Breastfeeding 1

Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect

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The importance of breastfeeding in low-income and middle-income countries is well recognised, but less consensus exists about its importance in high-income countries. In low-income and middle-income countries, only 37% of children younger than 6 months of age are exclusively breastfed. With few exceptions, breastfeeding duration is shorter in high-income countries than in those that are resource-poor. Our meta-analyses indicate protection against child infections and malocclusion, increases in intelligence, and probable reductions in overweight and diabetes. We did not find associations with allergic disorders such as asthma or with blood pressure or cholesterol, and we noted an increase in tooth decay with longer periods of breastfeeding. For nursing women, breastfeeding gave protection against breast cancer and it improved birth spacing, and it might also protect against ovarian cancer and type 2 diabetes. The scaling up of breastfeeding to a near universal level could prevent 823 000 annual deaths in children younger than 5 years and 20 000 annual deaths from breast cancer. Recent epidemiological and biological findings from during the past decade expand on the known benefits of breastfeeding for women and children, whether they are rich or poor.

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This is the first in a Series of two papers about breastfeeding

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See Online for appendix

Introduction

"In all mammalian species the reproductive cycle comprises both pregnancy and breast-feeding: in the absence of latter, none of these species, man included, could have survived", wrote paediatrician Bo Vahlquist in 1981.[1] 3 years earlier, Derek and Patrice Jelliffe in their classic book *Breast Milk in the Modern World*[2] stated that "breast-feeding is a matter of concern in both industrialised and developing countries because it has such a wide range of often underappreciated consequences".[3] The Jelliffes anticipated that breastfeeding would be relevant to "present-day interest in the consequences of infant nutrition on subsequent adult health".[3] These statements were challenged by the American Academy of Pediatrics, which in its 1984 report on the scientific evidence for breastfeeding stated that "if there are benefits associated with breast-feeding in populations with good sanitation, nutrition and medical care, the benefits are apparently modest".[4]

In the past three decades, the evidence behind breastfeeding recommendations has evolved markedly (appendix p 3). Results from epidemiological studies and growing knowledge of the roles of epigenetics, stem cells, and the developmental origins of health and disease lend strong support to the ideas proposed by Vahlquist and the Jelliffes. Never before in the history of science has so much been known about the complex importance of breastfeeding for both mothers and children.

Here, in the first of two Series papers, we describe present patterns and past trends in breastfeeding throughout the world, review the short-term and long-term health consequences of breastfeeding for the child and mother, estimate potential lives saved by scaling up breastfeeding, and summarise insights into how breastfeeding might permanently shape individuals' life course. The second paper in the Series[5] covers the determinants of breastfeeding and the effectiveness of promotion interventions. It discusses the role of breastfeeding in HIV transmission and how knowledge about this issue has evolved in the past two decades, and examines the lucrative market of breastmilk substitutes, the environmental role of breastfeeding, and its economic implications. In the context of the post-2015 development agenda, the two articles document how essential breastfeeding is for building a better world for future generations in all countries, rich and poor alike.

Search strategy and selection criteria

We obtained information about the associations between breastfeeding and outcomes in children or mothers from 28 systematic reviews and meta-analyses, of which 22 were commissioned for this review. See appendix pp 23–30 for the databases searched and search terms used. We reviewed the following disorders for young children: child mortality; diarrhoea incidence and admission to hospital; lower respiratory tract infections incidence, prevalence, and admission to hospital; acute otitis media; eczema; food allergies; allergic rhinitis; asthma or wheezing; infant growth (length, weight, body-mass index); dental caries; and malocclusion. For older children, adolescents, and adults, we did systematic reviews for systolic and diastolic blood pressure; overweight and obesity; total cholesterol; type 2 diabetes; and intelligence. For mothers, we did systematic reviews covering the following outcomes: lactational amenorrhoea; breast and ovarian cancer; type 2 diabetes; post-partum weight change; and osteoporosis.

For the **Demographic and Health Surveys** see http://www.measuredhs.com/aboutsurveys/dhs/start.cfm

For the **Multiple Indicator Cluster Surveys** see http://mics.unicef.org/surveys

Key messages

- Children who are breastfed for longer periods have lower infectious morbidity and mortality, fewer dental malocclusions, and higher intelligence than do those who are breastfed for shorter periods, or not breastfed. This inequality persists until later in life. Growing evidence also suggests that breastfeeding might protect against overweight and diabetes later in life.
- Breastfeeding benefits mothers. It can prevent breast cancer, improve birth spacing, and might reduce a woman's risk of diabetes and ovarian cancer.
- High-income countries have shorter breastfeeding duration than do low-income and middle-income countries. However, even in low-income and middle-income countries, only 37% of infants younger than 6 months are exclusively breastfed.
- The scaling up of breastfeeding can prevent an estimated 823 000 child deaths and 20 000 breast cancer deaths every year.
- Findings from studies done with modern biological techniques suggest novel mechanisms that characterise breastmilk as a personalised medicine for infants.
- Breastfeeding promotion is important in both rich and poor countries alike, and might contribute to achievement of the forthcoming Sustainable Development Goals.

Breastfeeding indicators and data sources for this review

WHO has defined the following indicators for the study of feeding practices of infants and young children:[6] early initiation of breastfeeding (proportion of children born in the past 24 months who were put to the breast within an hour of birth); exclusive breastfeeding under 6 months (proportion of infants aged 0–5 months who are fed exclusively with breastmilk. This indicator is based on the diets of infants younger than 6 months during the 24 h before the survey [to avoid recall bias], not on the proportion who are exclusively breastfed for the full 6-month period); continued breastfeeding at 1 year (proportion of children aged 12–15 months who are fed breastmilk); and continued breastfeeding at 2 years (proportion of children aged 20–23 months who are fed breastmilk).

Because few high-income countries report on the aforementioned indicators, we calculated additional indicators to allow global comparisons: ever breastfed (infants reported to have been breastfed, even if for a short period); breastfed at 6 months (in high-income countries, the proportion of infants who were breastfed from birth to 6 months or older; in low-income and middle-income countries [LMICs] with standardised surveys, the proportion of infants aged 4–7 months [median age of 6 months] who are breastfed); and breastfed at 12 months (in high-income countries, the proportion of children breastfed for 12 months or longer; in LMICs, the proportion of children aged 10–13 months [median age of 12 months] who are breastfed).

For this review, we used the last three, additional indicators for comparisons between high-income countries and LMICs only. Otherwise, we reported on the standard international indicators (appendix p 4).

For LMICs, we reanalysed national surveys done since 1993, including Demographic and Health Surveys, Multiple Indicator Cluster Surveys, and others (appendix pp 5–12). Nearly all surveys had response rates higher than 90% and used standardised questionnaires and indicators.

For all high-income countries with 50 000 or more annual births, we did systematic reviews of published studies and the grey literature and contacted local researchers or public health practitioners when data from a particular country were not available or when there was ambiguity (appendix pp 13–17). Information about breastfeeding from national samples was not available from many countries. Although 27 out of 35 countries had some information about breastfeeding at a national level, response rates were often in the 50–70% range, indicators were rarely standardised, and recall periods tended to be long. We used administrative or other data when surveys were not available. If necessary, we estimated the proportion of infants breastfed at 12 months on the basis of information available for breastfeeding at 6 months and vice versa. We calculated time trends using multilevel linear regression models (hierarchical mixed models) that take into account that two or more surveys were included in the analyses for each country. We explored departures from linearity with fractional polynomial regression models.[7] In all analyses, we weighted country data by their populations of children younger than 2 years of age (see appendix pp 18–22 for statistical methods).

We did systematic searches of the published literature, and, when possible, meta-analyses for outcomes postulated to be associated with breastfeeding (appendix pp 23–30). These systematic reviews and meta-analyses were specially commissioned by WHO to provide background information for this Series.

We used the Lives Saved Tool[8] to predict how many deaths of children younger than 5 years would be prevented if breastfeeding patterns as of 2013 were scaled up in the 75 countries that are part of the Countdown to 2015 effort,[9] which account for more than 95% of all such deaths worldwide. We assumed that 95% of children younger than 1 month and 90% of those younger than 6 months would be exclusively breastfed, and that 90% of those aged 6–23 months would be partly breastfed. We applied the relative risks for the protection against all infectious causes of death obtained from our new meta-analyses[10] to all infectious causes of death in children younger than 2 years, and also to the 15% of deaths caused by complications of prematurity that occur after the first week of life

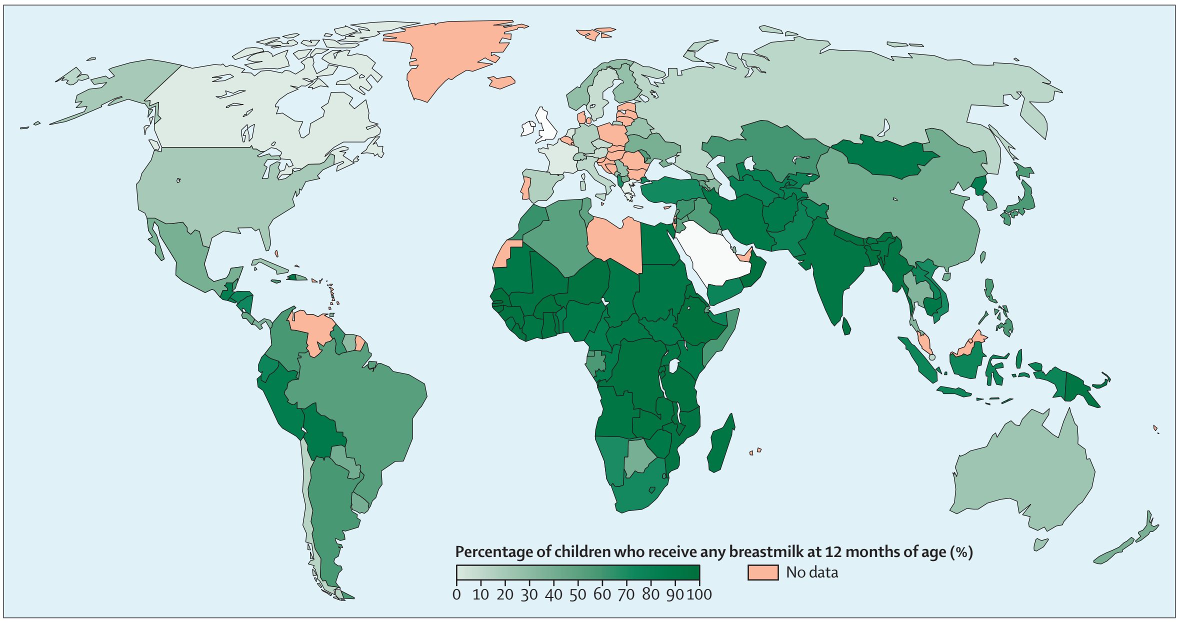

Figure 1: **Global distribution of breastfeeding at 12 months**
Data are from 153 countries between 1995 and 2013.

(appendix pp 31–36). We also estimated the potential number of deaths from breast cancer that could have been prevented by extending the duration of breastfeeding (appendix pp 37–38).

Epidemiology: levels and trends

We obtained complete information about 127 of the 139 LMICs (appendix pp 5–12), accounting for 99% of children from such countries. For high-income countries, we obtained data for 37 of 75 countries, but for several countries, only a subset of the indicators were available (appendix pp 13–17): these data should, therefore, be interpreted with caution.

Globally, the prevalence of breastfeeding at 12 months is highest in sub-Saharan Africa, south Asia, and parts of Latin America (figure 1). In most high-income countries, the prevalence is lower than 20% (appendix pp 13–17). We noted important differences—eg, between the UK (<1%) and the USA (27%), and between Norway (35%) and Sweden (16%).

We assessed breastfeeding indicators according to country income groups (figure 2). Information about early initiation or exclusive or continued breastfeeding at 2 years was not available for most high-income countries. We noted a strong inverse correlation (Pearson's $r=-0\cdot84$; $p<0\cdot0001$; appendix p 39) between breastfeeding at 6 months and log gross domestic product per person; our regression analyses showed that for each doubling in the gross domestic product per head, breastfeeding prevalence at 12 months decreased by ten percentage points.

Most mothers in all country groups started breastfeeding; only three countries (France, Spain, and the USA) had rates below 80% for ever breastfeeding. However, early initiation was low in all settings, as was exclusive breastfeeding (figure 2). Breastfeeding at 12 months was widespread in low-income and lower-middle-income settings, but uncommon elsewhere.

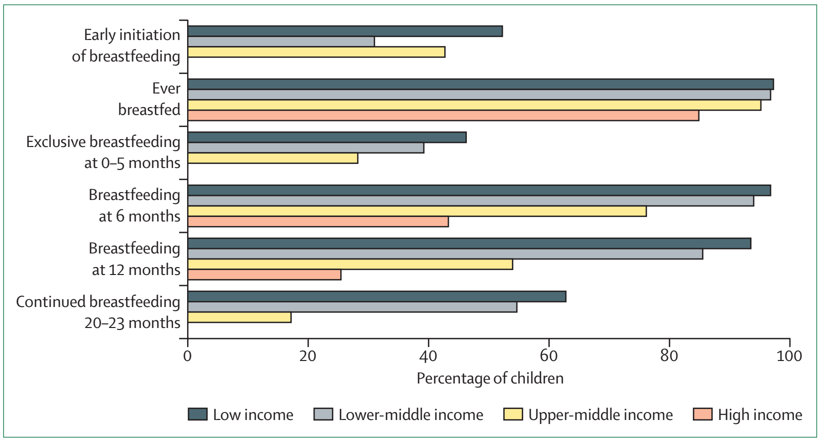

Figure 2: **Breastfeeding indicators by country income group in 2010**
Data are from national surveys that used standard indicators, and were weighted by national populations of children under 2 years. Data for up to 153 countries.

Except for early initiation, prevalence of all indicators decreased with increasing national wealth. Low-income countries had a high prevalence of breastfeeding at all ages, but the rates of initiation and exclusive breastfeeding are unsatisfactory even in these countries.

Surprisingly, most national level breastfeeding indicators were not strongly correlated (appendix p 39). We found only a moderate correlation (Pearson's $r=0\cdot54$) between exclusive and continued breastfeeding at 1 year in LMICs. Although the prevalence of

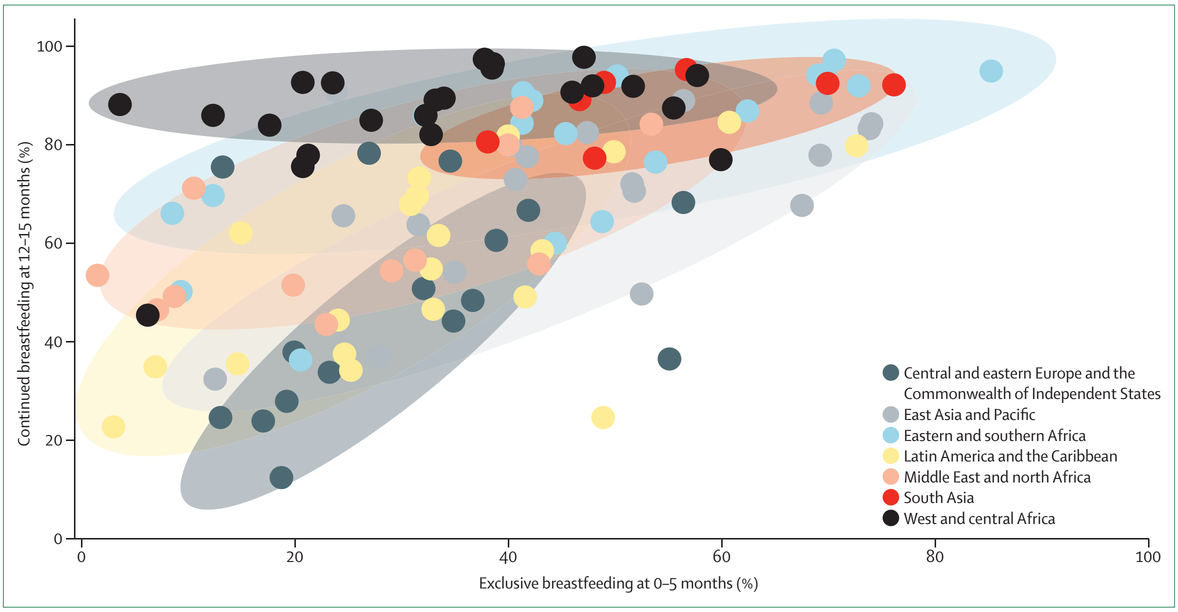

Figure 3: **The relation between exclusive breastfeeding at 0–5 months and continued breastfeeding at 12–15 months, by region**
Datapoints are countries (values from the most recent survey from 117 countries, 2000–13) and are coloured according to their region. The shaded ellipses include at least 80% of the points in each region.

continued breastfeeding was high throughout west and central Africa, rates of exclusive breastfeeding varied widely (figure 3). Countries from eastern and southern Africa tended to have on average lower rates of continued breastfeeding but higher rates of exclusive breastfeeding than did those in west Africa. In Latin America and the Caribbean, and in central and eastern Europe and the Commonwealth of Independent States, both indicators tended to be lower than in Africa. South Asian countries had high rates of both indicators whereas countries in the Middle East and north Africa had lower rates. Countries from east Asia and the Pacific region had moderate to high prevalence of both indicators.

In children younger than 6 months in LMICs, 36·3 million (63%) were not exclusively breastfed at the time of the most recent national survey. The corresponding percentages were 53% in low-income countries, 61% in lower-middle-income countries, and 63% in upper-middle-income countries. In children aged 6–23 months in LMICs, 64·8 million (37%) were not receiving any breastmilk at the time of the most recent national survey, with corresponding rates of 18% in low-income, 34% in lower-middle-income, and 55% in upper-middle-income countries. 101·1 million children in LMICs were not breastfed according to international recommendations.

In most LMICs, data were available from several surveys over time, making it possible to explore time trends both at the national level and for children in the poorest and richest 20% of families. Our analyses were restricted to surveys for which breakdown of breastfeeding indicators by wealth quintiles was possible (214 surveys for exclusive and 217 for continued breastfeeding; appendix pp 18–22), accounting for 83% of the total 2010 population of children younger than 2 years of age in LMICs. We reported linear trends because there was no evidence of departures from linearity. Exclusive breastfeeding rates increased slightly from 24·9% in 1993 to 35·7% in 2013 (figure 4). In the richest 20% of families, the increase was much steeper, whereas the poorest 20% followed the general trend. Continued breastfeeding at 1 year (12–15 months) dropped slightly at the global level (from 76·0% to 73·3%), partly due to a decline among the poorest 20% in each country (figure 4).

Epidemiology: within-country inequalities

We analysed 98 surveys from LMICs to investigate within-country inequalities according to wealth quintile (appendix p 40). Wealth-related inequalities in exclusive breastfeeding were small but disparities in continued breastfeeding rates were consistent: poorer people tend to breastfeed for longer than their richer counterparts in all country groupings, but especially in middle-income countries. Similar results based on 33 countries have been reported elsewhere.[11]

Our review of studies from high-income countries showed that high-income, better-educated women breast-feed more commonly than do those in low-income groups with fewer years of formal education.[12–20] Breastfeeding initiation in the USA was more common in mothers with lower education up until the 1960s, but the social gradient has since reversed.[4]

Breastfeeding is one of few positive health-related behaviours in LMICs that is less frequent in rich people, both between and within countries. The low rates of continued breastfeeding in richer families raises the possibility that poorer mothers will move towards breastmilk substitutes as their income increases, a concern that is reinforced by decreasing rates in poor populations.

