Estimated neonatal survival of very preterm births across the care pathway: a UK cohort 2016–2020

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ABSTRACT

Objective Currently used estimates of survival are nearly 10 years old and relate to only those babies admitted for neonatal care. Due to ongoing improvements in neonatal care, here we update estimates of survival for singleton and multiple births at 22^{+0} to 31^{+6} weeks gestational age across the perinatal care pathway by gestational age and birth weight.

Design Retrospective analysis of routinely collected data.

Setting A national cohort from the UK and British Crown Dependencies.

Patients Babies born at 22^{+0} to 31^{+6} weeks gestational age from 1 January 2016 to 31 December 2020.

Interventions None.

Main outcome measures Survival to 28 days.

Results Estimates of neonatal survival are provided for babies: (1) alive at the onset of care during the birthing process (n=43 763); (2) babies where survival-focused care was initiated (n=42 004); and (3) babies admitted for neonatal care (n=41 158). We have produced easy-to-use survival charts for singleton and multiple births. Generally, survival increased with increasing gestational age at birth and with increasing birth weight. For all births with a birthweight over 1000 g, survival was 90% or higher at all three stages of care.

Conclusions Survival estimates are a vital tool to support and supplement clinical judgement within perinatal care. These up-to-date, national estimates of survival to 28 days are provided based on three stages of the perinatal care pathway to support ongoing clinical care. These novel results are a key resource for policy and practice including counselling parents and informing care provision.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Up-to-date neonatal survival estimates for preterm babies are vital for counselling parents and informing care.

⇒ Currently used estimates of survival were created using data which are nearly 10 years old and relate to only those babies admitted for neonatal care.

WHAT THIS STUDY ADDS

⇒ We provide easy-to-use neonatal survival charts by gestational age, multiplicity and birth weight which can be used for all babies born very preterm.

⇒ Estimates of survival to 28 days after birth are provided for babies alive at the onset of the birthing process, babies where active survival focused care was initiated and babies admitted for neonatal care.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ These survival estimates based on different stages throughout the perinatal pathway allow, for the first time, ongoing counselling of parents through the early care pathway.

⇒ The survival estimates are a key resource for policy and practice including counselling parents and informing care.

INTRODUCTION

Reliable up-to-date estimates of survival for very preterm babies are a key resource for policy and practice including counselling parents and informing care. Babies born before 32 weeks gestational age account for 1% of all live births in the UK.[1] While survival in this cohort has increased in recent years,[2] these babies still account for over half of all neonatal deaths.[1]

Statistical modelling of neonatal data has the potential to offer accurate evidence-based estimates of survival and, in combination with clinical assessment, can provide parents and clinicians with more information to improve care throughout the perinatal pathway.[3] With ongoing improvements in survival following preterm birth, it is vital that such results are kept up-to-date. Furthermore, models based on different points along the care pathway allow a flexible and dynamic approach to discussions around clinical decision-making and may assist parents' understanding during an extremely stressful time.

Many existing estimates of neonatal survival are derived using data from individual hospitals, often tertiary centres, rather than from a population based on residence or national data.[4 5] The organisation of neonatal care into providers offering different levels of care means that survival estimates derived from a hospital-based cohort may not accurately reflect survival in the whole population. While estimates for neonatal survival exist, these are relatively out-of-date, based on regional data[6] or focused on neonatal care admissions.[2] This limitation supports the need for a development of a new model using national data rather than recalibration of historical models.

In this paper, we use national data for the UK and British Crown Dependencies for births from 2016 to 2020 to develop a prediction model

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which aimed to describe neonatal survival for babies born at 22^{+0} to 31^{+6} weeks gestational age. We provide this by birth weight and gestational age for three different stages of care along the perinatal care pathway from the onset of the care during the birthing process through to admission for neonatal care.

