

Supplementary Table 6: Neurodevelopmental outcomes associated with Intrapartum-Related Neonatal Encephalopathy

Author (ref)	Grades reported	Outcomes reported	USUAL CARE						INTERVENTION						Denominator		
			Events	N	%	Gr I N	Gr I events	Gr II-III N	Gr II-III events	Events	N	%	Gr I N	Gr I events		Gr II-III N	Gr II-III events
Aker 2021	Grades II and III combined	i) death or CP with GMFCS level 3-5 or BSID-III cognitive and/or motor score <85 or blindness or deafness	12	23	52			23	12	5	24	21			24	5	denominator = children with known outcome
		ii) death	6	23	26			23	6	2	24	8			24	2	denominator = children with known outcome
		iii) GMFCS level 3-5 or BSID-III cognitive and/or motor score <85 or blindness or deafness	6	17	35			17	6	3	22	14			22	3	Denominator = children with known outcome who did not die
		iv) BSID-III cognitive score <70	3	17	18			17	3	0	22	0			22	0	denominator = children evaluated with BSID-III, Griffiths (n=1) or phone (n=1)
		v) BSID-III cognitive score 70-84	3	17	18			17	3	2	22	9			22	2	denominator = children evaluated with BSID-III, Griffiths (n=1) or phone (n=1)
		vi) BSID-III motor score <70	3	17	18			17	3	0	22	0			22	0	denominator = children evaluated with BSID-III, Griffiths (n=1) or phone (n=1)
		vii) BSID-III motor score 70-84	1	17	6			17	1	2	22	9			22	2	denominator = children evaluated with BSID-III, Griffiths (n=1) or phone (n=1)
		viii) CP (any grade) - data also available for divided grades	3	17	18			17	3	1	22	5			22	1	denominator = children evaluated with BSID-III, Griffiths (n=1) or phone (n=1)
Ballot 2020	Excluded from Figure 3 as only examined survivors -> mortality data not available presuming that TH = grade II-III combined, CP data available disaggregated by grades but grades are not disaggregated by TH	i) death or any adverse outcome as below	NA						NA	NA							
		ii) death	NA						NA	NA							
		iii) any developmental delay (BSID-III motor, cognitive or language <70)	NA							NA	NA						denominator = children evaluated with BSID-III
		iv) BSID-III motor <70	8	35	23					5	49	10			49	5	denominator = children evaluated with BSID-III
		v) BSID-III cognitive <70	7	35	20					5	49	10			49	5	denominator = children evaluated with BSID-III
		vi) BSID-III language <70	6	35	17					2	49	4			49	2	denominator = children evaluated with BSID-III
		vii) CP	8	35	23	14	1	21	7	5	49	10		49	5	denominator = children evaluated with BSID-III	
		i) combined death or moderate to severe disability	46	79	58			79	46	27	76	36		76	27	Denominator = children with known outcome	
		ii) death	29	79	37			79	29	22	76	29		76	22	Denominator = children with known outcome	

Catherine 2021	Grades II and III combined	iii) any moderate or severe delay (as below)	17	50	34	50	17	5	54	9	54	5	Denominator = children with known outcome who did not die
		i) combined death or moderate to severe disability	NA	NA	NA			NA	NA	NA	NA	NA	Denominator = children with known outcome
		ii) death	29	79	37	79	29	22	76	29	76	22	Denominator = children with known outcome
		iii) any moderate or severe delay	NA	NA	NA			NA	NA	NA	NA	NA	Denominator = children with known outcome who did not die
		Excluded from Figure 3 due to lack of combined outcome, which was presented in the above report with same patients.											
		iii) DASII mental <70%	14	50	28	50	14	4	54	7	54	4	Denominator = children with known outcome who did not die
		iii) DASII motor <70%	17	50	34	50	17	5	54	9	54	5	Denominator = children with known outcome who did not die
		iv) hearing (abnormal BERA)	1	50	2	50	1	0	54	0	54	0	Denominator = children with known outcome who did not die
		v) vision	1	50	2	50	1	0	54	0	54	0	Denominator = children with known outcome who did not die
Catherine 2020	Grades II and III combined	vi) speech	12	50	24	50	12	2	54	4	54	2	Denominator = children with known outcome who did not die
		i) combined death or moderate to severe disability as below						21	29	72	29	21	Denominator = children with known outcome
		ii) death						11	29	38	29	11	Denominator = children with known outcome
		iii) Severe disability = BSID-III cognitive, language, or motor combined score <- 2 SD, total loss of vision, or cerebral palsy						10	18	56	18	19	Denominator = children with known outcome who did not die
		iv) Neuromotor retardation (=mild disability) = BSID-III cognitive, language, or motor combined score											Denominator = children with known outcome who did not die
Celik * 2016	Grades II and III combined	-1 SD...-2 SD						1	18	6	18	1	Denominator = children with known outcome who did not die
		i) combined death or severe disability as below	0	7	0	7	0						Denominator = children with known outcome
		ii) death	0	7	0	7	0						Denominator = children with known outcome
		iii) Severe disability = BSID-III cognitive, language, or motor combined score <- 2 SD, total loss of vision, or cerebral palsy	0	7	0	7	0						Denominator = children with known outcome who did not die
		iv) Neuromotor retardation (=mild disability) = BSID-III cognitive, language, or motor combined score											Denominator = children with known outcome who did not die
Celik * 2015	Grade I in usual care. Grades II-III were same patients as above	-1 SD...-2 SD	0	7	0	7	0						Denominator = children with known outcome who did not die

