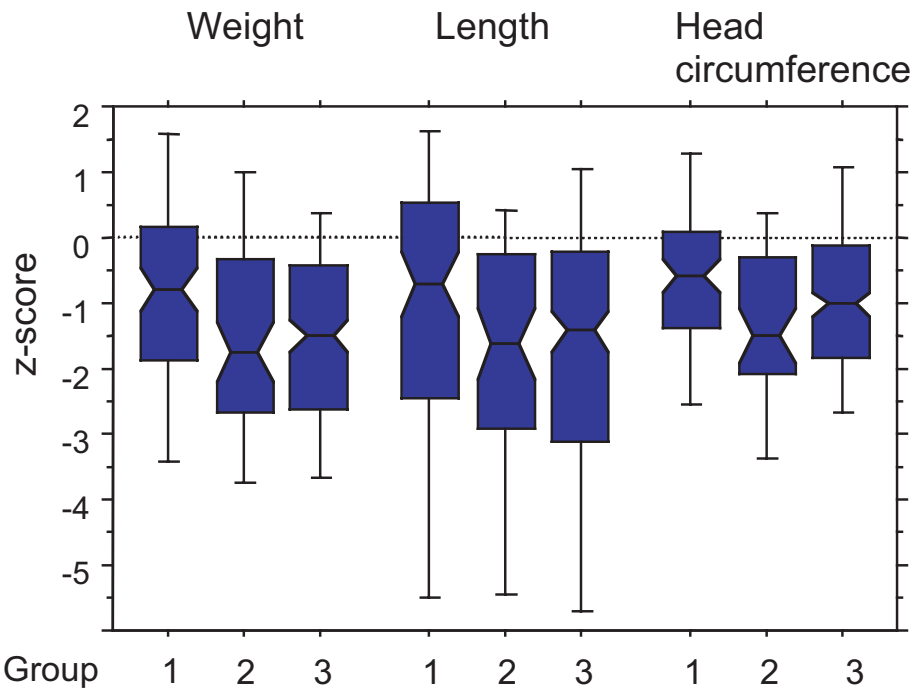


Figure 2

Growth at 24 months corrected for prematurity. Box plots display the 10th, 25th, 50th, 75th and 90th z-score percentile. Z-scores indicate how far and in what direction weight, length and head circumference deviate from their mean, expressed in units of their standard deviation.



at birth, a "fair" or impairment-free outcome correlated closely with increased gestation, starting at 0% at 24 weeks and raising to 85% at 30 weeks of gestation (fig. 4). A similar trend was seen when the infants were classified by birthweight with a "fair outcome" increasing from 0% for birthweights <500 g to 83% for birthweights >1499 g.

Discussion

This study provides outcome data from a geographically defined high-risk population, namely from infants born very pre-term or with a very low birth weight in 1996 in Switzerland.

Before we consider the significance of our results and compare them with those from other countries, we discuss some methodological aspects.

Completeness of recruitment?

All neonatal units in Switzerland participated in this study. A comparison with the numbers published by the Swiss Federal Statistical Office for newborn infants <1500 g shows an 85% recruitment. The large majority of the 15% infants not included most probably died in the delivery room soon after birth, and were therefore not trans-

Table 1

Neonatal data of three groups.