Short-term effects in children: mortality and morbidity

The results of 28 meta-analyses on the associations between breastfeeding and outcomes in the children and mothers, of which 22 were commissioned for this Series, are summarised in the table. Because studies varied with regard to their feeding classifications, for several outcomes we compared longer versus shorter breastfeeding durations (eg, never *vs* ever breastfed, breastfed for less or more than a given number of months, and for a few outcomes longer *vs* shorter durations of exclusive breastfeeding). We tested for heterogeneity due to the type of breastfeeding categorisation, and in its absence we pooled the different studies. We described the results of randomised trials on how breastfeeding promotion affects health, nutrition, or developmental outcomes, but not of trials in which the endpoint was restricted to breastfeeding indicators; these are reviewed in the second article in the Series.[5]

Only three studies in LMICs provide information about mortality according to exclusive, predominant, partial, or no breastfeeding in the first 6 months of life (table). A strong protective effect was evident, with exclusively breastfed infants having only 12% of the risk of death compared with those who were not breastfed.[10] Another three studies in LMICs showed that infants younger than 6 months who were not breastfed had 3·5-times (boys) and 4·1-times (girls) increases in mortality compared with those who received any breastmilk, and that that protection decreased with age.[33] These results are lent support by studies of children aged 6–23 months, in whom any breastfeeding was associated with a 50% reduction in deaths (table).

Breastfeeding might also protect against deaths in high-income countries. A meta-analysis of six high-quality studies showed that ever breastfeeding was associated with a 36% (95% CI 19–49) reduction in sudden infant deaths.[34] Another meta-analysis of four randomised controlled trials showed a 58% (4–82) decrease in necrotising enterocolitis,[34] a disorder with high case-fatality in all settings.[35]

In terms of child morbidity, overwhelming evidence exists from 66 different analyses, mostly from LMICs and including three randomised controlled trials, that breastfeeding protects against diarrhoea and respiratory infections (table).[21] About half of all diarrhoea episodes and a third of respiratory infections would be avoided by breastfeeding. Protection against hospital admissions due to these disorders is even greater: breastfeeding could prevent 72% of admissions for diarrhoea and 57% of those for respiratory infections. We discuss the risks associated with breastmilk substitutes in terms of biological and chemical contamination in appendix p 41.

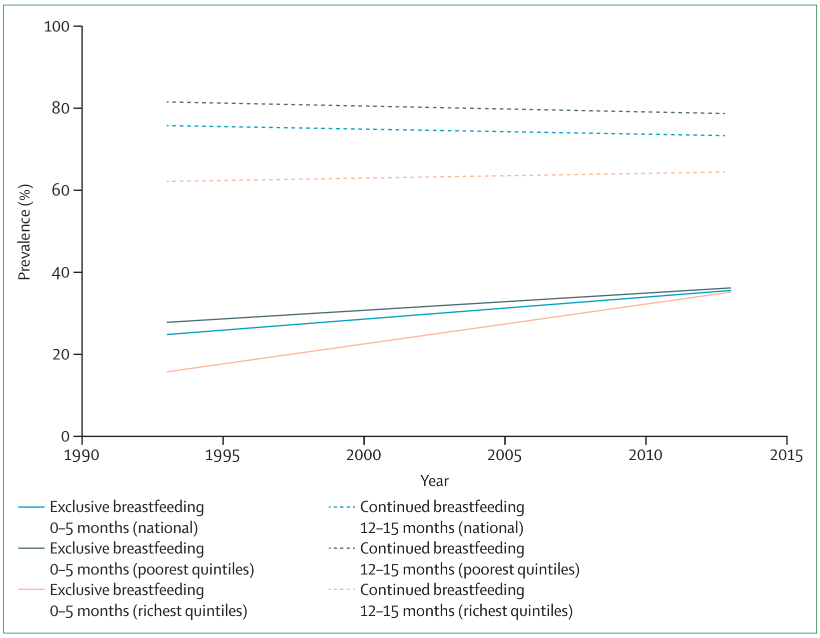

Figure 4: **National and wealth quintile-specific time trends in exclusive and continued breastfeeding, 1993–2013**
Data are weighted by national populations of children younger than 2 years at the time of the survey. Analyses restricted to 66 countries with information about household wealth.

Our reviews suggest important protection against otitis media in children younger than 2 years of age, mostly from high-income settings, but inconclusive findings for older children (table).[22] We saw no clear evidence of protection against allergic disorders: no association with eczema or food allergies and some evidence of protection against allergic rhinitis in children younger than 5 years.[23] When we analysed the 29 studies of asthma, we noted statistically significant evidence of a 9% (95% CI 2–15) reduction in asthma with breastfeeding, but effects were smaller and non-significant when we restricted analyses to the 16 studies with tighter control of confounding (a reduction of 5% [–6 to 15]) or to the 13 cohort studies (6% reduction [–11 to 20]).

On the basis of 49 studies done mostly in LMICs, our analyses of oral health outcomes (table) showed that breastfeeding was associated with a 68% reduction (95% CI 60–75) in malocclusions.[26] Most studies were restricted to young children with deciduous teeth, but malocclusion in this age group is a risk factor for malocclusion in permanent (adult) teeth.[36,37] However, breastfeeding for longer than 12 months and nocturnal feeding were associated with 2–3-times increases in dental caries in deciduous teeth, possibly due to inadequate oral hygiene after feeding.[25]

	Outcome	Types of comparison (breastfeeding categories)	Studies (n)	Age range of outcome	Pooled effect (95% CI)	Confounding and effect modification	Other biases	Conclusions
Effects on children, adolescents, or adults according to breastfeeding pattern								
Sankar et al (2015)[10]	Mortality due to infectious diseases	Exclusive versus predominant	3	<6 months	OR 0·59 (0·41–0·85)	All studies from LMICs, where confounding by SEP would probably underestimate the effect of breastfeeding. Confounder-adjusted studies showed similar effects	Studies that avoided reverse causation (breastfeeding stopped because of illness) showed similar effects. No evidence of publication bias but very few studies available	Consistent evidence of major protection. Few studies used the four breastfeeding categories in young infants, but evidence from other studies comparing any versus no breastfeeding is very consistent
Sankar et al (2015)[10]	Mortality due to infectious diseases	Exclusive versus partial	3	<6 months	OR 0·22 (0·14–0·34)	See above	See above	See above
Sankar et al (2015)[10]	Mortality due to infectious diseases	Exclusive versus none	2	<6 months	OR 0·12 (0·04–0·31)	See above	See above	See above
Sankar et al (2015)[10]	Mortality due to infectious diseases	Any versus none	9	6–23 months	OR 0·48 (0·38–0·60)	See above	See above	See above
Horta et al (2013)[21]	Diarrhoea incidence	More versus less breastfeeding (eg, exclusive *vs* non-exclusive; predominant *vs* partial; partial *vs* none; any breastfeeding *vs* no breastfeeding)	15	<5 years	RR 0·69 (0·58–0·82)	Most studies were from LMICs, where confounding would probably underestimate an effect. Confounder-adjusted studies showed similar effects. Three RCTs of breastfeeding promotion (not included in the meta-analysis) showed protection against diarrhoea morbidity (pooled OR 0·69 [0·49–0·96])	Few studies that allowed for reverse causation also showed protection. Publication bias is unlikely to explain the findings because results from large and small studies were similar	Strong evidence of major protection against diarrhoea morbidity and admissions to hospital, particularly in young infants, based on a large number of studies
Horta et al (2013)[21]	Diarrhoea incidence	See above	23	<6 months	RR 0·37 (0·27–0·50)	See above	See above	See above
Horta et al (2013)[21]	Diarrhoea incidence	See above	11	6 months to 5 years	RR 0·46 (0·28–0·78)	See above	See above	See above
Horta et al (2013)[21]	Admission to hospital for diarrhoea	See above	9	<5 years	RR 0·28 (0·16–0·50)	See above	See above	See above
Horta et al (2013)[21]	Lower respiratory infections (incidence or prevalence)	See above	16	<2 years	RR 0·68 (0·60–0·77)	Most studies were from LMICs, where confounding would probably underestimate the effect of breastfeeding. Confounder-adjusted studies showed similar effects	Studies that avoided reverse causation showed similar effects. No evidence of publication bias	Strong evidence of a reduction in severe respiratory infections in breastfed children, based on a large number of studies
Horta et al (2013)[21]	Admissions to hospitals for respiratory infections	See above	17	<2 years	RR 0·43 (0·33–0·55)	The only available RCT showed an RR of 0·85 (0·57–1·27), a non-significant reduction in admissions to hospital	See above	See above

(Table continues on next page)

Information about breastfeeding and child growth was derived from 17 studies, including 15 randomised controlled trials, mostly from middle-income countries.[24] Attained weight and length at about 6 months did not differ, but there was a small reduction (*Z* score –0·06 [95% CI –0·12 to 0·00]) in body-mass index (BMI) or bodyweight for length in children whose mothers received the breastfeeding promotion intervention compared with those whose mothers did not receive the promotion intervention (table).

Long-term effects in children: obesity, non-communicable diseases, and intelligence

We updated existing meta-analyses[38] on the associations between breastfeeding and outcomes related to non-communicable diseases (table). Most studies are from high-income settings. Based on all 113 studies identified, longer periods of breastfeeding were associated with a 26% reduction (95% CI 22–30) in the odds of overweight or obesity.[27] The effect was consistent across income classifications. The only breastfeeding promotion trial

	Outcome	Types of comparison (breastfeeding categories)	Studies (n)	Age range of outcome	Pooled effect (95% CI)	Confounding and effect modification	Other biases	Conclusions
(Continued from previous page)								
Bowatte et al (2015)[22]	Acute otitis media	More versus less breastfeeding (ever *vs* never; exclusive breastfeeding at 6 months *vs* not exclusive breastfeeding at 6 months; any breastfeeding for ≥3–4 months *vs* <3–4 months)	11	≤2 years	OR 0·67 (0·62–0·72)		Egger's test for small study effects showed weak evidence for publication bias (p=0·360)	Consistent evidence of reduction in acute otitis media during the first 2 years of life associated with longer durations of breastfeeding, based on 11 studies. No evidence of protection after 2 years
Bowatte et al (2015)[22]	Acute otitis media	See above	5	>2 years	OR 1·21 (0·60–2·45)	Most studies were done in HICs. Several studies did not adjust for important confounders	High heterogeneity (I^2=84%) among the five studies of children older than 2 years	See above
Lodge et al (2015)[23]	Eczema	More versus less breastfeeding (ever *vs* never; exclusive breastfeeding at 6 months *vs* not exclusive breastfeeding at 6 months; any breastfeeding for ≥3–4 months *vs* <3–4 months)	17	≤2 years	OR 0·95 (0·85–1·07)	About a third of the studies were from LMICs, and results are similar to those from HICs. Few studies in young children account for reverse causation. Several studies did not adjust for essential confounders	Some evidence of publication bias, with smaller pooled effect sizes in larger studies	No evidence of an association between breastfeeding and eczema
Lodge et al (2015)[23]	Eczema	See above	20	>2 years	OR 1·09 (0·99–1·20)	See above	See above	See above
Lodge et al (2015)[23]	Food allergies	See above	10	≤5 years	OR 1·07 (0·90–1·26)	See above	The ten studies on food allergy in children ≤5 years were highly heterogeneous (I^2=88%)	No evidence of an association between breastfeeding and food allergies
Lodge et al (2015)[23]	Food allergies	See above	4	>5 years	OR 1·08 (0·73–1·26)	See above	See above	See above
Lodge et al (2015)[23]	Allergic rhinitis	See above	5	≤5 years	OR 0·79 (0·63–0·98)	See above	See above	Possible protection against allergic rhinitis in children <5 years, based on only five studies
Lodge et al (2015)[23]	Allergic rhinitis	See above	9	>5 years	OR 1·05 (0·99–1·12)	See above	See above	No evidence for those older than 5 years
Lodge et al (2015)[23]	Asthma or wheezing	See above	29	5–18 years	OR 0·91 (0·85–0·98)	The protective effect of asthma was smaller and not significant in 16 studies with thorough control for confounders (OR 0·95 [0·85–1·06]) and in the 13 cohort studies (OR 0·94 [0·80–1·11]). There were too few studies to estimate association with asthma in adults	See above	Inconclusive evidence for the association between breastfeeding and the risk of asthma or wheezing

(Table continues on next page)

that reported on this outcome did not detect an association; in this trial, the investigators reported important early differences between intervention and comparison groups in terms of exclusive breastfeeding, but at 12 months of age only 19% of children in the intervention group and 11% of children in the comparison group were breastfed.[39,40] A 2005 meta-analysis[41] of breastfeeding and mean BMI included 36 articles of which 11 included adjustment for socioeconomic status, maternal smoking, and maternal BMI; their pooled effect did not suggest an association with breastfeeding. In our review,[27] 23 high-quality studies with sample sizes of

	Outcome	Types of comparison (breastfeeding categories)	Studies (n)	Age range of outcome	Pooled effect (95% CI)	Confounding and effect modification	Other biases	Conclusions
(Continued from previous page)								
Giugliani et al (2015)[24]	Length	Randomised trials or quasi-experiments comparing children receiving breastfeeding promotion interventions with control children	17	About 6 months (range 3–24)	Z score 0·03 (–0·02 to 0·08)	Most studies are from middle-income countries. Confounding is unlikely because 15 of the 17 studies were randomised trials. Analyses were by intent to treat, so that low compliance with breastfeeding promotion might underestimate the magnitude of the effect	Evidence of publication bias for BMI, with small studies showing larger reductions	No evidence of an effect on breastfeeding promotion on length at 6 months of age
Giugliani et al (2015)[24]	Weight	See above	16	See above	Z scores 0·03 (–0·06 to 0·12)	See above	See above	No evidence of an effect on breastfeeding promotion on weight at 6 months of age
Giugliani et al (2015)[24]	BMI or weight for length	See above	11	See above	Z scores –0·06 (–0·12 to 0·00)	See above	See above	Some evidence supporting a reduction in BMI or weight for length
Tham et al (2015)[25]	Dental caries	Breastfeeding >12 months versus ≤12 months	4	<6 years	OR 2·69 (1·28–5·64)	Most studies did not control for the introduction of sugary foods and drinks. Most studies were from HICs, where high SEP would be expected to negatively confound the association	Publication biases veer toward studies that show an association between breastfeeding beyond 12 months or on demand and dental caries	Consistent evidence that breastfeeding >12 months has detrimental effects on deciduous teeth
Tham et al (2015)[25]	Dental caries	Breastfeeding on demand or nocturnal feeding versus not (in breastfed children)	6	<6 years	OR 2·90 (2·33–3·60)	See above	See above	Consistent evidence that breastfeeding on demand has detrimental effects on deciduous teeth
Peres et al (2015)[26]	Malocclusion	Never versus ever breastfeeding; longer versus shorter duration of exclusive breastfeeding; or longer versus shorter duration of any breastfeeding	41	Childhood, adolescence, and adulthood	OR 0·32 (0·25–0·40)	80% of the studies were from LMICs. Because malocclusions are not associated with SEP or any other known determinant of breastfeeding patterns, it is unlikely that these results are affected by confounding	Some evidence of publication bias but the association was also present in the larger and better designed studies	Consistent evidence of a major, two-thirds reduction in malocclusions in deciduous teeth in breastfed individuals
Horta et al (2015)[27]	Systolic blood pressure	Never versus ever breastfed; or longer versus shorter breastfed duration	43	Childhood, adolescence and adulthood	–0·80 mm Hg (–1·17 to –0·43)	Three-quarters of the studies were from LMICs. Evidence of residual confounding as effect in studies from HIC but not in those from LMICs	Evidence of publication bias in systolic blood pressure studies	No evidence of a reduction in blood pressure associated with breastfeeding
Horta et al (2015)[27]	Diastolic blood pressure	Never versus ever breastfed; or longer versus shorter breastfeeding duration	38	Childhood, adolescence, and adulthood	–0·24 mm Hg (–0·50 to 0·02)	See above	Evidence of publication bias in diastolic blood pressure studies	See above
Horta et al (2015)[27]	Overweight or obesity	Never versus ever breastfed; longer versus shorter duration of exclusive breastfeeding; or longer versus shorter duration of any breastfeeding	113	Childhood, adolescence, and adulthood	OR 0·74 (0·70–0·78)	In HICs, residual confounding by SEP is a possibility; however, the effect size was similar in studies from LMICs (a third of all studies). 23 high-quality studies showed a smaller pooled reduction of 13% (95% CI 6–19)	Some evidence of publication bias with larger effects in small studies, but even large and well controlled studies showed a 20% reduction in prevalence	Suggestive evidence of protection, including high-quality studies and those from low-income or middle-income settings

(Table continues on next page)

	Outcome	Types of comparison (breastfeeding categories)	Studies (n)	Age range of outcome	Pooled effect (95% CI)	Confounding and effect modification	Other biases	Conclusions
(Continued from previous page)								
Horta et al (2015)[27]	Total cholesterol	Never versus ever breastfed; or longer versus shorter breastfeeding duration	46	Childhood, adolescence, and adulthood	−0·01 mmol/L (−0·05 to 0·02)	No evidence of heterogeneity with nearly all studies showing small effects. Three-quarters of the studies were from HICs	No evidence of an association	No evidence of an association
Horta et al (2015)[27]	Type 2 diabetes	Never versus ever breastfed; longer versus shorter duration of exclusive breastfeeding; or longer versus shorter duration of any breastfeeding	11	Childhood, adolescence, and adulthood	OR 0·65 (0·49–0·86)	Only two of 11 studies were from LMICs; these studies showed 14% reduction; residual confounding might have affected HIC studies	Few available studies; no evidence of publication bias	Restricted evidence of protection, based on 11 studies
Horta et al (2015)[28]	Intelligence	Never versus ever breastfed; or longer versus shorter breastfeeding duration	16	Childhood, adolescence, and adulthood	IQ points: 3·44 (2·30–4·58)	In HICs (14 of the 16 studies), residual confounding by SEP was a possibility; however, the effect was also present in two studies from LMICs. One high-quality RCT showed a statistically significant increase in IQ of more than 7 points	Some evidence of publication bias with larger effects in small studies, but even large studies showed an effect. Nine studies with adjustment for maternal IQ showed difference of 2·62 points (1·25–3·98)	Consistent effect of about 3 IQ points in observational studies; also present a large RCT on this topic
Effects on women who breastfed								
Chowdhury et al (2015)[29]	Lactational amenorrhoea	Highest versus lowest duration of breastfeeding	13	Women (<1 year post partum)	RR 1·17 (1·04–1·32)	Most studies were from LMICs. Residual confounding unlikely. Strongest effects when exclusive or predominant breastfeeding are compared with partial (RR 1·21) or no breastfeeding (RR 1·23)	No evidence of publication bias	Consistent effect on prolonging lactational amenorrhoea, especially for exclusive or predominant breastfeeding
Chowdhury et al (2015)[29]	Breast cancer	Highest versus lowest duration of breastfeeding	76	Adult women	OR 0·81 (0·77–0·86)	Three-quarters of the studies were from HICs. Parity reduces the risk of breast cancer and is also associated with greater lifetime breastfeeding duration. Most studies did not adjust appropriately for parity and therefore tended to exaggerate effect size. A thoroughly adjusted pooled analysis of 47 studies shows an OR of 0·96 for each 12 months of breastfeeding[30]	Some evidence of publication bias but the association was also present in the larger and better designed studies	Consistent protective effect of breastfeeding against breast cancer in 47 well designed studies, of a 4·3% reduction per 12 months of breastfeeding in the better controlled studies
Chowdhury et al (2015)[29]	Ovarian cancer	Highest versus lowest duration of breastfeeding	41	Adult women	OR 0·70 (0·64–0·75)	Only six studies from LMICs. Confounding by parity might affect the results but socioeconomic confounding is unlikely. Studies with fine adjustment for parity and exclusion of nulliparous women showed less protection with an OR of 0·82 (0·75–0·89)	Some evidence of publication bias, with smaller pooled effect sizes in the 22 studies with samples larger than 1500 women (OR 0·76 [0·69–0·84])	Suggestive evidence of a protective effect of breastfeeding
Chowdhury et al (2015)[29]	Osteoporosis (distal radius)	Highest versus lowest duration of breastfeeding	4	Adult women	SDS −0·132 (−0·260 to −0·003)	All studies from HICs. High heterogeneity in the distal radius analyses with the largest study showing no association and smaller studies showing protection	Not assessed because of small number of studies	Insufficient evidence