		disability	NA	NA			NA	NA						
		ii) death	NA	NA			NA	NA						
	Excluded from Figure 3 as only death or DAMA available	iii) psychomotor delay by DASII-III Grades I to III combined	16	84	19	Control group included 15 % Grade I NE, but outcomes are not detailed by grade	13	72	18			72	13	Denominator = children with known outcome who did not die
Charki 2020		iv) sensorineural disorder	24	84	29		11	72	15			72	11	Denominator = children with known outcome who did not die
		i) combined death or neurodevelopmental disability	18	30	60		6	30	20	na	na	30	6	Denominator = children with known outcome
		ii) death	9	30	30		3	30	10			30	3	Denominator = children with known outcome
		iii) DASII motor or mental development quotient <80%	9	21	43		3	27	11			27	3	Denominator = children with known outcome who did not die
		iv) Blindness = < 20/200 in both eyes	7	21	33		2	27	7			27	2	Denominator = children with known outcome who did not die
	II and III combined (has also segregated grade II and III)	v) Deafness = need of amplification	8	21	38		3	27	11			27	3	Denominator = children with known outcome who did not die
Das 2017		vi) Seizures = abnormal EEG or need of AED	18	21	86		10	27	37			27	10	Denominator = children with known outcome who did not die
		i) death or moderate to severe developmental disability					2	5				5	2	Denominator = children with known outcome at > 12m
		ii) death												
Gucuyener 2012	Grades II and III combined	iii) Cerebral Palsy					2	5				5	2	Denominator = children with known outcome at > 12 m
		i) death or severe disability (unclear definition)	NA			only reports neonatal death	NA							
		ii) death	NA				NA							
Jia 2018	Excluded from Figure 3 because of non-standard outcome definition	iii) severe disability (unclear definition)	35	82	43		16	61	26					Denominator = children with known outcome who did not die neonatally
		i) combined death or moderate to severe disability	NA				NA	NA	NA	NA		NA	NA	Denominator = children with known outcome at 2 yrs
	Excluded from Figure 3 due to lack of data on moderate disability	ii) death	NA				6	19	32			19	6	Denominator = children with known outcome at 2 yrs

Lally 2014	Grade II-III based on Thompson >5 within 6 hrs. Also has data on each Sarnat grade Day 3.	vii) composite motor score <82 or composite cognitive score <85 on BSID-III	3	26	12	38	3						Denominator = children with known outcome who did not die
		Severe disability: GMFCS grade 3 to 5, hearing impairment requiring hearing aids, bilateral cortical visual impairment with no useful vision or BSID- i) death or moderate or severe II Mental Development <70. disability**	35	50	70	50	35	20	50	40	50	20	Denominator = children with known outcome
		**Moderate disability: BSID-II Mental Developmental 70...84 and any one of the following: GMFCS grade 2, hearing impairment with no amplification, or persistent seizure disorder											
		ii) death	8	50	16	50	8	8	50	16	50	8	Denominator = children with known outcome
		iii) any disability	15	42	36	42	15	12	42	29	42	12	Denominator = children with known outcome who did not die
		iv) CP	19	42	45	42	19	10	42	24	42	10	Denominator = children with known outcome who did not die
		v) hearing impairment requiring amplification	2	42	5	42	2	2	42	5	42	2	Denominator = children with known outcome who did not die
		vii) seizures requiring AED	17	42	40	42	17	8	42	19	42	8	Denominator = children with known outcome who did not die
		vii) BSID-II mental <70	15	40	38	40	15	8	40	20	40	8	Denominator = children who completed BSID-II
		iiiv) BSID-II mental 70-84	6	40	15	40	6	5	40	13	40	5	Denominator = children who completed BSID-II
		ix) BSID-II psychomotor <70	15	40	38	40	15	9	40	23	40	9	Denominator = children who completed BSID-II
Malla 2017	Grade II-III combined, separate for outcome i)	x) BSID-II psychomotor 70-84	5	40	13	40	5	4	40	10	40	4	Denominator = children who completed BSID-II
		i) death or any neurodevelopmental disorder	13	18	72	18	13	7	16	44	16	7	Denominator = children with known outcome

