The impact of breastfeeding practices on under-five mortality in sub-Saharan Africa. Systematic review, meta-analysis and evaluation of its attributable costs

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PREFACE

Firstly, I would like to thank my heavenly Father for blessing me with a healthy mind and for giving me the strength to pursue my dreams.
I want to thank my beloved mother, father and sister for providing me with an abundance of love and support throughout my studies. I am truly blessed and grateful.

To my dear friends thank you for every word of encouragement and motivation. You kept me in a good state of mind on rainy days and late nights. I will forever cherish the good moments together.

With deep sense of gratitude, I thank Dr Cristian Ricci and Prof. Salome for your mentorship, guidance and contributions during the course and completion of my dissertation. I am also very thankful for your kindness and patience throughout the process.

I am grateful to all the other co-authors for their meaningful inputs and expert revision of the article.

"Desire is the key to motivation, but it's determination and commitment to an unrelenting pursuit of your goal – a commitment to excellence – that will enable you to attain the success you seek." – Mario Andretti

ABSTRACT

Background: Sub-Saharan Africa has lower exclusive breastfeeding rates compared to other low- and middle-income countries, and globally holds the highest under-five mortality rates. The aims of this project were: to conduct a literature review with regards to breastfeeding; to conduct a systematic review and meta-analysis of breastfeeding practices in relation to under-five mortality; to estimate the prevalence of breastfeeding practices and the population attributable fraction; and to determine the economic impact of breastfeeding on child mortality, in sub-Saharan Africa.

Methods: A literature review was conducted on the benefits of breastfeeding for both the child and the mother, the protection against mortality for children, the indicators of breastfeeding and determinants of breastfeeding, breastfeeding as a public health responsibility and as a human right, and breastfeeding in the context of HIV. A systematic review was conducted on observational studies (from 1 January 2000 to 31 May 2019) which reported an estimate of risk compared with exclusive and early initiation of breastfeeding and mortality in children under-five years of age, in sub-Saharan Africa. The systematic review included databases from Medline and CINAHL. Meta-analysis of mortality risk estimates was conducted using random and fixed effect methods. Heterogeneity was evaluated using the Cochrane Q test and the I^2 statistic. Publication bias was assessed by funnel plot visual inspection and the Egger's test. The prevalence for the breastfeeding practices were determined using UNICEF's database (2000-2018). Prevalence estimates by regions were compared using a linear meta-regression approach. The prevalence and all relative risk estimates were merged to provide population attributable fraction (PAF). Non-Health Gross Domestic Product Loss

(NHGDPL) attributable to child deaths in relation to inappropriate breastfeeding practices was calculated using data from the World Health Statistics 2015.

Results and discussion: The systematic review produced 1,511 records with the initial search. After title and abstracts screening, 51 records were assessed for eligibility. After the exclusion of 39 full text articles,16 studies were included in the qualitative synthesis. Nine were prospective studies, two were retrospective studies and four studies were surveys. The pooled relative mortality risk to any kind of infant feeding with respect to non-exclusive breastfeeding and delayed breastfeeding initiation were 5.71 (95%CI:2.14;15.23;N=6;I^2=96.3%) and 3.3 (95%CI:2.49;4.46;N=5;I^2=0%), respectively. According to our calculations, no indication of publication bias was observed. The overall exclusive breastfeeding and early initiation of breastfeeding prevalence were 35% and 47%, respectively. A large variability was observed between individual sub-Sahara African countries and regions for both exclusive breastfeeding and early initiation of breastfeeding prevalence. The PAF for non-exclusive breastfeeding was 75.7% and for late initiation of breastfeeding was 55.3%. The total NHGDPL attributable to inappropriate breastfeeding practices resulted in about 19.5 United States billion dollars (USB$). When considering deaths avoidable by exclusive breastfeeding and early breastfeeding initiation, the NHGDPL would be 8.3 and 8.4 USB$ in sub-Saharan Africa, respectively.

Conclusion: Our results confirm that scaling up breastfeeding would be greatly beneficial for saving children's lives and to reduce the negative economic impact of the under-five mortality rate in Sub-Saharan Africa. Therefore, public health interventions should prioritize breastfeeding practices to decrease the under-five mortality burden and its related costs in sub-Saharan Africa.

Keywords: exclusive breastfeeding, under-five mortality, economic, sub-Saharan Africa.

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LIST OF ABBREVIATIONS

AFASS	Acceptable, Feasible, Affordable, Sustainable, And Safe
ART	Antiretroviral Treatment
ARV	Antiretroviral
BFHI	Baby Friendly Hospital Initiative
BSc.	Bachelor of Science
CD4	Cluster of Differentiation-4
CI	Confidence Interval
Dr.	Doctor
EBF	Exclusive Breastfeeding
EIBF	Early Initiation of Breastfeeding
GDP	Gross Domestic Product
HIV	Human Immunodeficiency Virus
HMO	Human Milk Oligosaccharides
ICC	Intraclass Correlation Coefficient
IQ	Intelligence Quotient
LAM	Lactational Amenorrhoea Method
MeSH	Medical Subject Headings
MDG	Millennium Developing Goal
M. Pharm	Master of Pharmacy
M.Sc.	Master of Science

NCD	Non-communicable Disease
NHGDPL	Non-Health Gross Domestic Product Loss Attributable oo Child Deaths
NOS	Newcastle Ottawa Scale
NWU	North-West University
PAF	Population Attributable Fraction
PhD	Doctor of Philosophy
PMTCT	Prevention of Mother to Child Transmission
PRISMA	Preferred Reporting Items of Systematic Reviews and Meta-Analysis
RR	Relative Risk
SDG	Sustainable Development Goal
SSA	Sub-Saharan Africa
U5MR	Under-Five Mortality Rate
UNICEF	United Nations Children's Fund
USB$	United States Billion Dollars
WHO	World Health Organization
$	Dollars

CHAPTER 1 INTRODUCTION

1.1 Background and motivation

Globally, from 1990 to 2015, child mortality was estimated to have claimed the lives of 236.3 million children before their fifth birthday (You *et al.*, 2015). Accordingly, in 2000 the Millennium Developing Goals (MDG) target-4 called for a two-thirds reduction in the under-5 mortality rate (U5MR) (UN, 2000). Despite impressive improvements in most regions, this global target was not met. Only a reduction of 53% from 1990-2015 was observed for the global U5MR, and sub-Saharan Africa contributed to roughly half (49.6%) of U5MR reduction among the ten MDG regions (You *et al.*, 2015). Continuing with the current rate of progress, it was estimated that it would take ten more years to reach the global target-4 (Ki-Moon, 2015). Subsequently, the Sustainable Development Goal sets its target for 2030 to an U5MR of 25 or fewer deaths per 1000 live births (Anon, 2015). Currently, sub-Saharan Africa holds the highest U5MR of 83.1 deaths per 1000 live births. Specifically, the West and Central African sub-regions have the highest U5MR worldwide of 98.7 per 1000 live births. Therefore, sub-Saharan Africa faces unique challenges to reduce the U5MR, due to an additional demand generated by an increase in birth rates, its related child population growth (UN. Department of Economic and Social Affairs, 2015) and the negative economic impact attributable to child deaths in Africa (Kirigia *et al.*, 2015).

The nutritional status of children is one of the main modifiable risk factors for mortality (Lartey, 2008; Lim *et al.*, 2012; Pelletier & Frongillo, 2003). The Global Strategy for Infant and Young Child Feeding recognises that malnutrition has been responsible, directly or indirectly, for 60% of the 10.9 million deaths reported annually among children under-five years in 2003. Well over two-thirds of these deaths, which are often associated with inappropriate feeding practices, occur during the first year of life (WHO *et al.*, 2003). Therefore, breastfeeding is essential to sustain a child's health and nutritional status in the early stages of life. In the last years, a significant improvement in exclusive breastfeeding prevalence was observed in sub-Saharan Africa. Exclusive breastfeeding prevalence more than doubled in West and Central Africa (from 12% in 1995 to 28% in 2015), and from 35% to 47%, in East and Southern Africa (You *et al.*, 2015). Despite these improvements and the well-recognised importance of exclusive breastfeeding (Victora *et al.*, 2016b), sub-Saharan Africa still has lower exclusive breastfeeding rates (35%) when compared to other low- and middle-income countries including Asia (39%) (Cai *et al.*, 2012). These disparities raise questions about how inappropriate breastfeeding practices may determine why sub-Saharan Africa had the highest U5MR worldwide.

Several systematic reviews and meta-analyses investigated the association of breastfeeding practices and neonatal- or infant- or/and child mortality (Debes *et al.*, 2013; Horta & Victora, 2013; Khan *et al.*, 2015; Lamberti *et al.*, 2011; Lamberti *et al.*, 2013; Sankar *et al.*, 2015; Smith *et al.*, 2017a). However, none of them specifically focused on the sub-Saharan Africa region. Furthermore, there is a knowledge gap regarding the economic impact of breastfeeding practices in relation to child mortality in Sub-Saharan Africa.

This study integrates epidemiological-, public health- and economic data, providing novel information regarding how improved recommended breastfeeding practices (exclusive breastfeeding and early initiation of breastfeeding) may impact sub-Saharan African society. This impact will be determined by the population attributable fraction, by merging the prevalence of the recommended breastfeeding practices in sub-Saharan Africa, with the estimated risks for mortality obtained from the systematic review and meta-analysis. Furthermore, estimating the cost to which inappropriate breastfeeding practices and under-five mortality contribute, it is possible to determine how much can be saved if the recommended breastfeeding practices are fully implemented. Knowing the social and economic impact of breastfeeding practices and under-five mortality in sub-Saharan Africa will emphasise the need of national policies and breastfeeding promotion interventions in sub-Saharan Africa, so as to improve breastfeeding practices for the reduction under-five mortality in the region.

1.2 Aims and objectives

The primary aim of this project was to perform a systematic review and meta-analysis of the association between breastfeeding practices (particularly on exclusive breastfeeding and early initiation of breastfeeding) and the risk of mortality in children under-five years in sub-Saharan Africa. A second aim was to estimate the prevalence of exclusive breastfeeding and of early initiation of breastfeeding to determine the population attributable fraction of children affected, in sub-Saharan Africa. For a third aim, a cost analysis was performed by using the results from the previous aims to evaluate how improved breastfeeding practices may reduce the economic impact attributable to the U5MR in sub-Saharan Africa.

The objectives were:

- to systematically review the association between breastfeeding practices and the risk for mortality in children under-five years in sub-Saharan Africa from 2000-2019;

- to conduct a meta-analysis of the association of breastfeeding practices with the risk for mortality in children under-five years in sub-Saharan Africa from 2000-2018;
- to estimate the prevalence of exclusive breastfeeding and the early initiation of breastfeeding among mothers of infants aged 0-6 months in sub-Saharan Africa from 2000-2018;
- to estimate the population attributable fraction associated with favourable breastfeeding practices as recommended by the World Health Organization; and
- to calculate the Non-Health Gross Domestic Product Loss attributable to under-five mortality, which is related to inappropriate breastfeeding practices in sub-Saharan Africa.

1.3 Research outputs emanating from this project

The following outputs emanated from this project:

- a presentation which was presented at the 10th Child Health Priorities Conference, at the North-West University, Potchefstroom, on the 29th of November 2019 with the given title "The impact of breastfeeding practices on under-five mortality in sub-Saharan Africa: Systematic review, meta-analysis and evaluation of attributable cost of breastfeeding practices";
- a mini dissertation; and
- a paper submitted to and published by the European Journal of Paediatrics (as seen in Chapter 3 and Annexure F).

1.4 Structure of the dissertation

This dissertation will be presented in article format according to the postgraduate guidelines of the North-West University (NWU). It consists of four chapters and decimal numbers are used to ensure a logical structure. All relevant references will be provided at the end of each chapter. The references used in chapters One, Two and Four are presented as stipulated by the NWU mandatory referencing style. The references for the article in chapter Three will be cited according to the relevant journal's author guidelines (Annexure G), where the article has been submitted for publication.

Chapter One provides a brief introduction to and rationale for the research project, as well as the aim and objectives of the project and the research outputs that will emanate from this study. Details regarding members of the research team and their contributions towards this research project are also provided. Chapter Two consists of a review of the available literature that focuses on the benefits of breastfeeding for both the mother and the child, breastfeeding's protection against mortality outcomes, breastfeeding indicators and its determinants, breastfeeding as a public health responsibility and in the context of HIV. Chapter Three includes the article containing all information regarding this research project, viz. the background, methodology, and results found, discussion and conclusion for the article. The article was submitted for publication to the European Journal of Paediatrics. The style, format and referencing for this article followed the author guidelines and instructions of this journal and therefore the numbering of headings, tables and figures differ from those in the other chapters. Chapter Four completes this dissertation, providing a summary of the work and findings of this research project together with recommendations on future research and concluding remarks.

1.5 Authors' contributions

The following table lists the authors and their contributions to this research project.

Table 1-1: Summary of authors and their contributions.

Miss Cianté Elizabeth Pretorius	BSc Dietetics	Conceptualised and designed the project, designed the data collection instruments, collected data, drafted the initial manuscript, and reviewed and revised the manuscript.
Dr. Cristian Ricci	PhD Biostatistics	Conceptualised and designed the project, coordinated and supervised data collection, carried out the initial analyses and revised the manuscript.
Miss Hannah Asare	MSc Nutrition	Collected data and reviewed and revised the article.
Dr. Jon Genuneit	PD Dr. Med., Paediatrics	Contributed to the interpretation of data and revised the article critically for important intellectual content.
Prof. Herculina Salome Kruger	PhD Nutrition M Pharm	Contributed to the conception/design of the study and revised the manuscript critically for important intellectual content.

BSc: Bachelor of Science; Dr: doctor; M.Sc.: Master of Science; PhD: Doctor of Philosophy; M. Pharm: Master of Pharmacy

1.6 Signed declaration by the research team

I declare with my signature that as a co-author I have approved the article titled “Impact of Breastfeeding on Mortality in Sub-Saharan Africa: A Clinical Evaluation and Cost-Analysis”, that my role in the study as indicated above is representative of my actual contribution and that I hereby give permission that the article may be included as part of the M Sc dissertation of Ms CE Pretorius.