(Table continues on next page)

	Outcome	Types of comparison (breastfeeding categories)	Studies (n)	Age range of outcome	Pooled effect (95% CI)	Confounding and effect modification	Other biases	Conclusions
(Continued from previous page)								
Chowdhury et al (2015)[29]	Osteoporosis (femoral neck)	Highest versus lowest duration of breastfeeding	4	Adult women	SDS −0·142 (−0·426 to 0·142)	All studies from HICs. None of the studies showed an association	Not assessed because of small number of studies	Insufficient evidence
Aune et al (2013)[31]	Type 2 diabetes	Highest versus lowest duration of breastfeeding	6	Adult women	RR 0·68 (0·57–0·82)	Several confounding factors were adjusted for. Significant protection also seen for 3-month and 12-month increases in breastfeeding duration. Five of the six studies were from HICs. All six studies showed protection	Few available studies; no evidence of publication bias	Restricted evidence of protection against type 2 diabetes in women who breastfed for longer periods
Neville et al (2014)[32]	Post-partum weight change	Qualitative review	45	Women (<2 years post partum)	Not estimated because of different outcome measures at variable post-partum ages	Studies were highly variable. Most studies saw no association. Of the five studies with high methodological quality, four reported beneficial effects. Nearly all studies from HICs	Not assessed in the published review	The role of breastfeeding on post-partum weight change is uncertain

Data are odds ratio (95% CI), risk ratio (95% CI), *Z* score (95% CI), mm Hg (95% CI), mmol/L (95% CI), intelligence quotient (95% CI), or standard deviation scores (95% CI). In 22 sets of analyses, the summary effect sizes are the pooled results of studies comparing longer versus shorter breastfeeding durations (either never *vs* ever breastfed; exclusive breastfeeding for more than a specific number of months *vs* less than that number of months; or any breastfeeding for more than a specific number of months *vs* less than that number of months). Separate results for each type of categorisation are available in the appendix. OR=odds ratio. LMICs=low-income and middle-income countries. SEP=socioeconomic position. RR=risk ratio. RCT=randomised controlled trial. HICs=high-income countries. BMI=body-mass index. IQ=intelligence quotient. SDS=SD score.

Table: **Results of meta-analyses on the associations between breastfeeding and outcomes in children and mothers**

more than 1500 participants and adjustment for socioeconomic status, maternal BMI and perinatal morbidity showed a pooled reduction in the prevalence of overweight or obesity of 13% (95% CI 6–19).

For the incidence of type 2 diabetes, the pooled results from 11 studies indicate a 35% reduction (95% CI 14–51). We deemed only three studies to be of high quality, which indicated a potentially important, but not statistically significant, reduction of 24% (95% CI ranging from a 60% reduction to a 47% increase).[27] The direction and magnitude of the association with diabetes are consistent with findings for overweight. An earlier review of six studies indicated a possible protective effect against type 1 diabetes.[34] The meta-analyses for systolic (43 studies) and diastolic (38 studies) blood pressure, and total cholesterol (46 studies) showed no evidence of protective effects of breastfeeding.[27]

Breastfeeding was consistently associated with higher performance in intelligence tests in children and adolescents, with a pooled increase of 3·4 intelligence quotient (IQ) points (95% CI 2·3–4·6) based on the findings of 16 observational studies that controlled for several confounding factors including home stimulation (table).[28] Nine studies also adjusted for maternal intelligence, showing a pooled effect of 2·6 points (1·3–4·0). A large randomised trial reported an increase of more than 7 IQ points at 6·5 years of age,[42] and a similar effect was reported in a non-randomised trial in which preterm infants were fed formula or breastmilk.[43] Positive associations with attained schooling were reported from the UK,[44,45] New Zealand,[46] and Brazil,[47] but a joint analysis of four cohorts in LMICs showed mixed results.[48] A study in Brazil including 30 years of follow-up suggested an effect of breastfeeding on intelligence, attained schooling, and adult earnings, with 72% of the effect of breastfeeding on income explained by the increase in IQ.[49] A review of 18 studies suggested that breastfeeding is associated with a 19% reduction (95% CI 11–27) in the incidence of childhood leukaemia.[50]

Effects on the mother

The table shows the results of new reviews (published in July, 2015) on lactational amenorrhoea, breast and ovarian cancer, type 2 diabetes, and osteoporosis.[29] We also cite existing reviews on diabetes, weight retention, and maternal depression. Most studies were from high-income countries, except for those on lactational amenorrhoea.

The role of breastfeeding in birth spacing is well recognised. In 2003, it was estimated that in countries where continued breastfeeding is prevalent, eg, Uganda and Burkina Faso, 50% more births would be expected in the absence of breastfeeding.[51] Our review confirms that increased breastfeeding, and especially exclusive or predominant breastfeeding, were associated with longer periods of amenorrhoea.[29] Findings from randomised controlled trials of breastfeeding promotion interventions also confirm this effect.[52]

Evidence exists of a robust inverse association between breastfeeding and breast cancer (table). The largest individual-level analysis on this topic included about 50 000 patients with cancer from 47 studies,[30] which is about half those included in our meta-analysis. Each 12-month increase in lifetime breastfeeding was associated with a reduction of 4·3% (95% CI 2·9–6·8) in the incidence of invasive breast cancer. This analysis included thorough adjustment parity and other confounders; nulliparous women were excluded. The results did not vary substantially according to menopausal status. Our meta-analysis suggests a higher magnitude of protection, but when restricted to the 14 studies with fine adjustment for parity and exclusion of nulliparous women, the reduction comparing longer versus shorter breastfeeding durations was 7% (95% CI 3–11).[29]

The meta-analysis of 41 studies on breastfeeding and ovarian cancer shows a 30% reduction associated with longer periods of breastfeeding (95% CI 25–36). Confounding by parity might affect the results but socioeconomic confounding is unlikely because socioeconomic status is only weakly associated with ovarian cancer incidence. The pooled reduction, based on studies with fine adjustment for parity and exclusion of nulliparous women, was 18% (14–42).[29] We also reviewed the evidence on osteoporosis, finding no evidence of an association between breastfeeding and bone mineral density in the four studies available (table).[29]

A meta-analysis of six cohort studies on type 2 diabetes showed an odds ratio of 0·68 (95% CI 0·57–0·82).[31] In view of this finding, an association could be predicted with overweight, but a review of 54 articles on the possible role of breastfeeding on post-partum weight change was inconclusive.[32] Few studies are available for the long-term association between nursing and adiposity. After the review of studies on overweight and breastfeeding was published, an analysis of 740 000 British women with long-term follow-up showed that mean BMI was 1% lower for every 6 months that the woman had breastfed.[53] A qualitative review of 48 studies showed clear associations between breastfeeding and reduced maternal depression,[54] but it is more likely that depression affects breastfeeding than the opposite.

Estimating lives saved for children and mothers

The Lives Saved Tool[8] estimates that 823 000 annual deaths would be saved in 75 high-mortality LMICs in 2015 if breastfeeding was scaled up to near universal levels. This corresponds to 13·8% of the deaths of children under 2 years of age. For preventable deaths, 87% would have occurred in infants younger than 6 months due to a combination of high death rates and low prevalence of exclusive breastfeeding.

We also estimated the potential effect of breastfeeding on breast cancer mortality (appendix pp 31–37). Using the estimates of protection from the pooled study, we estimate that existing global rates of breastfeeding avert 19 464 annual breast cancer deaths compared with a scenario in which no women breastfed (table).[30] The low-income regions with long breastfeeding durations (Africa and south Asia) account for 58% of currently prevented deaths, despite only accounting for 36% of the global population included in this analysis. We also estimate that an additional 22 216 lives per year would be saved by increasing breastfeeding duration from present levels to 12 months per child in high-income countries and 2 years per child in LMICs. We cannot model the same effect in all countries given the differences in data availability and the fact that very few children in high-income countries are breastfed for longer than 12 months. Latin America, central and eastern Europe, the Commonwealth of Independent States, and high-income countries would benefit most because of their higher incidence of breast cancer and also shorter breastfeeding durations at present.

Conclusions

The fact that the reproductive cycle includes breastfeeding and pregnancy[1] has been largely neglected by medical practice, leading to the assumption that breastmilk can be replaced with artificial products without detrimental consequences. This neglect is particularly important in high-income countries, where fewer than one in every five children are breastfed by the age of 12 months. For each doubling in national gross domestic product per person, breastfeeding prevalence at 12 months decreases by 10 percentage points.

Findings from epidemiology and biology studies substantiate the fact that the decision to not breastfeed a child has major long-term effects on the health, nutrition, and development of the child and on women's health. Possibly, no other health behaviour can affect such varied outcomes in the two individuals who are involved: the mother and the child. Findings from immunology, epigenetic, microbiome, and stem-cell studies done over the past two decades that elucidate potential mechanisms through which breastfeeding can improve outcomes will probably be followed by other, even more exciting discoveries on the exquisite personalised medicine provided by human milk (panel).

Our global analyses show that more than 80% of neonates receive breastmilk in nearly all countries. However, only about half begin breastfeeding within the first hour of life, even though such a recommendation was issued by WHO more than 25 years ago.[70] Because 60% of the world's children are now delivered by skilled assistants,[9] further promotion of early initiation is possible. In most countries, rates of exclusive breastfeeding are well below 50%, and the correlation with the duration of any breastfeeding is only moderate. This finding signals the need to tailor breastfeeding support strategies to specific patterns recorded in each country. In the poorest countries, late initiation and low rates of exclusive breastfeeding are the main challenges. In middle-income and high-income

***Panel:* Breastmilk—a personalised medicine**

The nutritional advantages of breastfeeding and its protection against infection are well known. In the past two decades, the possibility that crucial imprinting events might be modulated during breastfeeding, with potential lifelong effects for the infant, has become apparent.[55] These events might be mediated directly or through effects on the infant microbiome. The ability of the microbiome to regulate host responses in infancy depends on individual bacterial species, which modulate T-cell polarisation and immune regulation, metabolic responses, adipogenesis, and possibly even brain development and cognitive functioning.[56,57] Abnormal colonisation patterns have a deleterious long-term effect on immune and metabolic homoeostasis. It is therefore remarkable that a mother's breastmilk transmits elements of her own microbiome and immune responses, and also provides specific prebiotics to support growth of beneficial bacteria.

Delivery mode initially established whether the gut flora of the mother (vaginal delivery) or the skin flora of the birth attendants (caesarean section) dominates the initial colonisers,[58] which induce an important immune response in the infant. Feeding mode is the second fundamental determinant of the infant microbiome. Breastfed infants maintain persistent microbial differences, independent of delivery mode,[59,60] owing to the effects of human milk oligosaccharides (HMOs). Human milk contains a much wider variety of sugars than other mammalian milks: up to 8% of its calorific value is provided in the form of indigestible HMOs, which function as prebiotics to support growth of specific bacteria. They cannot be used by most enteric organisms, but support growth of *Bifidobacterium longum* biovar *infantis*, which has co-evolved to express the enzymes needed for the utilisation of HMOs.[55] Substantial inter-individual variation exists in maternal HMO production, which in turn underpins the pattern of flora acquisition by the infant.[61] Therefore, there is specificity of the interaction between breastmilk and the infant microbiome, causing different bacterially induced effects on the infant's metabolism and immunity.

This specificity of interaction is further underpinned by the mother's enteromammary axis. To maintain her own gut homoeostasis, the mother's intestinal dendritic cells take up individual bacteria from the lumen and transport them to gut lymphoid follicles,[56] where T cells are committed to a regulatory phenotype and B cells shifted towards immunoglobulin A. Programmed dendritic cells and lymphocytes then re-enter the circulation before homing back to the gut through interaction between their induced β7 integrins and locally expressed mucosal vascular addressin cell adhesion molecule (MAdCAM-1). MAdCAM-1 is expressed in the mammary endothelium during pregnancy, allowing selective uptake by the breast of gut-programmed cells.[62] The consequences of enteromammary trafficking include the release of dendritic cells containing live maternal gut bacteria, T cells expressing gut-derived β7 integrins, and plasma cells producing immunoglobulin A specific for maternal gut bacteria into the colostrum and breastmilk. Breastmilk therefore contains a dominance of immune cells of gut-related phenotype (γδ cells, β7+ cells) that have matured within the mother's intestine.[63] Breastmilk cytokines also vary depending on the mother's immunological experiences. Therefore, there is coordinated input to the infant's nascent mucosal immune system, specific for the mother's microbiome, in which individual bacterial types are favoured and tolerogenic immune responses are transmitted. Caesarean section, perinatal antibiotics, and failure to breastfeed are the three major factors that affect this co-evolved imprinting process. Findings from a study of flora acquisition and immune responses in primates identified clear differences in both gut bacterial composition and mucosal immune responses in breastfed compared with formula-fed macaques, with the responses persisting into adult life.[64]

In addition to changes mediated through the flora, individual breastmilk components might directly affect epigenetic programming of the infant.[65] The usual adverse effect of peroxisome proliferator-activated receptor-γ polymorphisms on adiposity and metabolism is prevented by breastfeeding, possibly due to the content of peroxisome proliferator-activated receptor-modulating constituents such as long-chain polyunsaturated fatty acids and prostaglandin J.[66] Protection against breast cancer for a breastfeeding mother might also be mediated through peroxisome proliferator-activated receptor modulation.[66] Lactoferrin, a major breastmilk component, binds bacterial CpG motifs and blunts mucosal NF-κB responses to the flora. Microvesicles called exosomes are secreted into breastmilk, and might inhibit atopic sensitisation dependent on maternal immune experience.[67] Breastmilk fat globules contain many secreted micro-RNAs, the expression of which is modulated by maternal diet, which are predicted to target several genes in the infant.[68] Evidence also exists that multipotential stem cells are secreted into breastmilk and can persist within infants.[69]

Human breastmilk is therefore not only a perfectly adapted nutritional supply for the infant, but probably the most specific personalised medicine that he or she is likely to receive, given at a time when gene expression is being fine-tuned for life. This is an opportunity for health imprinting that should not be missed.

countries, short overall duration of breastfeeding is an additional challenge.

Our time-trend analyses show that, for LMICs as a whole, exclusive breastfeeding has increased by about 0·5 percentage points per year since 1993, reaching 35% in 2013. In 2012, the 56th World Health Assembly set as a target for 2025 to "increase the rate of exclusive breastfeeding in the first 6 months up to at least 50%".[71]

To achieve this goal would need a doubling of the recent annual increase, to more than 1 percentage point a year in the next decade, which is already the rate for the richest 20% of people. In view of the benefits of exclusive breastfeeding and of present achievements by leading countries, could a more ambitious target not be aimed for? The Assembly did not set a goal for continued breastfeeding.

In terms of inequalities, our findings show that breastfeeding is one of the few positive health behaviours that is more prevalent in poor than in rich countries. They also show that poor women breastfeed for longer than rich women in LMICs, whereas in high-income countries the pattern is reversed. These results suggest that breastfeeding patterns are contributing to reducing the health gaps between rich and poor children in LMICs, which would be even greater in the absence of breastfeeding.

In LMICs, there are no inequalities between rich and poor mothers in exclusive breastfeeding rates. Findings from our time-trend analyses suggest that this is because rich mothers are adopting exclusive breastfeeding at a much faster rate than are poor mothers—only 20 years ago, the poorer mothers had substantially higher rates of exclusive breastfeeding. Continued breastfeeding is still more common in poor mothers than in wealthy mothers, but rates seem to be dropping among these while remaining stable in rich mothers. Protecting breastfeeding in the world's poorest populations is therefore a major priority.

Our systematic reviews emphasise how important breastfeeding is for all women and children, irrespective of where they live and of whether they are rich or poor. Appropriate breastfeeding practices prevent child morbidity due to diarrhoea, respiratory infections, and otitis media. Where infectious diseases are common causes of death, breastfeeding provides major protection, but even in high-income populations it lowers mortality from causes such as necrotising enterocolitis and sudden infant death syndrome. Available evidence shows that breastfeeding enhances human capital by increasing intelligence. It also helps nursing women by preventing breast cancer. Additionally, our review suggests likely effects on overweight and diabetes in breastfed children, and on ovarian cancer and diabetes in mothers. The only harmful consequence of breastfeeding we detected was an increase in tooth decay in children breastfed for more than 12 months. In view of the many benefits of breastfeeding, this observation should not lead to discontinuation of breastfeeding but rather to improved oral hygiene.

Findings from our systematic reviews are restricted by the observational nature of most of the available data for breastfeeding and by the limitations of meta-analyses.[72,73] Experimental data are scarce because breastfeeding promotion activities must be highly effective to change feeding patterns to an extent that leads to a measurable effect on short-term and long-term outcomes. Moreover, confounding can occur because breastfeeding is associated with higher socioeconomic position in high-income countries. Our reviews included subanalyses of studies with tight control for confounding. Whenever possible, we also did separate analyses of studies from LMICs, because poor individuals tend to breastfeed for longer than rich people in these countries (appendix p 40), an association that is reversed in high-income countries. Interpretation of associations is also affected by the fact that non-breastfed infants receive different diets in different countries—eg, animal milk in most poor societies and formula in middle-income and high-income populations. The association between breastfeeding and overweight, for example, is probably affected by the diet of infants who are not breastfed.

No consensus exists about whether or not breastfeeding can protect against a child's later risk of overweight or diabetes,[34,38,41] largely because of potential residual confounding. Although the evidence is not as strong as it is for infections or intelligence, we argue that the evidence linking breastfeeding with protection from later overweight or diabetes is growing. Findings from our meta-analyses showed that the association persisted when restricted to only high-quality studies, and also when restricted to studies from only low-income and middle-income settings. The association seems to be specific—eg, we noted no effect on blood pressure or blood lipid concentrations, for which confounding patterns are similar. Finally, findings from randomised trials of breastfeeding promotion in infancy indicate a reduction in adiposity.

