

Appendices

NNRD variable	Data items
<i>Primary Clinical Reason For Admission</i>	<i>Admission details:</i> HIE Suspected/Confirmed
<i>Principal Diagnosis At Discharge</i>	<i>Discharge details, terms:</i> <ul style="list-style-type: none"> • HIE • Hypoxic ischaemic encephalopathy • Neonatal encephalopathy • Perinatal asphyxia • Hypoxic ischaemic brain damage • Birth asphyxia • Birth (perinatal) asphyxia • Intrauterine hypoxia

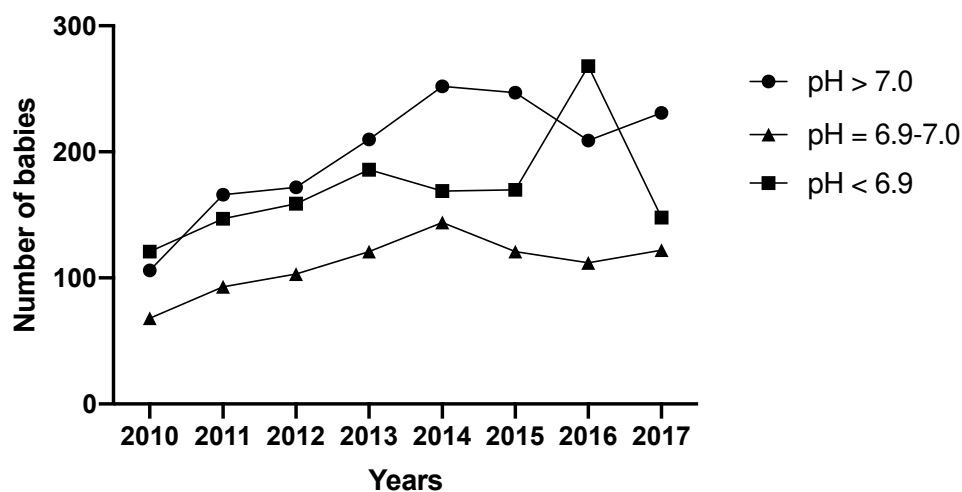
Supplemental table 1. NNRD data set items used for selection of babies corresponding to the inclusion criteria.

<i>Birth characteristics</i>	Sex Birth weight Gestation weeks; was calculated
<i>Demographics</i>	Lower Super Output Area (LSOA); categorized into deciles, with 0 being the most underprivileged areas. Ethnicity of mother Maternal age; was calculated
<i>Labour and delivery characteristics</i>	Mode of delivery Instrument used for delivery Multiple births Primiparous; no previous pregnancies
<i>Antenatal characteristics</i>	Medical problems prior to pregnancy; hypothyroid and diabetes Obstetric issues during pregnancy; maternal pyrexia, cord and/or placenta problems ¹ , suspected chorioamnionitis ² and rupture of membranes Smoking during pregnancy
<i>Neonatal care</i>	Post-natal transfer

Supplemental table 2. Descriptive characteristics of the population included in the study from 2009 to 2018 in England, Wales and Scotland. ¹Placental abruption and/or placenta praevia, ²Intrapartum antibiotics given.