Dr Cristian Ricci

Prof Herculina S. Kruger

Ms Hannah Asare

Dr Jon Genuneit

CHAPTER 2 LITERATURE REVIEW

2.1 Background

The WHO recommends early initiation of breastfeeding (within the first hour after birth), exclusive breastfeeding for the first six months of life and continued breastfeeding up to two years of age (WHO *et al.*, 2003). The importance of breastfeeding is well established for both women and infants over decades of science. Evidence suggests that long-term negative effects may be prevented in the health, nutrition, and development of both women and children if appropriate breastfeeding is to be implemented (Victora *et al.*, 2016a). This literature review will firstly explore the many given benefits of breastfeeding for both the child and the mother, secondly how breastfeeding may prevent the risk for mortality under-five years of age, thirdly the indicators and determinants of breastfeeding, and finally, breastfeeding as a public health responsibility and in the context of HIV will be discussed.

2.2 Breastfeeding benefits for the infant and child

Breast milk provides protective, developmental, and growth factors for children (Vieira Borba *et al.*, 2018). In the early stages of life, the first breast milk also known as colostrum is produced, and this contains more than 250 potentially immunologically active proteins (Donovan, 2016). Breast milk also contains micro biota, which determines the child's immune response and may hold many future benefits for the child including protection against inflammation of the mucosa, autoimmune pathology, and allergies in children and adults (Guaraldi & Salvatori, 2012).

2.2.1 Prevention of infections

Breastfeeding plays an important role in the prevention of non-specific gastrointestinal infections (Kramer *et al.*, 2002) in both low- and middle-income countries (Ip *et al.*, 2007). Breast milk was also found to protect against gastrointestinal infections in children exposed to Human Immunodeficiency Virus (HIV) (González *et al.*, 2013). Breast milk contains beneficial bacteria, protecting infants until their digestive mucosa matures and increases the ability to produce its own antibodies, around the age of 4-6 months (Hegar & Vandenplas, 2018).

Longer breastfeeding duration has been associated with a reduced risk for otitis media, also known as acute middle ear infection (Eidelman, 2012). Breastfeeding also protects against respiratory infections. Breastfeeding exclusively preferably for the first six months, will decrease the child's risk for hospitalisation related to lower respiratory infection during the first year of life (Duijts *et al.*, 2010). Breast milk is characterised as a personalised medicine for premature infants since it provides a 58% to 77% reduction in the risk of developing necrotising enterocolitis (Eidelman, 2012).

2.2.2 Cognitive, brain and visual development of infants and children

Breast milk contains the precursors of the n-3 and n-6 long-chain polyunsaturated fatty acids, especially docosahexaenoic acid, and arachidonic acid, which plays an important role in neurogenesis, improving the cognitive, brain and visual development in children up unto adolescence (Innis, 2014; Lechner & Vohr, 2017). A systematic review reported that breastfeeding is associated with an improved performance in intelligence tests (Horta *et al.*, 2015) which could be accountable to the presence of the long-chain polyunsaturated fatty acids in breast milk. Furthermore, longer duration of breastfeeding and greater exclusivity of breastfeeding have been reported to be associated with better receptive language and with higher verbal and nonverbal intelligence quotient (IQ), at three and seven years of age, respectively (Belfort *et al.*, 2013).

2.2.3 Protective role against non-communicable diseases

Growing evidence suggests that breastfeeding plays a protective role against non-communicable diseases, and related medical conditions, during adulthood including obesity, hypertension, dyslipidaemia and type 2 diabetes mellitus (Roya & Sanam, 2014). Globally, other studies reported similar results, where the relationship between the duration of breastfeeding and obesity is inversely related with a reduced risk of 4% for each month of breastfeeding for the child (Aguilar Cordero *et al.*, 2015; Eidelman, 2012; Gillman *et al.*, 2001; Hediger *et al.*, 2001; Hess *et al.*, 2015). Breast milk protects against certain cancers in children. Systematic reviews concluded that there is a reduced risk for developing leukaemia (Amitay & Keinan-Boker, 2015), acute lymphocytic leukaemia, and acute myelogenous leukaemia during childhood in relation to prolonged breastfeeding duration (Ip *et al.*, 2007).

2.2.4 Optimal nutrition for infants

Breast milk is seen as the optimal nutrition for infants. Breast milk contains the correct amounts and ratio of carbohydrates, protein, fat, vitamins, minerals, digestive enzymes and hormones (Gura, 2014). Breast milk is also rich in immune cells and other bioactive molecules which are protein-derived and lipid-derived, while others are protein-derived and indigestible, such as oligosaccharides. These human milk oligosaccharides (HMOs) provide protection against pathogens in the gastrointestinal tract of the infant. HMOs also contribute to the development of a diverse and balanced microbiota, which is essential for appropriate innate and adaptive immune responses and contributes to the 90% colonisation of the infant's biome (Walker, 2013).

The composition of breast milk adjust itself to suit the changing needs of a growing child. Therefore, breast milk is dynamic as it changes over time, even during a single nursing session. The first milk which is expressed during a nursing session is called the fore milk, which is thinner with a higher content of lactose, and therefore, satisfies a baby's thirst. Following the foremilk, is the hindmilk, which is creamier with a much higher content of fat for the baby's needs. Variations may also occur according to the mother's diet, maternal health and environmental exposures (Guo, 2014).

2.2.5 Association with growth/prevention of undernutrition

Exclusive breastfeeding is associated with a reduced risk of undernutrition especially in low- and middle-income countries. A few studies reported that exclusively breastfed infants are less likely to develop stunting and/or to be underweight (Kamudoni *et al.*, 2015; Kuchenbecker *et al.*, 2015). However, there has been some conflicting results among small and more slowly growing infants which are breastfed for longer durations, in low- and middle-income countries, which has led to speculations that breastfeeding may be associated with poor growth (Marquis *et al.*, 1997; Simondon & Simondon, 1998). Taking into consideration, the conditions of poor-nutritional-quality complementary foods, lack of variety in food groups, provision of watery porridges (Dewey, 2003), and commercially marketed complementary foods lacking essential nutrients (WHO, 2013), which is prevalent in many socially deprived households. The continuation of complementary breastfeeding on-demand up to two years of life, contributes to the prevention of child malnutrition (Dewey & Brown, 2003).

2.2.6 Allergies and eczema

Breast milk contains multiple compounds which can be seen as an immunological complex solution, therefore facilitates the host defence mechanism (Hoppu *et al.*, 2001).

Breast milk contains bioactive compounds such as immunoglobulin A and G, which plays a role in passive immunity and also contain factors that can actively stimulate the infant's immune system (Friedman & Zeiger, 2005). Moreover, breast milk provides beneficial effects on immune function development and decrease the susceptibility to allergic disorders (Hoppu *et al.*, 2001). Most studies have found a protective effect of breastfeeding against allergic diseases (Kull *et al.*, 2002; Oddy *et al.*, 1999), however several others have reported that breastfeeding may not provide such protective effects (Burgess *et al.*, 2006; Sears *et al.*, 2002). The evidence mainly supports the protective role of breastfeeding against asthma or allergic diseases including eczema (Burgess *et al.*, 2006; Dogaru *et al.*, 2014; Lowe *et al.*, 2006; Matheson *et al.*, 2007; Wright *et al.*, 2001).

2.3 Benefits for the mother

2.3.1 Protection against non-communicable diseases

Breastfeeding provides protection against numerous non-communicable diseases (NCD's). Studies have found that breastfeeding protect mothers against certain cancers, such as breast cancer (Lancet, 2002) and ovarian cancer (Chowdhury *et al.*, 2015).

Breastfeeding may also protect mothers against the risk for other NCD's such as diabetes, hypertension, hyperlipidaemia and cardiovascular diseases. The protective effect of breastfeeding all starts at the milk production which requires approximately 500 kcal per day for an exclusively breast-fed infant, therefore reduces maternal obesity in later life (Bobrow *et al.*, 2013). Furthermore, studies have found that breastfeeding mothers present with less visceral obesity and smaller waist circumferences when they are older (McClure *et al.*, 2011). These findings, therefore, strengthen the evidence, regarding the reduced maternal risk to develop diabetes mellitus (Jäger *et al.*, 2014) and hyperlipidaemia (Stuebe *et al.*, 2010). Moreover, the risk for gestational diabetes may also be reduced by lactation (Chouinard-Castonguay *et al.*, 2013). A study reported that mothers who never breastfed were 29% more likely to develop hypertension compared to mothers who breastfed according to national guidelines (Schwarz *et al.*, 2009; Stuebe *et al.*, 2011). Other studies reported the protective effect of breastfeeding against cardiovascular diseases (Schwarz *et al.*, 2009) and coronary heart disease (Stuebe *et al.*, 2009).

2.3.2 Birth spacing

Mothers who exclusively breastfeed can also benefit from improved birth spacing (Chowdhury *et al.*, 2015). Exclusive breastfeeding may serve as a contraceptive known as the lactational amenorrhoea method (LAM) which is available and accessible to many women (Kennedy, 1988). During breastfeeding the ovarian activity is suppressed by the suckling stimulus of the infant which reduces the pulsatile secretion of gonadotropin releasing-and luteinizing hormone (McNeilly, 2001). LAM can provide contraceptive protection for more than 98% of pregnancies in the first six months postpartum if implemented correctly (Kennedy & Visness, 1992; Labbok *et al.*, 1994). However, studies have shown that only a few women actually implement or use the method correctly (Romero-Gutierrez *et al.*, 2007; Sebastian *et al.*, 2012; Sipsma *et al.*, 2013).

2.3.3 Mother-infant relationship

The positive effects that breastfeeding may have on the mother-infant relationship are extensively promoted (Jansen *et al.*, 2008). According to studies, the hormones oxytocin and prolactin that stimulate milk production and milk ejection, have been shown to affect maternal caregiving behaviour and improve mother-infant pair bonding. Furthermore, this non-nutritive feature of breastfeeding, between the mother and infant during breastfeeding, may promote infant attachment (Feldman, 2007; Schore, 2001; Siegel, 2001). The number of daily feedings can also influence maternal bonding, due to sufficiently elevated oxytocin in mothers who feed more frequently (Ari *et al.*, 2007).

2.4 Breastfeeding can protect against mortality in infants

Interventions delivered early in the postnatal period have the highest potential for impacting mortality, since they reach new-borns when their risk of mortality are at its peak. Numerous studies have investigated the benefit of early initiation of breastfeeding (i.e. within one hour after birth) and duration of breastfeeding on mortality risk. A systematic review, which included prospective cohort studies, reported a relative risk reduction of 44%(95%CI:20;61) of all-cause mortality during the first 28 days among live births surviving the first 48 hours of life, if early breastfeeding initiation was introduced.

The relative risk reduction for the association between early breastfeeding initiation and infection-related mortality was 45%(RR=0.55 [95%CI:0.36;0.84]) for both healthy weight and low birth weight babies (Debes *et al.*, 2013). Another systematic review confirmed that delayed initiation of breastfeeding beyond the first hour of life is associated with an increased risk of neonatal mortality. It also indicated that neonates who are partially breastfed are at greater risk of all-cause mortality and infection-related mortality in the first month of life, compared with those who are exclusively breastfed. Infants are also at greater risk of sepsis, acute respiratory and gastrointestinal infection if they are partially breastfed compared to exclusively breastfed (Khan *et al.*, 2015).

The Neovita pooled group study reported that compared with infants initiating breastfeeding within the first hour of life, neonatal mortality between enrolment into the study, and 28 days, was higher in infants initiating breastfeeding at 2-23h with an adjusted relative risk of 1.41(95%CI:1.24;1.62), and 1.79(95%CI:1.39;2.30) in those who initiated breastfeeding at 24-96h. Exclusive breastfeeding was also associated with a reduced mortality risk in the first six months of life (1–3 months mortality: exclusive vs. partial breastfeeding at one month 1.83(1.45;2.32), and exclusive breastfeeding vs no breastfeeding at one month 10.88(8.27;14.31) (2016).

Breastfeeding promotion is crucial in low- and middle-income countries and might contribute to achievement of the majority of the forthcoming Sustainable Development Goals (SDGs), specifically SDG3, which is to ensure healthy lives and promote well-being for all at all ages. The promotion of breastfeeding can prevent an estimated 823,000 child deaths and 20 000 breast cancer deaths every year (Horton & Lo, 2013).

2.5 Indicators of breastfeeding

Lack of precision and consistency of breastfeeding have led to misinterpretation of data and problems with comparability between studies. Consistent and valid definitions of breastfeeding are needed, not only to ensure accurate conclusions by policymakers, but also to increase comparability of data collected from several countries or regions (Labbok & Krasovec, 1990). The most common indicators for the classification of breastfeeding and feeding practices of infants and young children defined by The World Health Organization (WHO) are presented in Table 2-1 below (WHO, 1991; WHO, 2008). Current recommendations regarding early infant feeding include breastfeeding initiation within one hour of birth, exclusive breastfeeding for six months, and continued breastfeeding for up to two years or more, combined with complementary feeding (WHO, 2016).

Table 1-1: Indicators of breast- and infant feeding.

	Indicator	Explanation
Before 6 months	Early initiation of breastfeeding	Proportion of children born in the past 24 months, who were put to the breast within an hour of birth, in exclusion all other substances other than breast milk.
	Exclusive breastfeeding under six months	Proportion of infants aged 0–5 months who are fed exclusively with breast milk, no other liquids or solids except for drops or syrups consisting vitamins, minerals, supplements or medicines). It can be measured by the age when the first supplement of any kind was given, including water.
	Predominant breastfeeding under six months	Proportion of infants 0–5 months of age who are predominantly breastfed, however the infant may also receive water and water-based drinks, fruit juice, oral rehydration solution, drop and syrup forms of vitamins, minerals and medicines, ritual fluids (in limited quantities).No food-based fluids is allowed with the exception of fruit juice and sugar water). The duration can be measured by the age at which other fluids or solid foods was first added.
	Partial breastfeeding or mixed feeding	Breastfeeding combined with other milks and/or solid foods. Includes three levels of substantial feeding: "high," "medium," and "low" (nearly all feeds are breast feeds, about half are breast feeds, almost none are breast feeds).
After 6 months	Timely complementary feeding	When the child is receiving both breast milk and solid food (or semi-solid), after 6 months and is measured in infants older than 6 months but less than 10 months.