Procianoy 2019	Grade II-III combined (reports separate grade II and III)	micro- cephaly removed from original	i) death or moderate to severe neurodevelopmental delay (BSID-III <85 or hearing impairment or visual impairment)									numerator = 16 deaths + 18 abnormal BSID + 3 blind/deaf. Denominator = children with known outcome = 72-13 lost to follow-up		
			ii) death									denominator = children with known outcome		
			iii) any neurodevelopmental delay (as defined above)										who attended could not be evaluated because of blindness or deafness)	
			iv) motor score <85										denominator = those with BSID-III done (3 children who attended could not be evaluated because of blindness or deafness)	
			v) language score <85										denominator = those with BSID-III done (3 children who attended could not be evaluated because of blindness or deafness)	
			vi) cognitive score <85										denominator = those with BSID-III done (3 children who attended could not be evaluated because of blindness or deafness)	
			iv) microcephaly										Denominator = children with known outcome who did not die	
		v) hearing impairment										Denominator = children with known outcome who did not die		
		vi) visual impaired										Denominator = children with known outcome who did not die		
Sun 2012	Grade II-III combined, but 20% Grade I	Excluded from Figure 3 and 4 due to mixing grade I and II-III, also only severe disability reported.	i) death or severe developmental delay BSID-III mental or physical development index <70	18	28	64	na	na	7	23	30	na	na	denominator = children with known outcome
			ii) death	1	28	4			0	23	0			denominator = children with known outcome
			iii) developmental delay BSID-III mental or physical development index <70	17	27	63			7	23	30			Denominator = children with known outcome who did not die
			iv) BSID-III mental development index <70	13	27	48			5	23	22			Denominator = children with known outcome who did not die
			v) BSID-III physical development index <70	12	27	44			5	23	22			Denominator = children with known outcome who did not die
			vi) CP	3	27	11			2	23	9			Denominator = children with known outcome who did not die

(Severe disability: BSID-III cognitive score <70, GMFCS 3...5, profound hearing impairment requiring hearing aids or a cochlear implant, or blindness.)	i) death or moderate to severe disability	94	199	47	na	na	199	94	98	195	50	195	98	denominator = children with known outcome	
	ii) death	63	201	31			201	63	84	198	42	198	84	denominator = children with known outcome	
	iii) Severe disability	28	136	21			136	28	14	112	13	112	14	Denominator = children with known outcome who did not die	
	iv) Moderate disability	3	135	2			135	3	0	111	0	111	0	Denominator = children with known outcome who did not die	
	v) Severe Microcephaly (<5th centile)	23	135	17			135	23	19	110	17	110	19	Denominator = children with known outcome who did not die	
	(Moderate disability BSID-III cognitive 70–84 and one or more of the following: GMFCS 2, a hearing impairment with no amplification, or a persistent seizure disorder)	vi) BSID-III cognitive score 70-84	22	133	17			133	22	25	108	23	108	25	Denominator = children with known outcome who did not die
	vii) BSID-III cognitive score <70	24	133	18			133	24	11	108	10	108	11	Denominator = children with known outcome who did not die	
	viii) BSID-III motor score 70-84	7	133	5			133	7	6	108	6	108	6	Denominator = children with known outcome who did not die	
	ix) BSID-III motor score <70	26	133	20			133	26	11	108	10	108	11	Denominator = children with known outcome who did not die	
	x) BSID-III language score 70-84	47	133	35			133	47	29	108	27	108	29	Denominator = children with known outcome who did not die	
	xi) BSID-III language score <70	27	133	20			133	27	18	108	17	108	18	Denominator = children with known outcome who did not die	
	xii) persistent seizures	9	133	7			133	9	3	111	3	111	3	Denominator = children with known outcome who did not die	
	Microcephaly removed	xiii) CP (GMFCS 2..5)	28	136	21			136	28	12	111	11	111	12	Denominator = children with known outcome who did not die
		xiv) Blindness	10	135	7			135	10	5	111	5	111	5	Denominator = children with known outcome who did not die
Grades II and III combined	xv) Hearing impairment	6	136	4			136	6	3	112	3	112	3	Denominator = children with known outcome who did not die	
Thayil 2021	i) death or severe neurodevelopmental disorder (any BSID-III < 70)								6	19	32	19	6	denominator = children with known outcome	
	ii) death								3	19	16	19	3	denominator = children with known outcome	
	iii) severe motor disorder BSID-III <70								1	13	8			denominator = children >1yr with known outcome who did not die	
	iv) moderate motor disorder BSID 70-84								1	13	8			denominator = children >1yr with known outcome who did not die	
	v) severe language develop								2	13	15			denominator = children >1yr with known outcome who did not die	
	vi) moderate language dev								3	13	23			denominator = children >1yr with known outcome who did not die	
	vii) severe cognitive								0	13	0			denominator = children >1yr with known outcome who did not die	