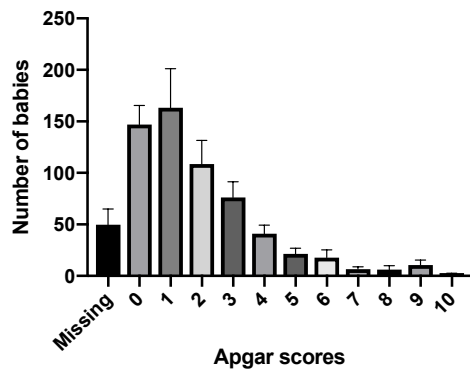
Variable	Data items
Intubation at resuscitation	<i>Labour and Delivery Details</i> NEONATAL RESUSCITATION METHODE – Code 15
Chest compressions	<i>Labour and Delivery Details</i> NEONATAL RESUSCITATION METHOD – Code 16
Resuscitation drugs	<i>Labour and Delivery Details</i> NEONATAL RESUSCITATION METHOD – Code 17 (Adrenaline) or 88 (any other drug)
Apgar score at 1 minute	<i>Labour and Delivery Details</i> APGAR SCORE (1 MINUTE)
Apgar score at 5 minute	<i>Labour and Delivery Details</i> APGAR SCORE (5 MINUTE)
Umbilical cord pH	<i>Labour and Delivery Details</i> UMBILICAL CORD BLOOD PH LEVEL (ARTERIAL)
Seizures recorded	<i>Daily Care Neurology</i> on day 1 only; CONVULSIONS
Invasive ventilation	<i>Daily Care Respiratory</i> on day 1 only; RESPIRATORY SUPPORT MODE – Code 1
Nitric oxide administered	<i>Daily Care Respiratory</i> on day 1 only, NITRIC OXIDE GIVEN INDICATOR
Inotropes administered	<i>Daily Care Cardiovascular</i> on day 1 only, INOTROPE INFUSION RECEIVED INDICATOR or <i>Daily Care Medication</i> on day 1 only, 500098 DOPAMINE, 500096 DOBUTAMINE, 500056 ADRENALINE, 500210 NORADRENALINE, 500116 HYDROCORTISONE, 1010173 MILRINONE

Supplemental table 3. NNRD data set items used for the clinical characteristics of babies

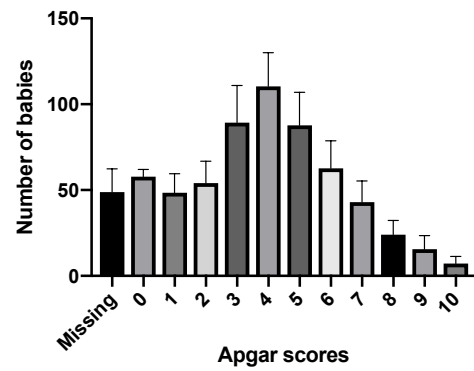


Supplemental figure 1. Line chart of the number of babies that had a diagnosis of hypoxic ischaemic encephalopathy and received therapeutic hypothermia for 3 days or died during that period by umbilical arterial cord pH at birth.

