

Table 1. Baseline characteristics of mothers and infants by breastfeeding initiation time

	Timing of initiation of breastfeeding					
	≤1 hours N=56981		2-23 hours N=38043		24 - 96 hours N=4608	
	n	%	n	%	N	%
<i>Infant characteristics</i>						
Male sex	29558	51.9%	19685	51.7%	2455	53.3%
Birthweight (mean [sd])	2928 (479)		2784 (454)		2726 (477)	
Low birth weight (<2500g)	8517	14.9%	8303	21.8%	1240	26.9%
Multiple births	1394	2.5%	922	2.4%	153	3.3%
Colostrum given	55026	96.6%	33346	87.7%	2164	47.0%
Vitamin A supplementation	14720	49.8%	9862	50.1%	1252	51.0%
<i>Maternal/delivery characteristics</i>						
Age						
Mothers age in years (median [iqr])	25 (21,29)		24 (21,28)		24 (21,27)	
Mothers age <20 years	6710	11.8%	3719	9.8%	338	7.3%
Education						
None or less than primary	15577	27.3%	16025	42.1%	1998	43.4%
Primary completed and secondary incomplete	30093	52.8%	12583	33.1%	1347	29.2%
Secondary completed and higher	11311	19.9%	9435	24.8%	1263	27.4%
Primiparous	13160	23.1%	11293	29.7%	1617	35.1%
Skilled birth attendant at delivery	44369	77.9%	24095	63.3%	3262	70.8%
Caesarean delivery	2120	3.7%	2664	7.0%	1461	31.7%
Family characteristics						
Wealth quintile						
1 (most poor)	10001	17.6%	8255	21.7%	1239	26.9%
2	12558	22.0%	7666	20.2%	964	20.9%
3	8826	15.5%	6934	18.2%	817	17.7%
4	14828	26.0%	7769	20.4%	758	16.5%
5 (least poor)	10768	18.9%	7419	19.5%	830	18.0%

Table 2. Neonatal and infant mortality risk by hour of breastfeeding initiation

	Deaths (per 1000)	Newborns	Univariable		Multivariable Model 1 ^a		Multivariable Model 2 ^b	
			RR (95% CI)	p value	RR (95% CI)	p value	RR (95% CI)	p value
I.A Neonatal mortality (enrolment to 28 days) ^c		N=99632						
Initiation ≤1 hour	623 (10.9)	56981	1.00	.	1.00	.		
Initiation 2-23 hours	559 (14.7)	38043	1.53(1.34,1.74)	<0.001	1.41(1.24,1.62)	<0.001		
Initiation 24-96 hours	79 (17.1)	4608	1.82(1.42,2.33)	<0.001	1.79(1.39,2.30)	<0.001		
I.B Neonatal mortality (5 to 28 days) ^d		N=98480						
Initiation ≤1 hour	301 (5.4)	56135	1.00	.	1.00	.	1.00	.
Initiation 2-23 hours	313 (8.3)	37768	1.43(1.19,1.7)	<0.001	1.32(1.10,1.58)	0.003	1.33(1.10,1.60)	0.003
Initiation 24-96 hours	53 (11.6)	4577	1.97(1.45,2.69)	<0.001	1.90(1.38,2.62)	<0.001	1.80(1.29,2.52)	0.001
II. Infant mortality from 1 to <3 months (29 to 90 days) ^e		N=97707						
Initiation ≤1 hour	332 (6.0)	55772	1.00	.	1.00	.	1.00	.
Initiation 2-23 hours	359 (9.6)	37416	1.40(1.18,1.66)	<0.001	1.34(1.13,1.59)	0.001	1.28(1.08,1.52)	0.005
Initiation 24-96 hours	49 (10.8)	4519	1.46(1.07,2.00)	0.018	1.48(1.07,2.06)	0.017	1.25(0.90,1.72)	0.180
III. Infant mortality from 3 to <6 months (91 to 180 days) ^f		N=96606						
Initiation ≤1 hour	286 (5.2)	55145	1.00	.	1.00	.	1.00	.
Initiation 2-23 hours	289 (7.8)	36998	1.49(1.23,1.79)	<0.001	1.42(1.18,1.72)	<0.001	1.39(1.15,1.68)	0.001
Initiation 24-96 hours	33 (7.4)	4463	1.36(0.93,1.99)	0.108	1.35(0.93,1.97)	0.113	1.21(0.83,1.76)	0.317