Group	1: <32 wks		2: <1500 g		3: <32 wks & <1500 g		p
N	156		103		368		
Boys	96	61.50%	47	45.60%	181	49.20%	1–2*, 1–3**
Girls	60	38.50%	56	54.40%	187	50.80%	ns
Gestational age wks (25, 50, 75 perc)	31⅙ (30⅗, 31⅓)		33⅖ (32⅗, 34⅖)		28⅘ (27⅖, 30⅙)		1–2***, 1–3***, 2–3***
Birth weight g (25, 50, 75 perc)	1650 (1580, 1795)		1340 (1195, 1440)		1110 (908, 1300)		1–2***, 1–3***, 2–3***
Inborn	128	82.10%	83	80.60%	328	89.10%	ns
Spontaneous delivery	48	30.80%	15	14.60%	79	21.50%	1–2**, 1–3*
Caesarean section	100	64.10%	85	82.50%	279	75.80%	ns
Singelton	107	68.60%	72	69.90%	268	72.80%	ns
Twins	39	25.00%	24	23.30%	62	16.80%	ns
Triplets	10	6.40%	7	6.80%	19	5.20%	ns
Malformation	13	8.30%	14	13.60%	29	7.90%	1–2**, 2–3**
Respiratory distress syndrome	121	77.60%	45	43.70%	315	85.60%	1–2***, 1–3**, 2–3***
Hyaline membrane disease (surfactant treatment)	27	17.30%	1	1.00%	106	28.80%	1–2***, 1–3*, 2–3***
Patent ductus arteriosus	13	8.30%	5	4.90%	76	20.70%	1–3***, 2–3***
Sepsis	4	2.60%	5	4.90%	40	10.90%	1–3***, 2–3***
Necrotising enterocolitis	2	1.30%	1	1.00%	17	4.60%	ns
Cerebral ultrasound							
– not examined	11	7.10%	9	8.70%	5	1.40%	ns
– normal	110	75.90%	82	87.20%	270	74.40%	ns
– intracranial haemorrhage all grades	25	17.20%	8	8.50%	79	21.80%	ns
– grade 3 and 4	2	1.40%	2	2.10%	14	3.90%	ns
– cystic periventricular leucomalacia	7	4.80%	0	0.00%	10	2.80%	ns
Retinopathy of prematurity (ROP)							
– not examined	47	30.10%	18	17.50%	18	4.90%	ns
– no ROP	101	92.70%	78	91.80%	288	82.30%	ns
– all ROP stages	8	7.30%	7	8.20%	62	17.70%	ns
– stage 3 and 4	3	2.80%	5	5.90%	14	4.00%	ns
Bronchopulmonary dysplasia (oxygen dependent at 36 gestational weeks)	13	8.30%	1	1.00%	150	40.80%	ns
Chronic lung disease (oxygen dependent at day 28)	6	3.80%	12	11.70%	62	16.80%	ns
Mechanical ventilation	49	31.40%	12	11.70%	192	52.20%	1–2***, 1–3***, 2–3***
– mean days per infant	5.5		2.3		9.3		1–2***, 1–3***, 2–3***
Nasal CPAP	60	38.50%	20	19.40%	208	56.50%	1–2***, 1–3***, 2–3***
– mean days per infant	3.9		1.2		11.8		1–2***, 1–3***, 2–3***
Poor neonatal outcome	13	8.30%	13	12.60%	84	22.80%	1–2***, 1–3***, 2–3***

1–2: group 1 vs group 2, 1–3: group 1 vs group 3; 2–3: group 2 vs group 3
ns: p >0.05; * p <0.05; ** p <0.01; *** p <0.001

ferred to a neonatal unit. A comparison of infants transferred from one hospital to another and therefore recruited twice, showed a high agreement between the two records indicating a high number of infants reported and a good quality of data.

Reporting bias?

Follow-up information could only be obtained for two thirds of the infants. This loss however is unlikely to affect the main results as follow-up rates were similar in all three groups, and as the percentage of a poor neonatal outcome is higher in the infants followed up than in those that are not. A reporting bias excluding infants with major impairment and lost to follow-up therefore seems very unlikely.

Born too soon or too small?