	Continued breastfeeding at 1 year	Proportion of children aged 12–15 months who are fed breast milk but is also given solid food.
	Continued breastfeeding at 2 years	Proportion of children aged 20–23 months who are fed breast milk.
	Children ever breastfed	Proportion of children born in the last 24 months who were ever breastfed.

The main purpose of these indicators is to provide a given set of measures to assess breastfeeding practices, and they must be limited in number, relatively easy to measure and interpret, and operationally useful. Current recommendations regarding early infant feeding include breastfeeding initiation within one hour of birth, exclusive breastfeeding for six months, and continued breastfeeding for up to two years or more, combined with complementary feeding (WHO, 2016).

2.6 Determinants of breastfeeding

During the Innocenti Declaration in 1990, the WHO and United Nations Children's fund (UNICEF) called for policies that would promote breastfeeding culture and encourage women to breastfeed their infants exclusively for the first six months of life (WHO *et al.*, 2003). Since then, much effort has gone into scaling up breastfeeding rates especially in low- and middle-income countries (Pérez-Escamilla *et al.*, 2012).

The Lancet Series Breastfeeding 2 reviewed and revised previous conceptual frameworks to identify the determinants of breastfeeding (Rollins *et al.*, 2016). The model operates at three nested levels (see *Figure 2-1*) which can affect breastfeeding decisions and behaviours regarding the initiation, intensity, and continuation of breastfeeding over time.

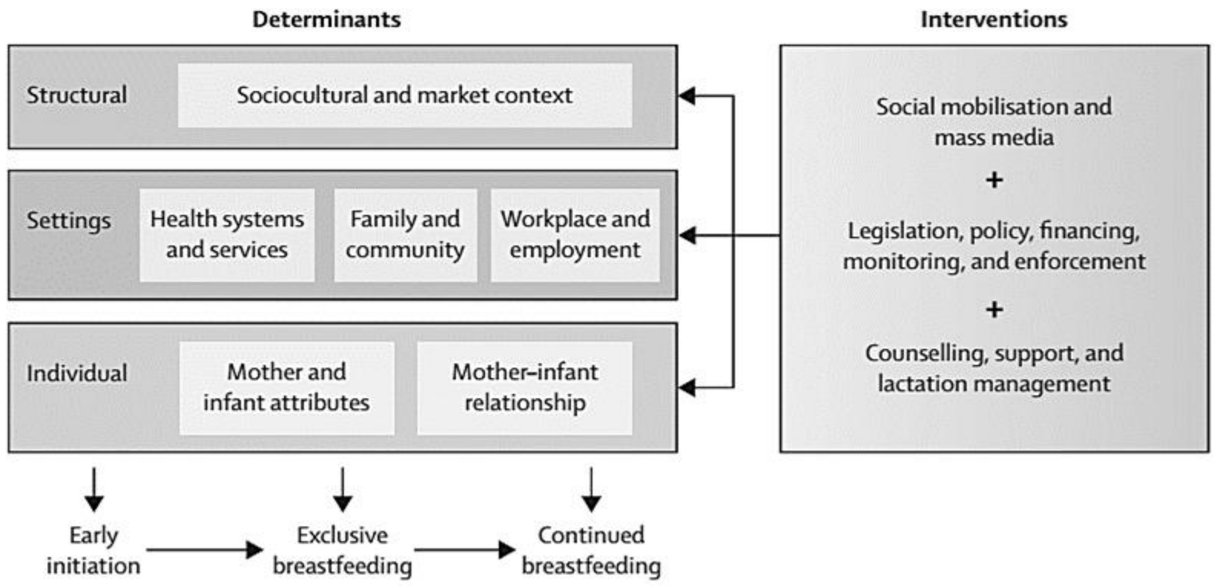

Figure 2-1: The conceptual framework of breastfeeding determinants (Rollins *et al.*, 2016).

2.6.1 Structural level: social, cultural and market context factors

The structural level of breastfeeding includes social, cultural, and market context factors. These factors may consist of social trends, advertising, media, products available in stores, legislation, policy, and media and social mobilisation, which can change social attitudes and practices. An example of how the factors on structural level can determine breastfeeding is when after reports that many infants were malnourished and dying due to formula malpractice, which lead to diluted or contaminated breast milk substitutes, the International Code of Marketing of Breast milk Substitutes was adopted at the 34th World Health Assembly in 1981 (Myres, 1982).

2.6.2 The setting: health systems and services, family and community, workplace and employment

The next level is in context of the setting, which includes health systems and services; family and community; and finally, workplace and employment. Health-care providers can influence and support feeding decisions at the crucial moments right before and after birth (McAllister *et al.*, 2009), as they are equipped to provide knowledge and support (Leviniene *et al.*, 2009). Several health care related factors have been associated with breastfeeding practices (Kennell, 1994; Kozhimannil *et al.*, 2014; Prior *et al.*, 2012; Simmons *et al.*, 2005; Thurston *et al.*, 2013). For this reason, the WHO has created the *Baby-Friendly* hospital initiative to protect and promote breastfeeding during the early phases to improve the practices of early breastfeeding initiation (WHO, 2009c). Mothers who are supported by the community and their families for breastfeeding, are more likely to initiate and prolong the duration of breastfeeding (Meedya *et al.*, 2010).

The workplace has a significant influence on mother's ability to continue breastfeeding. Short maternity leave of less than six weeks may have an odds ratio of four times the increase of either not initiating breastfeeding or early cessation thereof (Guendelman *et al.*, 2009). Studies found that formal employment has a negative effect on breastfeeding (Dearden *et al.*, 2002; Ogbuanu *et al.*, 2011; Ong *et al.*, 2005), and that women who planned to return to work after childbirth were less likely to decide to breastfeed from the start or continue breastfeeding (Hawkins *et al.*, 2007; Mirkovic *et al.*, 2014).

The HIV epidemic in the past 20 years has caused misunderstanding of the policy and programmatic recommendations by communities, families, and health care workers alike. This has harmfully affected the mother's confidence to breastfeed, due to guidelines that was originally against breastfeeding if the mother was HIV positive. Later, further research confirmed that mothers with HIV can breastfeed their baby up to two years if given the correct antiretroviral medications (Arpadi *et al.*, 2009; Donovan, 2016; Gillman *et al.*, 2001; Innis, 2014; Rollins *et al.*, 2013; Shapiro *et al.*, 2010; Silverstein *et al.*, 2007; Smith *et al.*, 2017b; WHO, 2010b).

2.6.3 Individual level: Mother infant attributes and mother-infant relationship

At the most intimate level, a women's breastfeeding behaviour is influenced by personal attributes such as age, weight, education, and confidence, and by attributes of the baby, such as sex, wellbeing, and temperament (Rollins *et al.*, 2016). The intention to breastfeed is a strong predictor for the initiation (Rebecca *et al.*, 2012) and duration of breastfeeding among mothers (DiGirolamo *et al.*, 2005). A mother's intention to breastfeed is superior to all the other factors determining breastfeeding, but the intention can be influenced by many contributing factors. Among others, mothers often abandon breastfeeding due to poor latching (Odom *et al.*, 2013); unsuccessful breastfeeding from first child (Da Vanzo *et al.*, 1990); assumptions that they have insufficient breast milk (Howard *et al.*, 2006), due to fussiness of the baby (Wasser *et al.*, 2011); perceived hunger and the inability to settle the infant (McCann & Bender, 2006); smoking (Leung *et al.*, 2002; Liu *et al.*, 2006); overweight and obesity (Turcksin *et al.*, 2014); and depression (Dennis & McQueen, 2007).

Several studies have been done to identify the determinants of exclusive breastfeeding in sub-Saharan Africa. Among others there is a significant association between exclusive breastfeeding and higher education (Aidam *et al.*, 2005; Lawoyin *et al.*, 2001) and income status (Agho *et al.*, 2011; Ogbo *et al.*, 2015), delivery at health care facilities (Aidam *et al.*, 2005; Bbaale, 2014; Seid *et al.*, 2013; Tampah-Naah & Kumi-Kyereme, 2013), vaginal delivery (Seid *et al.*, 2013), pre- and post-natal care, and breastfeeding counselling (Agho *et al.*, 2011; Lawoyin *et al.*, 2001; Ogbo *et al.*, 2015; Teka *et al.*, 2015), breastfeeding at own home or region (Agho *et al.*, 2011; Aidam *et al.*, 2005). There is also a significant association between a decrease and cessation of breastfeeding and increased infant's age (Agho *et al.*, 2011; Lawoyin *et al.*, 2001; Seid *et al.*, 2013; Teka *et al.*, 2015);

perceived infant size to be small (Tampah-Naah & Kumi-Kyereme, 2013); infant gender (Agho *et al.*, 2011); birth intervals under 24 months (Bbaale, 2014); and decreased maternal age (Lawoyin *et al.*, 2001).

2.7 Breastfeeding as a public health responsibility and human right for the child and mother

2.7.1 The role of governments

Our behaviour as individuals can be affected by the systems and structures of the environment and it is widely acknowledged that social, economic, and political factors all influence our knowledge, attitudes and ability to make healthy choices (Bronfenbrenner, 1986). Therefore, it is the government's responsibility to ensure that the environment enables and influence individuals to make informed decisions for the welfare of themselves and their children. The United Nations Convention on Rights of the Child has stated that governments have the responsibility "to ensure that all segments of society, in particular parents and children, are informed, have access to education and are supported in the use of basic knowledge of child health and nutrition, the advantages of breastfeeding, hygiene and environmental sanitation and the prevention of accidents" (Anon, 1990).

The foundation of the right for breastfeeding lies in the Universal Declaration of Human Rights, which asserts in article 25 that "everyone has the right to a standard of living adequate for the health and well-being of himself and his family, including food…"(UN, 1948).

This right was reaffirmed in two major binding international agreements. In the International Covenant on Economic, Social and Cultural Rights, which came into force in 1976, article 11 states that "The States Parties to the present Covenant recognize [sic] the right of everyone to an adequate standard of living for himself and his family, including adequate food, clothing, and housing...” and also recognises “the fundamental right of everyone to be free from hunger..."(Assembly, 1966; UN, 1976).

2.7.2 Rights of the child

In the Convention on the Rights of the Child, which came into force in 1990, it is reported in article 24 that "States Parties recognize [sic] the right of the child to the enjoyment of the highest attainable standard of health..." (section (1)) and shall take appropriate measures "to combat disease and malnutrition...through the provision of adequate nutritious foods, clean drinking water, and health care" (section (2c)) (Anon, 1990).

It declares that children have the right to life, survival, and development and to the highest attainable standard of health, as well as to safe and nutritious foods (Kent, 2006). Some would argue that the obligation to seek the highest attainable standard of health implies that breast milk substitutes should not be used except in very special circumstances, such as cases in which children have a rare metabolic disorder, such as galactosemia (Kent, 2006).

2.7.3 Rights of the mother

Breastfeeding is also a human rights issue for the mother. The WHO and UNICEF declare that “all women should be enabled to practise exclusive breastfeeding and all infants should be fed exclusively on breast milk from birth to 6 months of age” (WHO, 2009c). Women have the right to accurate, unbiased information needed to make an informed decision about breastfeeding and the right to an environment that enables them to carry it out (Galtry, 2015). However, a mother may not be obliged to breastfeed her child. Others would argue that women should be free to use breast milk substitutes so long as they can be used in ways that are acceptable, feasible, affordable, sustainable and safe (AFASS) which is according to the WHO criteria (WHO, 2009a).

2.7.4 Public health considerations

Breastfeeding is recognised as an important public health issue with enormous social and economic implications. Infants who do not receive breast milk are likely to experience poorer health outcomes than breastfed infants; mothers who do not breastfeed increase their own health risks (Victora *et al.*, 2016a).

Current breastfeeding policies create severe pressure on women to breastfeed and may have ethically problematic consequences for individual women. Some women may experience physical and emotional difficulties when trying to breastfeed, while others might have other good reasons not to breastfeed. In certain contexts, such as in low- and middle-income countries, the reason to promote breastfeeding is crucial where clean water is not available, or parents are poor and might dilute formula, babies will run the risk of becoming undernourished (Jones *et al.*, 2003). For this reason, the International Code of Marketing of Breast-milk Substitutes prohibits the promotion of breast-milk substitutes.

It is the responsibility of providers of information on infant feeding and health care providers to encourage parents to make an informed, individual choice. The mother, in consultation with other family members, should be the one who decides how the child is to be fed.

2.8 Breastfeeding in the context of HIV

Infant feeding by HIV-infected mothers has been a major global public health dilemma since HIV was discovered in human milk 1985 and linked to child infection (Thiry *et al.*, 1985; Ziegler *et al.*, 1985). Infant feeding by HIV-infected mothers has been a controversial matter throughout the years, as evidence regarding the transmission of the HIV virus from the mother to the child emerged. Recommendations regarding infant feeding throughout the years have been refined to address the needs of infants born to HIV-infected mothers.

2.8.1 Early recommendations

After the first findings of HIV to be present in breast milk, the risk to obtain the HIV transmission was initially uncertain and believed to be relatively small. In low-and middle-income settings, the feeding method of choice was to breastfeed by means of the biological mother regardless of the HIV status. The risk for transmission of the HIV virus was not the only factor to consider with regards to infant feeding guidelines, where in addition, the risk for malnutrition and gastro-intestinal - and respiratory infections became evident. The WHO discussion in 1992 concluded that “Where infectious diseases and malnutrition are the main cause of infant deaths and the infant mortality rate is high, breastfeeding should be the usual advice given to pregnant women including those who are HIV-infected” (WHO, 1992).