The scaling up of breastfeeding practices to almost universal levels is estimated to prevent 823 000 annual deaths, or 13·8% of all deaths of children younger than 24 months in the 75 Countdown to 2015[9] countries. The target of 95% of all infants younger than 6 months having exclusive breastfeeding is ambitious because at present the highest national prevalences are 85% in Rwanda and 76% in Sri Lanka. We also used a target of 90% for any breastfeeding from 6–23 months, but five countries already have levels that are above this target (Nepal, Rwanda, Ethiopia, Burundi, and Guinea). We acknowledge that these targets are ambitious, but the estimates show the potential for lives saved if mothers and children adhered to international recommendations. Despite differences in methods, our estimates about potential lives saved are consistent with those from the 2013 *Lancet* Nutrition Series (804 000 deaths)[74] but higher than those from the 2010 Global Burden of Disease study (540 000 deaths),[75] in which the assumptions and methods were not sufficiently detailed to understand the reasons for the discrepancy. Breastfeeding is potentially one of the top interventions for reducing under-5 mortality, and the modest changes in breastfeeding rates since 2000 have contributed to the fact that most LMICs did not reach the fourth Millennium Development Goal, to reduce under-5 mortality by two-thirds.[76] We show that increasing exclusive breastfeeding should be among the top priorities for reducing infant deaths.

As an example of the potential to save women's lives, we estimated that present rates of breastfeeding prevent almost 20 000 annual deaths from breast cancer, and an additional 20 000 are preventable by scaling up breastfeeding practices (appendix). To achieve its full effect, breastfeeding should continue up to the age of 2 years. Protection against mortality and morbidity from infectious diseases extends well into the second year of life—eg, breastfeeding prevents half of deaths caused by infections in children aged 6–23 months. Protection against otitis media, a common childhood illness throughout the world, also extends to 2 years and possibly beyond. Findings from studies of overweight and obesity show that longer durations of breastfeeding are associated with lower risk, as do studies of IQ showing a clear dose–response association with duration. Breast cancer is reduced by lifetime duration of breastfeeding in women, with a 6% reduction for every 12 months.[50] Findings from ethnographical research show that total duration of breastfeeding ranges between 2 and 4 years in most traditional societies,[77] and our review of the literature lends support to international recommendations about the total duration of breastfeeding, in both high-income and low-income countries.

Data availability for breastfeeding patterns shows an unusual distribution. Health authorities and researchers in high-income countries seem to neglect breastfeeding to such an extent that most of these countries are unable to report on reliable, standardised indicators. This situation contrasts sharply with the high quality of data for breastfeeding in LMICs, as a consequence of the regular conduct of standardised surveys such as the Demographic and Health Surveys and Multiple Indicator Cluster Surveys.

Our findings show how essential the protection, promotion, and support of breastfeeding is for the achievement of many of the newly launched Sustainable Development Goals by 2030. Breastfeeding is clearly relevant to the third sustainable goal, which includes not only maternal and child health but also non-communicable diseases such as breast cancer and diabetes as well as overweight and obesity. It is also relevant to the second goal (on nutrition). The effect of breastfeeding on intelligence and on human capital is relevant to the fourth goal (education), the first goal (poverty), and the eighth goal (inclusive economic growth). Finally, by helping close the gap between rich and poor, breastfeeding can contribute to goal number ten—reducing inequalities.

Contributors

CGV and NCR had the idea for the paper. CGV was the primary author. The other co-authors contributed specific sections: SM (biological mechanisms), SH (breast cancer cases averted), NW (child lives saved), MJS (meta-analysis on child mortality), and RB (early initiation of breastfeeding). AJDB, GVAF, and JK collected and analysed the data. All authors revised the draft report and approved the final version.

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Declaration of interests

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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

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Webappendix 1. Brief history of breastfeeding recommendations

Virtually all women are able to fully nourish their infants through BF.[1, 2] For example, over 95% of rural mothers in most countries in Sub-Saharan Africa currently nurse their one year old children. BF, either by the biological mother or less commonly by a wet nurse, was universal until the mid 1800's when the development of the feeding bottle and of condensed milk offered mothers the option of not breastfeeding.[3] In the early 1900's, epidemiological studies were already showing high mortality rates among non-breastfed infants.[4, 5] Bottle feeding became increasingly common, and by the 1970's breastfeeding was the exception rather than the rule in middle and high-income settings.[6]

Breastfeeding recommendations evolved with time. While the expression "exclusive BF" was in common use in the early 1980's[7], it failed to recognize that many if not most young infants received non-nutritive fluids such as water and herbal teas in addition to breastmilk.[8] In the late 1980's, exclusive BF was redefined when research documented the risks of giving fluids to breastfed infants[9-11] while others showed that even in hot climates breastfed babies had no need for additional water.[12] Since 1989, the World Health Organization recommends that mothers should initiate BF "*within a half-hour of birth*"[13] and in 1990 the landmark Innocenti Declaration recommended that breastmilk alone was sufficient to nurture infants up to 4-6 months of life, and that breastfeeding should be continued until "*2 years or beyond*". [14] In 2001, the recommended duration of exclusive breastfeeding was extended from 4-6 months to 6 months [15] based on a systematic review of the evidence. [16, 17] In 2001, the recommended duration of exclusive breastfeeding was extended from 4-6 months to 6 months.[15] Although – particularly in European circles – there is still debate on this issue, [18-20] a recent meta-analysis concluded that *"the available evidence demonstrates no apparent risks in recommending, as a general policy, exclusive breastfeeding for the first six months of life in both developing and developed-country settings".* [17]

Webappendix 2. Breastfeeding definitions

The following indicators were included in the analyses, using internationally agreed upon definitions:[21]

- Early initiation of BF: proportion of children born in the last 24 months who were put to the breast within one hour of birth;
- Exclusive BF under 6 months: proportion of infants 0–5 months of age who are fed exclusively with breast milk;
- Continued BF at 1 year (12-15 months): proportion of children 12–15 months of age who are fed breast milk;
- Continued BF at 2 years (20-23 months): proportion of children 20-23 months of age who are fed breast milk.

Feeding practices were defined as follows:[22]

Indicator	Permitted to Receive
Exclusive Breastfeeding	• Breast milk from mother or wet nurse or expressed breast milk • NO other liquids or solids except vitamin drops or syrups, mineral supplements, or prescribed medicines
Predominant Breastfeeding	• Breast milk from mother or wet nurse or expressed breast milk • Water and water-based drinks • NO food-based fluid with the exception of fruit juice and sugar water • Vitamin drops or syrups, mineral supplements, or prescribed medicines
Partial Breastfeeding	• Breast milk from mother or wet nurse or expressed breast milk • Any other liquids or non-liquids, including both milk and non-milk products
No Breastfeeding	• Formula, animal's milk and/or solid, semisolid or soft food • NO breast milk
Any Breastfeeding	• Breast milk from mother or wet nurse or expressed breast milk • Includes children exclusively, predominantly, fully or partially breastfed

Because few high-income countries (HICs) report on the above indicators, we calculated the following additional indicators to allow global comparisons:

- Ever BF: infants reported to have been breastfed, even if for a short period; for LMICs, this refers to children born in the 2 years before the survey; for HICs, the reference age groups vary from country to country.
- BF at 6 months: in HICs, the proportion of infants who were breastfed for 6 months or longer; in LMICs with standardized surveys, the proportion of infants aged 4-7 full months (midpoint 6 months) who are breastfed.
- BF at 12 months: in HICs, the proportion breastfed for 12 months or longer; in LMICs, the proportion of 10 to 13-month old children (midpoint 12 months) who are breastfed.

These three indicators are not included in the standard, internationally recommended indicators. They were only used exclusively for comparisons between HICs and LMICs. Otherwise, we report on the standard indicators.

Webappendix 3. Data sources and estimates: countries with standardized surveys (mostly low and middle income countries)

Nationally representative surveys are available for the vast majority of low and middle-income countries (LMICs). The surveys include Demographic and Health Surveys or DHS (http://www.measuredhs.com/aboutsurveys/dhs/start.cfm), Multiple Indicator Cluster Surveys or MICS (http://mics.unicef.org) and a few other national surveys. We obtained the original datasets from 127 surveys, and reanalyzed them using the standard international definitions.

Table 3.1 shows the most recent survey from each country, which was included in the analyses.

Table 3.1. Most recent survey from each country included in the analyses.

Country	Year	Source	Early initiation of BF	Ever BF	Exclusive BF 0-5 mo	BF at 6 mo	BF at 12 mo	Continued BF 20-23 mo	BF 6-23 mo
Afghanistan	2003	MICS					94.3	54.0	
Albania	2008	DHS	43.5	97.4	38.6	86.2	72.3	31.0	53.8
Algeria	2006	MICS			6.9		55.1	22.2	
Argentina	2011	MICS	52.7	95.8	32.7	77.1	62.0	29.1	48.7
Armenia	2010	DHS	35.7	97.3	34.6	75.5	52.3	22.8	38.7
Azerbaijan	2006	DHS	30.9	87.4	11.8	65.8	36.1	16.2	34.7
Bahrain	1995	Gulf Family Health Survey					71.8		
Bangladesh	2012	MICS			56.4		97.0	87.5	
Barbados	2012	MICS							
Belarus	2012	MICS	53.0	92.5	19.0	46.5	32.0	11.5	26.3
Belize	2011	MICS	61.5	91.9	14.7	65.6	63.7	34.9	53.0
Benin	2011	DHS	50.8	94.0	32.5	91.2	85.6	67.9	75.8
Bhutan	2010	MICS	59.0	98.9	48.7	99.4	95.7	65.7	86.5
Bolivia	2008	DHS	63.0	98.0	60.4	95.6	88.1	40.0	73.5
Bosnia and Herzegovina	2012	MICS			18.5			12.2	
Botswana	2007	Other NS			20.3		44.5	5.9	
Brazil	2006	Other NS	41.7	95.8	41.3	72.6	56.0	26.0	47.1
Burkina Faso	2012	Other NS			38.2		97.2		
Burundi	2010	DHS	74.2	98.8	69.3	98.6	96.4	79.1	92.1
Cambodia	2010	DHS	66.4	96.3	73.5	94.1	89.7	43.4	75.6
Cameroon	2011	DHS	40.2	97.4	21.0	96.7	85.5	24.3	67.4
Cape Verde	2005	DHS			59.6		83.1	12.7	
Central African Republic	2010	MICS	43.5	94.8	33.7	96.6	90.9	32.1	75.8

Table 3.1. Most recent survey from each country included in the analyses. (continued)

Country	Year	Source	Early initiation of BF	Ever BF	Exclusive BF 0-5 mo	BF at 6 mo	BF at 12 mo	Continued BF 20-23 mo	BF 6-23 mo
Chad	2010	MICS	28.7	95.6	3.4	95.9	90.4	59.1	83.0
China	2008	Other NS	41.0		27.6	76.2	46.2	9.1	
Colombia	2010	DHS	63.6	97.0	42.9	88.5	62.0	32.5	55.3
Comoros	2012	DHS	34.1	93.5	12.1	95.4	79.4	56.7	73.1
Congo, Dem. Rep.	2013	DHS	52.4	98.2	47.6	97.3	95.6	66.3	87.5
Congo, Rep.	2011	DHS	24.0	94.9	20.5	93.3	86.2	17.0	60.9
Costa Rica	2011	MICS	59.6	97.0	32.5	90.7	50.6	27.5	49.1
Cote d'Ivoire	2011	DHS	31.3	96.6	12.1	95.9	92.1	38.1	76.2
Croatia	1996	MICS							
Cuba	2010	MICS	76.7	98.1	48.6	70.8	30.9	17.1	29.0
Djibouti	2006	MICS	54.9	88.4	1.3	84.9	55.0	18.4	49.3
Dominican Republic	2013	DHS			6.7		43.0	14.4	
Ecuador	2013	Encuesta Nacional de Salud y Nutrición					77.5	18.9	
Egypt, Arab Rep.	2014	DHS			39.7		85.5	20.4	
El Salvador	2008	FESAL			31.4		80.0	54.0	
Equatorial Guinea	2011	DHS					60.4		
Eritrea	2010	Eritrean Population and Health Survey			68.7		96.3	72.8	
Ethiopia	2011	DHS	52.1	97.5		97.6	97.3		92.7
Fiji	2004	Other NS			39.8				
Gabon	2012	DHS	32.7	90.3	6.0	81.1	60.5	3.9	41.3
Gambia, The	2013	DHS			46.8		98.7	42.2	

Table 3.1. Most recent survey from each country included in the analyses. (continued)

Country	Year	Source	Early initiation of BF	Ever BF	Exclusive BF 0-5 mo	BF at 6 mo	BF at 12 mo	Continued BF 20-23 mo	BF 6-23 mo
Georgia	2009	Other NS			54.8		44.7	16.6	
Ghana	2011	MICS	45.9	98.9	45.7	98.8	95.2	37.4	78.4
Guatemala	2008	ENSMI			49.6		84.4	46.2	
Guinea	2012	DHS	16.6	98.3	20.5	97.7	94.9	66.0	90.3
Guinea-Bissau	2010	MICS			38.3		97.8	64.9	
Guyana	2009	DHS	61.0	93.7	33.2	83.9	65.7	49.3	63.9
Haiti	2012	DHS	46.8	96.8	39.7	95.3	90.7	30.8	72.0
Honduras	2012	DHS			31.2		76.8	43.3	
India	2005	DHS	23.3	97.3	46.4	97.6	91.8	72.7	86.8
Indonesia	2012	DHS	49.5	96.0	41.5	88.5	78.0	55.3	73.3
Iran, Islamic Rep.	2010	Other NS			53.1		88.8	51.0	
Iraq	2011	MICS	42.8	92.2	19.6	74.9	57.9	22.7	47.3
Jamaica	2011	MICS	64.7	95.4	23.8	83.3	57.9	31.2	48.2
Jordan	2012	DHS	18.6	93.1	22.7	75.2	54.8	12.9	41.6
Kazakhstan	2010	MICS	67.8	96.4	31.8	85.4	63.0	26.1	49.7
Kenya	2008	DHS	56.1	97.6	31.9	99.3	89.4	53.6	80.9
Kiribati	2009	Other NS			69.0		92.1	81.7	
Korea, Dem. Rep.	2012	National Nutrition Survey			68.9		83.8	21.5	
Kuwait	1996	Gulf Family Health Survey					28.1		
Kyrgyz Republic	2012	DHS	84.1	98.8	56.1	96.5	79.6	37.0	69.8
Lao PDR	2011	MICS	39.1	95.6	40.4	90.2	79.4	40.0	67.0
Lesotho	2009	DHS	50.4	92.6	53.5	85.4	79.8	35.1	66.4
Liberia	2013	DHS	61.4	98.0	55.2	97.6	95.2	44.2	79.6

Table 3.1. Most recent survey from each country included in the analyses. (continued)

Country	Year	Source	Early initiation of BF	Ever BF	Exclusive BF 0-5 mo	BF at 6 mo	BF at 12 mo	Continued BF 20-23 mo	BF 6-23 mo
Macedonia, FYR	2011	MICS	21.0	93.9	23.0	70.1	43.3	12.8	37.5
Madagascar	2012	Other NS			41.9		92.5	83.1	
Malawi	2014	MICS			70.2		98.3	74.5	
Malaysia	1996	National Health and Morbidity Survey			29.0				
Maldives	2009	DHS	60.5	98.2	47.8	92.9	84.5	68.9	78.5
Mali	2012	DHS	58.1	97.3	32.9	95.4	94.1	73.0	86.5
Marshall Islands	2007	Other NS			31.3		71.6	53.1	
Mauritania	2011	MICS			26.9		89.5	35.5	
Mauritius	2002	Other NS			21.0				
Mexico	2012	ENSN			14.4		43.7	14.1	
Moldova	2012	MICS			36.4		57.0	12.2	
Mongolia	2013	MICS			47.1		87.5	52.6	
Montenegro	2013	MICS			16.8		31.2	9.0	
Morocco	2003	DHS	48.2	95.6	31.0	81.8	66.0	14.7	48.9
Mozambique	2011	DHS	77.2	97.3	41.1	97.7	93.0	51.6	82.5
Myanmar	2009	MICS			23.6		94.0	65.4	
Namibia	2013	DHS			48.5		72.1	21.0	
Nauru	2007	NRU			67.2		75.1	64.9	
Nepal	2011	DHS	44.6	98.2	69.6	99.5	95.4	92.6	95.3
Nicaragua	2006	ENDESA			30.6		75.3	42.9	
Niger	2012	DHS	53.2	98.8	23.3	98.6	95.8	50.2	85.8
Nigeria	2013	DHS	33.4	98.1	17.4	95.5	88.7	35.3	74.4

Table 3.1. Most recent survey from each country included in the analyses. (continued)

Country	Year	Source	Early initiation of BF	Ever BF	Exclusive BF 0-5 mo	BF at 6 mo	BF at 12 mo	Continued BF 20-23 mo	BF 6-23 mo
Oman	2000	Other NS					96.8		
Pakistan	2012	DHS	18.4	94.5	37.8	87.6	80.5	56.1	74.8
Panama	1995	MICS			25.0		42.3	21.2	
Papua New Guinea	2006	PNG Demographic and Health Survey			56.1		92.5	71.6	
Paraguay	2008	ENDSSR			24.4		45.8	14.3	
Peru	2013	DHS			72.3		85.3	53.8	
Philippines	2013	DHS	49.8	93.8		77.8	61.5	40.9	
Qatar	1998	Gulf Family Health Survey					40.1		
Romania	2004	Other NS			15.8				
Rwanda	2010	DHS	71.7	98.7	84.9	99.1	95.7	83.5	92.8
Sao Tome and Principe	2008	DHS	43.4	98.4	51.4	99.6	95.8	20.0	68.2
Senegal	2012	DHS	32.1	98.5	37.5	99.5	99.4	47.1	85.7
Serbia	2014	MICS			12.8		32.0	8.9	
Sierra Leone	2013	DHS	54.3	97.4	32.0	94.7	87.8	47.9	79.8
Solomon Islands	2007	DHS			73.7		88.9	67.4	
Somalia	2006	MICS	26.3	93.2	9.1	86.5	61.0	35.4	57.1
South Africa	2003	DHS			8.3		73.7	30.6	
South Sudan	2010	MICS			45.1		87.4	38.0	
Sri Lanka	2006	DHS			75.8		94.8	83.9	
St. Lucia	2012	MICS	49.6	95.5		67.7	52.4		42.5
Sudan	2010	MICS			41.0		91.5	40.1	

Table 3.1. Most recent survey from each country included in the analyses. (continued)

Country	Year	Source	Early initiation of BF	Ever BF	Exclusive BF 0-5 mo	BF at 6 mo	BF at 12 mo	Continued BF 20-23 mo	BF 6-23 mo
Suriname	2010	MICS	44.7	90.4	2.8	63.9	37.0	14.9	27.5
Swaziland	2010	MICS	54.5	90.9	44.1	83.3	66.5	10.7	46.7
Syrian Arab Republic	2009	PAP			42.6		64.2	24.9	
Tajikistan	2012	DHS	49.9	98.7	34.3	92.2	82.3	49.5	72.8
Tanzania	2010	DHS	45.5	97.1	49.9	97.6	95.8	51.0	83.5
Thailand	2012	MICS			12.3		40.4	17.8	
Timor-Leste	2009	DHS	80.2	98.1	51.5	97.5	81.9	33.4	69.8
Togo	2013	DHS			57.4		96.2	61.7	
Tonga	2012	Other NS			52.2		58.2	30.3	
Trinidad and Tobago	2006	MICS	41.2	89.0		61.5	42.1		35.1
Tunisia	2011	MICS	39.9	96.6	8.5	78.0	53.7	19.1	45.0
Turkey	2008	DHS			41.6		74.2	21.6	
Turkmenistan	2000	DHS			13.0		81.8	26.9	
Tuvalu	2007	DHS			34.7		62.5	50.6	
Uganda	2011	MICS	52.7	98.3	62.1	97.0	91.8	45.8	78.7
Ukraine	2012	MICS	65.7	95.4	19.7	87.0	44.1	22.0	39.6
Uzbekistan	2006	MICS	67.1	97.3	26.7	96.0	83.7	37.9	68.6
Vanuatu	2007	MICS	71.9	90.7	39.9	95.3	79.4	31.6	67.9
Vietnam	2014	MICS			24.3		73.2	21.8	
West Bank and Gaza	2010	MICS	61.5	95.8	28.8	91.2	67.3	13.2	47.7
Yemen, Rep.	2013	DHS			10.3		78.2	45.3	
Zambia	2013	DHS			72.5		94.7	41.8	
Zimbabwe	2014	MICS			41.0		89.0	17.1	

Some available surveys from LMICs were not used, either because of data quality concerns (e.g. Afghanistan 2010 MICS) or because they were not nationally representative (Angola 2001 MICS and Lebanon 2009 MICS).