METHODS

Data

Data for births between 1 January 2016 and 31 December 2020 to mothers resident in the UK and British Crown Dependencies were obtained from the perinatal mortality surveillance programme (MBRRACE-UK). MBRRACE-UK has been commissioned by the Healthcare Quality Improvement Partnership (HQIP) to collect UK perinatal mortality surveillance data since 2013.[1] MBRRACE-UK links detailed information on all deaths reported by UK hospitals with birth notifications from the Patient Demographic Service (formerly the NN4B birth notification system) from NHS Digital for England, Wales and Isle of Man and birth and stillbirth and neonatal death registration data from the Office for National Statistics for England and Wales, National Records Scotland and Public Health Scotland for Scotland, Northern Ireland Maternity System for Northern Ireland, Health and Social Services Department (Bailiwick of Guernsey) and Health Intelligence Unit (Bailiwick of Jersey). Stillbirth and neonatal death registrations from statutory sources are used to optimise ascertainment of deaths and to provide underlying information about all births.

Inclusion/exclusion

We included data for all births from 22^{+0} to 31^{+6} weeks gestational age. We excluded babies where a congenital anomaly was recorded as the primary cause of death as these deaths have a particular underlying aetiology often unrelated to gestational age.

We imputed birth weight for births where birth weight was missing or considered implausible (birth weight outside the 0.4% and 99.6% centiles (based on sex and gestation-specific birth weight centiles developed by MBRRACE-UK[7])) by assigning a birth weight from a normal distribution based on the mean and SD for babies of the same gestational age, multiplicity of birth and survival status.

We investigated survival to 28 days relating to three different stages of care along the perinatal care pathway:

1. Babies alive at the onset of care for the birthing process, that is, during labour, commencement of induction of labour or caesarean section excluding those where death was confirmed before onset of care.
2. Babies where survival-focused care was initiated, that is, resuscitation or ventilation was provided following birth and/or the baby survived to be admitted for neonatal care.
3. Babies admitted to a neonatal care unit, that is, the baby was known to be admitted for neonatal care and/or the baby survived beyond the first day after birth.

Statistical analyses

Logistic regression models were developed to estimate the probability of survival to 28 days after birth for each of the three stages of care. Gestational age (measured in completed weeks), birth weight of the baby and multiplicity of birth (singleton vs multiple) were included in the model as these are known to be key predictors of survival.[4]

Non-linear functions were investigated for gestational age and birth weight using fractional polynomials,[8] with the final form selected using the change in deviance. Two-way interactions between the non-transformed variables were investigated between the main effects (gestational age, birth weight and multiplicity of birth) and retained in the model if their inclusion was statistically significant at the 5% level. Estimated survival percentages were calculated for babies according to week of gestational age at birth, multiplicity and birth weight in increments of 100 g.

The overall model fit was assessed by investigating the Briers score for each of the optimised linear predictors where a score closer to 0 indicates a better fit of the model.[9] The internal validation of the model was checked by examining the calibration and discrimination (c-statistic and Hosmer-Lemeshow test) overall and in predefined subgroups based on birth weight (less than 50th centile vs ≥50th centile), multiplicity (singleton vs multiple) and gestational age (22^{+0}–26^{+6} weeks; 27^{+0}–29^{+6} weeks; 30^{+0}–31^{+6} weeks).

RESULTS

There were 44 122 babies (33 173 singletons and 10 949 multiples) alive at the onset of care during the birthing process born at 22^{+0} to 31^{+6} weeks' gestational age in the UK and British Crown Dependencies between 1 January 2016 and 31 December 2020. A total of 359 babies were excluded because their primary cause of death was a congenital anomaly (0.8%).

There were 43 763 babies alive at the onset of care during the birthing process (around 8800 babies per year). Birth weight was imputed due to being missing for 7086 (16%) births or implausible for 1160 (2.7%) births. Survival-focused care was provided for 42 004 babies (96.0%) and 41 158 babies (94.0%) were admitted to a neonatal care unit. The observed survival is provided in table 1 by week of gestational age and stage of care.

In tables 2–7, we display survival graphically using a grid approach for ease of use in practical situations and as seen in previous research.[6] The predicted survival for the midpoint birth weight of each hundred gram band is displayed. For example, at 24 weeks of gestational age, survival to 28 days for singletons

Table 1 Percentage and number of babies surviving to 28 days after birth by gestational age (weeks) for the three different stages throughout the perinatal pathway