2.8.2 Promotion of replacement feeding

The WHO published new infant feeding guidelines in 1997-98, which advised that all mothers should be counselled about possible feeding options, and thus, be allowed to make their own decision about infant feeding (UNAIDS, 1998). Subsequently, there was a huge policy shift towards the promotion of replacement feeding and the distribution of free infant formula to HIV positive women enrolled in the prevention of mother-to-child transmission (PMTCT) programmes was initiated in some countries (Coutsoudis *et al.*, 2002).

Emerging evidence at that stage suggested the possibility that exclusive breastfeeding could be safer than mixed feeding, and that replacement feeding represents a risk to child health and survival. Based on the shift in the policy, the WHO accommodated this possibility in 2001 (WHO, 2001), and introduced the AFASS criteria (WHO, 2001; WHO, 2003b). The AFASS criteria was understood as “when replacement feeding is acceptable, feasible, affordable, sustainable, and safe, avoidance of all breastfeeding by HIV-infected mothers is recommended, otherwise, exclusive breastfeeding for the first few months of life is recommended” (WHO, 2001). The infant feeding recommendations, which were focused on feeding guidelines for HIV-infected mothers in 2001, consisted of the following options: replacement feeding with commercial infant formula or modified animal milk, exclusive breastfeeding with early and rapid cessation at six months, expressed heat-treated breast milk or wet-nursing by an HIV-negative mother, the latter two receiving less attention due to their perceived local inapplicability.

A large majority of HIV-infected mothers had experienced extreme difficulty to adhere both to exclusive breastfeeding and replacement feeding (Leshabari *et al.*, 2007; Moland *et al.*, 2010), which caused major challenges for the implementation of AFASS criteria in the local programmes (Sellen *et al.*, 2007).

2.8.3 Evidence on the risk of replacement feeding

In 2006, the WHO infant feeding guidelines were updated and launched a major shift in the previous policy (WHO, 2006). Strong evidence indicating the risks of childhood infections and malnutrition associated with replacement feeding, and with the path-breaking documentation of a higher HIV free survival rate among exclusively breastfed than among replacement fed infants (Coovadia *et al.*, 2007). Therefore, the updated guidelines emphasised breastfeeding as follows: “Exclusive breastfeeding is recommended for HIV-infected mothers for the first six months of life unless replacement feeding is acceptable according to the AFASS criteria for them and their infants before that time. When replacement feeding is acceptable, feasible, affordable, sustainable and safe, avoidance of all breastfeeding by HIV-infected mothers is recommended" (WHO, 2006).

New evidence emerged regarding how the risk of HIV transmission through breastfeeding can be reduced by antiretroviral (ARV) interventions for HIV-infected mothers or HIV-exposed infants. In 2009, the WHO introduced the Rapid Advice (WHO, 2009b), which was based on the evidence of HIV-free infant survival, thus by the provision of safe breast milk in HIV infected women which have access to ARV treatment. The 2010 HIV and infant feeding guidelines followed the rapid advice, providing the following recommendations (WHO, 2010a):

- Mothers known to be HIV-infected should exclusively breastfeed their infants for the first six months of life, introducing appropriate complementary food thereafter, and continue breastfeeding for the first 12 months of life;
- Mothers who decide to stop breastfeeding should stop gradually within one month; stopping breastfeeding abruptly is not advisable;
- Mothers known to be HIV-infected should only give commercial infant formula milk as a replacement feed to their HIV uninfected infants or infants who are of unknown status, when specific conditions are met (referred to as AFASS); and
- Mothers known to be HIV-infected should be provided with lifelong antiretroviral therapy (ART) or antiretroviral prophylaxis interventions.

The Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection recommended lifelong ART for HIV infected mothers, regardless of their cluster of differentiation-4 (CD4) count or clinical stage for the maternal postnatal period and ARV prophylaxis from birth to six weeks for the infant (WHO, 2016a), where the mother could continue breastfeeding.

In 2016, the WHO updated the recommendations on HIV and infant feeding. The guidelines are as follows (WHO, 2016b):

- Mothers living with HIV should breastfeed for at least 12 months and may continue breastfeeding for up to 24 months or longer (similar to the general population) while being fully supported for ART adherence (see the WHO consolidated guidelines on ARV drugs for interventions to optimize adherence)
- National and local health authorities should actively coordinate and implement services in health facilities and activities in workplaces, communities and homes to protect, promote and support breastfeeding among women living with HIV.
- Mothers living with HIV and health-care workers can be reassured that ART reduces the risk of postnatal HIV transmission in the context of mixed feeding. Although exclusive breastfeeding is recommended, practising mixed feeding is not a reason to stop breastfeeding in the presence of ARV drugs.
- Mothers living with HIV and health-care workers can be reassured that shorter durations of breastfeeding of less than 12 months are better than never initiating breastfeeding at all.

These guidelines correspond with the most recent evidence, which reports that the adherence to antiretroviral drugs for both the mother and the child ought to allow the child to safely breastfeed exclusively for six months, and it would be safe for the mother to continue breastfeeding up unto two years of age. Even though HIV can pass from a mother to her child during pregnancy, labour or delivery, and also through breast milk, the evidence on HIV and infant feeding show that giving ART to mothers living with HIV significantly reduces the risk of transmission through breastfeeding, and also improves the mother's health (WHO, 2016a).

2.9 Conclusion

It is quite evident that breast milk is the optimal nutrition for infants for the first six months of life, prevents malnutrition, promotes optimal growth during the early stages of life and improves cognitive development. Moreover, breastfeeding also provides non-nutritive benefits for the child such as short- and long-term protection against infections and prevent the onset of non-communicable diseases. Breastfeeding also provides numerous benefits for the breastfeeding mother such as protection against certain cancers and other non-communicable diseases, birth spacing and improved mother-infant relationship. However, despite all these benefits of breastfeeding, there are many determinants which may increase or decrease the prevalence of breastfed children around the world. HIV transmission has been a main contributor towards the public health dilemma regarding breastfeeding mothers who are HIV positive. Most importantly appropriate breastfeeding practices may protect against child mortality, especially during the early stages of life. Breastfeeding is a public health responsibility and should extensively be promoted globally, especially in countries where the breastfeeding prevalence remain sub-optimal.

CHAPTER 3 ARTICLE

Impact of Breastfeeding on Mortality in Sub-Saharan Africa: A Clinical Evaluation and Cost-Analysis

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Abstract: Sub-Saharan Africa has lower breastfeeding rates compared to other low- and middle-income countries, and globally holds the highest under-five mortality rates. The aims of this review were to estimate mortality risk for inadequate breastfeeding, prevalence of breastfeeding, population attributable fraction, and the economic impact of breastfeeding on child mortality, in sub-Saharan Africa. The systematic review included databases from Medline and CINAHL. Meta-analysis of mortality risk estimates was conducted using random effect methods. The prevalence of breastfeeding in Sub-Saharan African countries was determined using UNICEF's database. The population attributable fraction was derived from the prevalence and relative risk data. Non-Health Gross Domestic Product Loss attributable to child deaths in relation to inappropriate breastfeeding was calculated using data from the World Health

Statistics data. The pooled relative mortality risk to any kind of infant feeding compared to exclusive and early breastfeeding initiation was 5.71(95%CI:2.14;15.23) and 3.3(95%CI: 2.49;4.46), respectively. The overall exclusive and early initiation of breastfeeding prevalence were 35%(95%CI: 32%;37%) and 47%(95%CI: 44%;50%), respectively. The population attributable fraction for non-exclusive breastfeeding was 75.7% and for late breastfeeding initiation was 55.3%. The Non-Health Gross Domestic Product Loss resulted in about 19.5 USB$. Conclusion: Public health interventions should prioritize breastfeeding practices to decrease the under-five mortality burden and its related costs in sub-Saharan Africa.

Key words: "Child"; "Mortality"; "Breastfeeding"; "Prevalence"; "Public health"; "Africa South of the Sahara"

1. INTRODUCTION

Globally, from 1990 to 2015, child mortality was estimated to have claimed the lives of 236.3 million children before their fifth birthday [1]. The Sustainable Development Goal in 2015 set its target for 2030 to an under-five mortality rate (U5MR) of 25 or fewer deaths per 1000 live births [2]. Currently, sub-Saharan Africa holds the highest U5MR of 83.1 deaths per 1000 live births [1].

The nutritional status of children is one of the main modifiable risk factors for mortality [3-7]. The World Health Organization (WHO) and United Nations Children's Fund (UNICEF) strongly recommend early initiation of breastfeeding (EIBF) and exclusive breastfeeding (EBF) during the first 6 months of life for the widely acknowledged health and nutritional benefits [8].

In recent years, a large improvement in EBF prevalence was observed in sub-Saharan Africa. The prevalence more than doubled in West and Central Africa (from 12% in 1995 to 28% in 2015) and went from 35% to 47% in East and Southern Africa [1]. Despite these improvements, sub-Saharan Africa still has lower EBF rates (35%) when compared to other low- and middle-income countries (39%) [9].

Several systematic reviews and meta-analyses investigated the association of appropriate breastfeeding practices and child mortality [10-16]. However, none have specifically focused on the sub-Saharan Africa region. Furthermore, there is a gap of knowledge regarding the economic impact of breastfeeding practices in relation to child mortality in sub-Saharan Africa.

Therefore, the primary aim of this study was to perform a systematic review and meta-analysis of the association between breastfeeding practices (particularly EBF and EIBF) and the risk of mortality in children under-five years in sub-Saharan Africa. A second aim was to evaluate how improved breastfeeding practices may reduce the economic impact attributable to U5MR in sub-Saharan Africa.

The primary aim of this study was to perform a systematic review and meta-analysis of the association between breastfeeding practices (particularly on EBF and EIBF) and the risk of mortality in children under-five years in sub-Saharan Africa. A second aim was to determine the impact of breastfeeding practices on U5MR in sub-Saharan Africa. Thirdly, a cost analysis was performed to evaluate how improved breastfeeding practices may reduce the economic impact attributable to U5MR in sub-Saharan Africa.

2. MATERIALS AND METHODS

2.1 Eligibility Criteria of Included Studies for Systematic Review and Meta-analysis

The literature search was conducted on observational studies published from 01 January 2000 to 31 May 2019,with no language restrictions used. Eligible papers were included if they reported an estimate for breastfeeding practices (EBF, EIBF, continued breastfeeding, any breastfeeding vs other inappropriate breastfeeding practices) and all-cause or infectious mortality in children under five years of age in sub-Saharan Africa. The eligibility criteria for the meta-analysis were limited to studies reporting estimates for strength of association (with 95% CI) between EBF and/or EIBF and all-cause mortality in children under five years of age in sub-Saharan Africa. EBF and EIBF was defined by the proportion of infants aged 0-5 months of age who are fed exclusively with breast milk and the proportion of children who were put to the breast within the first hour after birth, respectively [17].

2.2 Data Sources

The literature search was conducted by searching electronic databases and scanning through reference lists of the included studies, and relevant systematic reviews and meta-analyses.

Medical Subject Headings (MeSH) and key terms (Annexure E (Supporting material: Text 1)) were used to define the search and the North-West University library search engine (powered by EBSCO*host*) was used to identify existing evidence. Databases such as MEDLINE and CINAHL were included in the search engine (Annexure E (Supporting material: Text 3)).

2.3 Study Selection and Quality Assessment

The paper selection was conducted independently by two investigators following the Preferred Reporting Items of Systematic reviews and Meta-Analysis (PRISMA) [18]. The titles and the abstracts of the citations retrieved by the searches were screened for relevance (CP, HA). The investigators independently checked the full papers for eligibility (CP, HA). The quality assessment was conducted independently by the same investigators using the Newcastle–Ottawa Scale (NOS) (Wells *et al.*, 2000). Agreement between the two investigators was reported using Cohen`s K, intraclass correlation coefficient (ICC) and percentage of agreement. Thereafter, the data (author; year published; country; number of subjects in study; number of deaths; persons year of follow-up; exposure of feeding (per age group); estimate risk for all-cause mortality including HR, OR, RR (95%CI); other specific mortality outcome (only if reported); covariates) from eligible studies were extracted independently by the two investigators. Disagreements were resolved by consensus and a third author (CR) was consulted in such case that no agreement could be reached.

2.4 Statistical Analysis

We conducted a meta-analysis to estimate relative risk of mortality due to non-EBF and delayed breastfeeding initiation. Afterwards, we estimated EBF and EIBF prevalence in sub-Saharan Africa. Then, prevalence and all relative risk estimates (OR, RR and HR)were merged to provide population attributable risks. Finally, population attributable risk was used, along with data on sub-Saharan Africa population structure gross domestic product, and health cost to estimate how improved breastfeeding practices may reduce the economic impact attributable to U5MR in sub-Saharan Africa.

2.4.1 Meta-analytic Estimates

Meta-analysis of mortality relative risk estimates was determined by random and fixed effect methods. Heterogeneity was evaluated using the Cochrane Q test and the I^2 statistic. Stratification, study exclusion and meta-regression analyses were conducted to identify sources of heterogeneity. Publication bias was assessed by funnel plot visual inspection and the Egger's test [20]. Influence analyses were conducted excluding one study at a time.

2.4.2 Breastfeeding Prevalence in sub-Saharan Africa

Breastfeeding prevalence (EBF and EIBF) in Sub-Saharan African countries was estimated during the period 2000-2018 using data from the UNICEF database [21]. A mixed model having the arcsine of the breastfeeding prevalence as outcome and random intercept by country, was used to estimate marginal least squared means and 95% confidence limits by country. Breastfeeding prevalence by country was computed by retro-transformed sin values and meta-analysed by a fixed effect model having country under-five median population during the period 2000-2018 as weight variable. Prevalence estimates by regions were compared using a linear meta-regression approach.

2.4.3 Population Attributable Risk Estimates

The relative risk for mortality and the prevalence of population at risk (complementary to breastfeeding practice prevalence) were merged, resulting in the population attributable fraction (PAF = (Pr (RR-1))/((Pr (RR-1)) +1) where Pr is the prevalence of the population at risk and RR is the estimate of the relative risk of mortality.