Blank cells in the above table refer to indicators that were not collected in a given survey, or for which there were local questionnaire adaptations that did not allow the internationally standardized indicator to be calculated.

Webappendix 4. Data sources and estimates: countries without standardized surveys (mostly high-income countries)

The objective of this systematic review of the literature was to identify data on breastfeeding levels and trends in countries where standardized national surveys (i.e. DHS or MICS) are not available. Such surveys are routinely carried out in low and middle-income countries, so that the systematic review was focused on studies from high-income countries.

The first step was to identify all high-income countries according to the World Bank Classification.[1] We prioritized countries with 250,000 or more children aged under five years, which did not have international surveys such as DHS (Demographic Health Survey) or MICS (Multiple Indicator Cluster Surveys).

Once these countries were identified, a search strategy was developed and the following databases were searched: PubMed[2], Web of Science[3], EMBASE[4] and CINAHL[5] (Box 4.1). The search was carried out in late 2014 and 1,872 references were obtained of publications dated 2000 or later.

Box 4.1. Search strategy (keywords)

(United States of America OR Russian Federation OR Japan OR United Kingdom OR France OR Germany OR Saudi Arabia OR Italy OR Spain OR Republic of Korea OR Poland OR Canada OR Australia OR Chile OR Netherlands OR Israel OR Belgium OR Czech Republic OR Greece OR Sweden OR United Arab Emirates OR Portugal OR Austria OR Switzerland OR Ireland OR Denmark OR New Zealand OR Norway OR Finland OR Oman OR Kuwait OR Slovakia OR Singapore OR Uruguay) **AND** (breastfeeding OR breast feeding OR breastfeeding practices OR breastfed OR breastfeed OR infant feeding OR infant feeding practices) **AND** (National Health and Nutrition Examination Survey OR Nutrition Survey OR Nutritional Surveys OR Health Survey OR Surveys, Health).

In addition to the formal literature search on the four databases described above, we carried out a thorough search of the grey literature. This included governmental webpages for the above countries relating to health, nutrition and statistical information. Google searches for “country name” and “nutritional survey”/“health survey”/”breastfeeding” were systematically carried out. Snowball techniques were employed based on references to national surveys or databases in the published articles identified in the formal search described in Box 4.1.
All references to articles, reports, databases or websites were inserted in an Endnote database.[6] All such documents were read to ensure that they included nationally representative data using standard international breastfeeding indicators.

References were excluded in the following cases: methodological flaws (such as low response rates or biased sampling); non-standard definitions of breastfeeding; inadequate distinction among feeding groups; studies on local populations. In this review, we were not interested in

[1] Available from: http://data.worldbank.org/country
[2] Available from: www.pubmed.com
[3] Available from: http://thomsonreuters.com/thomson-reuters-web-of-science/
[4] Available from: http://www.elsevier.com/online-tools/embase
[5] Available from: http://health.ebsco.com/products/cinahl-complete
[6] Available from: www.endnote.com

specific studies on factors affecting breastfeeding duration, nor on breastfeeding promotion or support policies or programs or impact of breastfeeding on health.

The main difficulty we faced was the variability in the terminology and indicators related to breastfeeding (see Table 4.1).

Table 4.1. Different classifications of breastfeeding (BF) used in the reviewed literature. The top line represents the World Health Organization classification.

<table>
<tr><th rowspan="2">Exclusive BF</th><th colspan="2">Predominant BF</th><th colspan="2">Partial</th><th>No BF</th></tr>
<tr><td>BF + Water</td><td>BF + Tea</td><td>BF + Food</td><td>BF + Milk</td><td rowspan="3">No BF</td></tr>
<tr><td colspan="4">Only breast (natural) milk (regardless of non-milk foods)</td><td>Mixed Milk</td></tr>
<tr><td colspan="5">Any BF</td></tr>
</table>

After the review of the literature was completed, we identified countries with limited or no information, and wrote to investigators from such countries to inquire about additional sources of data that we may have failed to detect. The following countries were contacted:

- Canada
- Czech Republic
- Denmark
- Germany
- Ireland
- Italy
- Japan
- Korea
- New Zealand
- Norway
- Russia
- Saudi Arabia
- Spain
- Switzerland
- United Kingdom

In most cases, the investigators who were contacted reanalyzed national datasets to produce the estimates that we needed.

Figure 4.1 shows that 94 publications/data sources were selected for identifying the following indicators for breastfeeding (BF): early initiation of BF; exclusive BF (< 4 months and < 6 months); ever BF; any BF at 6 and 12 months.

Results are available in Table 4.2. It is important to note that for many countries, only a few of the required indicators are presented. For example, definitions of "exclusive BF" varied so markedly from country to country that we opted not to present them.

Of the 34 high income countries with 50,000 or more annual births, we were unable to obtain national information for following countries: Belgium, Israel, Kuwait, Poland, Portugal, Slovakia, and United Arab Emirates.

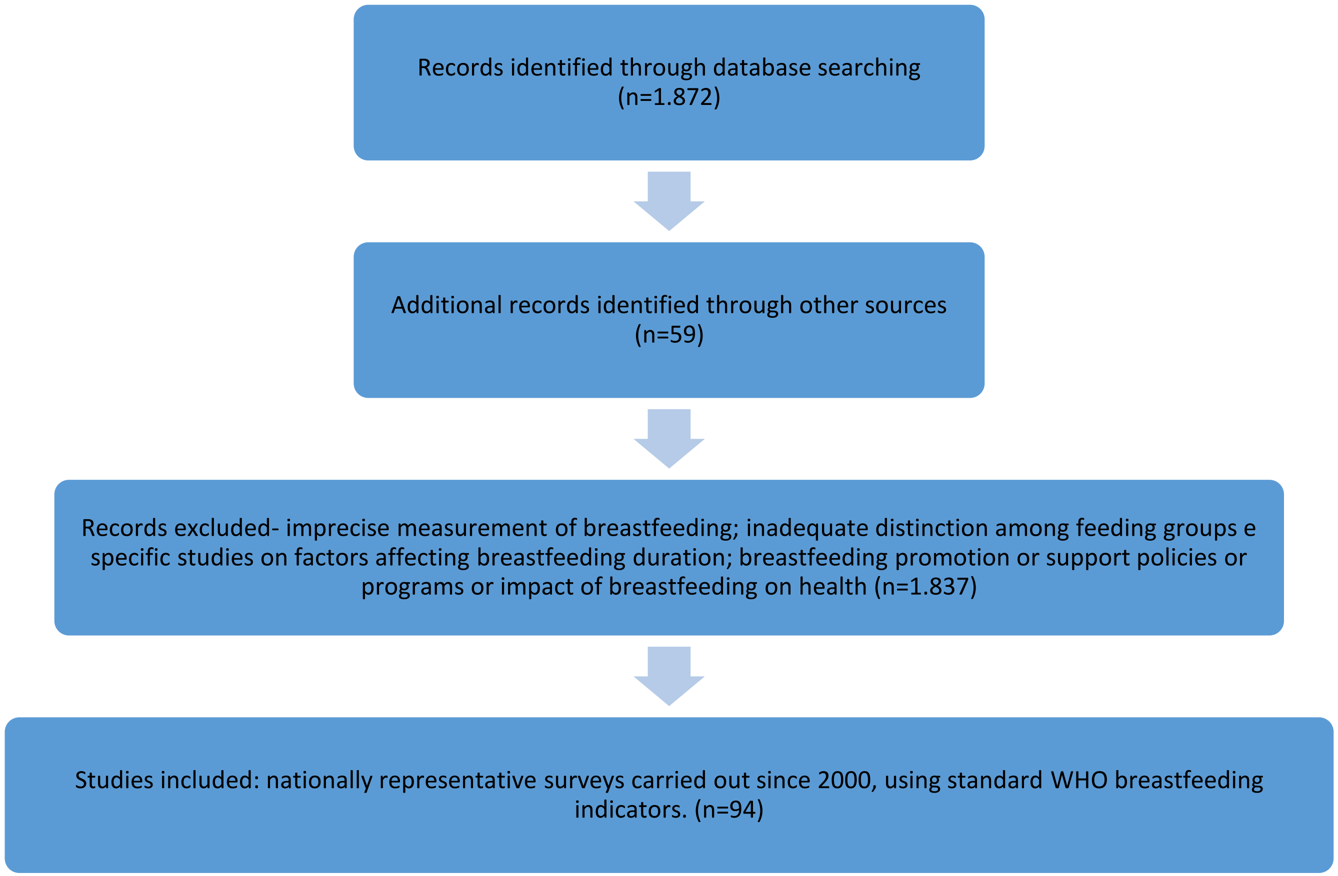

Figure 4.1. Literature review procedure, showing the number of articles/records identified.

Table 4.2. Results from the systematic review of the literature on BF practices in high-income countries.

Country	Publication date	Reference period	Ever BF	Early initiation of BF	Any BF at age 6 mo	Any BF at age 12 mo	Data source	Response rate	Source
Australia	2011	2010	92	NA	56	30	National survey	56%	Australian Institute of Health and Welfare, 2011 [23]
Austria	2009	2006	93	80	42*	16	National survey	16%	Schlögel, 2009 [24]
Canada	2013	2011-12	89	NA	30*	9	National survey	72%	Gionet, 2013 [25]
Chile	2012	2011-12	95	NA	41	21	Health records	95%	Atalah,2004 [26]
Czech Republic	2013	2005	96	NA	42*	16	Health records	NA	OECD, 2013 [27] and 12mo from personal communication (Dagmar Schneidrová)
Denmark	2014	2013	NA	NA	13	3*	Health records	NA	Statens Serum Institut, 2014 [28]
Finland	2012	2010	92	NA	58	34	National survey	NA	Uusitalo, 2012 [29]
France	2012-13	2012-13	63	NA	23	9	National survey	35%	Institut de Veille Sanitaire, 2014 [30]
Germany	2014	2009-12	82	NA	50*	23	National survey	67%	von der Lippe, 2015 [31] and personal communication (Elena von der Lippe)
Greece	2007-08	2007-08	88	27	22	6	National survey	66%	Institute of Child Health, 2009 [32]
Ireland Republic	2014	2012	55			2*	National cohort	69%	Growing Up in Ireland
Italy	2013	2013	86	94	46	19	National survey	NA	Italian National Institute of Statistics, 2013 [33]
Japan	2009	2009	95	NA	63*	60	National survey	NA	Personal communication (Naho Morizaki)
Netherlands	2009	2006-08	NA	75	32	11*	National survey	54%	Statistics Netherlands, 2009 [34]

Table 4.2. Results from the systematic review of the literature on BF practices in high-income countries. (continued)

Country	Publication date	Reference period	Ever BF	Early initiation of BF	Any BF at age 6 mo	Any BF at age 12 mo	Data source	Response rate	Source
New Zealand	2014	2006	NA	NA	60	44	National survey	NA	New Zealand Ministry of Health, 2014 [35] and personal communication (Riz Firestone)
Norway	2014	2013	95	NA	71	35	National survey	NA	Norway Helsedirektoratet, 2014 [36]
Oman	2013	2007-11	NA	85	15*	95	National survey	NA	UNICEF, 2013 [37]
Republic of Korea	2013	2012	88	NA	61	46	National survey	NA	Chung [38] and personal communication (Chong-Woo Bae)
Russian Federation	2015	2013	96	NA	36	20	Health records	NA	Personal communication (Elena Keshishian) based on pediatric records (range 18-22% by region)
Saudi Arabia	2005	2004-05	92	23	10	2	National survey	NA	El Mouzan, 2009 [39]
Singapore	2014	2011	96	NA	42	19*	National survey	NA	Singapore Goverment, 2014 [40]
Spain	2013	2011	77	NA	47	23*	National survey	71%	Gobierno de España, 2013 [41]
Sweden	2012	2010	98	NA	52	16	National survey	NA	Official Statistics of Sweden, 2012 [42]
Switzerland	2010	2003	94	NA	62	28	National survey	74%	Merten, 2005 [43]
United Kingdom	2004	2005-10	81	74	34	0.5	National survey	35%	McAndrew, 2012 [44]
United States of America	2011	2011	79	NA	49	27	National survey	60%	CDC, 2014 [45]
Uruguay	2011	2011	98	59	64*	45	National survey of facility users	97%	Ministerio de Salud Pública, 2011 [46]

*Estimates modelled using fractional polynomial regression (BF at 6 months modeled from BF at 12 months and vice-versa). NA = not available

Webappendix 5: Statistical methods

Weighting

The paper presents in Figures 2, 4 and 5 averages of breastfeeding rates at global level, and by UN regions and World Bank country income classification. In each of the analyses we calculated averages for the relevant estimates using only available data weighted by the size of population of children under two years of age in 2010. This year was selected because it was the median for the most recent surveys for the countries in study. The source for population estimates was the Population Division, Department of Economic and Social Affairs, United Nations (http://esa.un.org/wpp/Excel-Data/population.htm).

Time trends

Time trends for breastfeeding were estimated at national level and for the poorest and richest wealth quintiles. We used two indicators: exclusive breastfeeding for children 0-5 months of age and continued breastfeeding at 12 months of age (based on survey data for children 12-15 months). The inclusion criteria for surveys were:

1. All surveys for which the national and respective quintile-specific estimates were available were considered for inclusion in the analysis
2. The estimates of the resulting set of surveys went through a vetting process by Unicef, and those based on non-standard definitions or on data that were considered low quality were excluded.
3. Surveys with unweighted national sample size < 50 for a given indicator were excluded for the respective indicator. Surveys were not dropped only based on sample size for quintile-specific estimates.
4. After applying the previous rules, we excluded countries who had less than 2 surveys, and those where the time between 1st and last surveys was less than 3 years.

After applying these criteria, we included 66 countries and 214 surveys for the exclusive breastfeeding trend. For continued breastfeeding, we included 67 countries and 217 surveys. Table 5.1 presents the surveys used in the breastfeeding trend analysis.

The trends were estimated using multilevel linear regression models (hierarchical mixed models) that take into account that countries contribute with two or more surveys for the analysis. This allow us to estimate a trend that will, in a way, average country level trends over time. As countries differ widely in population size, the estimates were weighted by population size of children under the age of two years. We used estimates from the Population Division, Department of Economic and Social Affairs, United Nations (http://esa.un.org/wpp/Excel-Data/population.htm). Under-two population estimates are available at five year intervals, and we used estimates from the year closest to the starting date of the survey.

We started by fitting straight line models, and explored departures from linearity using fractional polynomial models. For all six models fitted, we found the polynomial models did not improve on the linear fits. We, thus, present the results of the linear fits for exclusive breastfeeding for children 0-5 months and continued breastfeeding for age 12 at national level and for the extreme wealth quintiles in Table 5.2. The coefficients of the models obtained can be interpreted as average annual change in percentage points of breastfeeding.

Table 5.1. Set of surveys used for the breastfeeding trend analyses. These are restricted to surveys with information on household assets that allow disaggregation by wealth quintile.