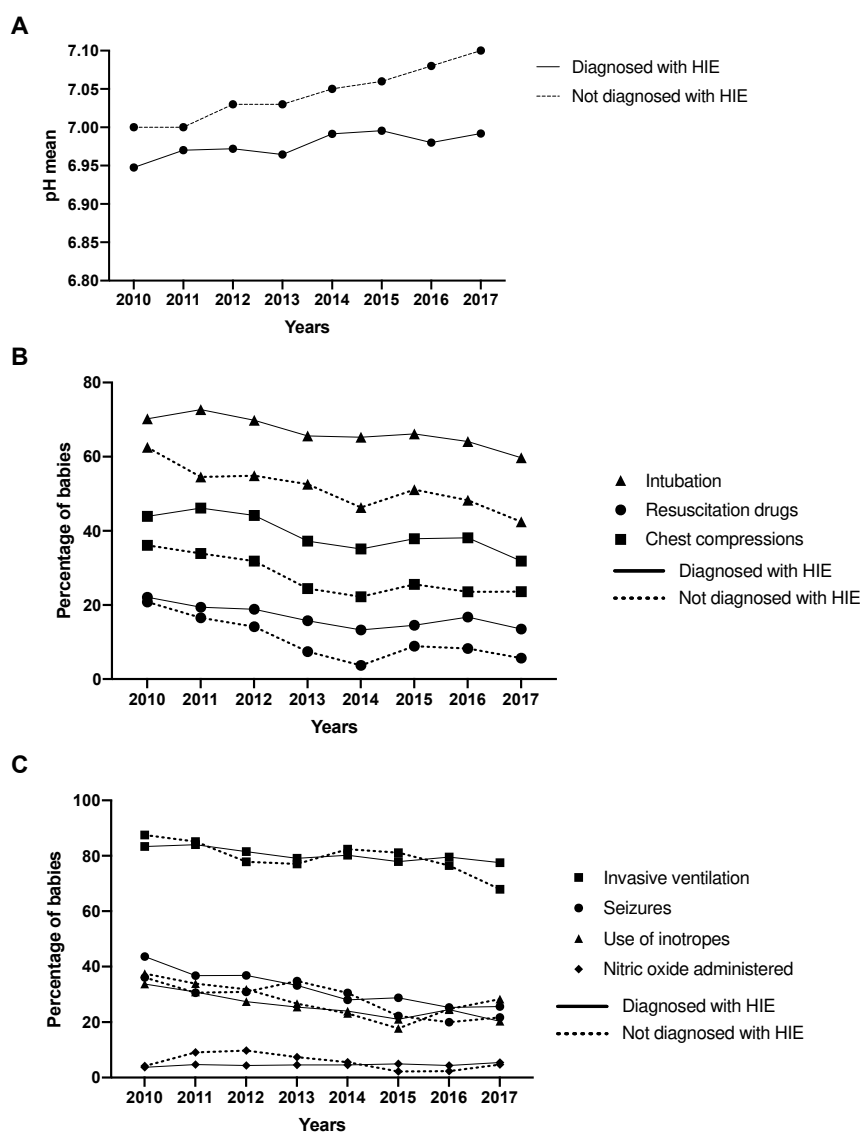
A



B



Supplemental figure 2. Bar charts of the number of babies that had a diagnosis of hypoxic ischaemic encephalopathy and received therapeutic hypothermia for 3 days or died during that period, by Apgar score at 1 minute (A) and 5 minutes (B), from 2010 to 2017.



Supplemental figure 3. Line charts of the clinical characteristics of babies who have received therapeutic hypothermia from 2010 to 2017. (A) The mean umbilical arterial cord pH at birth, **(B)** the resuscitation characteristics and **(C)** the condition on the first day of admission in the neonatal unit for babies who were admitted for HIE (continuous lines) and for babies who were not admitted for HIE (dashed lines).

Sarnat staging		Years								
Recorded HIE score (grade)		2010	2011	2012	2013	2014	2015	2016	2017	
Count	Missing data	19	12	23	34	22	44	39	84	
	1	31	71	68	109	94	112	113	133	
	2	141	158	185	253	238	231	255	293	
	3	212	316	297	284	409	384	328	209	
Percentage	Missing data	4.71	2.15	4.01	5.00	2.88	5.71	5.31	11.68	
	1	7.69	12.75	11.87	16.03	12.32	14.53	15.37	18.50	
	2	34.99	28.37	32.29	37.21	31.19	29.96	34.69	40.75	
	3	52.61	56.73	51.83	41.76	53.60	49.81	44.63	29.07	
Statistical analysis	Spearman correlation	Coefficient			-0.11					
		95% CI			[-0.14;-0.08]					
		p-value			<0.0001					

Supplemental table 4. Statistical analysis of the initial conditions prior to treatment variables over the years.

Diagnosis		Year								Total
		2010	2011	2012	2013	2014	2015	2016	2017	
Acidosis	count	4	12	7	20	15	10	11	14	93
	frequency	5.56	9.92	6.19	14.81	13.89	11.11	12.94	13.21	11.2
Sepsis	count	12	23	24	49	49	47	39	55	298
	frequency	16.67	19.01	21.24	36.3	45.37	52.22	45.88	51.89	35.9
Seizures	count	0	4	2	5	5	5	3	4	28
	frequency	0	3.31	1.77	3.7	4.63	5.56	3.53	3.77	3.37
Encephalopathy (not hypoxic)	count	1	2	3	2	2	0	2	3	15
	frequency	1.39	1.65	2.65	1.48	1.85	0	2.35	2.83	1.81
Meconium aspirate syndrome	count	2	18	22	16	13	17	13	22	123
	frequency	2.78	14.88	19.47	11.85	12.04	18.89	15.29	20.75	14.82
Respiratory issues	count	6	37	30	49	46	38	45	36	287
	frequency	8.33	30.58	26.55	36.3	42.59	42.22	52.94	33.96	34.58
Poor clinical condition	count	0	2	4	6	6	15	9	13	55
	frequency	0	1.65	3.54	4.44	5.56	16.67	10.59	12.26	6.63