2.4.4 Assessment of Breastfeeding Mortality Costs

Non-Health Gross Domestic Product Loss attributable to child deaths (NHGDPL) was undertaken as proposed by Kirigia et al.,[22] (based on World Health Statistics 2015).

$$\text{NHGDPL}_{area} = \sum_{i}^{n}\sum_{t}^{k}\frac{1}{(1+r^{t})}\Delta GDP_{i}Mort_{i}$$

where i represents i-th country in a region; n the total number of countries within a region; t the t-th year of life loss; k the total number of working years lost (difference between the retirement age (assumed 65) and the age at starting work (assumed 20)); ΔGDP_i the difference between the per-capita gross domestic product (GDP) and the per-capita health expenditure of the i-th country; r the discount rate (r =3%) which takes into account the variation of the economic productivity during the working period. Finally, $Mort_i$ represents the number of child deaths from that given country and it was estimated considering the median under-five mortality attributable to inappropriate breastfeeding practices by country during the period 2000-2018. This element was calculated multiplying the total under-five deaths by country to the proportion of under-five deaths due to inappropriate breastfeeding practices. We assumed 15% of the total under-five child deaths are attributable to poor breastfeeding practices dividing the worldwide 800,000 child deaths attributable to poor breastfeeding practices observed in 2017 by the 5.5 million under-five child deaths that occurred in the same year [1]. The NHGDPL preventable by proper breastfeeding practices was computed multiplying deaths by the PAF. The NHGDPL was reported as US billion dollars (USB$).

3. RESULTS

3.1 Systematic Review

The initial literature search yielded 1,511 after the removal of duplicates. After title and abstracts screening, 51 records were assessed for eligibility. After the exclusion of 39 full text articles (Figure 3-1), 16 studies were included in the qualitative synthesis [23-37]. Two of these studies were not eligible to be retained for the meta-analysis. One study did not report the 95% confidence intervals [24] and the other study conducted a pooled analysis which included a country from Peru, outside sub-Saharan Africa [23] (Figure 3-1). Of the sixteen studies included for qualitative synthesis, nine were prospective studies [23,26-29,34-36,32], two were retrospective studies [31,37] and four were surveys [30,33,24,38]. The quality of the studies according to the NOS score ranged between a minimum of six points to a maximum of eight points out of nine, with a median of seven points. Agreement between the two investigators rating the study quality was satisfactory (Cohen K=0.52, ICC=0.82, agreement =73%). Study characteristics were reported in Table 3-1. The relative risk estimates for non-EBF vs EBF ranged from 3.6(95%CI:2.5;5.2) [36] to 33.3(95%CI:25;50) [26]. The relative risk estimates for predominant breastfeeding and partial breastfeeding vs EBF ranged from 0.94(95%CI 0.41;3.45) [37] to 1.46(95%CI:0.75;2.86) [23] and from 0.80(95%CI:0.14;4.61) [28] to 3.82(95%CI:1.99;7.34) [29], respectively. The median number of adjusting factors among studies was seven and only four studies reported less than five factors [25,33-35], of which two of these studies did not report any adjusting factors [33,34].

3.2 Mortality Risk in Relation to Exclusive Breastfeeding and Early Initiation of Breastfeeding and Their Population Attributable Fractions

Mortality risk in association with any kind of infant feeding with respect to EBF, was 5.71(95%CI:2.14;15.23) relevant heterogeneity was observed (I^2=96.3%;$P_{Cochrane\text{-}test} < .001$) (Figure 3-4). Here, the exclusion of the study from Motsa et al. [37], reduced the between study heterogeneity the most (I^2=90.2%; $P_{Cochrane\text{-}test} < 0.01$). Further heterogeneity reduction was obtained when applying meta-regression considering NOS score I^2=35%. Delayed compared to early breastfeeding initiation increased the relative mortality risk to

3.33(95%CI:2.49;4.46), with no heterogeneity (I^2=0%,$P_{Cochrane\ test}$=.406). According to this sensitivity analysis, the RR estimate for mortality due to non-EBF and delayed breastfeeding initiation would have been 4.21(95%CI:1.5;12.2) and 3.19(95%CI:1.6;6.34); which overlap with the initial estimates of 5.71(95%CI:2.14;15.23) and 3.33(95%CI:2.49;4.46), respectively. According to funnel plot visual inspection (Supporting: Figures 1 & 2) and Egger test, no indication of publication bias was observed (P_{Egger}>0.1).

3.3 Prevalence of Exclusive Breastfeeding and Early Initiation of Breastfeeding in Sub-Saharan Africa

We estimated an EBF prevalence in Sub-Saharan African countries of 34%(95%CI:32%;37%) during the period 2000-2018 (Figure 3-2), with a large variability among the countries (5% in Chad to 86% in Rwanda). When considering different regions, we observed the highest EBF prevalence which was 50% in East Africa (95%CI:47%;54%,I^2=94.3%). EBF prevalence were 40%(95%CI:33%;47%,I^2=81.9%), 29%(95%CI:23%;36%,I^2=91.1%) and 22%(95%CI:18%;26%, I^2=89.7%) in Southern Africa, Central Africa and West Africa, respectively. Overall difference between region was non-significant (P=0.068), East Africa had statistically significant higher EBF prevalence with respect to Southern Africa (P=0.029), Central Africa (P=0.034) and West Africa (P=0.043). EIBF prevalence was 47%(95%CI: 44%;50%) (Figure 3-3). Also, EIBF prevalence had a large range of variability among countries going from 26% (Somalia) to 87% (Eritrea). Southern Africa had the highest EIBF prevalence (60% (95%CI:51%;70%,I^2=33.6%). East Africa, Central Africa and West Africa had a prevalence of 59%(95%CI:54%;64%,I^2=79.8%), 43%(95%CI:35%;51%,I^2=70.8%), and 35%(95%CI:30%;41%,I^2=73.2%), respectively. The overall difference between region was strongly significant (P<0.001) as for the difference between early breastfeeding prevalence of Central Africa with respect to West Africa (P<0.001) and East Africa (P=0.004), West Africa with respect to East Africa (P=0.003) and East Africa with respect to South Africa (P<0.001). Also, the difference EIBF prevalence in West Africa and in South Africa was statistically significant (P=0.031).

3.4 Population Attributable Fraction and Breastfeeding Mortality Costs

Finally, we estimated that the PAF for non-EBF was 75.7% in sub-Saharan Africa , ranging from 70.2% in East Africa to 77% in West Africa. The PAF for late breastfeeding initiation was 55.3% in sub-Saharan Africa, ranging from 48.2% in Southern Africa to 60.2% in West Africa (Table 3-2). The NHGDPL attributable to under-five child deaths was 130 USB$. The NHGDPL attributable to inappropriate breastfeeding practices resulted in about 19.5 USB$. When considering deaths avoidable by EBF and early breastfeeding initiation, the NHGDPL would be 8.3 and 8.4 USB$ in sub-Saharan Africa, respectively (Table 3-3).

4. DISCUSSION

We reported a five-fold increased risk for mortality was observed with suboptimal breastfeeding practices. The overall prevalence for EBF and EIBF were 34% and 47%, respectively. The PAF for non-EBF and for late breastfeeding initiation were 75.7% and 55.3% respectively. Finally, the total NHGDPL attributable to under-five child deaths and inappropriate breastfeeding practices were calculated to be 130 USB$ and 19.5 USB$, respectively.

Our results agree with previous systematic reviews and meta-analysis of breastfeeding practices and mortality in sub-Saharan Africa [39,11-16]. We confirm that breastfeeding is a cost-effective intervention with potential to prevent child deaths [40]. Feeding colostrum during EIBF and practicing EBF may protect against infections, such as sepsis, acute respiratory tract infection, meningitis, omphalitis and diarrhoea, which is the main cause of child deaths in developing countries [41]. According to a systematic review and meta-analysis, peer counselling as a community intervention reduces the risk of non-EBF significantly, especially in low- and middle-income countries [42]. However, some education interventions have not proven effective in reducing mortality [43]. Adherence to the Baby-friendly Hospital Initiative (BFHI) *Ten Steps* has been proven to have a positive impact on short- and long-term breastfeeding outcomes. Community support interventions is part of the step ten of the BFHI and appears to be essential for sustaining breastfeeding impacts of BFHI in the longer term [44]. Therefore, emphasis ought to be placed on encouraging mothers to deliver in a health institution [45], together with continued support of breastfeeding through community interventions [44].

In the present systematic review, large variability among studies was observed for mortality risk estimates for exclusive breastfeeding. This large variability could be better understood for example considering the study of Shifa et al.[37] which provided the lower RR estimate and the study of Biks et al.[26] which provided the higher RR estimate. These two studies were both performed in Ethiopia and in rural areas but were located in the South and North-western regions respectively, which are completely different from a geographic viewpoint. The study from Shifa et al.[37] was conducted in a pluvial area while the study from Biks et al.[26] was conducted in a desert area with a different rate of exclusive breast feeding of 50% and 80%, respectively. Notably and as reported by the authors, the large food availability in the south area may have influenced both exclusive breastfeeding and child mortality.

The overall EBF prevalence for infants under 6 months was estimated to be poor (34%) compared to the 2025 WHO’s target of at least 50%. Our estimated prevalence of EBF among infants younger than 6 months, was consistent with the results by Cai et al. [9], who reported a prevalence of 35% of EBF in Africa in 2010. We also estimated that the prevalence of EIBF was just less 50%. This result is confirmed by the WHO Global Survey, which reported that the prevalence of EIBF is approximately 50% in many low- and middle-income countries [46]. However, this survey was conducted more than ten years ago (2004-2005) in Africa, which indicates the poor improvement of EIBF in sub-Saharan Africa, specifically.

In the present work, large variability was observed between individual sub-Sahara African countries and regions for both EBF and EIBF prevalence. This variability can be explained by the multiple factors associated with breastfeeding practices [47], or the risk of bias, which may have occurred through the retrospective evaluation methods used by UNICEF's database [48]. Another factor may have been the existing disparities towards adopting the WHO guidelines from 1997-1998 [49] to 2006 [50] for feeding with respect to the postnatal prevention of mother to child transmission (PMTCT) of human immunodeficiency virus (HIV). The infant feeding guidelines in 1997-1998 [49] and 2001 [51] created a huge policy shift towards the promotion of replacement feeding and the distribution of free infant formula to HIV positive women enrolled in the PMTCT programmes [52]. As new evidence was emerging, the updated 2006 guidelines emphasized EBF among HIV positive mothers after the risks of childhood infections, malnutrition associated with replacement feeding, and higher HIV free survival rate among exclusively breastfed than among replacement fed infants were reported [50].

According to the population at risk and the mortality risk, we estimated that about 55% to75% of child deaths are due to inappropriate breastfeeding practices among affected children, and that a portion of those deaths is avoidable if the prevalence of appropriate breastfeeding practices would improve in sub-Saharan Africa. Moreover, we estimated that child mortality due to inappropriate breastfeeding practices results in a loss of GDP of about 19.5 USB$. Thus, if EBF and EIBF prevalence would grow, this cost would potentially be reduced, with child deaths avoided, to the tune of 8.4 and 7 USB$, respectively. The present cost analysis is in agreement with previous reports [22] and results in an immediate and remarkable economic saving that will be maintained in the long-term.

It was reported that the cost of a community intervention aimed to improve EBF practice in South Africa would be in the range of 200-300 US$ per woman [53]. Such an intervention for improving breastfeeding would result in a total cost of 1.1 USB$ across sub-Saharan Africa if it was applied extensively, that is, to all mothers who experienced a child death in the last year. Notably, this cost represents approximately 6% of the overall GDP loss due to child mortality in relation to poor breastfeeding practices [54,55].

Our work has limitations. Due to missing information, we limited our analysis to EBF and EIBF. It would have been of interest to as well consider other exposures such as mixed feeding and timing of breastfeeding initiation. Another weakness of our work is that we provided results for sub-Saharan Africa as a whole, while a country-specific evaluation of breastfeeding practices impact may be of greater interest for practitioners. Finally, we pooled different RR estimates such as HR, RR and odds ratio, which could have generated a bias. On the other hand, a sensitivity analysis was performed considering only the most reliable prospective studies.

This study is unique because it integrates epidemiological-, public health- and economic data providing novel information regarding how improved breastfeeding practices may impact sub-Saharan African society. In addition, breastfeeding prevalence, U5MR, child population and costs were obtained from reliable population-based surveys. It is not merely speculation that sub-Saharan Africa would greatly benefit by an extensive plan of interventions aimed to improve beneficial breastfeeding practices. Public health interventions aimed to improve EBF and EIBF may prevent 55%-75% of lives lost due to inappropriate breastfeeding practices, saving more than 10 USB$.

AUTHOR CONTRIBUTION

CP and CR conceptualized and designed the study and data collection instruments and drafted the initial manuscript. CP and HA collected data and CR carried out the initial analyses. HA, JG and SK contributed to the acquisition, analysis, or interpretation of data reviewed and revised the manuscript critically for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

COMPLIANCE WITH ETHICAL STATEMENTS

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Table 1-1: Characteristics of included studies for the systematic review of breastfeeding practices and child mortality.

