

Supplemental table 1 Annual number of study subjects, deaths, and active treatment

year of birth	period 1					period 2						
	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012		
National population <sup>a)</sup>	847	832	845	892	937	4353	886	886	876	867	888	4403
Registered to the database in this study <sup>b)</sup>	242	278	360	362	399	1641	397	426	393	404	388	2008
Transferred after birth	30	28	29	37	38	162	37	45	37	28	22	169
Study subjects	212	250	331	325	361	1479	360	381	356	376	366	1839
Not admitted to the NICU				12	5	17	9	6	8	13	7	43
Active treatment, n	209	247	328	320	355	1459	354	376	346	366	362	1804
%	98.6%	98.8%	99.1%	98.5%	98.3%	98.6%	98.3%	98.7%	97.2%	97.3%	98.9%	98.1%
Admitted to the NICU	212	250	331	313	356	1462	351	375	348	363	359	1796
Death in the NICU	77	77	116	104	97	471	102	76	76	89	74	417
Death at discharge	77	77	116	116	102	488	111	82	84	102	81	460
Death at discharge: unknown	0	0	0	0	0	0	0	0	1	0	1	2
Death after discharge	1	0	1	4	2	8	2	2	2	0	1	7

a), numbers of the national population were obtained from E-stat. Vital statistics of Japan, live births by the period of gestation (reference 34).

b), numbers of infants registered to the NRNJ database from 52 tertiary centers in Japan included in this study.

Supplemental table 2 Comparison of demographic, prenatal, and neonatal characteristics of study subjects between surviving infants with and without follow-up data at 3 years of age

	With follow-up data		Without follow-up data		p
	n=1463		n=892		
Maternal age, mean (SD)	31.2 (5.1)	n=1416	31.0 (5.7)	n=874	0.365
Birth weight, mean (SD)	612 (100)	n=1463	613 (104)	n=892	0.902
GA, mean (SD)	23.9 (0.7)	n=1463	23.9 (0.7)	n=892	0.745
GA distribution					0.831
22 w	118/1463	8.1%	71/892	8.0%	
23 w	522/1463	35.7%	308/892	34.5%	
24 w	823/1463	56.3%	513/892	57.5%	
Male	745/1461	51.0%	455/892	51.0%	1.000
Multiple births	223/1463	15.2%	155/892	17.4%	0.183
Congenital anomalies	32/1452	2.2%	14/886	1.6%	0.358
Pregnancy-related hypertension	70/1463	4.8%	45/888	5.1%	0.768
Clinical CAM	564/1442	39.1%	285/853	33.4%	0.006
Antenatal steroids	736/1460	50.4%	450/878	51.3%	0.701
Cesarean section	941/1462	64.4%	540/889	60.7%	0.078
RDS	1134/1455	77.9%	671/889	75.5%	0.172
PDA	908/1455	62.4%	554/889	62.3%	0.965
CLD on day 28	1234/1642	84.4%	759/886	85.7%	0.440
CLD at 36 weeks	791/1449	54.6%	498/878	56.7%	0.323
NEC and/or intestinal perforation	83/1463	5.7%	65/892	7.3%	0.136
Sepsis	273/1455	18.8%	181/890	20.3%	0.360
IVH (grades 3-4)	123/1449	8.5%	95/881	10.8%	0.067
Cystic periventricular leukomalacia	45/1460	3.1%	28/886	3.2%	0.903

Received surfactant	1209/1454	83.1%	719/890	80.8%	0.148
PDA indomethacin for prophylaxis	167/1454	11.5%	98/887	11.0%	0.788
PDA treated with indomethacin	936/1454	64.4%	552/887	62.2%	0.309
PDA ligation	300/1015	22.8%	198/797	24.8%	0.291
LCC treated with steroids	377/1453	25.9%	217/887	24.5%	0.434
CLD treated with steroids	549/1452	37.6%	355/880	40.3%	0.189
Received antibiotics	1282/1447	88.6%	790/883	89.5%	0.541
Retinopathy of prematurity, treated	675/1447	46.6%	443/877	50.5%	0.072
Parenteral nutrition	1152/1462	78.8%	700/890	78.7%	0.959
Home oxygen therapy at discharge	327/1450	22.6%	188/875	21.5%	0.571

Values are the number/number of measurement and percentages unless otherwise stated.