Valera 2017	Grades II and III combined	viii) moderate cognitive	NA						1	13	8			16	3	denominator = children >1yr with known outcome who did not die	
Zhou 2010	All NE grades. (has data on separate)	i) death or severe disability (GMFCS 3-5 or GCDAS <70)	46	94	49	18	0	76	46	31	100	31	21	0	79	31	denominator = children with known outcome
		ii) death	27	94	29	18	0	76	27	20	100	20	21	0	79	20	denominator = children with known outcome
		iii) severe disability (GMFCS 3-5 or GCDAS <70)	19	67	28	18	0	49	19	11	80	14	21	0	59	11	Denominator = children with known outcome who did not die
		iv) GCDAS <70	13	63	21	15	0	48	13	4	75	5	19	0	56	4	Denominator = children with known outcome who did not die
		v) GCDAS 70-84	17	63	27	15	7	48	10	23	75	31	19	6	56	17	Denominator = children with known outcome who did not die
Zhou 2010		vi) cerebral palsy	19	67	28			NA	NA	10	80	13			NA	NA	Denominator = children with known outcome who did not die. NE grade of cases unknown.
Zhu 2009	Grades II and III combined and separated	i) death or moderate to severe disability (CP GMFCS 3...5, severe hearing loss, blindness, and BSID-II MDI < 70)	35	80	44			80	35	18	73	25			73	18	denominator = children with known outcome
		ii) death	4	80	5			80	4	3	73	4			73	3	denominator = children with known outcome
		iii) CP	14	76	18			76	14	5	70	7			70	5	Denominator = children with known outcome who did not die
Zhu 2009		iv) MDI <70	17	76	22			70	7	70	10			70	7	Denominator = children with known outcome who did not die	
Zou 2019	All NE grades combined	i) death or abnormal neurodevelopmental outcome (BSID-III cognitive or motor score <85)	26	42	62			na	na	16	44	36			na	na	denominator = children with known outcome
		ii) death	6	42	14					6	44	14					denominator = children with known outcome
		iii) abnormal neurodevelopment (BSID-III cognitive or motor score <85)	20	36	56					10	38	26					Denominator = children with known outcome who did not die
Weng 2021	Grades II and III combined	i) death or severe disability (BSID-II MDI < 70, GMFCS 3 to 5, hearing impairment requiring hearing aids, or blindness)	10	25	40			25	10	2	36	6			36	2	denominator = children with known outcome
		ii) death	4	25	16			25	4	0	36	0			36	0	denominator = children with known outcome
		iii) severe disability	6	21	29			21	6	2	36	6			36	2	Denominator = children with known outcome who did not die
		SUM Combined Outcome:	361	712	51					#VALUE!	####	#VALUE!					
		SUM CP:	95	426	22					56	476	12					

BSID = Bayley Scales of Infant Development

CP = Cerebral Palsy
 DAMA = discharge against medical advice
 DASII = Developmental Assessment Scale for Indian Infants
 EEG = electroencephalography
 GCDAS = Griffiths Scales of Developmental Assessment
 MDI = Mental Development Index
 GMFCS = Gross Motor Function Classification Scale
 GMDS = Griffiths Mental Development Scale
 SD = Standard Deviation

Additional notes:

Number of abnormal cases were calculated based on percentages provided in the article and are not the same as reported in Table 5 of the article, which does not consider loss to follow-up.

Usual care group group N=18, 7 died hospital, 11 were followed, 5 were normal = 6 were abnormal. Total N= 7+6+5 = 18, abnormal = 7+6 = 13

Intervention 19, 3 died in hospital and 1 after hospital, 13 Were followed, 9 were normal = 4 were abnormal. Total N = 3+13=16, abnormal = 3+4=7

† Maoulaine

3 children were lost to follow-up and outcome for 5 was not included as they were not 1 year at time of report

‡ Valera