



Lives Saved Tool Technical Note

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Breastfeeding effect sizes on mortality in LiST

This documentation is in response to the challenge of separating out the independent effects of early initiation of breastfeeding (EIBF, defined as beginning breastfeeding <1 hour of birth) and exclusive breastfeeding (EBF, during the first 6 months of life) on neonatal and post-neonatal child mortality, which has not been adequately addressed in most published studies to date, raising the concern of confounding or double-counting of effects.

Neonatal (<1 mo) period

The University of Pelotas group led by Cesar Victora has done a reanalysis of the data from their 2000 Lancet publication¹, using data from three countries (Brazil, Pakistan, and Philippines). Unfortunately they only have data on the mortality risk of not breastfeeding. Excluding deaths in the first week to reduce reverse causality (i.e., those children that are too sick to breastfeed), the risk of death from all infectious causes in neonates is 5.4 (2.3, 13.0) relative to EBF.

A reanalysis of the NEOVITA study² data (from Tanzania, Ghana and India) also has results for neonates (excluding deaths in the first 4 days and for all causes, no cause of death available). In this study, the risk for initiation 2+ hours after birth (data were collected for <2h, so <1h was not available) in neonates is 1.35 (1.13, 1.62), controlling for breastfeeding pattern, but they only enrolled breastfeeding infants. According to this study, there is no significant risk of neonatal mortality for partial or predominant breastfeeding compared to EBF, controlling for time of initiation.

Effect sizes in LiST:

- EIBF: Risk of late initiation is 1.35 (relative to EIBF) for infectious causes of mortality in the neonatal period (diarrhea, sepsis, and pneumonia) – among breastfed infants only.
- EBF: Risk of not breastfeeding is 5.4 (relative to EBF) for infectious causes of mortality in the neonatal period (diarrhea, sepsis, and pneumonia). There is no elevated risk for predominant or partial breastfeeding.

¹ WHO Collaborative Study Team on the Role of Breastfeeding on the Prevention of Infant Mortality. Effect of breastfeeding on infant and child mortality due to infectious diseases in less developed countries: a pooled analysis. *Lancet* 2000; <https://www.ncbi.nlm.nih.gov/pubmed/10841125>.

² NEOVITA Study Group. Timing of initiation, patterns of breastfeeding, and infant survival: prospective analysis of pooled data from three randomised trials. *Lancet Global Health* 2016; <https://www.ncbi.nlm.nih.gov/pubmed/27013313>.

These effect sizes may be somewhat conservative, but eliminate the issue of double-counting of risks. This is operationalized in LiST as:

	Exclusive	Predominant	Partial	No breastfeeding
Early initiation	1 (ref)	1	1	5.4 (2.3, 13.0)
Late initiation	1.35 (1.13, 1.62)	1.35 (1.13, 1.62)	1.35 (1.13, 1.62)	5.4 (2.3, 13.0)*

* For simplicity's sake, no children are assumed to fall into this category (i.e. if they are not breastfeeding, they never initiated at all).

Post-neonatal (1-5 mo) period

In the Pelotas reanalysis, the mortality risk of not breastfeeding is 3.2 (2.5, 4.3) relative to EBF. As mentioned above, this analysis only looks at the risk of not breastfeeding (not predominant or partial relative to EBF).

In the NEOVITA reanalysis, the risk of predominant is not significant (0.99, or 0.96 adjusting for time of initiation), partial is 1.85 (1.56, 2.2), and not breastfeeding is 12.14 (9.97, 14.8) for all-cause deaths, controlling for time of initiation.

Based on Lamberti 2011³ and Lamberti 2013⁴, the following risks apply for the period of 0-5 mo:

	Exclusive	Predominant	Partial	No breastfeeding
Diarrhea mortality	1 (ref)	2.28 (0.85, 6.13)	4.62 (1.81, 11.76)	10.52 (2.79, 39.6)
Pneumonia mortality	1 (ref)	1.66 (0.53, 5.23)	2.50 (1.03, 6.04)	14.97 (0.67, 332.74)
All-cause mortality	1 (ref)	1.48 (1.14, 1.92)	2.84 (1.63, 4.97)	14.40 (6.13, 33.86)

Effect sizes in LiST:

We recommend keeping the cause-specific mortality risks for diarrhea and pneumonia from Lamberti 2011 and 2013, as is currently in LiST. (Although they are risks for 0-5 mo, we apply them to 1-5 mo in LiST, due to the separate neonatal risks detailed above.)

In addition, we recommend applying Lamberti's all-cause mortality risks to other infectious disease causes of mortality, specifically meningitis, measles, and pertussis. (A risk relationship will not be applied to mortality due to malaria as there is currently not evidence to support this linkage.)

Note: The NEOVITA all-cause mortality risk is not statistically significant for predominant breastfeeding. We have used the Lamberti analysis in LiST, including the non-significant risk for predominant for diarrhea and pneumonia mortality, because the all-cause for predominant was significant. While the NEOVITA analysis does not confirm this for predominant, it does for partial and not. We believe that we should continue to use risks for all three breastfeeding categories.

³ Lamberti LM, Fischer Walker CL, Noiman A, et al. Breastfeeding and the risk for diarrhea morbidity and mortality. BMC Public Health 2011; <https://www.ncbi.nlm.nih.gov/pubmed/21501432>.

⁴ Lamberti LM, Zakarija-Grković I, Fischer Walker CL, et al. Breastfeeding for reducing the risk of pneumonia morbidity and mortality in children under two: a systematic literature review and meta-analysis. BMC Public Health 2013; <https://www.ncbi.nlm.nih.gov/pubmed/24564728>.

Post-neonatal (6-23 mo) period

Lamberti 2011 and 2013 provide risks for not breastfeeding in the 6-11 and 12-23 mo periods.

	6-11 mo		12-23 mo	
	Breastfeeding	Not breastfeeding	Breastfeeding	Not breastfeeding
Diarrhea mortality	1 (ref)	1.47 (0.67, 3.25)	1 (ref)	2.57 (1.10, 6.01)
Pneumonia mortality	1 (ref)	1.92 (0.79, 4.68)	1 (ref)	1.92 (0.79, 4.68)
All-cause mortality	1 (ref)	3.69 (1.49, 9.17)	1 (ref)	3.69 (1.49, 9.17)

Effect sizes in LiST:

We recommend these values be included/updated in LiST, including applying the all-cause mortality risks to meningitis, measles, and pertussis mortality.