Prospective studies						
Author, year	**Country**	**Sample**	**Exposure *(age-group)***	**Mortality**	**Covariates**	**NOS**
Bahl et al., 2005 ° °°	Ghana, India and Peru	N: 9,424 D: 104 P-year: 3,264	EBF VS. PRE *(6-26 w)* PBF VS. PRE NBF VS. PRE	HR_{EBF}: 1.46 (0.75;2.86) HR_{EBF-DS}: 1.36 (0.37;5.03) HR_{PBF}: 2.46 (1.44;4.18) HR_{PBF-DS}: 3.37 (1.46;7.75) $HR_{PBF-ALRI-S}$: 3.57 (0.93;13.7) HR_{NBF}: 10.5 (5.0;22.0) HR_{NBF-DS}: 8.96 (2.56;31.4) $HR_{NBF-ALRI-S}$: 32.7 (6.82;157.2)	Infant's weight at enrolment, sex, twin status, birth order, ^ education, place of delivery, household water supply	7
Biks et al., 2015	Ethiopia	N: 1,752 D: 130 P-year: 1,473	NEBF VS. EBF *(<1y)* EI >1d VS. EI <1h EI 1-24h VS. EI <1h	RR_{NEBF}: 7.86 (5.11;12.10) RR_{EI}: 2.96 (1.76;4.96) RR_{EI}: 4.84 (2.94;7.99)	Nutrition factors, environmental factors, behavioral factors, residential factor, ^ biological factors, SES	6
Edmond et al., 2006	Ghana	N: 10,947 D: 268 P-year: 10,947	PRE VS. EBF *(<28 d)* PBF VS. EBF EI 1-24h VS. EI <1h EI >1d VS. EI <1h	HR_{PRE}: 1.30 (0.90;1.87) HR_{PBF}: 3.82 (1.99;7.34) HR_{EI}: 1.43 (0.88;2.31) HR_{EI}: 2.88 (1.87;4.42)	Parity, ^ age, ^ income, place of delivery, gender, gestational age, number of antenatal visits, place of birth, birth attendant, infant health at birth, infant health at the time of interview, ^ health at the time of delivery, household water supply, neonatal size at birth	6
Edmond et al., 2007	Ghana	N: 10, 942 D: 140 P-year: 840	PRE VS. EBF *(<28 d)* PBF VS. EBF	OR_{PRE}: 0.97 (0.45;2.04) OR_{PRE-IS}: 1.45 (0.90;2.34) OR_{PBF}: 0.80 (0.14;4.61)	^ education, ^ income, sanitation, overcrowding, antenatal care, delivery attendant, site of delivery, ^ ethnicity, ^ age, parity, ^	6

			EI >1d VS. EI <1d	OR_{PBF-IS}: 5.73 (2.75;11.91) OR_{EI}: 1.63 (0.85;3.11) OR_{EI-IS}: 2.61 (1.68;4.04)	perinatal health, sex, gestational age, neonatal perinatal health, other breastfeeding practices, household water supply, neonatal size at birth, congenital abnormalities	
Edmond et al., 2008	Ghana	N: 11,751 D: 320 P-year: 901	PRE VS. EBF *(<28 d)* EI >1d VS. EI <1d	HR_{PRE}: 1.05 (0.25;4.38) HR_{EI}: 2.94 (1.00;8.73)	^ education, sanitation, site of delivery, ^ age, ^^ age, ^ perinatal health, multiple births, gender, EI, infant perinatal health, pre-lacteal feeding	6
Mengesha et al., 2016	Ethiopia	N: 1,152 D: 68 P-year: 75	NEBF VS. EBF *(<28 d)*	HR_{NEBF}: 7.5 (3.77;15.60)	*	6
Neovita, 2016	Ghana	N: 22,995 D: 699 P-year: 11,498	*(1 to <3m)*EI 2-23h VS. EI <1h EI >1d VS. EI <1h *(3 to <6m)*EI 2-23h VS. EI<1h EI >1d VS. EI <1h	RR_{EI}: 2.22 (1.51;3.26) RR_{EI}: 2.37 (0.73;7.73) RR_{EI}: 1.54 (1.05;2.27) RR_{EI}: 1.84 (0.57;5.93)	Sex, study site, birth weight, singleton babies, ^ age, ^ education, parity, skilled birth attendant, caesarean section, wealth quartile	7
Neovita, 2016	Tanzania	N: 31,999 D: 1,112 P-year: 63,998	*(1 to <3m)*EI 2-23h VS. EI <1h EI >1d VS. EI <1h *(3 to <6m)*EI 2-23h VS. EI<1h EI >1d VS. EI <1h	RR_{EI}: 1.05 (0.66;1.66) RR_{EI}: 1.39 (0.34;5.56) RR_{EI}: 1.41(0.92;2.16) RR_{EI}: 0.66(0.41;6.66)	Sex, study site, birth weight, singleton babies, ^ age, ^ education, parity, skilled birth attendant, caesarean section, wealth quartile	7
Orsido et al., 2019	Ethiopia	N: 964 D: 159 P-year: 16	EI >1h VS. EI <1h (<28 d)	RR_{EI}: 2.62 (1.60;4.30)	^ and neonatal factors, neonatal illness, service-related factors	7
Rollins et al., 2013	South Africa	N: 2,589 D: 101 P-year: 2,589	PBF VS. EBF *(0-12m)* NEBF VS. EBF	HR_{PBF}: 2.6 (1.9;3.8) HR_{NEBF}: 3.6 (2.5;5.2)	Sex, age, HIV status, water source, ^^ age, enrolment clinic, ^ education	7

WHO team, 2000 °	Ghana	N: 1,099 D: 33	NBF VS. BF (<23m)	RR_{NBF}: 7.9 (1.2;53.2)	^ education, age-group	7
	Senegal	N: 3,534 D: 425	NBF VS. BF (<23m)	RR_{NBF}: 2.0 (1.4;3.1)		6
Retrospective studies						
Author, year	**Country**	**Sample**	**Exposure *(age-group)***	**Mortality**	**Covariates**	**NOS**
Girma et al., 2011	Ethiopia	N: 296 D: 74	nBF VS. eBF *(<5y)*	OR_{nBF}: 13.21 (3.28;53.16)	Ethnicity, religion, parity, floor materials of the house, ^^ age, eBF, vaccination history, wealth quintile	7
Shifa et al., 2018	Ethiopia	N: 1,143 D: *	nBF VS. eBF *(<5y)* PRE VS. EBF PBF VS. EBF EI >1h VS. EI <1h nBF VS. eBF *(<1y)* PRE VS. EBF PBF VS. EBF EI >1h VS. EI <1h	HR_{eBF}: 8.09 (4.08;16.05) HR_{PRE}: 0.94 (0.38;2.29) HR_{PBF}: 1.29 (0.86;1.94) HR_{EI}: 1.55 (0.95;2.51) HR_{eBF}: 14.19 (5.51;36.50) HR_{PRE}: 1.19 (0.41;3.45) HR_{PBF}: 0.91 (0.54;1.51) HR_{EI}: 1.43 (0.80;2.59)	Sex, ^ education, wealth index, husband's occupation, marital status of mother, first breastfeeding started, breastfeeding status within 6 months of age, eBF, bottle feeding, timing of first bath, anything applied to umbilical wound	8
WHO team, 2000 °	Gambia	N: 431 D: 202	NBF VS. BF *(<23m)*	OR_{NBF}: 0.9 (0.3;2.6)	^ age, age-group	6
Surveys						
Author, year	**Country**	**Sample**	**Exposure *(age-group)***	**Mortality**	**Covariates**	**NOS**
Ettarh & Kimani, 2012	Kenya	N: 16,162 D: *	CBF 6-12m VS. BF <6m *(<5y)* CBF >12m VS. BF *(<6m)*	HR_{CBF}: 0.55 (0.20;1.48) HR_{CBF}: 0.13 (0.02;0.84)	Place of residence, ^ age, ^ education, sex, birth order, household wealth quintile, place of delivery, province, duration of breastfeeding, postnatal visit at 2	-

					months; place of residence x breastfeeding duration	
Kayode et al., 2012	Nigeria	N: 28,647 D: 3,201	CBF 6-12m VS. NBF (<5y) CBF >12m VS. NBF	OR_{CBF}: 0.27 (0.24;0.30) OR_{CBF}: 0.10 (0.08;0.11)	*	-
Lindstrom et al., 2015°°	Ethiopia	N: 9,173 D: *	nBF *(0m)* nBF *(1-11m)* BF 11m *(1-4y)* BF 23m *(1-4y)* BF 35m *(1-4y)* BF 47m *(1-4y)*	OR_{nBF}: 115.35 ** OR_{nBF}: 2.85 OR_{BF}: 1.81 OR_{BF}: 1.5 OR_{BF}: 2.0 OR_{BF}: 7.9	SES, environmental factors, ^ education, ^ age, ^^ age, multiple births, sex	-
Motsa et al., 2016	Swaziland Lesotho, Zambia and Zimbabwe	N: 13,218 D: 677	EBF VS. NBF (<1y) PBF VS. NBF (<1y)	HR_{EBF}: 33.3 (25; 50) HR_{PBF}: 25 (25; 33.3)	^ demographic, environmental factors and SES, infant's bio-demographic variables	-

Notes: N: number of subjects; D: number of deaths; P-year: persons year of follow up; EBF: exclusive breastfeeding; PRE: predominant breastfeeding; w: week/s; PBF: partial breastfeeding; NBF: not breastfeeding; HR: hazard ratio; DS: diarrhea specific; ALRI-S: acute lower respiratory infection-specific; NEBF: not EBF; y: year/s; d: day/s; h: hours/s; EI: early initiation of breastfeeding; RR: relative risk; SES: socio-economic status; OR: odds ratio; IS: infection specific; m: month/s; nBF: never breastfed; eBF: ever breastfed; BF: breastfeeding; CBF: continued breastfeeding; °: stratified by country; °°: not eligible for meta-analysis *: not reported; **: confidence intervals not reported; ^ : maternal; ^^ : paternal.

Table 2-3: Population at risk and population attributable fraction for mortality attributable to breastfeeding practices.

Non-EBF vs. EBF			
Area	**°Pp risk (95% CIs)**	***RR (95% CIs)**	**PAF (95% CIs)**
Sub Saharan Africa	66% (63%; 68%)	5.71 (2.14, 15.23)	75.7% (42, 91)
Central Africa	71% (64%; 77%)		77.0% (42, 92)
West Africa	78% (74%; 82%)		78.6% (46, 92)
East Africa	50% (46%; 53%)		70.2% (34, 88)
Southern Africa	60% (53%; 67%)		73.9% (38, 91)
Late breastfeeding initiation vs. Early breastfeeding initiation			
Area	**°Pp risk (95% CIs)**	***RR (95% CIs)**	**PAF (95% CIs)**
Sub Saharan Africa	53% (50%; 56%)	3.33 (2.49, 4.46)	55.3% (45; 66)
Central Africa	57% (49%; 65%)		57.0% (48; 69)
West Africa	65% (59%; 70%)		60.2% (61; 71)
East Africa	41% (36%; 46%)		48.9% (30; 61)
Southern Africa	40% (30%; 49%)		48.2% (25; 63)

Notes: °: Population at risk derived from meta-analytical estimate of prevalence by area UNICEF 2000-2018; *: Relative risk of mortality derived from meta-analytical estimate of relative risk estimates from included studies; PAF: population attributable fraction PAF = Pp (RR-1)/(Pp (RR-1)+1).

Table 3-3: Economic gross domestic product loss attributable to child mortality in sub-Saharan Africa.

Area	**All-causes (USB$)[a]**	**Any type BF (USB$)[b]**	**Exclusive BF (USB$)[c]**	**Early initiation BF (USB$)[d]**
Sub Saharan Africa	129.973	16.753	8.359	8.394
Central Africa	29.117	3.754	1.876	1.878
West Africa	72.836	8.753	4.405	4.348
East Africa	9.321	1.456	0.742	0.714
Southern Africa	18.699	2.789	1.336	1.453

Notes: USB$: Billions of US dollars, BF: Breast feeding, a: Economic loss due to child mortality for all cause; b : Economic loss due to child mortality for inappropriate breast feeding; c : Economic loss due to child mortality for non-exclusive breast feeding; d : Economic loss due to child mortality for delayed breast feeding initiation.

LEGENDS FOR FIGURES

Figure 3-1. Flow chart of paper selection.

Figure 3-2. Exclusive breastfeeding prevalence in sub-Saharan Africa.

Figure 3-3. Early initiation of breastfeeding prevalence in sub-Saharan Africa.

Figure 3-4. Meta- analysis of breastfeeding practices in relation to mortality risk.

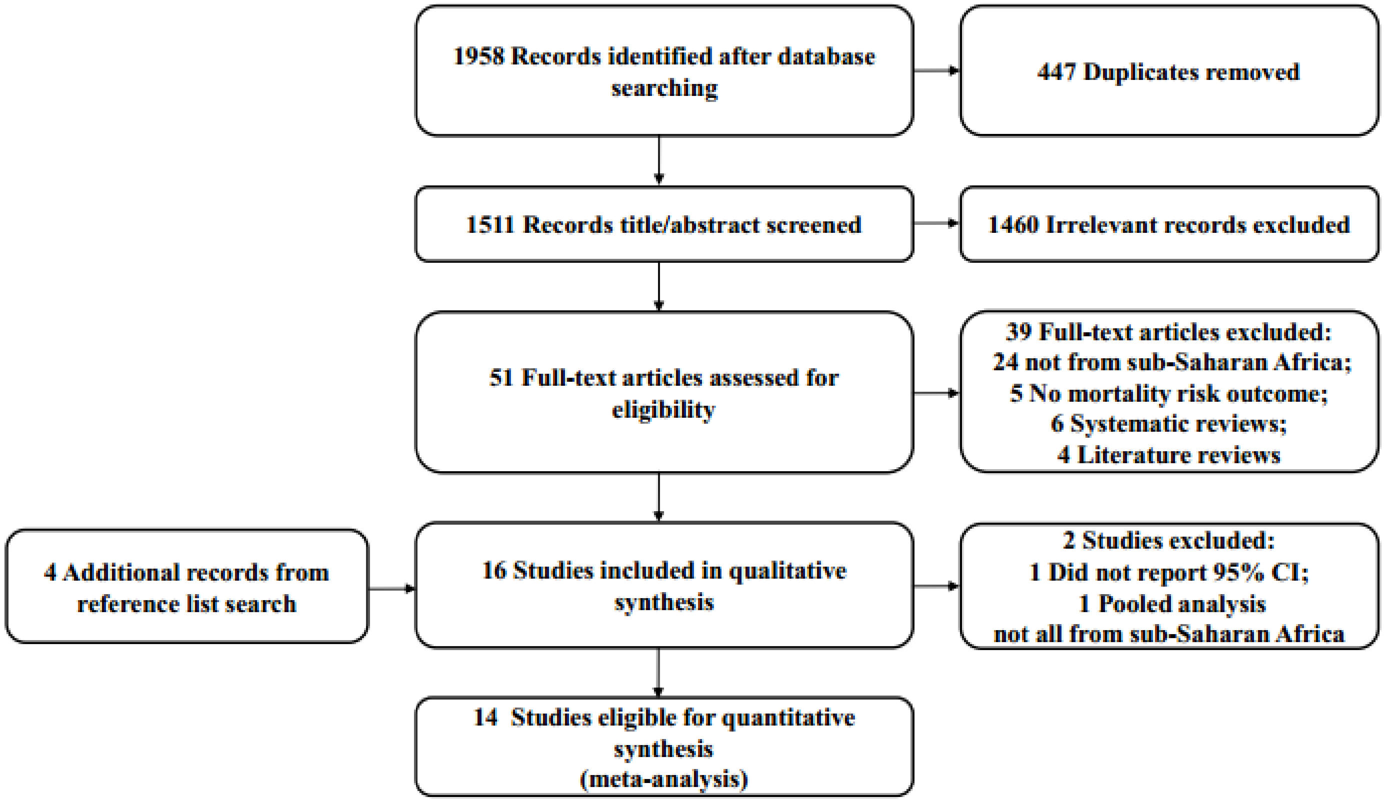


Figure 3-1: Flow chart of paper selection.