The newborn population can be classified according to gestational age or weight at birth. For both definitions thresholds are used to define a risk

Table 2

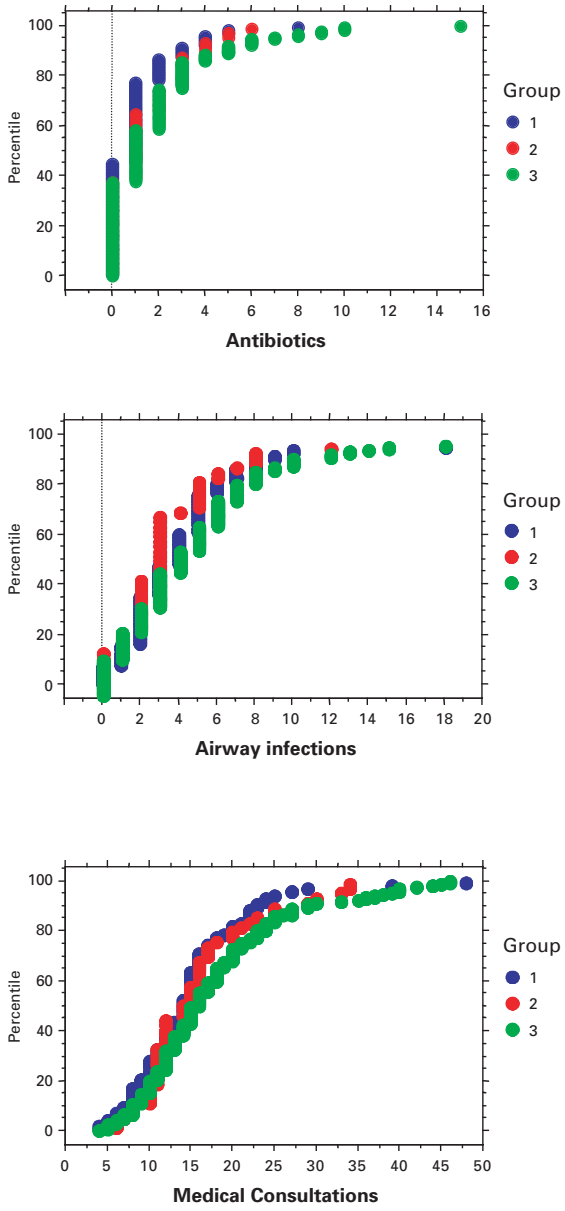
Outcome at 24 months corrected for prematurity.

Group	1: <32 wks		2: <1500 g		3: <32 wks & <1500 g	
N	156		103		368	
Examined at 24 months	92	59.0%	54	52.4%	220	59.8%
Neurological outcome*						
– normal	54	58.7%	25	46.3%	104	47.3%
– suspect	32	34.8%	26	48.1%	92	41.8%
– abnormal	6	6.5%	5	9.3%	24	10.9%
Neurological outcome specified						
Muscle tone abnormal	20	21.7%	20	19.4%	59	16.0%
Behaviour abnormal	2	2.2%	3	2.9%	15	4.1%
Movements abnormal	3	3.3%	1	1.0%	7	1.9%
Hearing problems	0	0.0%	0	0.0%	8	2.2%
Visual problems	3	3.3%	4	3.9%	21	5.7%
Epilepsy	1	1.1%	0	0.0%	4	1.1%

* Group 1 vs 2 p = 0.02, group 1 vs 3 p = 0.07, group 2 vs 3 p = 0.7

Figure 3

Management after hospital discharge.



group with high mortality and high impairment rates among survivors. Such thresholds are birth weight <1500 g (very low birth weight) and <1000 g (extremely low birth weight) or gestational age <32 completed weeks (very pre-term infants) or <26 completed weeks (extremely pre-term infants). There is an ongoing debate whether low birthweight or low gestational age is the better predictor for outcome [8–10]. Traditionally birthweight was considered to be more reliable than gestational age as long as the latter was based on the history of the last menstruation only. With the introduction of routine measurement of the length of the embryo with ultrasound in the first trimester, gestational age assessment became much more reliable, and consequently started to be used increasingly in studies classifying neonatal mortality, morbidity and long-term outcome. Our data show that both parameters are equally important and that the combination of both gives the best prediction. This finding is in agreement with a previous study showing that single and combined pre- and postnatal risk factors are less valuable for prediction than weight and gestational age [11].