Country	Surveys
Albania	MICS 2005 and MICS 2008
Armenia	DHS 2000, DHS 2005, and DHS 2010
Bangladesh	DHS 1993, DHS 1996, DHS 1999, DHS 2004, DHS 2006, DHS 2007, and DHS 2011
Belarus	MICS 2005 and MICS 2012
Belize	MICS 2006 and MICS 2011
Benin	DHS 1996, DHS 2001, DHS 2006, and DHS 2011
Bolivia	DHS 1994, DHS 1998, DHS 2003, and DHS 2008
Bosnia and Herzegovina	MICS 2006 and MICS 2011
Brazil	DHS 1996 and DHS 2006
Burkina Faso	DHS 1998, DHS 2003, DHS 2006, and DHS 2010
CAR	DHS 1994, DHS 2006, and DHS 2010
Cambodia	DHS 2000, DHS 2005, and DHS 2010
Cameroon	DHS 1998, DHS 2004, DHS 2006, and DHS 2011
Chad	DHS 1996, DHS 2004, and DHS 2010
China	UNICEF 2003 and UNICEF 2008
Colombia	DHS 1995, DHS 2000, DHS 2005, and DHS 2010
Comoros	DHS 1996 and DHS 2012
Congo (Brazzaville)	DHS 2005 and DHS 2011
Congo Democratic Republic	DHS 2007, DHS 2010, and DHS 2013
Côte d'Ivoire	DHS 1994, DHS 1998, DHS 2006, and DHS 2011
Dominican Republic	DHS 1996, DHS 1999, DHS 2002, and DHS 2007
Egypt	DHS 1995, DHS 2000, DHS 2005, and DHS 2008
Ethiopia	DHS 2000, DHS 2005, and DHS 2011
Gabon	DHS 2000 and DHS 2012
Ghana	DHS 1993, DHS 1998, DHS 2003, DHS 2006, DHS 2008, and DHS 2011
Guatemala	DHS 1995 and DHS 1998
Guinea	DHS 1999, DHS 2005, and DHS 2012
Guyana	MICS 2006 and MICS 2009
Haiti	DHS 1994, DHS 2000, DHS 2005, and DHS 2012
Honduras	DHS 2005 and DHS 2011
India	DHS 1998 and DHS 2005
Indonesia	DHS 1997, DHS 2002, DHS 2007, and DHS 2012
Jordan	DHS 1997, DHS 2002, DHS 2007, and DHS 2012
Kazakhstan	DHS 1995, DHS 1999, DHS 2006, and DHS 2010
Kenya	DHS 1993, DHS 1998, DHS 2003, and DHS 2008
Kyrgyzstan	DHS 1997, DHS 2005, and DHS 2012
Lao	MICS 2006 and MICS 2011
Lesotho	DHS 2004 and DHS 2009
Liberia	DHS 2007 and DHS 2013
Madagascar	DHS 1997, DHS 2003, and DHS 2008
Malawi	DHS 2000, DHS 2004, DHS 2006, and DHS 2010

Table 5.1. Set of surveys used for the breastfeeding trend analyses. These are restricted to surveys with information on household assets that allow disaggregation by wealth quintile. (continued)

Country	Surveys
Mali	DHS 1995, DHS 2001, DHS 2006, and DHS 2012
Mongolia	MICS 2005 and MICS 2010
Mozambique	DHS 1997, DHS 2003and DHS 2011
Namibia	DHS 2000 and DHS 2006
Nepal	DHS 1996, DHS 2001, DHS 2006, and DHS 2011
Nicaragua	DHS 1997 and DHS 2001
Niger	DHS 1998, DHS 2006, and DHS 2012
Nigeria	DHS 2003, DHS 2007, DHS 2008, DHS 2011 and DHS 2013
Pakistan	DHS 2006 and DHS 2012
Peru	DHS 1996, DHS 2000, DHS 2004, DHS 2005, DHS 2006, DHS 2007, DHS 2008, DHS 2009, DHS 2010, DHS 2011, and DHS 2012
Philippines	DHS 1993, DHS 1998, DHS 2003, DHS 2008, and DHS 2013
Rwanda	DHS 2000, DHS 2005, and DHS 2010
Senegal	DHS 1997, DHS 2005, DHS 2010, and DHS 2012
Serbia	MICS 2005 and MICS 2010
Sierra Leone	MICS 2005, MICS 2008, MICS 2010, and MICS 2013
Suriname	MICS 2006 and MICS 2010
Swaziland	DHS 2006 and DHS 2010
Tajikistan	MICS 2005 and MICS 2012
Tanzania	DHS 1996, DHS 1999, DHS 2004, and DHS 2010
Togo	DHS 1998, DHS 2006, and DHS 2010
Turkey	DHS 1993, DHS 1998, and DHS 2003
Uganda	DHS 1995, DHS 2006, and DHS 2011
Ukraine	MICS 2005, MICS 2007, and MICS 2012
Uzbekistan	DHS 1996 and DHS 2006
Vietnam	DHS 1997, DHS 2002, DHS 2006, and DHS 2010
Zambia	DHS 1996, DHS 2001, and DHS 2007
Zimbabwe	DHS 1994, DHS 1999, DHS 2005, DHS 2009, and DHS 2010

Table 5.2. Model coefficients for the breastfeeding trend analyses.

	Level of analysis	Number of countries/surveys	Average annual change (pct points)	P value
Exclusive breastfeeding for children 0-5 months	National	66/214	0.54	<0.001
	Q1 (poorest)		0.43	0.043
	Q5 (richest)		0.98	<0.001
Continued breastfeeding for children at 12 months	National	67/217	-0.13	0.149
	Q1 (poorest)		-0.14	0.200
	Q5 (richest)		0.12	0.339

Estimation of missing breastfeeding estimates at specific ages

Continued breastfeeding at 12 months for LMICs

Different sources of information on breastfeeding use different ways to estimate continued breastfeeding at 12 months. From survey data, the usual approach is to estimate BF for children aged 12-15 months of age, instead of using only children that are exactly 12 months old. This is done mostly to guarantee sample sizes big enough for fair precision of the estimates. However, as this is a period of rapid weaning, the inclusion of older children can produce underestimates.

For surveys where data is available, we recalculated breastfeeding prevalence for children age 10-13, so that enough sample was available and the age midpoint was 12 months. For countries where data was not available, and estimates were obtained from reports, these were usually based on children aged 12-15 months. To avoid using different reference age groups in our analyses we developed a model to predict breastfeeding at 10-13 months from estimates of breastfeeding at 12-15. For this model, we used all DHS and MICS surveys phase 3 onwards with data on breastfeeding – 181 DHS, 71 MICS and 3 from other sources. Breastfeeding at 10-13 and at 12-15 months was estimated for all these surveys. Logit transforms of both estimates were used in a fractional polynomials ordinary least squares model using the **fracpoly** subcommand in Stata 13. Logit transforms were used to avoid estimating predicted values outside the 0-100 range, given many surveys had rates very close to 100%. From 44 possible models, we selected the best fitting one that included the powers 1 and ½. The model presented an R^2 of 96%. Figure 5.1 shows the final predictive model used, with values back transformed to their original scale.

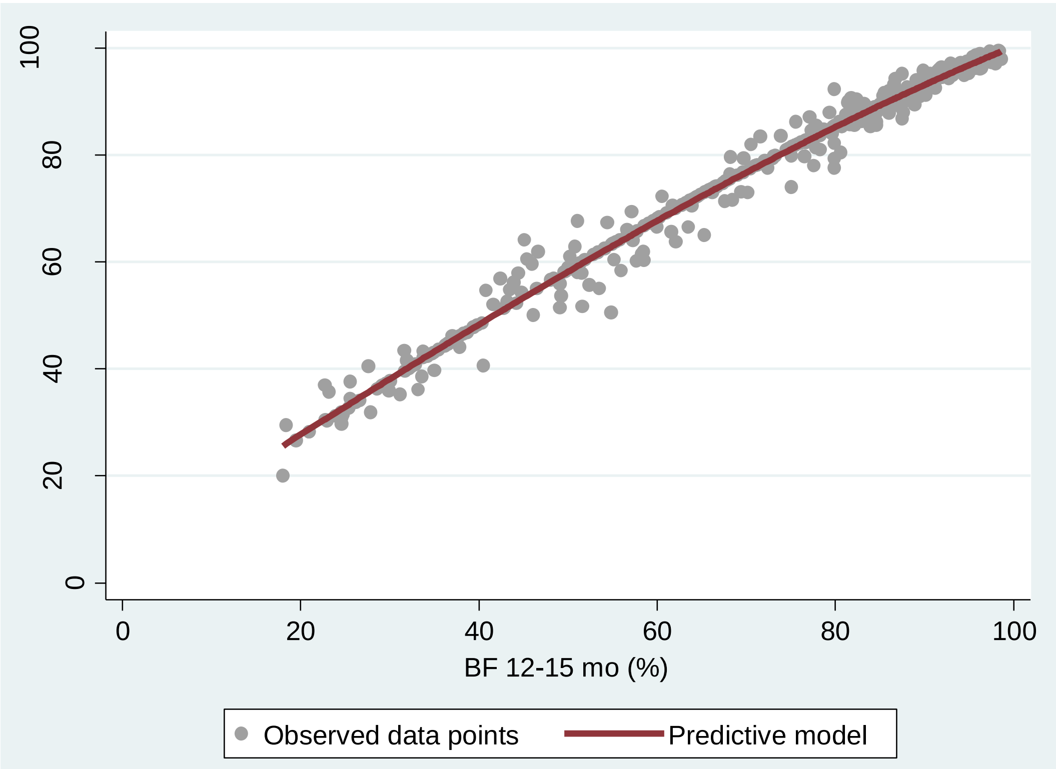

Figure 5.1. Predictive model to estimate breastfeeding at age 10-13 from breastfeeding at 10-15 months.

Any breastfeeding at 6 and 12 months for HICs

Our world map of breastfeeding presents the proportion of children receiving any breastfeeding at 12 months of age. Data on breastfeeding from HICs is limited, and for several countries only BF at 6 months or at 12 months is available. In order to complete the data for the map, we needed estimates at 12 months for as many countries as possible. Thus, we used data from HICs that had data for both ages to derive a predictive model for BF at 12 from BF at 6 months. The countries that contributed data for this model are listed in Table 5.3. The best predictive model was selected using fractional polynomials ordinary least squares models using the fracpoly subcommand in Stata 13. From 44 possible models, we selected the best fitting one that included the powers 3 and 3 again (applied to the logarithm of the predictor). The model presented an R^2 of 81%. Figure 5.2 shows the final predictive model used, with values back transformed to their original scale. A similar approach using the same data points was used to estimate BF at 6 months from BF at 12, in order to complete Table 4.2.

Table 5.3. Sources of data for predicting breastfeeding at 12 months from breastfeeding at 6 months for HICs.

Country	Year
Australia	2010
Belgium	2003-07
Chile	2011-12
Finland	2010
France	2012-13
Greece	2007-08
Italy	2013
Luxembourg	2008
Norway	2013
Republic of Korea	2012
Russian Federation	2014
Saudi Arabia	2004-05
Sweden	2010
Switzerland	2003
United States of America	2011

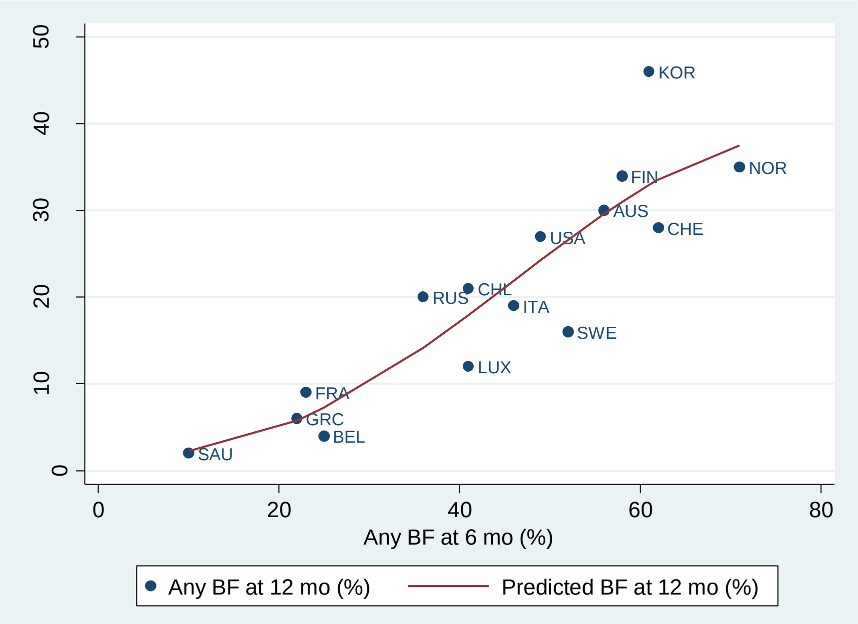

Figure 5.2. Predictive model to estimate breastfeeding at age 12 from breastfeeding at 6 months in HICs.

Webappendix 6. Systematic review – search terms

Search terms

Effects on children, adolescents or adults according to bf pattern

Neonatal, Infant, and Child Mortality Rates

Database	Search terms
PUBMED	#1 (("breast feeding"[MeSH Terms] OR ("breast"[All Fields] AND "feeding"[All Fields]) OR "breast feeding"[All Fields] OR "breastfeeding"[All Fields]) OR ("breast feeding"[MeSH Terms] OR ("breast"[All Fields] AND "feeding"[All Fields]) OR "breast feeding"[All Fields])) OR "human milk"[All Fields] OR "breast milk"[All Fields] OR ("exclusive breastfeeding"[All Fields] OR "exclusive breast feeding"[All Fields]) OR continuation[All Fields] OR continuing[All Fields] OR continued[All Fields] OR "stopping"[All Fields] OR stopped[All Fields] OR stop[All Fields] #2 ("mortality"[Subheading] OR "mortality"[All Fields] OR "mortality"[MeSH Terms]) OR ("infant mortality"[MeSH Terms] OR ("infant"[All Fields] AND "mortality"[All Fields]) OR "infant mortality"[All Fields] OR ("neonatal"[All Fields] AND "mortality"[All Fields]) OR "neonatal mortality"[All Fields]) OR ("infant mortality"[MeSH Terms] OR ("infant"[All Fields] AND "mortality"[All Fields]) OR "infant mortality"[All Fields]) OR ("child mortality"[MeSH Terms] OR ("child"[All Fields] AND "mortality"[All Fields]) OR "child mortality"[All Fields]) #3 ("pneumonia"[MeSH Terms] OR "pneumonia"[All Fields]) OR ("diarrhoea"[All Fields] OR "diarrhea"[MeSH Terms] OR "diarrhea"[All Fields]) OR ("sepsis"[MeSH Terms] OR "sepsis"[All Fields]) OR ("infection"[MeSH Terms] OR "infection"[All Fields] OR "infections"[All Fields]) OR (preterm[All Fields] OR ("infant, premature"[MeSH Terms] OR ("infant"[All Fields] AND "premature"[All Fields]) OR "premature infant"[All Fields] OR "prematurity"[All Fields])) OR ("malnutrition"[MeSH Terms] OR "malnutrition"[All Fields]) #4 (Addresses[ptyp] OR Autobiography[ptyp] OR Bibliography[ptyp] OR Biography[ptyp] OR pubmed books[filter] OR Case Reports[ptyp] OR Congresses[ptyp] OR Consensus Development Conference[ptyp] OR Directory[ptyp] OR Duplicate Publication[ptyp] OR Editorial[ptyp] OR Festschrift[ptyp] OR Guideline[ptyp] OR In Vitro[ptyp] OR Interview[ptyp] OR Lectures[ptyp] OR Legal Cases[ptyp] OR News[ptyp] OR Newspaper Article[ptyp] OR Personal Narratives[ptyp] OR Portraits[ptyp] OR Retracted Publication[ptyp] OR Twin Study[ptyp] OR Video-Audio Media[ptyp]) #1 AND (#2 OR #3) #5 NOT #4

Diarrhea incidence/hospitalization, lower respiratory infections incidence/prevalence and respiratory infections hospitalization

Database	Search terms
MEDLINE	Mortality: Infant mortality; pneumonia AND mortality; pneumonia and death; respiratory infection AND mortality; respiratory infection and death; lower respiratory tract infection and mortality; lower respiratory tract infection and death; diarrhea AND mortality; diarrhea AND death. Hospitalization: hospitalization; AND infant OR childhood; AND pneumonia OR respiratory infection OR lower respiratory tract infection OR diarrhea Incidence/prevalence: infant OR childhood; AND pneumonia OR respiratory infection OR lower respiratory tract infection OR diarrhea

Acute otitis media

Database	Search terms
PUBMED	#1 "Breast Feeding"[Mesh] #2 "Milk, Human"[Mesh] #3 Breast[All Fields] AND Feed*[All Fields] #4 Breast-fe*[All Fields] #5 Infant fe* [All Fields] #6 Infant nutrition* [All Fields] #7 #1 OR #2 OR #3 OR #4 OR #5 OR #6 #8 “Otitis Media” [Mesh] #9 Otitis media[All Fields] #10 Middle ear infection[All Fields] #11 #8 OR #9 OR #10 #12 #7 AND #11 #13 animals [mh] NOT humans [mh] #14 #12 NOT #13
EMBASE	#1 exp breast feeding/ #2 exp breast milk/ #3 Breast AND Feed* #4 Breast-fe*.mp. #5 Infant fe*.mp. #6 Infant nutrition*.mp. #7 1 OR 2 OR 3 OR 4 OR 5 OR 6 #8 exp otitis media/ #9 exp ear infection/ #10 otitis media.mp. #11 middle ear infection.mp. #12 8 OR 9 OR 10 OR 11 #13 7 AND 12 #14 limit 13 to human
CINAHL	#1 "Breast Feeding" #2 "Milk, Human" #3 Breast AND Feed* #4 Breast-fe* #5 Infant fe* #6 Infant nutrition* #7 S1 OR S2 OR S3 OR S4 OR S5 OR S6 #8 “Otitis Media” #9 Otitis media #10 Middle ear infection #11 S8 OR S9 OR S10 #12 S7 AND S11 **For S12 select the ‘edit’ option – tick limit option ‘Human’

Allergic disease

Database	Search terms
PUBMED	#1 "Breast Feeding"[Mesh] #2 "Milk, Human"[Mesh] #3 Breast[All Fields] AND Feed*[All Fields] #4 Breast-fe*[All Fields] #5 Infant fe* [All Fields] #6 Infant nutrition* [All Fields] #7 #1 OR #2 OR #3 OR #4 OR #5 OR #6 #8 “Asthma”[Mesh] #9 "Respiratory Sounds"[Mesh] #10 Wheez*[All Fields] #11 #8 OR #9 OR #10 #12 "Eczema"[Mesh] #13 "Dermatitis, Atopic"[Mesh] #14 atopic eczema* [All Fields] #15 #12 OR #13 OR #14 #16 "Rhinitis, Allergic, Seasonal"[Mesh] #17 "Rhinitis, Allergic, Perennial"[Mesh] #18 Allergic rhinitis [All fields] #19 Hay fever [All fields] #20 #16 OR #17 OR #18 OR #19 #21 "Food Hypersensitivity"[Mesh] #22 Food allerg*[All Fields] #23 Food hypersensit*[All Fields] #24 #21 OR #22 OR #23 #25 #7 AND (#11 OR #15 OR #20 OR #24) #26 animals [mh] NOT humans [mh] #27 #25 NOT #26
EMBASE	#1 exp breast feeding/ #2 exp breast milk/ #3 Breast AND Feed* #4 Breast-fe*.mp. #5 Infant fe*.mp. #6 Infant nutrition*.mp. #7 1 OR 2 OR 3 OR 4 OR 5 OR 6 #8 exp asthma/ #9 exp wheezing/ #10 wheez*.mp. #11 8 OR 9 OR 10 #12 exp eczema/ #13 exp atopic dermatitis/ #14 atopic eczema*.mp. #15 12 OR 13 OR 14 #16 exp allergic rhinitis/ #17 allergic rhinitis.mp. #18 hay fever.mp. #19 16 OR 17 OR 18 #20 exp food allergy/ #21 food allerg*.mp. #22 food hypersensit*.mp. #23 20 OR 21 OR 22 #24 7 AND (11 OR 15 OR 19 OR 23) #25 limit 24 to human
CINAHL	#1 "Breast Feeding"

	#2 "Milk, Human" #3 Breast AND Feed* #4 Breast-fe* #5 Infant fe* #6 Infant nutrition* #7 S1 OR S2 OR S3 OR S4 OR S5 OR S6 #8 "Asthma" #9 "Wheezing" #10 Wheez* #11 S8 OR S9 OR S10 #12 "Eczema" #13 "Dermatitis, Atopic" #14 atopic eczema* #15 S12 OR S13 OR S14 #16 "Rhinitis, Allergic, Seasonal" #17 "Rhinitis, Allergic, Perennial" #18 Allergic rhinitis #19 Hay fever #20 S16 OR S17 OR S18 OR S19 #21 "Food Hypersensitivity" #22 Food allerg* #23 Food hypersensit* #24 S21 OR S22 OR S23 #25 S7 AND (S11 OR S15 OR S20 OR S24) **For S24 select the 'edit' option – tick limit option 'Human'

Infant nutrition (length / weight / BMI or weight/length)