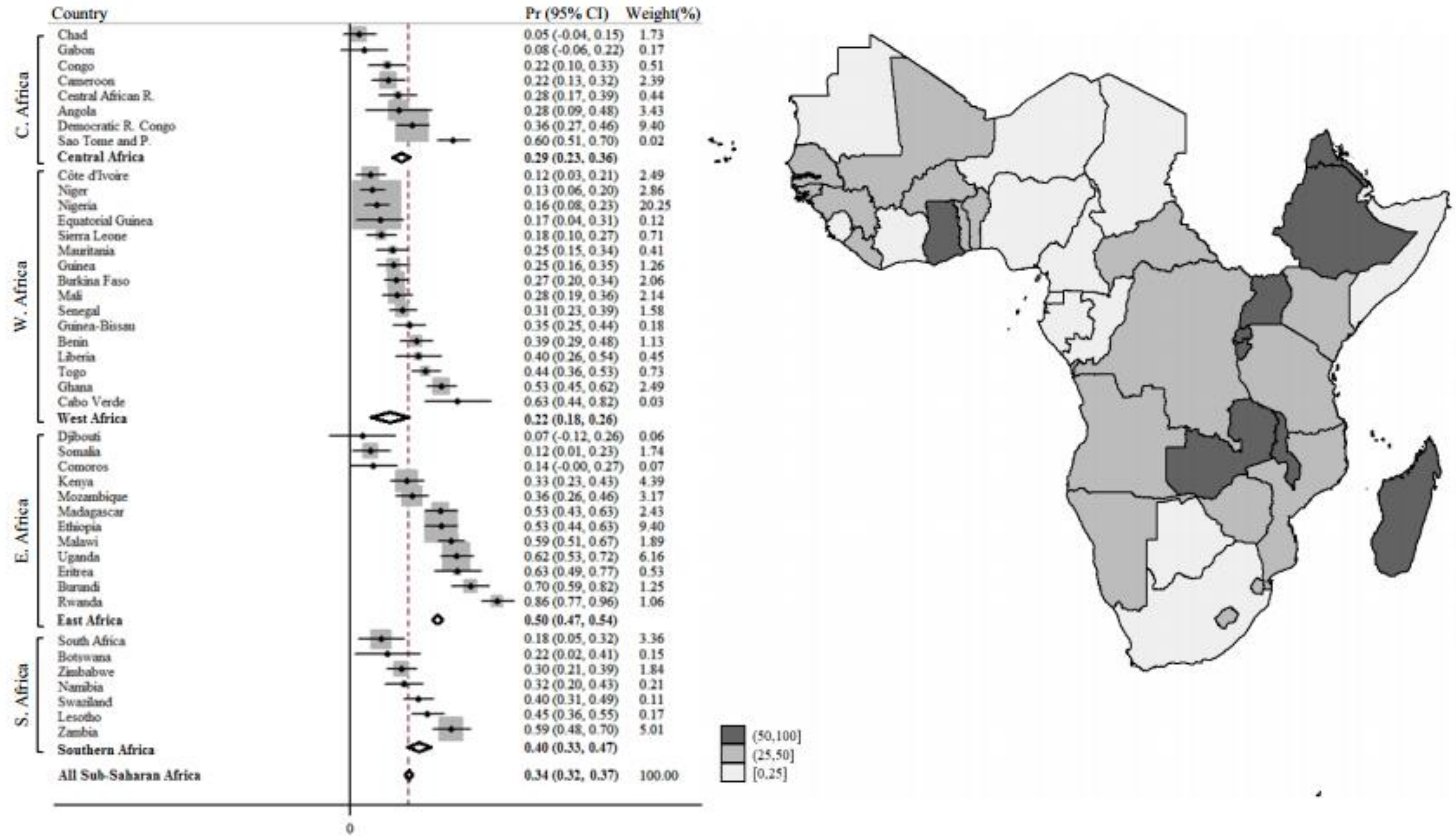


Figure 3-2: **Exclusive breastfeeding prevalence in sub-Saharan Africa.**

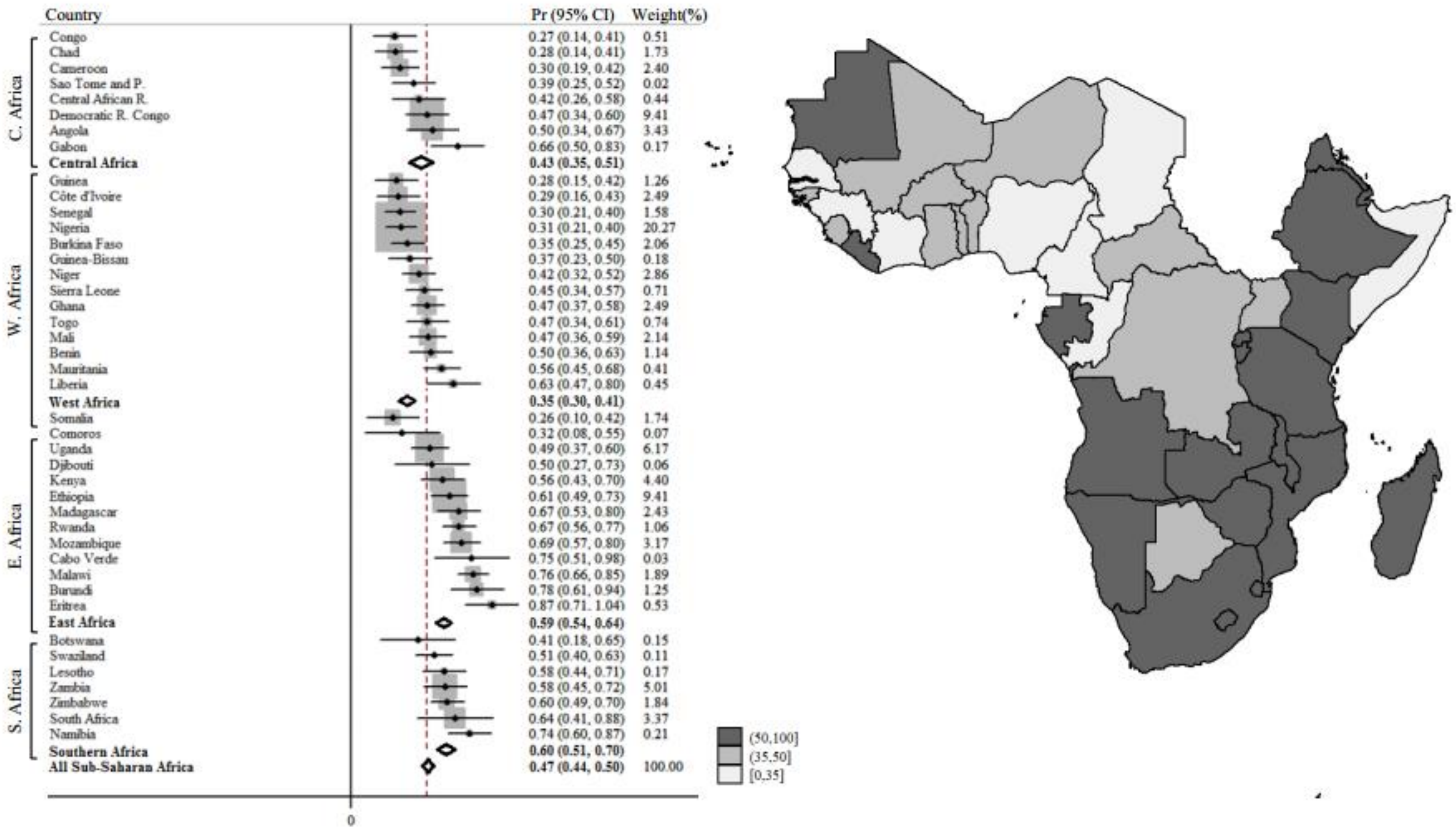


Figure 3-3: **Early initiation of breastfeeding prevalence in sub-Saharan Africa chart of paper selection.**

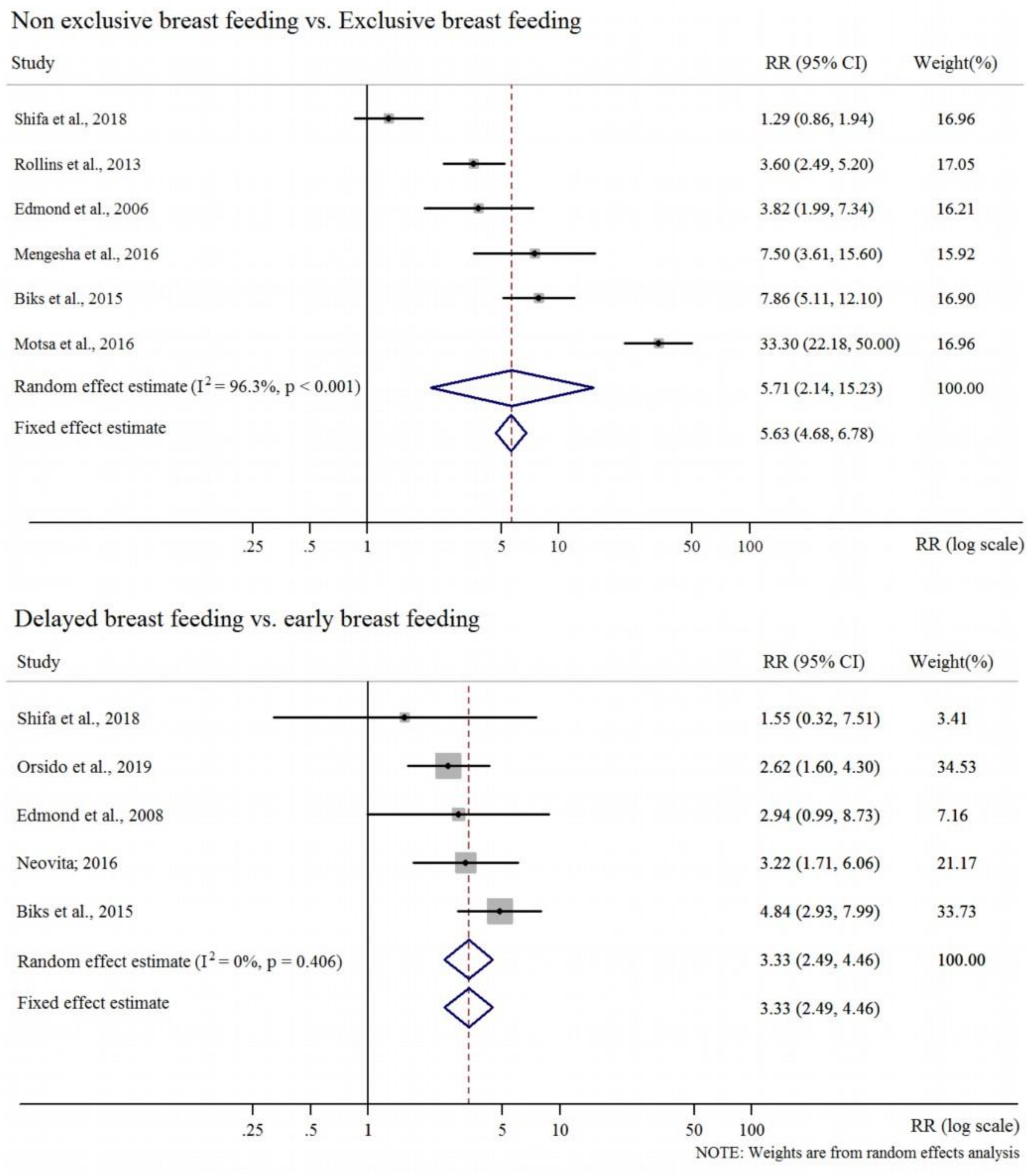


Figure 3-4: **Meta-analysis of breastfeeding practices in relation to mortality risk.**

CHAPTER 4 CONCLUSION AND RECOMMENDATIONS

4.1 Introduction

In 2000, The Millennium Developing Goals (MDG) target-4 called for a two-thirds reduction in the under-5 mortality rate (U5MR) (UN, 2000), however, this target was not reached since only a reduction of 53% from 1990-2015 was observed for the global U5MR (You *et al.*, 2015). However, despite the improvements according to the current rate of progress, it was estimated that it would take ten more years to reach the global target-4 (Ki-Moon, 2015). We are now working towards a new target, as set by the Sustainable Development Goal, to an U5MR of 25 or fewer deaths per 1000 live births for 2030 (Anon, 2015). Globally, Sub-Saharan Africa still holds the highest U5MR of 83.1 deaths per 1000 live births, even though they contributed to roughly half of the U5MR reduction in 2015 (You *et al.*, 2015). Sub-Saharan Africa faces unique challenges to reduce the U5MR, due to an additional demand of an increase in birth rates, its related child population growth (UN. Department of Economic and Social Affairs, 2015) and the negative economic impact attributable to child deaths in Africa (Kirigia *et al.*, 2015).