Gestational age (weeks)	Percentage (number) of babies surviving to 28 days					
	Babies alive at the onset of care during the birthing process		Babies where active survival focused care was initiated		Babies admitted to a neonatal care unit	
22	4.5	(1548)	14.4	(485)	23.2	(302)
23	36.5	(1949)	44.0	(1615)	50.6	(1405)
24	64.7	(2454)	68.6	(2312)	73.0	(2173)
25	79.5	(2566)	81.3	(2507)	84.4	(2415)
26	87.2	(3228)	88.3	(3186)	89.7	(3137)
27	92.3	(3867)	93.3	(3827)	94.2	(3790)
28	94.1	(5178)	94.7	(5146)	95.4	(5109)
29	97.0	(5693)	97.2	(5680)	97.6	(5654)
30	97.6	(7588)	97.8	(7572)	98.3	(7533)
31	98.5	(9692)	98.7	(9674)	99.0	(9640)
22^{+0}–31^{+6} weeks	87.1	(43 763)	90.8	(42 004)	92.7	(41 158)

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Table 2 Predicted percentage survival to 28 days after birth by birth weight and gestational age for singleton births alive at the onset of care during the birthing process

	Gestation at birth (completed weeks)									
	22	23	24	25	26	27	28	29	30	31
Birth weight (g)										
2200–2299										98%
2100–2199										98%
2000–2099									97%	98%
1900–1999									97%	98%
1800–1899									97%	98%
1700–1799								97%	97%	98%
1600–1699								97%	97%	98%
1500–1599							96%	97%	97%	98%
1400–1499							96%	97%	97%	98%
1300–1399						94%	96%	97%	97%	98%
1200–1299						94%	96%	97%	97%	97%
1100–1199					91%	94%	95%	96%	97%	97%
1000–1099					90%	93%	95%	96%	97%	97%
900–999				83%	90%	93%	95%	96%	97%	
800–899			70%	82%	89%	92%	94%	96%		
700–799	22%	46%	66%	80%	87%	91%	93%			
600–699	19%	40%	62%	76%	85%	89%				
500–599	14%	33%	53%	69%						
400–499	8%	21%	39%							
300–399	3%	8%	17%							

babies between 300 g and 800 g ranged between 17% and 70% for babies alive at the onset of care during the birthing process, 31%–73% for babies where active survival-focused care was initiated, and 40%–76% for babies admitted to a neonatal unit (tables 2–7).

The results for multiple births were very similar (tables 2–7). For singleton and multiple births with a birthweight of 1000g or more, 90% or more babies survived to 28 days across all three stages of the perinatal care pathway.

Details of the final models are given in online supplemental appendix 1.

Model fit

The model fit statistics are provided for the whole dataset and prior defined subgroups according to gestational age and birth weight (table 8). The observed and predicted number of babies surviving are provided and can be used to investigate specific

Table 3 Predicted percentage survival to 28 days after birth by birth weight and gestational age for multiple births alive at the onset of care during the birthing process

	Gestation at birth (completed weeks)									
	22	23	24	25	26	27	28	29	30	31
Birth weight (g)										
2200–2299										100%
2100–2199										99%
2000–2099									99%	99%
1900–1999									99%	99%
1800–1899									99%	99%
1700–1799								99%	99%	99%
1600–1699								99%	99%	99%
1500–1599							98%	99%	99%	99%
1400–1499							98%	99%	99%	99%
1300–1399						97%	98%	98%	99%	99%
1200–1299						97%	98%	98%	99%	99%
1100–1199					95%	96%	97%	98%	98%	99%
1000–1099					94%	96%	97%	98%	98%	98%
900–999				88%	93%	95%	97%	97%	98%	
800–899			76%	87%	92%	95%	96%	97%		
700–799	26%	52%	72%	84%	90%	93%	95%			
600–699	21%	44%	66%	80%	87%	91%				
500–599	15%	35%	56%	72%						
400–499	8%	22%	40%							
300–399	3%	7%	16%							

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Table 4 Predicted percentage survival to 28 days after birth by birth weight and gestational age for singleton births where survival-focused care was initiated