^a Controlling for study site, sex, birthweight, singleton, maternal age, maternal education, primiparity, skilled birth attendant, caesarean section, wealth quintile

^b Controlling for study site, sex, birthweight, singleton, maternal age, maternal education, primiparity, skilled birth attendant, caesarean section, wealth quintile, breastfeeding pattern

^c Among all live births who initiated breastfeeding

^d Among all live births who initiated breastfeeding, who survived until 5 days

^e Among all live births who initiated breastfeeding, who survived until 28 days

^f Among all live births who initiated breastfeeding, who survived until 90 days

Table 3. Neonatal and infant mortality risk by hour of breastfeeding initiation, stratified by exclusive breastfeeding status

	Deaths (per 1000)	Newborns	Univariable RR (95% CI)	p value	Multivariable ^a RR (95% CI)	p value
I. Neonatal mortality (5-28 days) by exclusively breastfed status at 4 days ^b (N=98203) (p value for interaction with exclusivity = 0.690)						
a. Among exclusively breastfed infants at 4 days		N=64097				
Initiation \leq 1 hour	244 (5.1)	47442	1.00	.	1.00	.
Initiation 2-23 hours	135 (8.4)	16128	1.53(1.22,1.91)	<0.001	1.41(1.12,1.77)	0.003
Initiation 24-96 hours	5 (9.5)	527	1.78(0.74,4.30)	0.201	1.51(0.63,3.65)	0.357
b. Among not exclusively breastfed infants at 4 days		N=34106				
Initiation \leq 1 hour	56 (6.5)	8678	1.00	.	1.00	.
Initiation 2-23 hours	177 (8.2)	21469	1.29(0.95,1.75)	0.106	1.22(0.9,1.66)	0.197
Initiation 24-96 hours	45 (11.4)	3959	1.79(1.20,2.67)	0.004	1.80(1.19,2.73)	0.006
II. Infant mortality (1-<3 months) by exclusively breastfed status at 1 month ^c (N=87576) (p value for interaction with exclusivity = 0.921)						
a. Among exclusively breastfed infants at 1 month		N=52655				
Initiation \leq 1 hour	127 (3.7)	34174	1.00	.	1.00	.
Initiation 2-23 hours	98 (5.8)	16998	1.37(1.02,1.85)	0.039	1.39(1.02,1.89)	0.036
Initiation 24-96 hours	10 (6.7)	1483	1.36(0.7,2.64)	0.371	1.65(0.82,3.31)	0.157
b. Among not exclusively breastfed infants at 1 month		N=34921				
Initiation \leq 1 hour	92 (6.8)	13577	1.00	.	1.00	.
Initiation 2-23 hours	189 (10.2)	18513	1.23(0.95,1.59)	0.116	1.17(0.9,1.52)	0.237
Initiation 24-96 hours	27 (9.5)	2831	1.10(0.71,1.70)	0.664	1.09(0.7,1.69)	0.710
III. Infant mortality (3-<6 months) by exclusively breastfed status at 3 months ^d (N=86692) (p value for interaction with exclusivity = 0.925)						
a. Among exclusively breastfed infants at 3 months		N=35579				
Initiation \leq 1 hour	75 (3.2)	23525	1.00	.	1.00	.
Initiation 2-23 hours	48 (4.3)	11095	1.40(0.93,2.09)	0.106	1.31(0.89,1.93)	0.177
Initiation 24-96 hours	4 (4.2)	959	1.32(0.46,3.74)	0.604	1.25(0.44,3.58)	0.675
b. Among not exclusively breastfed infants at 3 months		N=51113				
Initiation \leq 1 hour	128 (5.3)	24019	1.00	.	1.00	.
Initiation 2-23 hours	184 (7.7)	23832	1.25(0.98,1.59)	0.078	1.19(0.94,1.5)	0.154
Initiation 24-96 hours	27 (8.3)	3262	1.29(0.84,1.98)	0.246	1.17(0.76,1.8)	0.465