Comparison of outcome with published data

After discharge of their infant born much too early or much too small from the neonatal intensive care unit, the main concern of parents is the long-term prognosis. To answer this question, we combined outcome variables including death, major pulmonary, visual, hearing and cerebral impairment assessed during the neonatal period and at two years of life. Absence of any of these findings at the age of two allows major handicap in later life to be ruled out with a high degree of confidence. The percentage of infants without any of these high risk factors, and thus with a high chance for an undisturbed development is 86% in group 1, 81% in group 2 and 60% in group 3.

As there are only few geographically based studies and as outcome variables among these studies often differ, comparisons have to be made

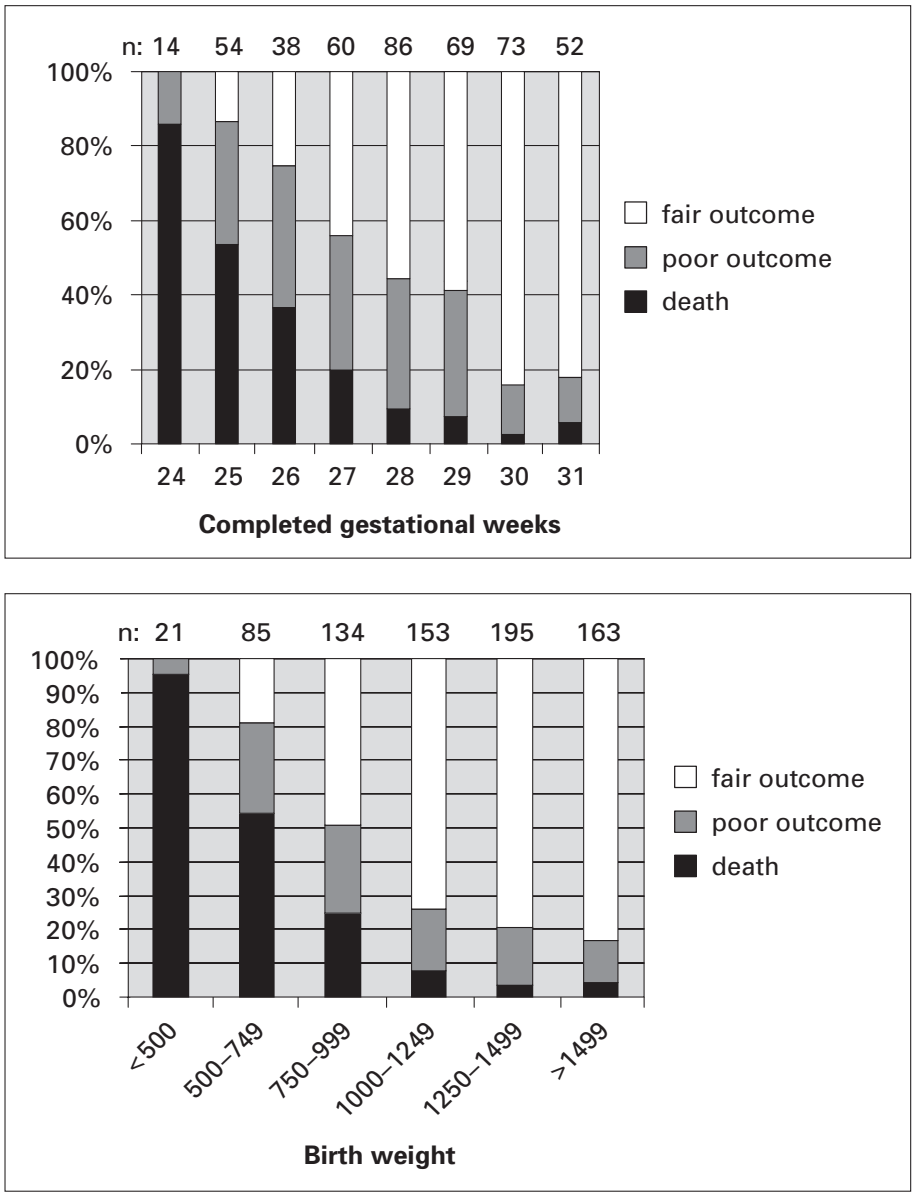


Figure 4
Outcome at 24 months.