Supplemental table 5. Frequency of the diagnosis recorded in the 'principal diagnosis at discharge' field in babies who have not been admitted for HIE but have been cooled from 2010 to 2017.

	Clinical characteristics		Year							Total years		
			2010	2011	2012	2013	2014	2015	2016	2017	Mean	Median
Babies cooled	Count		72	121	113	135	108	90	85	106	830	
Mortality rate	Count (%)		14 (19.44)	10 (8.26)	12 (10.62)	17 (12.59)	9 (8.33)	5 (5.56)	4 (4.71)	10 (9.43)	81 (9.76)	
Level of pH												
	Mean (s.d)		7.00 (0.20)	7.00 (0.16)	7.03 (0.18)	7.03 (0.19)	7.05 (0.16)	7.06 (0.19)	7.08 (0.17)	7.10 (0.19)	Mean	Median
	Count (%)	missing data	23 (31.94)	54 (44.63)	41 (36.28)	48 (35.56)	45 (41.67)	24 (26.67)	26 (30.59)	39 (36.79)	7.04	7.03
		< 6.9	15 (20.83)	21 (17.36)	20 (17.70)	21 (15.56)	11 (10.19)	10 (11.11)	6 (7.06)	7 (6.60)		
		[6.9;7.0]	17 (23.61)	16 (13.22)	8 (7.08)	22 (16.30)	14 (12.96)	14 (15.56)	17 (20.00)	15 (14.15)		
		> 7.0	17 (23.61)	30 (24.79)	44 (38.94)	44 (32.59)	38 (35.19)	42 (46.67)	36 (42.35)	45 (42.45)		
Apgar score at 1min												
	Median (IQR)		2 (2)	2 (3)	2 (4)	2 (3)	3 (4)	2 (4)	3 (4)	3 (4)	Mean	Median
	Count (%)	missing data	10 (13.89)	16 (13.22)	14 (12.39)	9 (6.67)	13 (12.04)	13 (14.44)	8 (9.41)	13 (12.26)	3.05	2.00
		[0;3]	48 (66.67)	70 (57.85)	68 (60.18)	82 (60.74)	59 (54.63)	49 (54.44)	46 (54.12)	59 (55.66)		
]3;7]	13 (18.06)	25 (20.66)	17 (15.04)	31 (22.96)	20 (18.52)	17 (18.89)	21 (24.71)	30 (28.30)		
]7;10]	1 (1.39)	10 (8.26)	14 (12.39)	13 (9.63)	16 (14.81)	11 (12.22)	10 (11.76)	4 (3.77)		
Apgar score at 5min												
	Median (IQR)		4 (3)	5 (4)	5 (5)	5 (3)	5 (4)	5 (3)	5 (4)	5 (4)	Mean	Median
	Count (%)	missing data	10 (13.89)	15 (12.40)	17 (15.04)	8 (5.93)	13 (12.04)	15 (16.67)	7 (8.24)	12 (11.32)	4.77	5.00
		[0;3]	30 (41.67)	41 (33.88)	35 (30.97)	35 (25.93)	27 (25.00)	25 (27.78)	22 (25.88)	30 (28.30)		
]3;7]	25 (34.72)	47 (38.84)	39 (34.51)	75 (55.56)	48 (44.44)	37 (41.11)	38 (44.71)	48 (45.28)		
]7;10]	7 (9.72)	18 (14.88)	22 (19.47)	17 (12.59)	20 (18.52)	13 (14.44)	18 (21.18)	16 (15.09)		
Intubation at resuscitation												
	Count (%)	missing data	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	Mean (%)	
	No	0.00	27 (37.50)	55 (45.45)	51 (45.13)	64 (47.41)	58 (53.70)	44 (48.89)	44 (51.76)	61 (57.55)	48.67	