^a Controlling for site, sex, birthweight, singleton, maternal age, maternal education, primiparity, skilled birth attendant, caesarean section, wealth quintile

^b Among all live births who initiated breastfeeding, who survived until 5 days, whose breastfeeding pattern at 4 days is known

^c Among all live births who initiated breastfeeding, who survived until 28 days, whose breastfeeding pattern at 1 month is known

^d Among all live births who initiated breastfeeding, who survived until 90 days, whose breastfeeding pattern at 3 months is known

Table 4. Mortality risk in by breastfeeding pattern at 4 days, 1 month and 3 months

	Deaths per 1000)	Newborns	Univariable RR (95% CI)	p value	Multivariable ^a RR (95% CI)	p value
I. Neonatal mortality (5-28 days) by patterns of breastfeeding at 4 days ^b (N=98203)						
Exclusively breastfed at 4 days	384 (6.0)	64097	1.00	.	1.00	.
Predominantly breastfed at 4 days	180 (7.9)	22785	1.10(0.88,1.39)	0.395	0.99(0.78,1.25)	0.927
Partially breastfed at 4 days	97 (8.6)	11316	1.19(0.91,1.56)	0.208	1.34(1.01,1.78)	0.042
Not breastfed at 4 days	1 (200.0)	5	- ^e	- ^e	- ^e	- ^e
II. Mortality from 1 to <3 months by patterns of breastfeeding at 1 month ^c (N=87576)						
Exclusively breastfed at 1 month	235 (4.5)	52655	1.00	.	1.00	.
Predominantly breastfed at 1 month	143 (5.5)	25785	0.87(0.7,1.08)	0.216	0.84(0.68,1.05)	0.132
Partially breastfed at 1 month	104 (12.7)	8173	2.01(1.58,2.55)	<0.001	1.83(1.45,2.32)	<0.001
Not breastfed at 1 month	61 (63.3)	963	12.05(9.13,15.91)	<0.001	10.88(8.27,14.31)	<0.001
III. Mortality from 3 to <6 months by patterns of breastfeeding at 3 months ^d (N=86692)						
Exclusively breastfed at 3 months	127 (3.6)	35579	1.00	.	1.00	.
Predominantly breastfed at 3 months	104 (3.9)	26652	0.93(0.71,1.22)	0.609	0.93(0.71,1.23)	0.623
Partially breastfed at 3 months	154 (6.7)	22850	1.70(1.33,2.18)	0.000	1.62(1.26,2.07)	<0.001
Not breastfed at 3 months	81 (50.3)	1611	12.19(9.08,16.36)	<0.001	11.98(8.98,16)	<0.001

^a Controlling for site, sex, birthweight, singleton, maternal age, maternal education, primiparity, skilled birth attendant, caesarean section, wealth quintile

^b Among all live births who initiated breastfeeding, who survived until 5 days, whose breastfeeding pattern at 4 days is known

^c Among all live births who initiated breastfeeding, who survived until 28 days, whose breastfeeding pattern at 1 month is known

^d Among all live births who initiated breastfeeding, who survived until 90 days, whose breastfeeding pattern at 3 months is known

^e Numbers too small to have a reliable estimate

Webappendix A. Probability of non-exclusive breastfeeding or no breastfeeding at 1 month by the hour of breastfeeding initiation

	Events (%)	Newborns	Univariable RR (95% CI)	p value	Multivariable ^b RR (95% CI)	p value
I. Non-exclusive breastfeeding at 1 month						
Initiation ≤1 hour	13577 (28.4%)	47751		.		.
Initiation 2-23 hours	18513 (52.1%)	35511	1.15(1.13,1.17)	<0.001	1.15(1.13,1.17)	<0.001
Initiation 24-96 hours	2831 (65.6%)	4314	1.25(1.22,1.28)	<0.001	1.27(1.24,1.31)	<0.001
II. Non breastfed at 1 month						
Initiation ≤1 hour	508 (1.1%)	47751		.		.
Initiation 2-23 hours	361 (1.0%)	35511	1.25(1.07,1.47)	0.006	1.26(1.07,1.48)	0.005
Initiation 24-96 hours	94 (2.2%)	4314	2.46(1.93,3.13)	<0.001	2.48(1.92,3.21)	<0.001