GA, gestational age; CAM, chorioamnionitis. RDS, Respiratory distress syndrome; PDA, patent ductus arteriosus; CLD, chronic lung disease; NEC, necrotizing enterocolitis, IVH, intraventricular hemorrhage; LCC, late-onset circulatory collapse.

Supplement table 3 Survival and neurodevelopmental outcomes at 3 years of age for periods 1 and 2 after simple imputations

	Total				22 w				23 w				24 w			
	Period 1		Period 2		Period 1		Period 2		Period 1		Period 2		Period 1		Period 2	
	n=1479		n=1839		n=183		n=271		n=544		n=686		n=752		n=882	
Not admitted to the NICU	17	1.1%	43	2.3%	4	2.2%	26	9.6%	11	2.0%	13	1.9%	2	0.3%	4	0.5%
Death at the NICU	471	31.8%	417	22.7%	114	62.3%	119	43.9%	198	36.4%	169	24.6%	159	21.1%	129	14.6%
Death after discharge	8	0.5%	7	0.4%	1	0.5%	1	0.4%	5	0.9%	4	0.6%	2	0.3%	2	0.2%
Survived	983	66.5%	1372 <sup>b)</sup>	74.6%	64	35.0%	125	46.1%	330	60.7%	500	72.9%	589	78.3%	747 <sup>b)</sup>	84.7%
Missing data were imputed as having impairments																
Cerebral palsy	469		669		33		60		168		241		268		368	
Visual impairments	474		701		31		72		162		243		281		386	
Hearing impairments	455		753		30		80		149		226		276		410	
DQ of KSPD <70	725		952		49		87		251		354		425		511	
Developmental delay	668		917		47		87		236		349		385		481	
NDI <sup>a)</sup>	745		1055		50		108		259		388		437		559	
Death or NDI <sup>a)</sup>	1242	84.0%	1522	82.8%	169	92.3%	254	93.7%	473	86.9%	574	83.7%	600	79.8%	964	78.7%
Missing data were imputed as having no impairments																
Cerebral palsy	97		74		10		10		44		28		43		36	
Visual impairments	80		31		4		9		33		10		43		12	
Hearing impairments	14		6		0		0		7		3		7		3	
DQ of KSPD <70	126		250		11		31		43		99		72		120	
Developmental delay	181		278		14		32		66		117		101		129	
NDI <sup>a)</sup>	269		322		19		40		109		130		141		152	
Death or NDI <sup>a)</sup>	765	51.7%	789	42.9% **	138	75.4%	186	68.6%	323	59.4%	316	46.1% **	304	40.4%	287	32.5% **

a), NDI, Neurodevelopmental impairments were defined as any of the following: cerebral palsy, hearing impairments, visual impairments, DQ of KSPD <70, or developmental delay.

b), two infants with missing data on death after NICU discharge in period 2 were estimated as having survived without follow-up data.

Supplement table 4 Adjusted odds ratios for neurodevelopmental impairments (NDI) at 3 years of age in period 2 versus period 1 after imputations

	Total n=3318	22 w n=454	23 w n=1230	24 w n=1634
Death or NDI <sup>a)</sup>	<b>0.83 (0.71–0.97)</b>	0.99 (0.57–1.72)	<b>0.64 (0.49–0.84)</b>	0.86 (0.68–1.07)
Death or NDI <sup>b)</sup>	1.01 (0.82–1.24)	1.11 (0.41–3.06)	0.81 (0.56–1.18)	1.00 (0.76–1.31)
Death or NDI <sup>c)</sup>	<b>0.75 (0.64–0.87)</b>	0.75 (0.44–1.25)	<b>0.57 (0.44–0.74)</b>	<b>0.79 (0.63–0.99)</b>

Death or NDI <sup>a)</sup>, values are the adjusted odds ratios (95% confidence intervals) by a logistic regression after multiple imputations as missing at random

Death or NDI <sup>b)</sup>, values are the adjusted odds ratios (95% confidence intervals) by a logistic regression after missing data were imputed as having impairments.

Death or NDI <sup>c)</sup>, values are the adjusted odds ratios (95% confidence intervals) by a logistic regression after missing data were imputed as having no impairments.

Adjusting variables were the center, gender, multiple gestation, maternal age, cesarean delivery, antenatal steroid use, pregnancy-related hypertension, clinical chorioamnionitis, life-threatening congenital anomalies, and birth weight.