	Gestation at birth (completed weeks)									
	22	23	24	25	26	27	28	29	30	31
Birth weight (g)										
2200–2299										97%
2100–2199										97%
2000–2099									97%	98%
1900–1999									97%	98%
1800–1899									97%	98%
1700–1799								96%	97%	98%
1600–1699								97%	97%	98%
1500–1599							95%	97%	98%	98%
1400–1499							95%	97%	98%	98%
1300–1399						94%	96%	97%	98%	98%
1200–1299						94%	96%	97%	98%	98%
1100–1199					90%	94%	96%	97%	98%	98%
1000–1099					90%	94%	96%	97%	98%	98%
900–999				84%	90%	93%	95%	97%	98%	
800–899			73%	83%	89%	93%	95%	96%		
700–799	38%	56%	71%	81%	88%	92%	94%			
600–699	33%	51%	66%	78%	85%	90%				
500–599	27%	43%	60%	72%						
400–499	19%	33%	48%							
300–399	10%	19%	31%							

subgroups where the model overestimates or underestimates survival. Overall, the model fit was good at all three stages of the care pathway (Briers scores: 0.07, 0.06 and 0.05). Generally, the Hosmer-Lemeshow test indicated good calibration, although there was a small number of subgroups where $p<0.01$. Overall, the discrimination of the models was good (c-statistics: 0.89, 0.86 and 0.85), although it was poorer (c-statistic around 0.62–0.65) in some of the subgroups based on gestational age at birth greater than 26 weeks.

DISCUSSION

In this paper, we have estimated the percentage of babies surviving to 28 days after birth for singleton and multiple births at 22^{+0}

Table 5 Predicted percentage survival to 28 days after birth by birth weight and gestational age for multiple births where survival-focused care was initiated

	Gestation at birth (completed weeks)									
	22	23	24	25	26	27	28	29	30	31
Birth weight (g)										
2200–2299										99%
2100–2199										99%
2000–2099									99%	99%
1900–1999									99%	99%
1800–1899									99%	99%
1700–1799								99%	99%	99%
1600–1699								99%	99%	99%
1500–1599							98%	99%	99%	99%
1400–1499							98%	99%	99%	99%
1300–1399						97%	98%	99%	99%	99%
1200–1299						97%	98%	98%	99%	99%
1100–1199					94%	96%	97%	98%	99%	99%
1000–1099					94%	96%	97%	98%	99%	99%
900–999				88%	93%	95%	97%	98%	98%	
800–899			78%	87%	91%	94%	96%	97%		
700–799	42%	60%	74%	84%	89%	93%	95%			
600–699	35%	53%	68%	79%	86%	91%				
500–599	27%	43%	59%	72%						
400–499	17%	30%	45%							
300–399	9%	16%	27%							

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Table 6 Predicted percentage survival to 28 days after birth by birth weight and gestational age for singleton births admitted to a neonatal care unit

	Gestation at birth (completed weeks)									
	22	23	24	25	26	27	28	29	30	31
Birth weight (g)										
2200–2299										98%
2100–2199										98%
2000–2099									97%	98%
1900–1999									97%	98%
1800–1899									98%	99%
1700–1799								97%	98%	99%
1600–1699								97%	98%	99%
1500–1599							95%	97%	98%	99%
1400–1499							96%	97%	98%	99%
1300–1399						93%	96%	97%	98%	99%
1200–1299						94%	96%	98%	98%	99%
1100–1199					90%	94%	96%	98%	98%	99%
1000–1099					91%	94%	96%	98%	98%	99%
900–999				85%	91%	94%	96%	98%	98%	
800–899			76%	85%	90%	94%	96%	97%		
700–799	47%	62%	75%	84%	90%	93%	96%			
600–699	43%	59%	72%	81%	88%	92%				
500–599	38%	53%	66%	77%						
400–499	29%	43%	56%							
300–399	17%	27%	40%							

to 31^{+6} weeks gestational age using national data from the UK and British Crown Dependencies. We have provided graphical representations of the percentage of babies surviving for three different stages of the perinatal care pathway: (1) babies alive at the onset of care during the birthing process; (2) babies provided with survival-focused care; and (3) those who were admitted to neonatal care. Using national data for 5 years, we were able to estimate survival for multiple births and babies born at the earliest weeks of gestational age where they may survive, particularly those born before 24 weeks of gestation. Previously, these groups have either not been included in estimates or included with very small sample sizes.