^a Among infants who initiated breastfeeding and who were alive at 1 month

^b Controlling for site, sex, birthweight, singleton, maternal age, maternal education, primiparity, skilled birth attendant, caesarean section, wealth quintile

Webappendix B. Probability of non-exclusive breastfeeding or no breastfeeding at 3 months by the hour of breastfeeding initiation

	Events (%)	Newborns	Univariable RR (95% CI)	p value	Multivariable ^b RR (95% CI)	p value
I. Non exclusive breastfeeding at 3 months						
Initiation \leq 1 hour	24019 (50.5%)	47544		.		.
Initiation 2-23 hours	23832 (68.2%)	34927	1.06(1.04,1.07)	<0.001	1.05(1.04,1.06)	<0.001
Initiation 24-96 hours	3262 (77.3%)	4221	1.07(1.05,1.08)	<0.001	1.06(1.04,1.08)	<0.001
II. Not breastfeeding at 3 months						
Initiation \leq 1 hour	675 (1.4%)	47544		.		.
Initiation 2-23 hours	755 (2.2%)	34927	1.21(1.08,1.36)	0.001	1.20(1.07,1.35)	0.001
Initiation 24-96 hours	181 (4.3%)	4221	2.01(1.69,2.39)	<0.001	1.88(1.56,2.26)	<0.001

^a Among infants who initiated breastfeeding and who were alive at 3 months

^b Controlling for site, sex, birthweight, singleton, maternal age, maternal education, primiparity, skilled birth attendant, caesarean section, wealth quintile

Footnote to Web appendices A and B

Is breastfeeding pattern a confounder or a mediator of the association between initiation of breastfeeding and mortality?

- The definition of a confounder is that it is a predictor of the exposure, is associated with the outcome, and is not on the causal pathway between the exposure and outcome. The definition of a mediator is that it is associated with the exposure and the outcome and is on the causal pathway.
- Breastfeeding pattern is not confounder of the association between initiation of breastfeeding and mortality for two reasons First, breastfeeding pattern occurs after breastfeeding initiation, and thus it cannot predict breastfeeding initiation. Second, we hypothesize that breastfeeding pattern is a potential mediator (i.e. on the causal pathway between breastfeeding initiation and mortality), which means that it cannot be a confounder, by definition.
- Breastfeeding pattern is a mediator of some, but not all, of the association between initiation of breastfeeding and mortality. There are multiple causal pathways between initiation and mortality. Breastfeeding pattern is on just one those pathways; early initiation of breastfeeding increases exclusive breastfeeding (shown in web appendix A,B,C) and exclusive breastfeeding reduces mortality (shown in Table 4)
- However the fact that there was an additional strong independent effect of early initiation after adjusting for breastfeeding pattern means that an important part of the effect of early initiation on mortality is mediated through other pathways.
- As early initiation also results in the provision of colostrum and provides the protective effect of thermal care, there is biological plausibility for these other pathways.
- The independent effect of early initiation on mortality is also seen clearly when the data are stratified by breastfeeding pattern (Table 3) i.e. There is a strong effect of early initiation on mortality in babies who are all exclusively breastfed.

Webappendix C Neonatal and infant mortality risk by hour of breastfeeding initiation (Control Group Only)