Database	Search terms
PUBMED	"Breast Feeding"[Mesh] AND ((Clinical Trial[ptyp] OR Clinical Trial, Phase III[ptyp] OR Controlled Clinical Trial[ptyp] OR Evaluation Studies[ptyp] OR Meta-Analysis[ptyp] OR Multicenter Study[ptyp] OR Randomized Controlled Trial[ptyp]) AND ("2006/01/01"[PDAT] : "2014/22/12"[PDAT]))
SCIELO	2006 or 2007 or 2008 or 2009 or 2010 or 2011 or 2012 or 2013 or 2014 [Ano de publicação] and aleitamento or breastfeeding or breastfeeding intervention or breastfeeding counseling or aleitamento materno or amamentação [Assunto] and peso or weight or altura or lenght or hight or indice de massa corporal or body mass index or hemoglobina or anemia or estado nutricional or medidas antropométricas or nutritional status or haemoglobin or ferro or anaemia or deficiência de ferro or iron deficiency [Todos os índices]
LILACS	"ENSAIO CLINICO" or "ENSAIO CLINICO CONTROLADO" or "ENSAIO CLINICO CONTROLADO ALEATORIO" or "ENSAIO CLINICO FASE III" or "ESTUDOS DE AVALIACAO" or "METANALISE" or "REVISAO" [Tipo de publicação] and ("ALEITAMENTO" or "ALEITAMENTO materno") or "amamentacao" [Descritor de assunto] and peso or weight or altura or length or hight or indice de massa corporal or body mass index or hemoglobina or anemia or estado nutricional or medidas antropométricas or nutritional satus or haemoglobin or ferro or anaemia or deficiência de ferro or iron deficiency [Palavras]
COCHRANE	tw:(aleitamento materno AND (instance:"regional") AND (collection:("02-cochrane"))) AND (instance:"regional") AND (mj:("Aleitamento Materno") AND type_of_study:("systematic_reviews") AND limit:("Humans"))
EMBASE	breastfeeding OR 'breastfeeding promotion' OR 'breast feeding' AND ([controlled clinical trial]/lim OR [randomized controlled trial]/lim OR [meta analysis]/lim) AND [article]/lim AND [humans]/lim NOT [medline]/lim AND [2006-2014]/py

Dental caries

Database	Search terms
PUBMED	#1 "Breast Feeding"[Mesh] #2 "Milk, Human"[Mesh] #3 Breast[All Fields] AND Feed*[All Fields] #4 Breast-fe*[All Fields] #5 Infant fe* [All Fields] #6 Infant nutrition* [All Fields] #7 #1 OR #2 OR #3 OR #4 OR #5 OR 6 #8 Dental caries (MeSH) #9 Tooth decay #10 "Early childhood caries" #11 "Nursing bottle caries" #12 #8 OR #9 OR #10 OR #11 #13 animals [mh] NOT humans [mh] #14 #7 AND #12 #15 #14 NOT #13
EMBASE	#1 'breast feeding'/exp #2 'breast milk'/exp #3 Breast AND Feed* #4 Breast-fe* #5 Infant fe* #6 Infant nutrition* #7 #1 OR #2 OR #3 OR #4 OR #5 OR 6 #8 'dental caries'/exp #9 Tooth decay #10 "Early childhood caries" #11 "Nursing bottle caries" #12 #8 OR #9 OR #10 OR #11 #13 [animals]/lim NOT [humans]/lim #14 #7 AND #12 #15 #14 NOT #13
CINAHL	#1 "Breast Feeding" #2 "Milk, Human" #3 Breast AND Feed* #4 Breast-fe* #5 Infant fe* #6 Infant nutrition* #7 S1 OR S2 OR S3 OR S4 OR S5 OR S6 #8 dental caries #9 tooth decay #10 early childhood caries #11 nursing bottle caries #12 S8 OR S9 OR S10 OR S11 #13 S7 AND S12 **For #13 limit to 'Human'

Malocclusion

Database	Search terms
PUBMED	(“Breast Feeding” OR “Bottle Feeding” OR “Infant Formula” OR “Milk, Human” OR “Weaning” OR “Breastfeeding” OR “Predominant Breastfeeding” OR “Continuing Breastfeeding” OR “Continued Breastfeeding” OR “Breastfed” OR “Breastfeed” OR “Formula milk” OR “Formula feed”) AND (“Malocclusion” OR “Openbite” OR “Overbite” OR “Malocclusion, Angle Class III” OR “Malocclusion, Angle Class II” OR “Malocclusion, Angle Class I” OR “Overjet” OR “Cross bite” OR “Canine relationship” OR “Molar relationship” OR “Deep bite” OR “Foster & Hamilton” OR “Dental Aesthetic Index”)
SCOPUS	TITLE-ABS-KEY ("Breast Feeding" OR "Breastfeeding" OR "Breast feeding" OR "Predominant Breastfeeding" OR "Continuing Breastfeeding" OR "Continued Breastfeeding" OR "Breastfed" OR "Breastfeed" OR "Bottle Feeding" OR "Bottle Feed" OR "Bottle fed" OR "Infant Formula" OR "Milk, Human" OR "Human Milk" OR "Formula milk" OR "Formula feed" OR "Formula fed" OR "Weaning") AND TITLE-ABS-KEY ("Malocclusion" OR "Openbite" OR "Overbite" OR "Overjet" OR "Open bite" OR "Over bite" OR "Cross bite" OR "Crossbite" OR "Over jet" OR "Openbite" OR "Canine relationship" OR "Molar relationship" OR "Deep bite" OR "Malocclusion, Angle Class III" OR "Malocclusion, Angle Class II" OR "Malocclusion, Angle Class I" OR "Foster & Hamilton" OR "Dental Aesthetic Index")
EMBASE AND WEB OF KNOWLEDGE	("Breast Feeding" OR "Breastfeeding" OR "Breast feeding" OR "Predominant Breastfeeding" OR "Continuing Breastfeeding" OR "Continued Breastfeeding" OR "Breastfed" OR "Breastfeed" OR "Bottle Feeding" OR "Bottle Feed" OR "Bottle fed" OR "Infant Formula" OR "Milk, Human" OR "Human Milk" OR "Formula milk" OR "Formula feed" OR "Formula fed" OR "Weaning") AND ("Malocclusion" OR "Openbite" OR "Overbite" OR "Overjet" OR "Open bite" OR "Over bite" OR "Cross bite" OR "Crossbite" OR "Over jet" OR "Openbite" OR "Canine relationship" OR "Molar relationship" OR "Deep bite" OR "Malocclusion, Angle Class III" OR "Malocclusion, Angle Class II" OR "Malocclusion, Angle Class I" OR "Foster & Hamilton" OR "Dental Aesthetic Index")
SCIELO AND LILACS	(tw: ("Breast Feeding" OR "Breastfeeding" OR "Breast feeding" OR "Predominant Breastfeeding" OR "Continuing Breastfeeding" OR "Continued Breastfeeding" OR "Breastfed" OR "Breastfeed" OR "Bottle Feeding" OR "Bottle Feed" OR "Bottle fed" OR "Infant Formula" OR "Milk, Human" OR "Human Milk" OR "Formula milk" OR "Formula feed" OR "Formula fed" OR "Weaning") AND tw: ("Malocclusion" OR "Openbite" OR "Overbite" OR "Overjet" OR "Open bite" OR "Over bite" OR "Cross bite" OR "Crossbite" OR "Over jet" OR "Openbite" OR "Canine relationship" OR "Molar relationship" OR "Deep bite" OR "Malocclusion, Angle Class III" OR "Malocclusion, Angle Class II" OR "Malocclusion, Angle Class I" OR "Foster & Hamilton" OR "Dental Aesthetic Index"))

Blood pressure

Database	Search terms
PUBMED	(breastfeeding OR "breast feeding" OR breastfed OR breastfeed OR “bottle feeding” OR “bottle fed” OR “bottle feed” OR “infant feeding” OR “human milk” OR “formula milk” OR “formula feed” OR “formula fed” OR weaning) AND ("blood pressure" or hypertension or "systolic blood pressure" or "diastolic blood pressure")

Overweight and/or obesity

Database	Search terms
PUBMED	(breastfeeding OR "breast feeding" OR breastfed OR breastfeed OR “bottle feeding” OR “bottle fed” OR “bottle feed” OR “infant feeding” OR “human milk” OR “formula milk” OR “formula feed” OR “formula fed” OR weaning) AND (overweight or obesity or "body mass index" or growth or weight or height or "child growth")

Total cholesterol

Database	Search terms
PUBMED	(breastfeeding OR "breast feeding" OR breastfed OR breastfeed OR “bottle feeding” OR “bottle fed” OR “bottle feed” OR “infant feeding” OR “human milk” OR “formula milk” OR “formula feed” OR “formula fed” OR weaning) AND (cholesterol or LDL or HDL or triglycerides or "blood lipids")

Type-2 diabetes

Database	Search terms
PUBMED	(breastfeeding OR "breast feeding" OR breastfed OR breastfeed OR “bottle feeding” OR “bottle fed” OR “bottle feed” OR “infant feeding” OR “human milk” OR “formula milk” OR “formula feed” OR “formula fed” OR weaning) AND (diabetes or glucose or glycemia)

Intelligence

Database	Search terms
PUBMED	(breastfeeding OR "breast feeding" OR breastfed OR breastfeed OR “bottle feeding” OR “bottle fed” OR “bottle feed” OR “infant feeding” OR “human milk” OR “formula milk” OR “formula feed” OR “formula fed” OR weaning) AND (schooling or development or intelligence)

Interventions to promote breastfeeding

Database	Search terms
PUBMED	#1 (Breastfeeding OR Breast Feeding OR (Exclusive AND Breastfeeding [All Fields]) OR (Continued AND Breast feeding [All Fields]) OR Lactation OR Human Milk OR Breast Milk [MeSH Majr]) #2 (Counseling OR Peer OR education OR health education OR (intervention[All Fields]) OR family practice OR support OR Groups OR health worker OR physician [MeSH terms]) #3 (Social media OR social networking OR mass media OR health campaigns OR (group AND meeting [All Fields]) OR health promotion OR community health services OR community health care OR community participation OR community networks [MeSH terms]) #4 (BFHI [All Fields] OR (Baby Friendly Hospital [All Fields]) OR Rooming in OR Perinatal Care OR Comprehensive health care OR Primary care OR health services OR Hospital OR Facility OR health care system OR health program[MeSH terms]) #5 ((Infant food Marketing [All Fields]) OR (Code of Marketing [All Fields]) OR (Infant milk substitutes [All Fields]) OR (Breast milk substitutes [All Fields]) OR Policy OR Legislations OR law [MeSH terms]) #6 (Addresses[ptyp] OR Autobiography[ptyp] OR Bibliography[ptyp] OR Biography[ptyp] OR pubmed books[filter] OR Case Reports[ptyp] OR Congresses[ptyp] OR Consensus Development Conference[ptyp] OR Directory[ptyp] OR Duplicate Publication[ptyp] OR Editorial[ptyp] OR Festschrift[ptyp] OR Guideline[ptyp] OR In Vitro[ptyp] OR Interview[ptyp] OR Lectures[ptyp] OR Legal Cases[ptyp] OR News[ptyp] OR Newspaper Article[ptyp] OR Personal Narratives[ptyp] OR Portraits[ptyp] OR Retracted Publication[ptyp] OR Twin Study[ptyp] OR Video-Audio Media[ptyp]) #7 «#1 AND (#2 OR #3 OR #4 OR #5)» #8 «#7 NOT #6»

Effects on women who breastfed

Database	Search terms
-PUBMED	#1 Breastfeeding OR Breast Feeding OR Lactation OR Human Milk OR Breast Milk #2 Women OR Maternal OR Postpartum OR puerperal OR postnatal OR Birth OR gestation Diabetes OR (Breast AND (Cancer OR carcinoma OR tumor OR malignancy)) OR (Ovarian OR Ovary AND (Cancer OR carcinoma OR tumor OR malignancy)) OR (depression OR Blues OR psychosis) OR (Amenorrhea OR Contraception) OR (Osteoporosis OR Bone mineral density) OR Weight OR BMI OR body mass index #3 (Addresses[ptyp] OR Autobiography[ptyp] OR Bibliography[ptyp] OR Biography[ptyp] OR pubmed books[filter] OR Case Reports[ptyp] OR Congresses[ptyp] OR Consensus Development Conference[ptyp] OR Directory[ptyp] OR Duplicate Publication[ptyp] OR Editorial[ptyp] OR Festschrift[ptyp] OR Guideline[ptyp] OR In Vitro[ptyp] OR Interview[ptyp] OR Lectures[ptyp] OR Legal Cases[ptyp] OR News[ptyp] OR Newspaper Article[ptyp] OR Personal Narratives[ptyp] OR Portraits[ptyp] OR Retracted Publication[ptyp] OR Twin Study[ptyp] OR Video-Audio Media[ptyp]) #4 #1 AND #2 AND #3 #1 #5 NOT #4

Webappendix 7. LiST methods and assumptions

In this section of the web annex we present two pieces related to the LiST analyses presented in the paper. The first section provides a brief overview and background of the Lives Saved Tool. More details on the models and previous use are available at the LiST web site (www.livessavedtool.org). The second section then presents explicit details of the methods used in the analyses and also provides a link to the country-specific models that were used in the analyses. These models which include all of the country-specific information can be downloaded and run to reproduce the analyses presented in the main text.

General Overview of the Lives Saved Tool (*LiST*)[7]

Background and history

The ***Lives Saved Tool (LiST***) has been developed over the past 10 years. The initial version of the software was developed as part of the work for the Child Survival Series in Lancet in 2003.[47] The purpose of the program was to estimate the impact that scaling up community-based interventions would have on under-five mortality [48], but the program had a very limited demographic capability. - Starting from this initial point the software was expanded first to handle a new set of interventions that focused more on facility-based care with the primary impact being on neonatal mortality.[49, 50] The model was then improved to handle populations and cohorts and to include wasting and stunting as risk factors as part of the work for the Lancet Nutrition Series.[51] At about the same time, the Bill & Melinda Gates foundation provided on-going support to the further development and maintenance of the software as part of the work of the Child Health and Epidemiology Reference Group (CHERG). At that point, the software was shifted into the free and publicly available Spectrum software package, to take advantage of the demographic capabilities in that software and to provide links to the AIM module that had been developed to estimate the impact of HIV/AIDS.[52] Since that time *LiST* has expanded its scope to look at the impact of interventions on birth outcomes and stillbirths [53], maternal mortality, and incidence of pneumonia and diarrhea [54] as well as neonatal and child mortality.

Theoretical approach and basic modelling structure of LiST

The Lives Saved tool has been characterized as a linear, mathematical model that is deterministic.[55] It describes fixed relationships between inputs and outputs that will produce the same outputs each time one runs the model. In *List* the primary inputs are coverage of interventions and the outputs are changes in population level of risk factors (such as wasting or stunting rates, birth out comes such a prematurity or size at birth) and cause-specific mortality (neonatal, child mortality 1-59m, maternal mortality and stillbirths). The relationship between an input (change in intervention coverage) with one or more outputs is specified in terms of the effectiveness of the intervention in reducing the probability of that outcome. The outcome can be cause-specific mortality or a risk factor. The overarching assumption in *LiST* is that mortality rates and cause of death structure will not change except in response to changes in coverage of interventions. The model assumes that changes in distal variables such as increase in per capita income or mothers' education will affect mortality by increasing coverage of interventions or reducing risk factors.

Currently there are around 70 separate interventions within *LiST*. These interventions have an impact on stillbirths, neonatal mortality, mortality in children 1-59 months, maternal mortality

[7] This overview document is based on a paper by N Walker, Y Tam and I Friberg.

or risk factors within the model. Interventions can be linked to multiple outcomes, with some interventions linked to multiple causes of death and risk factors. A key feature of *LiST* is that it allows one to look at the impact of scaling up coverage of multiple interventions simultaneously, instead of a single intervention and one cause as is done in many natural history models.

There are several structural features about the model that must be considered in order to estimates the impact of scaling up coverage of multiple interventions and changes in risk factors on mortality. First, the effectiveness or efficacy of an intervention must be described in terms of reduction in cause-specific mortality rather than in overall mortality. With cause-specific estimates of efficacy we can then compute the combined impact of interventions. Within *LiST,* efficacy of an intervention is defined in terms of the reduction of a cause of death or risk factor. When there is a single intervention the calculation of impact is simple as one has change in coverage times the efficacy of the intervention and this is applied to the cause specific mortality. For example if we have 10,000 diarrhea deaths in children aged 1-59 months and we introduce a new vaccine that would be 50% effective in reducing diarrhea mortality. If we have coverage of 50% we would then reduce diarrhea mortality to 7,500 (10000 – (10,000 *.5 * .5)). When there is a second or a third intervention, the same approach is followed except that the second diarrhea intervention would be applied to the residual diarrhea deaths. So if the second new diarrhea intervention is also 50% effective and coverage reaches 50% we would then reduce diarrhea mortality to 5,626. By using cause-specific efficacy and applying each intervention to the residual deaths after the previous intervention we ensure that we are not double counting impact of interventions.

Age structure within LiST

LiST has a fairly simple age structure within the model that serves as a pseudo cohort. The age periods in *LiST* include pregnancy, 0-1 month, 1-5m, 6-11, 12-23 and 24-59. Within the model impact at one age period has a cascading effect of what happens at the next. For example, if we scale up interventions that have an impact of neonatal mortality, more children will survive that period and then be exposed to the risk of death in the 1-59 month period. So the number of deaths in this period will increase, but the rate of mortality will remain the same. These time periods are also linked to the impact of sub-optimal breastfeeding on mortality.

For pregnancy, neonatal and 1-59 months there is a fixed cause of death structure in the base year (during pregnancy it is period of stillbirths). There is also a mortality rate that is applied to the age period. Within the 1-59 month period it is adjusted to reflect the higher mortality at earlier ages. Interventions within LiST can have an impact on one or more age periods.

Links to other modules in Spectrum

The Lives Saved Tool is a linked module within the Spectrum program. Currently *LiST* is linked directly to three other modules in Spectrum. A required linkage in Spectrum is between LiST and the demographic module, ***DemProj***. DemProj is a fully functioning demographic package that allows users to define populations via inputs on age-specific fertility, migration, population structure by age and sex, and other factors. The software contains the most recent population projections from the United Nations Population Division for 192 countries. When using *LiST*, users select a country, base year and end year and then LiST automatically loads in the population projection for that time period. Users can then use this as the population projection or they can use DemProj to update or alter as they deem appropriate.

FamPlan is a second module within Spectrum that is linked to *LiST*. FamPlan was developed to estimate the impact of scaling up family planning on fertility. As with the other modules, when one selects a country the most recent information on family planning, contraceptive prevalence, unmet need for contraception and contraceptive method mix is loaded. The user can then create scenarios where one reduces unmet need, increase contraceptive use and changes the contraceptive method mix. By changing these parameters in FamPlan several outputs change when it feeds into LiST as inputs. First, if one changes contraceptive prevalence then there is an impact on fertility. When a user specifies changes in FamPlan, this overrides the predicted fertility assumptions and alters assumptions about abortion from DemProj and passes this new information to LiST. For example, if one scales up contraceptive prevalence to very high rates in a country with low contraceptive use, then the number of births will decrease and therefore the number of under-five and maternal deaths predicted by *LiST* will decrease.