with caution. A recently published study from England gives survival rates for pre-term infants according to birthweight and to gestational age [12]. These results show a significantly higher survival for infants born at 23 and 24 weeks and similar values for gestational ages of 26 weeks and more. Several studies show lower mortality at the lower end of birthweight or gestational age, but high rates of disability in survivors [11–15]. As we did not measure disability but rather preconditions likely to be followed by disability, the outcome data are not fully comparable.

Nevertheless, differences in outcome may be due to differences in performance or may reflect different attitudes among neonatologists in withholding or withdrawing intensive care [16–17]. Our results can be interpreted as Swiss neonatologists are generally reluctant to resuscitate extremely immature infants [18].

Conclusions

This study gives estimates for mortality, poor and fair outcome at 24 months corrected age for both very low birth weight infants (<1500 g) and for very pre-term infants (<32 completed gestational weeks). Gestational age is as important for predicting outcome as birth weight and should therefore be integrated into national statistics.

Information on the outcome of high-risk preterm infants has to be improved. A standardised test for psychomotor development should be applied nationwide and there is a need to assess school performance, quality of life and coping of a family with disabled child.

Cooperating neonatal units

Genève (Prof. M. Berner, PD Dr. R. Pfister), Lausanne (PD Dr. C. L. Fawer, PD Dr. J. L. Micheli), Neuchâtel (Dr. P. Pilloud, Dr. B. Laubscher), Fribourg (Dr. F. Renevey), Biel/Bienne (Dr. A. Blumberg), Sion (Dr. G. Délèze), Bern, Kinderspital (Prof. E. Bossi), Bern, Frauenspital (Dr. K. von Känel, Prof. A. Moessinger, Dr. J. Hentschel), Basel (Dr. R. Glanzmann, Prof. P. Nars), Bruderholz (PD Dr. M. Amato, Prof. J. Lütschg), Aarau (Dr. G. Zeilinger), Baden (Dr. M. Wopmann,

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Correspondence:
Prof. H. U. Bucher
Clinic of Neonatology
University Hospital
CH-8091 Zürich
E-Mail: HansUlrich.Bucher@fhk.usz.ch

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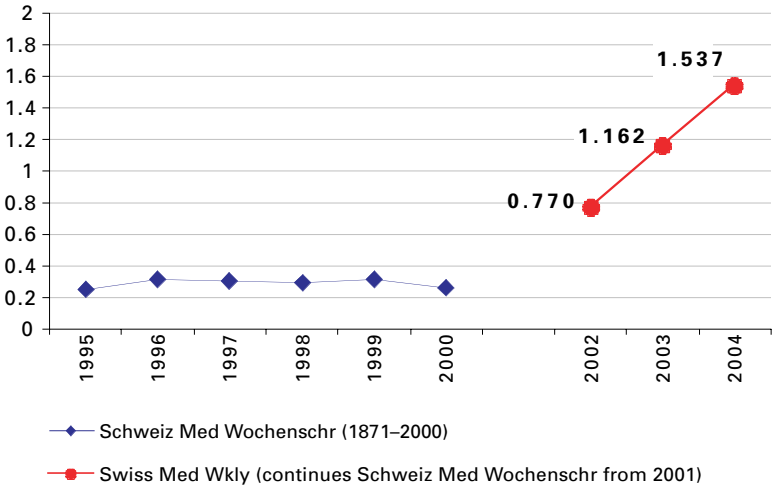

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