			Univariable		Multivariable Model 1 ^a		Multivariable Model 2 ^b	
	Deaths (per 1000)	Newborns	RR (95% CI)	p value	RR (95% CI)	p value	RR (95% CI)	p value
I.A Neonatal mortality (enrolment to 28 days) ^c		N=49,816						
Initiation ≤1 hour	296 (10.4)	28586		.	.			
Initiation 2-23 hours	291 (15.3)	18973	1.69(1.41,2.04)	<0.001	1.55(1.28,1.86)	<0.001		
Initiation 24-96 hours	37 (16.4)	2257	1.84(1.28,2.64)	<0.001	1.7(1.18,2.45)	0.005		
I.B Neonatal mortality (5 to 28 days) ^d		N=49,258						
Initiation ≤1 hour	136 (4.8)	28182		.	.			
Initiation 2-23 hours	168 (8.9)	18833	1.65(1.28,2.13)	<0.001	1.53(1.18,1.97)	0.001		
Initiation 24-96 hours	26 (11.6)	2243	2.11(1.35,3.29)	<0.001	1.98(1.25,3.12)	0.003		
II. Infant mortality from 1 to <3 months (29 to 90 days) ^e		N=48,880						
Initiation ≤1 hour	161 (5.7)	28016		.	.			
Initiation 2-23 hours	186 (10.0)	18649	1.5(1.18,1.91)	<0.001	1.44(1.13,1.83)	0.003	1.4(1.1,1.79)	0.007
Initiation 24-96 hours	24 (10.8)	2215	1.5(0.96,2.36)	0.077	1.45(0.91,2.31)	0.114	1.23(0.76,1.98)	0.397
III. Infant mortality from 3 to <6 months (91 to 180 days) ^f		N=48,329						
Initiation ≤1 hour	138 (5.0)	27712		.	.			
Initiation 2-23 hours	147 (8.0)	18430	1.38(1.06,1.79)	0.018	1.31(1.01,1.71)	0.044	1.28(0.98,1.67)	0.073
Initiation 24-96 hours	19 (8.7)	2187	1.39(0.84,2.3)	0.198	1.32(0.79,2.22)	0.293	1.13(0.68,1.87)	0.648

^a Controlling for study site, sex, birthweight, singleton, maternal age, maternal education, primiparity, skilled birth attendant, caesarean section, wealth quintile

^b Controlling for study site, sex, birthweight, singleton, maternal age, maternal education, primiparity, skilled birth attendant, caesarean section, wealth quintile, breastfeeding pattern

^c Among all live births who initiated breastfeeding

^d Among all live births who initiated breastfeeding, who survived until 5 days

^e Among all live births who initiated breastfeeding, who survived until 28 days

^f Among all live births who initiated breastfeeding, who survived until 90 days

Webappendix D. Neonatal and infant mortality risk by hour of breastfeeding initiation in each site

GHANA Neonatal and infant mortality risk by hour of breastfeeding initiation

	Deaths (per 1000)	Newborns	Univariable RR (95% CI)	p value	Multivariable Model 1 ^a RR (95% CI)	p value
I.A Neonatal mortality (enrolment to 28 days) ^c						
Initiation ≤1 hour	125 (8.8)	14186
Initiation 2-23 hours	135 (16.0)	8455	1.81(1.42,2.31)	0.000	1.6(1.24,2.08)	0.000
Initiation 24-96 hours	14 (45.6)	307	5.18(3.01,8.89)	0.000	3.71(2.12,6.48)	0.000
I.B Neonatal mortality (5 to 28 days) ^d						
Initiation ≤1 hour	73 (5.2)	14134
Initiation 2-23 hours	73 (8.7)	8393	1.68(1.22,2.33)	0.002	1.41(1.01,1.98)	0.044
Initiation 24-96 hours	9 (29.8)	302	5.77(2.91,11.42)	0.000	3.68(1.82,7.46)	0.000
II. Infant mortality from 1 to <3 months (29 to 90 days) ^e						
Initiation ≤1 hour	48 (3.4)	14031
Initiation 2-23 hours	70 (8.4)	8293	2.47(1.71,3.56)	0.000	2.22(1.51,3.26)	0.000
Initiation 24-96 hours	3 (10.3)	292	3(0.94,9.59)	0.063	2.37(0.73,7.73)	0.151
III. Infant mortality from 3 to <6 months (91 to 180 days) ^f						
Initiation ≤1 hour	56 (4.0)	13931
Initiation 2-23 hours	58 (7.1)	8196	1.76(1.22,2.54)	0.002	1.54(1.05,2.27)	0.027
Initiation 24-96 hours	3 (10.4)	288	2.59(0.82,8.23)	0.106	1.84(0.57,5.93)	0.311

^a Controlling for study site, sex, birthweight, singleton, maternal age, maternal education, primiparity, skilled birth attendant, caesarean section, wealth quintile