Use of national data provides a population-based overview of neonatal survival. Previous research in the UK[6] has

Table 7 Predicted percentage survival to 28 days after birth by birth weight and gestational age for multiple births admitted to a neonatal care unit

	Gestation at birth (completed weeks)									
	22	23	24	25	26	27	28	29	30	31
Birth weight (g)										
2200–2299										100%
2100–2199										100%
2000–2099									99%	100%
1900–1999									99%	100%
1800–1899									99%	100%
1700–1799								99%	99%	100%
1600–1699								99%	99%	100%
1500–1599							98%	99%	99%	99%
1400–1499							98%	99%	99%	99%
1300–1399						97%	98%	99%	99%	99%
1200–1299						96%	98%	99%	99%	99%
1100–1199					94%	96%	98%	98%	99%	99%
1000–1099					93%	96%	97%	98%	99%	99%
900–999				88%	93%	95%	97%	98%	99%	
800–899			79%	87%	91%	95%	96%	98%		
700–799	48%	64%	76%	84%	90%	93%	96%			
600–699	42%	57%	70%	80%	87%	91%				
500–599	34%	48%	62%	73%						
400–499	23%	36%	49%							
300–399	12%	20%	30%							

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Table 8 Model fit statistics for each of the three cohorts overall and by subgroups based on birth weight, multiplicity and gestational age at birth

			Birth weight		Gestational age (weeks)			Multiplicity	
Birth cohort	Variable	Overall	<50th centile	≥50th centile	22^{+0}–26^{+6}	27^{+0}–29^{+6}	30^{+0}–31^{+6}	Singleton	Multiple
Alive at onset of birth process	Number of babies	43 763	21 880	21 883	11 745	14 738	17 280	32 853	10 910
	Number surviving	38 133	18 834	19 299	7221	13 962	16 950	28 310	9823
	Predicted surviving	38 133	18 786	19 345	7178	14 050	16 905	28 310	9823
	C-statistic	0.89	0.89	0.88	0.83	0.63	0.62	0.88	0.92
	Hosmer-Lemeshow test	0.97	0.99	<0.001	0.76	<0.001	0.99	0.89	0.95
	Briers score	0.07	0.07	0.06	0.16	0.05	0.02	0.07	0.05
Provided active survival-focused care	Number of babies	42 004	20 847	21 157	10 105	14 653	17 246	31 412	10 592
	Number surviving	38 133	18 834	19 299	7221	13 962	16 950	28 310	9823
	Predicted surviving	38 133	18 794	19 339	7188	14 011	16 934	28 310	9823
	C-statistic	0.86	0.86	0.85	0.76	0.62	0.64	0.84	0.89
	Hosmer-Lemeshow test	0.91	0.99	0.29	0.89	<0.001	0.99	0.89	0.73
	Briers score	0.06	0.06	0.06	0.16	0.04	0.02	0.07	0.05
Neonatal admission	Number of babies	41 158	20 341	20 817	9432	14 553	17 173	30 665	10 493
	Number surviving	38 133	18 834	19 299	7221	13 962	16 950	28 310	9823
	Predicted surviving	38 133	18 784	19 349	7189	13 996	16 948	28 310	9823
	C-statistic	0.85	0.85	0.84	0.74	0.62	0.65	0.83	0.89
	Hosmer-Lemeshow test	0.15	0.80	0.01	0.98	<0.001	0.78	0.83	<0.001
	Briers score	0.05	0.05	0.05	0.15	0.04	0.01	0.06	0.04

predominantly investigated babies who were admitted to neonatal care, representing a biased cohort as these represent a highly selective subset of all babies. This is most marked at the earliest gestations where those babies who die following comfort care without admission to neonatal care have not been captured in previous estimates and these babies can represent a large cohort. For example, of those babies born at 22 weeks, less than 20% survived to be admitted for neonatal care. Our inclusion of this important group is unique and the results we provide can facilitate the counselling of parents about potential outcomes and how they change before, during and immediately following birth.

Comparison of our data with those from two previous neonatal mortality estimates in the UK[6 10] demonstrates increases in survival over time with sustained improvements for all gestations up to 30 weeks with the largest improvements seen among the lower gestational age births. This confirms the need for these updated charts to inform future counselling of parents and clinical knowledge.