A third linked package is the AIDS Impact Module, ***AIM***, which is used to estimate the impact of HIV/AIDS on mortality. This module has been developed under the auspices of UNAIDS and the UNAIDS reference group on modeling and estimates.[56] This module describes the epidemic curve in terms of incidence for each country. The module also has coverage of interventions (e.g., treatment, prevention of mother-to-child transmission) and uses the information to estimate prevalence and mortality by age and sex. Estimating the impact of interventions to reduce AIDS mortality in children in not done in LiST, rather the calculations are done in AIM and then passed to *LiST*. Within Spectrum, when one selects a country it will automatically load in the most recent country-specific AIM module developed by UNAIDS and the national AIDS program.[57] As with other modules in Spectrum, the user can override the standard AIM inputs and can scale up interventions and change the epidemic curve to develop new scenarios for the future. This module then passes to *LiST* mortality due to AIDS to the *LiST* module.

Source of assumptions and process of updating LiST

The development of the Lives Saved Tool has been under the guidance of the Child Health Epidemiology Reference Group (CHERG) of WHO and UNICEF. CHERG, along with its institutional sponsors, has developed rules of evidence to decide what interventions should be included in the model as well as how to develop the estimates of efficacy and effectiveness used in the model.[58] While the assumptions used within *LiST* are drawn from various sources, most of the assumptions about efficacy and effectiveness of interventions come from a series of journal supplements. Previously three supplements containing over 70 articles have been published.[59-61] The set of assumptions and their sources can be found at the *LiST* website (www.livessavedtool.org).

The CHERG also supports efforts to compare the estimates that come from *LiST* to measured changes in intervention coverage and mortality. There have been several studies that have compared measured changes in mortality to *LiST* estimates of mortality change looking at different sets of interventions in different countries. For example, one study compared *LiST* estimates to measured reduction in neonatal mortality in community trials in South Asia.[62] Another study looked at community trials that focus on the scale up of use of insecticide treated nets (ITNs) in sub-Saharan Africa.[63] A third compared measured and estimated mortality for a community trial in Mozambique.[64] In all of these studies there was close agreement between the estimates of mortality from *LiST* based on coverage changes and the measured reductions in mortality. Additional studies doing comparisons of *LiST* have been published in the *LiST* journal supplements.[59-61]

Creating a projection scenario in LiST

The basic process to create a projection scenario is fairly simple. First, one must select a baseline year for a country (or region, district or any other area one choses). In that baseline year the country must be described in terms of a five broad sets of variables: mortality, exposure, risk factors, intervention coverage and demography. For mortality one must specific the neonatal, 1-59 month, stillbirth rates and maternal mortality rates, as well as the proportional causes of mortality (or stillbirths). Exposure variables include such factors as exposure to falciparum, level of deficiency of vitamin A and zinc, and percent of the population living in poverty. Risk factors include stunting and wasting rates by age, birth outcomes, breastfeeding patterns and diarrhea and pneumonia incidence. Coverage of interventions must be provided for all intervention in *LiST* in the baseline year. Finally, for *LiST* to operate basic demographic information must be provided including population structure by age and sex as well as age-specific fertility. Fortunately *LiST* allows readers to automatically load in this information for 90 low- and middle-income countries for any year from 2000 to 2011, where the information are typically compiled from large surveys such as DHS or MICS. Once one selects the country and base year, the information is automatically loaded into the program but the user can change any values if they have better data or if they would like to modify the population to reflect a region smaller than the national.

Once a baseline year is set for a country, the user can then create a projection scenario by scaling up coverage of a single or multiple interventions over a time period. For example, one could look at the impact of scaling up vitamin A supplementation from its current level of coverage of 50% in 2013 to 95% coverage in 2015. Or one could develop a treatment scenario where one scale up coverage of treatment for diarrhea with ORS, antibiotics for pneumonia and treatment for malaria with ACT from current levels of coverage to 90% by 2018.

Once one has created a scale up scenario, LiST then re-computes all of the inputs used in the base year based on the impact of the interventions in the scale up scenario. The levels of mortality, cause of deaths structure and levels of risk factors will be recomputed and applied to the new population structure that reflects not only the changes in DemProj but also any changes in intervention coverage from the *LiST* model and changes made in the FamPlan and AIM modules.

Methods and Assumptions of the LiST Analyses

Countries

The LiST analyses of the impact of increased appropriate breastfeeding practices were performed on the 75 countdown countries. We restricted the analyses to these 75 countries as we had estimates and data available to have good baseline models in LiST. These countries are responsible for over 95% of global under-five deaths.

LiST Assumptions

For all 75 countdown countries we created a baseline model for the year 2013. We chose 2013 as our baseline year as this is the last year for which we have country-specific estimates of mortality in children, which includes neonatal, infant and under-five mortality.[65] For the other assumptions in LiST we used the standard data sources and assumptions, with the exception of changes to the linkages between breastfeeding practices and cause-specific mortality risk.

Breastfeeding and mortality risk

In the standard version of LiST we treat sub-optimal breastfeeding as a risk factor. We characterize breastfeeding by type and age of the child.

For children under the age of six months, we specify the percent of children who are exclusively breastfed, predominantly breast fed, partial breastfed and not breast fed. We stratify these patterns of breastfeeding into two periods: under one month and 1-5 months. Using exclusive breastfeeding as the standard, we then have relative risks for cause-specific mortality for each of the three sub-optimal feeding practices.

For children aged six months to 2 years we specify the percent of children who are continuing to beast feed and those who do not. Here we stratify this into two age groups, 6-11 months and 12-23 months. The continued breastfeeding is the standard and we have higher relative risks for cause-specific mortality for the no breastfeeding group for both periods. For all age periods our estimates of breastfeeding practices are from the most recent household surveys for each country.

In LiST, under-five mortality is divided into two age periods (under one month and 1 to 59 months). For each of these periods we have estimates of cause-specific mortality. For the neonatal period there are 8 causes: N-diarrhea, N-pneumonia, N-sepsis, N-asphyxia, N-prematurity, N-tetanus, N-congenital abnormalities, and N-other. In the period 1-59 months we have 9 causes of death: diarrhea, pneumonia, meningitis, measles, malaria, pertussis, AIDS, Injury and other. In the standard version of LiST we only have increased relative risks for diarrhea and pneumonia, in both the neonatal and 1-59 month period. These causes of deaths are those categories used by WHO in their most recent estimates of cause-specific under-five mortality.[66]

For the analyses presented here we created links and relative risks between sub-optimal breastfeeding and all additional causes. In the neonatal period we added links between breastfeeding and sepsis, prematurity and neonatal other. For the period 1-59 months we added links between breastfeeding and meningitis, measles, malaria, pertussis and other.

Relative risks

For the relative risk associated with different breastfeeding practices we used the results of a meta-analysis.[67] These risks were applied to all of the causes listed above with the exception of N-other, N-prematurity and Other (1-59m). Table 7.1 shows the risks by age periods.

Table 7.1. Relative risks of breastfeeding practices by age of child.

Breastfeeding Practice	Less than 1 month	1 to 6 months	6 to 12 months	12 to 24 months
Exclusive	1.0	1.0	1.0	1.0
Predominant	1.7	1.7	_	_
Partial	4.56	4.56	_	_
None	8.60	8.60	2.09	2.09

For N-other, N-prematurity and Other (1-59m) we had to make adjustments to the relative risks. For N-other and other (1-59m) we had to adjust the relative risks to reflect the percentage of other deaths that were due to infectious diseases. For each country we obtained estimates of the percent of other causes for both the neonatal and 1-59 month periods and the relative risks were altered to reflect and impact on the percentage of other deaths that were due to infectious diseases. While these estimates were country specific, overall (all countries) the median percent of neonatal other due to infectious diseases was 84% while in the other 1-59 period it was 15.3%.

For N-prematurity we also made an adjustment. The key here is that we assumed that breastfeeding would have little impact on early deaths due to prematurity, but once a premature child had survived for the first few days, averting infectious via breastfeeding would have a strong impact. We used an estimate of 15% of premature deaths occurring after the first week of life and it was to those deaths we applied the relative risks.

Scenarios

We used a simple scenario for estimating the impact of improved breast feeding practices on mortality. For each of the 75 countdown countries we created a baseline for the year 2013. This included the most recent estimate of breastfeeding practices. Then in the year 2014 we scaled up breastfeeding practices to the rates shown in Table 7.2. If a country had a current rate higher than the scale up values we did not change the rates.

Table 7.2. Scaled rates of breast feeding by age of child.

	Less than 1 month	1 to 6 months	6 to 12 months	12 to 24 months
Exclusive	95%	90%	90%	90%
Predominant	3%	5%	_	_
Partial	1%	3%	_	_
None	1%	2%	10%	10%

Final LiST Models

The estimates of the impact of scaling up breast feeding on mortality were run using LiST version 5.25 beta 1. This version of the software along with the country specific models can be downloaded at (www.livedsavedtool.org).

Webappendix 8. Breast cancer estimates

Breastfeeding has benefits for mothers as well as for children. Studies for the US[68] and the UK[69] estimate the number of maternal deaths which could be averted by increased breastfeeding, primarily from breast cancer. The odds ratio used by Renfrew et al.[69] (drawn from Collaborative Group [70]) consider the impact of cumulative lifetime breastfeeding of the mother on incidence of breast cancer, and are 0.96 (ever versus never breastfed: CI 0.92-0.99); 0.98 (< 6 months versus never: CI 0.95-1.01), 0.94 (7-18 months versus never: CI 0.91-0.97); and 0.89 (18+ months versus never: CI 0.84-0.94). We make the assumption that the effect on breast cancer mortality is similar to that on breast cancer incidence.

The data available across countries are for breastfeeding duration of individual children, not for a woman's lifetime experience. For LMICs we use data on the proportion of children breastfed up to 2 years and apply the 0.89 odds ratio; for high income countries where we have data on the proportion of children breastfed up to 12 months, we use this rate and apply the 0.94 odds ratio. For a few high income countries where we have only data on the proportion breastfed to 6 months, we apply the odds ratio of 0.98. This method will provide a conservative estimate of the number of breast cancer deaths averted since women on average have more than one child.

Data on breast cancer mortality rates by country were drawn from Globocan 2012[71]. Data on breastfeeding usable for this analysis were available for 153 of the 197 countries and areas of the world listed in UNICEF[72], representing 97.5% of the world's population. Of the 153 countries with breastfeeding data, no data on breast cancer were available for 5 small island states.

We estimated what breast cancer mortality rates would have been in the absence of protection from breastfeeding, compared these to current breast cancer deaths, and hence calculated the number of lives saved by country, region and the global total for those countries with available data. We also estimated how many additional breast cancer deaths could be averted by a significant increase in the proportion of women breastfeeding for long durations (defined as 12 months per child in the high income countries, and 2 years per child in LMICs).

Globally, an estimated 19,494 breast cancer deaths are averted annually at existing rates of breastfeeding. The low income regions with long breastfeeding durations (Africa and South Asia) account for 58% of the current estimated lives saved, despite only accounting for 36% of the global population included in this analysis. Regions which would benefit disproportionately more if breastfeeding durations were to increase include Latin America, CEE/CIS and the high income countries – regions which have both higher rates of breast cancer and also shorter durations of breastfeeding.

Table 8.1. Breastfeeding and breast cancer cases averted, by region and global total.

Region	% of global population (excludes countries missing data)	Number of breast cancer deaths averted at current bf rates	% of global breast cancer deaths averted at current bf rates	Number of breast cancer deaths potentially averted at higher bf rates	% of global breast cancer deaths averted
Eastern and Southern Africa	6.4	1452	7.4	813	3.7
West and Central Africa	6.3	1264	6.5	1436	6.5
MENA (Middle East and North Africa)	6.3	853	4.4	1655	7.4
South Asia	23.8	8651	44.4	1861	8.4
East Asia and Pacific	29.2	2990	15.3	6535	29.4
Latin America and Caribbean	8.7	1266	6.5	2917	13.1
CEE/CIS	5.7	417	2.1	1991	9.0
High-income countries	13.6	2602	13.4	5008	22.5
World	10.0	19494	10.0	22216	10.0

Webappendix 9. Ecological correlation matrix

Table 9.1. Pearson correlation coefficients and P levels for associations among BF indicators and gross domestic product per capita, most recent survey in each country.

		Ever BF	Early initiation of BF	Exclusive BF 0-5mo	Any BF 6 mo	Any BF 12 mo	Continued BF 12-15 mo	Continued BF 20-23 mo
Log GDP per capita	Coefficient	-0.53	0.14	-0.41	-0.84	-0.84	-0.71	-0.60
	P value	<0.001	0.24	<0.001	<0.001	<0.001	<0.001	<0.001
	N	92	76	116	97	151	120	113
Ever BF	Coefficient		0.06	0.55	0.58	0.55	0.60	0.50
	P value		0.62	<0.001	<0.001	<0.001	<0.001	<0.001
	N		76	64	94	93	66	65
Early initiation of BF	Coefficient			0.47	-0.10	-0.11	0.06	0.11
	P value			<0.001	0.38	0.36	0.62	0.36
	N			65	78	77	67	66
Exclusive BF 0-5mo	Coefficient				0.44	0.53	0.54	0.53
	P value				<0.001	<0.001	<0.001	<0.001
	N				65	116	117	116
Any BF 6 mo	Coefficient					0.95	0.87	0.61
	P value					<0.001	<0.001	<0.001
	N					98	67	66
Any BF 12 mo	Coefficient						0.99	0.70
	P value						<0.001	<0.001
	N						124	117
Continued BF 12-15 mo	Coefficient							0.73
	P value							<0.001
	N							118

Webappendix 10. Within country inequalities in exclusive and continued breastfeeding.

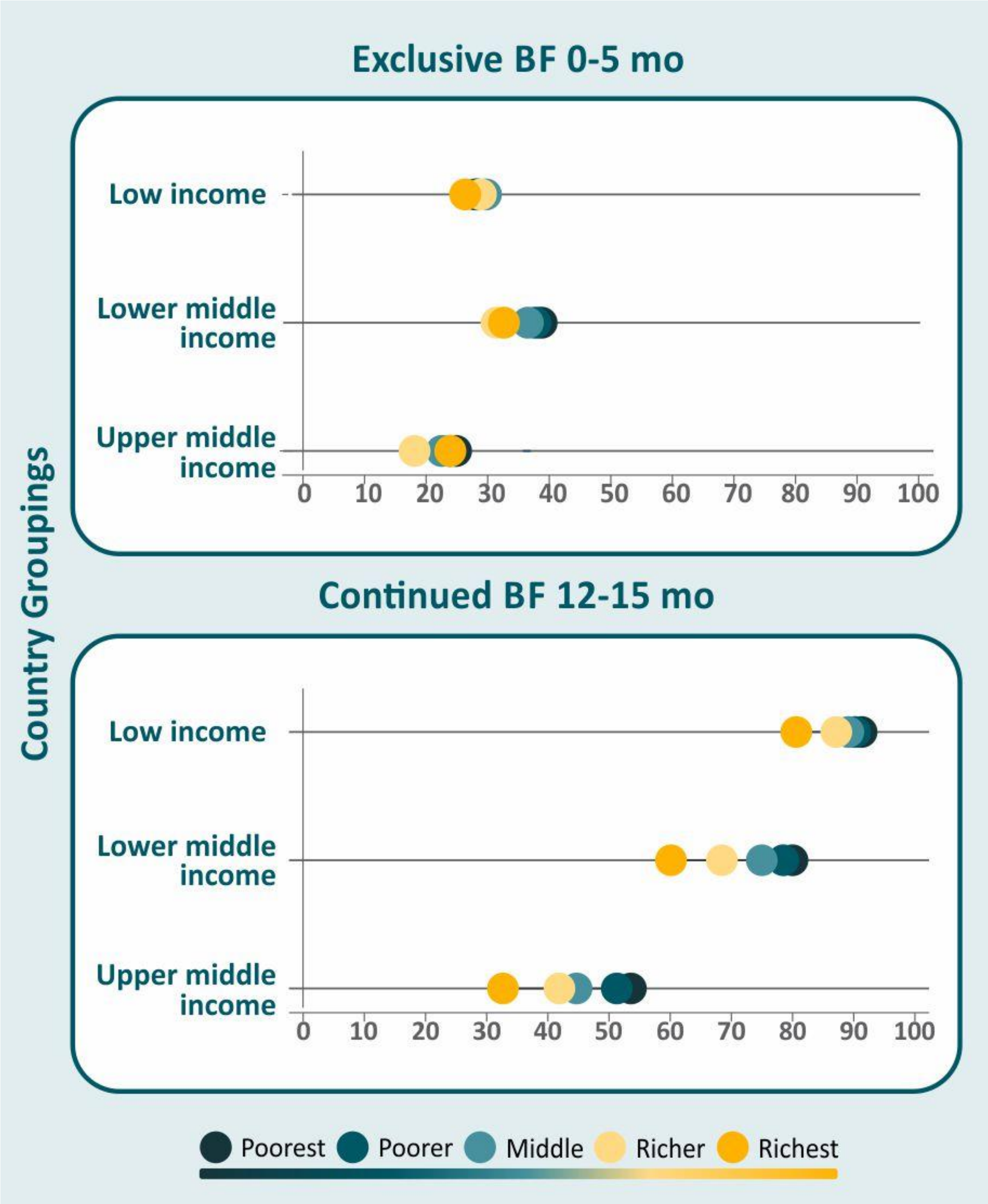

Figure 10.1. Wealth related inequalities in exclusive BF 0-5 mo and continued BF 12-15 months by country income groupings. Values are mean percentages by wealth quintile in 127 LMICs.

Webappendix 11. Risks associated with breastmilk substitutes

In 1974, Mike Muller raised a storm when he started his report– 'The Baby Killer' – stating that 'Third World babies are dying because their mothers bottle feed them with western style infant milk. Many that do not die are drawn into a vicious cycle of malnutrition and disease that will leave them physically and intellectually stunted for life.[73] He captured both the short and long term risks associated with breastmilk substitutes (BMS) when given in low resource settings and also the lure of practices among the rich on aspirations among the poor.

Infants who are not breastfed are given replacement feeds. In resource poor settings, because of the expense of commercial BMS, these infants may receive dilute cow's milk or skimmed milk powders that place infants at risk of electrolyte disorders and malnutrition.[74] Commercial BMS are susceptible to bacterial contamination when re-constituted for feeding,[75] as mothers in low resource settings are not able to consistently sterilize bottles or use boiling water to prepare every feed, and do not have clean utensils and fridges for preparation and storage. Contaminated water has also been associated with mortality among formula-fed infants.[76]

In addition, contamination of formula in the manufacturing process also place children at risk Outbreaks of Cronobacter sakazakii have occurred among preterm infants in high-income countries .[77, 78] In the US, powdered formula have been recalled due to possible contamination by beetle larvae.[79] In China, over 300,000 children were reported to have fallen ill when melamine was inadvertently added to manufactured formula.[80]

In contrast, breastmilk is exceptionally safe. Adverse effects have only very rarely been associated with its consumption in settings where environmental degradation has resulted in excess background levels of heavy metals, chemical residues and radioactive isotopes. Only in cases of industrial disasters would the risks of exposure to such contaminants potentially outweigh the benefits of breastfeeding.[81]

Webappendix 12. Acknowledgments

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