INDIA Neonatal and infant mortality risk by hour of breastfeeding initiation

	Deaths (per 1000)	Newborns	Univariable RR (95% CI)	p value	Multivariable Model 1 ^a RR (95% CI)	p value
I.A Neonatal mortality (enrolment to 28 days) ^c						
Initiation \leq 1 hour	163 (11.2)	14543
Initiation 2-23 hours	345 (13.2)	26192	1.18(0.98,1.41)	0.087	1.15(0.96,1.39)	0.128
Initiation 24-96 hours	61 (15.0)	4058	1.34(1,1.8)	0.049	1.42(1.05,1.92)	0.023
I.B Neonatal mortality (5 to 28 days) ^d						
Initiation \leq 1 hour	99 (6.8)	14479
Initiation 2-23 hours	213 (8.2)	26060	1.2(0.94,1.52)	0.141	1.18(0.93,1.49)	0.176
Initiation 24-96 hours	42 (10.4)	4039	1.52(1.06,2.18)	0.022	1.61(1.11,2.35)	0.013
II. Infant mortality from 1 to <3 months (29 to 90 days) ^e						
Initiation \leq 1 hour	123 (8.6)	14377
Initiation 2-23 hours	268 (10.4)	25840	1.21(0.98,1.5)	0.076	1.2(0.97,1.48)	0.096
Initiation 24-96 hours	44 (11.0)	3995	1.29(0.91,1.81)	0.148	1.35(0.94,1.94)	0.101
III. Infant mortality from 3 to <6 months (91 to 180 days) ^f						
Initiation \leq 1 hour	83 (5.8)	14245
Initiation 2-23 hours	206 (8.1)	25563	1.38(1.07,1.78)	0.012	1.34(1.04,1.73)	0.022
Initiation 24-96 hours	28 (7.1)	3950	1.22(0.79,1.86)	0.368	1.15(0.73,1.8)	0.557

^a Controlling for study site, sex, birthweight, singleton, maternal age, maternal education, primiparity, skilled birth attendant, caesarean section, wealth quintile

TANZANIA. Neonatal and infant mortality risk by hour of breastfeeding initiation

	Deaths (per 1000)	Newborns	Univariable RR (95% CI)	p value	Multivariable Model 1 ^a RR (95% CI)	p value
I.A Neonatal mortality (enrolment to 28 days) ^c						
Initiation \leq 1 hour	335 (11.9)	28252
Initiation 2-23 hours	79 (23.3)	3396	1.96(1.54,2.5)	0.000	1.85(1.46,2.35)	0.000
Initiation 24-96 hours	4 (16.5)	243	1.39(0.52,3.69)	0.511	1.31(0.49,3.53)	0.587
I.B Neonatal mortality (5 to 28 days) ^d						
Initiation \leq 1 hour	129 (4.7)	27522
Initiation 2-23 hours	27 (8.1)	3315	1.74(1.15,2.63)	0.009	1.61(1.06,2.44)	0.027
Initiation 24-96 hours	2 (8.5)	236	1.81(0.45,7.26)	0.404	1.9(0.47,7.62)	0.366
II. Infant mortality from 1 to <3 months (29 to 90 days) ^e						
Initiation \leq 1 hour	161 (5.9)	27364
Initiation 2-23 hours	21 (6.4)	3283	1.09(0.69,1.71)	0.718	1.05(0.66,1.66)	0.836
Initiation 24-96 hours	2 (8.6)	232	1.47(0.37,5.87)	0.590	1.39(0.34,5.56)	0.646
III. Infant mortality from 3 to <6 months (91 to 180 days) ^f						
Initiation \leq 1 hour	147 (5.5)	26969
Initiation 2-23 hours	25 (7.7)	3239	1.42(0.93,2.16)	0.107	1.41(0.92,2.16)	0.118
Initiation 24-96 hours	2 (8.9)	225	1.63(0.41,6.54)	0.490	1.66(0.41,6.66)	0.475

^a Controlling for study site, sex, birthweight, singleton, maternal age, maternal education, primiparity, skilled birth attendant, caesarean section, wealth quintile