Differences in adjustments

We made an a priori decision not to adjust for or make exclusions based on baby's ethnicity. Along with other work in similar fields, we believe including ethnicity could exacerbate existing disparities between ethnic groups.[11] We do not think clinical decision-making over care initiation or continuation is or should be based on the ethnicity of a baby. Similarly, we did not provide separate survival estimates according to the sex of the baby as we believe any differences were likely to be so small that they would not be clinically meaningful for conversations with parents.

Clinical use of these charts

These charts will help facilitate conversations between healthcare professionals and parents about the potential outcome for their baby (or babies). National estimates of survival are useful and vital to support clinical judgement and decision-making.[3] Both the British Association of Perinatal Medicine (BAPM)[12] and Yeoh *et al*[13] provide helpful guidance for such conversations with parents.

Strengths/limitations

In this work, we present results from a large national cohort, rather than from a specific region or hospital. We have been able to investigate care throughout the perinatal pathway rather than a potentially biased subset, for example, only those babies admitted to neonatal care. We have also focused on a cohort of babies alive at the onset of care during birthing process rather than only live births as this minimises the impact of the wide variation in the classification of deaths of babies born at less than 24 weeks as intrapartum losses or neonatal deaths.[14]

Our data relate to a time period encompassing the introduction of new guidance from BAPM in late 2019, which suggests potential provision of active care at 22 weeks of gestation.[12] Therefore, there may be ongoing and future significant changes in survival and other outcomes in babies born at 22 weeks requiring regular updates to this analysis.

We followed the recommendations within the Transparent Reporting of Multivariable Prediction Model for Individuals Prognosis or Diagnosis (TRIPOD) statement when developing this work.[15] Overall, the discrimination of the models was good, although it was poorer in some of the subgroups based on gestational age at birth greater than 26 weeks. This finding is not unexpected because gestational age is a strong predictor of survival, and its effect will not be seen for subgroups defined over a narrow range of gestational ages.

A limitation of our work is that we only had information on survival for up to 28 days after birth and some babies may have died after this time while receiving neonatal care. However, research has indicated that for babies born at <32 weeks' gestational age around half of deaths occur in the first 10 days after birth, and around 75% of deaths occurring within the first month.[16]

CONCLUSION

In this work, we have provided estimates of neonatal mortality for babies born at 22^{+0} to 31^{+6} weeks of gestational age to update and extend previous estimates. For the first time, estimates of survival have been provided using national data and

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at different points along the early care pathway, allowing for ongoing counselling of parents and care provision.

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Appendix 1: Final model details

The final logistic model to predict survival at 28 days for each of the three stages of care is as follows.

Survival is survival to 28 days of life

Gestation is the baby's gestational age in completed weeks

Birthweight is the baby's birthweight in grams

Multiplicity is 0 for singleton births and 1 otherwise

Model 1: Babies alive at onset of labour

Logit(Survival) = β0+ β1*$(Birthweight/1000)^{-2}$ + β2*$(Gestation)^{-2}$ + β3*$(Gestation)^{-2}$*ln(Gestation) + β4*Multiplicity + β5*Multiplicity*Birthweight + β6*Gestation*Multiplicity

Coefficients β0: =-1.5056412; β1: -0.35756955; β2: 42438.23; β3: 13865.879; β4 0.65555131; β5: 0.00075761; β6: 0.0144124

Model 2: Babies receiving active survival focused care

Logit(Survival) = β0 + β1*ln(Birthweight/1000) + β2ln$(Birthweight/1000)^{2}$ + β3*$Gestation^{-2}$ + β4 *Multiplicity+ β5*Multiplicity*Birthweight + β6 *Gestation*Multiplicity

Coefficients β0: 8.4231188; β1: 0.45646377; β2: -1.2870236; β3: -4207.6619; β4: -0.48652448; β5: 0.00098267; β6: 0.00289392

Model 3: Babies admitted to neonatal care

Logit(Survival) = β0 + β1*ln(Birthweight/1000) + β2*$(Birthweight/1000)^{0.5}$ + β3*$Gestation^{-1}$ + β5 *Multiplicity+ β6*Gestation*Birthweight+ β7 *Multiplicity*Birthweight+ β8 *Gestation*Multiplicity
Coefficients β0: 33.552105; β1: 8.954789; β2: -22.325092; β3: -289.95836; β4: -0.49235337; β5: 0.00008494; β6: 0.001155; β7: -0.01368192; β8: -0.01368192