	Yes	1.00	45 (62.50)	66 (54.55)	62 (54.87)	71 (52.59)	50 (46.30)	46 (51.11)	41 (48.24)	45 (42.45)	51.33	
Use of inotropes												
	Count (%)	missing data	0 (0.00)	0 (0.00)	1 (0.88)	1 (0.74)	0 (0.00)	2 (2.22)	3 (3.53)	1 (0.94)	Mean (%)	
	No	0.00	45 (62.50)	80 (66.12)	76 (67.26)	98 (72.59)	83 (76.85)	72 (80.00)	61 (71.76)	75 (70.75)	71.08	
	Yes	1.00	27 (37.50)	41 (33.88)	36 (31.86)	36 (26.67)	25 (23.15)	16 (17.78)	21 (24.71)	30 (28.30)	27.95	
Chest compressions												
	Count (%)	missing data	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	Mean (%)	
	No	0.00	46 (63.89)	80 (66.12)	77 (68.14)	102 (75.56)	84 (77.78)	67 (74.44)	65 (76.47)	81 (76.42)	72.53	
	Yes	1.00	26 (36.11)	41 (33.88)	36 (31.86)	33 (24.44)	24 (22.22)	23 (25.56)	20 (23.53)	25 (23.58)	27.47	
Resuscitation drugs												
	Count (%)	missing data	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	Mean (%)	
	No	0.00	57 (79.17)	101 (83.47)	97 (85.84)	125 (92.59)	104 (96.30)	82 (91.11)	78 (91.76)	100 (94.34)	89.64	
	Yes	1.00	15 (20.83)	20 (16.53)	16 (14.16)	10 (7.41)	4 (3.70)	8 (8.89)	7 (8.24)	6 (5.66)	10.36	
Nitric oxide administered												
	Count (%)	missing data	0 (0.00)	0 (0.00)	1 (0.88)	2 (1.48)	0 (0.00)	2 (2.22)	3 (3.53)	2 (1.89)	Mean (%)	
	No	0.00	69 (95.83)	110 (90.91)	101 (89.38)	123 (91.11)	102 (94.44)	86 (95.56)	80 (94.12)	99 (93.40)	92.77	
	Yes	1.00	3 (4.17)	11 (9.09)	11 (9.73)	10 (7.41)	6 (5.56)	2 (2.22)	2 (2.35)	5 (4.72)	6.02	
Invasive ventilation												
	Count (%)	missing data	0 (0.00)	0 (0.00)	1 (0.88)	2 (1.48)	0 (0.00)	1 (1.11)	2 (2.35)	0 (0.00)	Mean (%)	
	No	0.00	9 (12.50)	18 (14.88)	24 (21.24)	29 (21.48)	19 (17.59)	16 (17.78)	18 (21.18)	34 (32.08)	20.12	
	Yes	1.00	63 (87.50)	103 (85.12)	88 (77.88)	104 (77.04)	89 (82.41)	73 (81.11)	65 (76.47)	72 (67.92)	79.16	
Seizures												
	Count (%)	missing data	0 (0.00)	0 (0.00)	1 (0.88)	2 (1.48)	1 (0.93)	1 (1.11)	3 (3.53)	2 (1.89)	Mean (%)	
	No	0.00	46 (63.89)	84 (69.42)	77 (68.14)	86 (63.70)	74 (68.52)	69 (76.67)	65 (76.47)	81 (76.42)	70.12	
	Yes	1.00	26 (36.11)	37 (30.58)	35 (30.97)	47 (34.81)	33 (30.56)	20 (22.22)	17 (20.00)	23 (21.70)	28.67	

Supplemental table 6. Frequency of the clinical characteristics of babies who have not been admitted for HIE but have been cooled from 2010 to 2017.