It is widely known that a child's nutritional status is one of the main modifiable risk factors for mortality (Lartey, 2008; Lim *et al.*, 2012; Pelletier & Frongillo, 2003). Malnutrition has been responsible, directly or indirectly, for 60% of the 10.9 million deaths reported annually among children under-five years in 2003 (WHO *et al.*, 2003). Well over two-thirds of these deaths occur during the first year of life, when exclusive breastfeeding and continued breastfeeding are crucial to sustain a child's health and nutritional status (WHO, 2003a). In sub-Saharan Africa, a large improvement of exclusive breastfeeding prevalence was observed in the last years. The prevalence more than doubled in West and Central Africa (12% to 28%), and increased from 35% to 47%, in East and Southern

Africa, from 1995 to 2015 (You *et al.*, 2015). Despite these improvements and the well-recognised importance of exclusive breastfeeding (Victora *et al.*, 2016a), sub-Saharan Africa still has lower exclusive breastfeeding rates (35%) when compared to other low- and middle-income countries (39%) (Cai *et al.*, 2012).

Several systematic reviews and meta-analyses investigated the association of breastfeeding practices and neonatal- or infant- or/and child mortality (Debes *et al.*, 2013; Horta & Victora, 2013; Khan *et al.*, 2015; Lamberti *et al.*, 2011; Lamberti *et al.*, 2013; Sankar *et al.*, 2015; Smith *et al.*, 2017a). However, none of them specifically focused on the sub-Saharan Africa region. Furthermore, there is a knowledge gap regarding the economic impact of breastfeeding practices in relation to child mortality in sub-Saharan Africa.

The purpose of this study was to determine the clinical and economic impact which breastfeeding practices may have in sub-Saharan Africa. This impact was determined by the population attributable fraction, by merging the prevalence of the recommended breastfeeding practices in sub-Saharan Africa, with the estimated risks for mortality obtained from the systematic review and meta-analysis. Furthermore, by estimating the cost to which inappropriate breastfeeding practices and under-five mortality contribute, it is possible to determine how much USB$ may potentially be saved if the recommended breastfeeding practices are improved. Knowing the clinical and economic impact of breastfeeding practices and under-five mortality in sub-Saharan Africa will emphasise the need of national policies and healthcare professionals in sub-Saharan Africa, so as to improve breastfeeding practices for the reduction under-five mortality in the region.

4.2 Aim and Objectives

The primary aim of this study was to perform a systematic review and meta-analysis to estimate the risk of association between inappropriate breastfeeding practices and mortality in children under-five years, in sub-Saharan Africa. A second aim was to estimate the prevalence's of exclusive breastfeeding and early initiation of breastfeeding to determine the population attributable fraction of children affected, in sub-Saharan Africa. The third aim was to perform a cost analysis to calculate how much the recommended breastfeeding practices may reduce the economic impact attributable to the under-five mortality in sub-Saharan Africa.

The objectives of the study were:

- to systematically review the association between breastfeeding practices and the risk for mortality in children under-five years in sub-Saharan Africa from 2000-2019;
- to conduct a meta-analysis of the association of breastfeeding practices with the risk for mortality in children under-five years in sub-Saharan Africa from 2000-2018;
- to estimate the prevalence of exclusive breastfeeding and the early initiation of breastfeeding among mothers of infants aged 0-6 months in sub-Saharan Africa from 2000-2018;
- to estimate the population attributable fraction associated with favourable breastfeeding practices as recommended by the World Health Organization; and
- to calculate the Non-Health Gross Domestic Product Loss attributable to under-five mortality, which is related to inappropriate breastfeeding practices in sub-Saharan Africa.

4.3 The risk for under-five mortality in relation to breastfeeding practices

Sub-Saharan Africa holds the highest U5MR of 83.1 deaths per 1000 live births, which means that approximately 1 in every 12 children will die before their fifth birthday (You *et al.*, 2015). To reach the Sustainable Development Goal for an U5MR of 25 or fewer deaths per 1000 live births by 2030, the WHO African region must reduce their child mortality rate by 70% (Anon, 2015). According to our findings, poor breastfeeding practices contributes to the burden of under-five mortality in children. We estimated a three-fold and five-fold higher under-five mortality risk attributed to late breastfeeding initiation and non-exclusive breastfeeding practices, respectively. This observation indicates the vulnerability of Sub-Saharan African children with respect to poor breastfeeding practices. Therefore, the recommended breastfeeding practices (early breastfeeding initiation and exclusive breastfeeding for the first 6 months) as set by the WHO and UNICEF, may potentially prevent the lives lost due to poor breastfeeding practices and aid in the reduction of the U5MR.

4.4 The prevalence of breastfeeding practices in Sub-Saharan Africa

According to the findings, the overall prevalence of exclusive breastfeeding for sub-Saharan Africa is slightly more than one third (34%), and thus, we can estimate that only one in three children in sub-Saharan Africa is exclusively breastfed up to the age of six months. Our estimated prevalence of exclusive breastfeeding among infants younger than six months in sub-Saharan Africa was consistent with the results of Cai *et al.* (2012), who reported a prevalence of 35% of exclusive breastfeeding in Africa in 2010. These findings indicate the poor improvement of the exclusive breastfeeding rate in sub-Saharan Africa, as that study was done 10 years ago. We also estimated that almost half of the children (47%) are put to the breast within the first hour of life. This result is confirmed by the WHO Global Survey, which reported that the prevalence of early breastfeeding initiation is approximately 50% in many low- and middle-income countries (Takahashi *et al.*, 2017). Sub-Saharan Africa still has a long road ahead towards improving breastfeeding practices to reach the Global Nutrition Target for an exclusive breastfeeding prevalence of 50% among infants <6 months of age, by 2025 (WHO, 2014).

4.5 The population attributable fraction for under-five mortality in relation to breastfeeding practices

The population attributable fraction is the proportional reduction in a disease or mortality within a population, that would occur if exposure to a risk factor were reduced to an alternative ideal exposure scenario. The population attributable fraction attributable to non-exclusive breastfeeding practices, was estimated to be approximately 75% of under-five deaths. This indicates that three quarters of under-five deaths attributed to non-exclusive breastfeeding may potentially be prevented in Sub-Saharan Africa, if exclusive breastfeeding were implemented. The principle can also be applied for early breastfeeding initiation, which may prevent 50% of under-five deaths attributed to late breastfeeding initiation. Based on a report published in the Lancet, scaling up breastfeeding to a near universal level could prevent 823 000 deaths annually in children younger than five years (Victora *et al.*, 2016a). Our results confirm that scaling up breastfeeding would be greatly beneficial for saving children's lives in Sub-Saharan Africa.

4.6 The economic impact of under-five mortality in relation to breastfeeding practices in Sub-Saharan Africa

Our findings confirmed that the recommended breastfeeding practices may help to reduce the negative economic impact of the under-five mortality rate in sub-Saharan Africa. The Non-health Gross Domestic Product loss in relation to breastfeeding practices resulted in about 19.5 USB$. Thus, if exclusive breastfeeding and early breastfeeding initiation would be improved, this cost would be reduced in parallel with child deaths avoided, to 8.4 and 7 USB$, respectively. Sub-Saharan Africa consists of low- and middle-income countries, thus the economy can benefit from scaling up of breastfeeding practices in the long term. In southeast Asia, it was estimated that investing in a national breastfeeding promotion strategy in Vietnam could result in preventing 200 child deaths per year, and generate monetary benefits of 2.39 US$ for every 1 US$ invested, or a 139% return on investment (Walters *et al.*, 2016). These reassuring results suggest that there are feasible and affordable opportunities to accelerate progress towards achieving the Global Nutrition Target for exclusive breastfeeding by 2025 (WHO, 2014).

4.7 Conclusions and practical recommendations

This study has contributed to new knowledge by the integration of epidemiological-, public health- and economic data, providing novel information regarding how the scaling up of recommended breastfeeding practices (exclusive breastfeeding and early initiation of breastfeeding) may positively impact Sub-Saharan Africa, with regards to the U5MR and its economic burden.

This clinical impact was determined by the population attributable fraction, by merging the prevalence of the recommended breastfeeding practices in sub-Saharan Africa with the estimated risks for mortality obtained from the systematic review and meta-analysis. Furthermore, we estimated the cost to which under-five mortality, attributed to poor breastfeeding practices, may contribute. Thus, observed how much USB$ can be saved if those under-five deaths could be prevented, by scaling up the recommended breastfeeding practices in sub-Saharan Africa.

Knowledge of the clinical and economic impact of poor breastfeeding practices and under-five mortality in sub-Saharan Africa, will emphasise the need of national policies and health care professionals to scale up breastfeeding practices. It is inevitable that the improvement of the breastfeeding prevalence in sub-Saharan Africa may lead to an even more meaningful reduction in under-five mortality and may substantially reduce related costs. According to Rollins et al., countries with pro-breastfeeding social national policies can make a difference in improving breastfeeding practices (2016).

4.8 Limitations of this research project

Due to missing information, we limited our analysis to exclusive breastfeeding and early initiation of breastfeeding, while it would have been of interest to consider other feeding practices as well, such as mixed feeding and continued breastfeeding.

Another weakness of our work is that we provided results for the overall sub-Saharan Africa and its regions, while a country-specific evaluation of breastfeeding practices impact could have been of greater interest for practitioners, as well as some readers. However, the original data we identified did not allow these extensions.

Furthermore, we did not look specifically at HIV-related mortality in relation to breastfeeding practices, because data on the prevalence of HIV in children under-five years, and the relative risk of mortality of children exposed to different types of breastfeeding practices and HIV were not available.

4.9 Future studies

The most recent amendment of the WHO's infant and young child feeding guidelines recommends that HIV exposed children may continue breastfeeding up to two years of age if the mother adheres to her ARV treatments. Taking the HIV prevalence among children under-five into context may be a future consideration by investigating the mortality risk associated with non-exclusive breastfeeding compared to exclusive breastfeeding among HIV positive children in Sub-Saharan Africa.

Another suggestion would be to add the cost of investing in different breastfeeding promotion interventions to the economic analysis and to determine which interventions might be more cost effective, but still to ensure significant increases in breastfeeding prevalence. This may improve the promotion of breastfeeding practices in individual countries, where it is necessary to adjust prioritisation according to the county's need for scaling up breastfeeding, because there is, in fact, a wide heterogeneity in prevalence of optimal breastfeeding practices among sub-Saharan African countries.

In conclusion, the aim and objectives of this study were reached and the findings of this research project, irrespective of its limitations, add value to the current literature. An update regarding the association between breastfeeding practices and child mortality has been provided by the estimate of mortality risk reduction attributed to exclusive breastfeeding and early breastfeeding initiation. An estimate of the prevalence of population at risk by country and sub-Saharan Africa region was conducted. Furthermore, an estimate of the population attributable fraction for child mortality associated with different breastfeeding practices in sub-Saharan Africa countries were also provided. Finally, the estimated costs attributable to under-five deaths, related to inappropriate breastfeeding practices and estimate of costs savings attributable to the implementation of optimal breastfeeding practices were calculated.

ANNEXURES

LAST UPDATED: 10 AUGUST 2020

ANNEXURE A: APPROVAL OF ETHICAL CLEARANCE FOR HEALTH RESEARCH ETHICS COMMITTEE NORTH-WEST UNIVERSITY

NWU® NORTH-WEST UNIVERSITY NOORDWES-UNIVERSITEIT YUNIBESITI YA BOKONE-BOPHIRIMA

Private Bag X1290, Potchefstroom
South Africa 2520

Tel: 086 016 9698
Web: http://www.nwu.ac.za

North-West University Health Research Ethics Committee (NWU-HREC)

Tel: 018 299-1206
Email: Ethics-HRECApply@nwu.ac.za (for human studies)

15 November 2019

RESEARCH ETHICS COMMITTEE LETTER OF DECISION: NO RISK

Based on the review by the North-West University Health Research Ethics Committee (NWU-HREC) on 13/11/2019, the NWU-HREC hereby clears your study as a no risk study. This implies that the NWU-HREC grants its permission that, provided the general conditions specified below are met, the study may be initiated, using the ethics number below.

Study title: The impact of breastfeeding practices on under-five mortality in sub-Saharan Africa. Systematic review, meta-analysis and evaluation of its attributable costs
Principal Investigator/Study Supervisor/Researcher: Dr C Ricci
Student: CE Pretorius - 25947729

Ethics number: N W U - 0 0 9 7 4 - 1 9 - A 1

Institution | Study Number | Year | Status

Status: S = Submission; R = Re-Submission; P = Provisional Authorisation; A = Authorisation

Application Type: Single study
Commencement date: 15/11/2019

Risk: No Risk

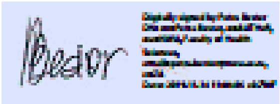
General conditions:

The following general terms and conditions will apply:

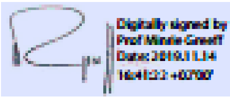
- *The commencement date indicates the first date that the study may be started.*
- *In the interest of ethical responsibility, the NWU-HREC reserves the right to:*
  - *request access to any information or data at any time during the course or after completion of the study;*
  - *to ask further questions, seek additional information, require further modification or monitor the conduct of your research;*
  - *withdraw or postpone clearance if:*
    - *any unethical principles or practices of the study are revealed or suspected;*
    - *it becomes apparent that any relevant information was withheld from the NWU-HREC or that information has been false or misrepresented;*
    - *submission of the required amendments, or reporting of adverse events or incidents was not done in a timely manner and accurately; and/or*
    - *new institutional rules, national legislation or international conventions deem it necessary.*
- *NWU-HREC can be contacted for further information via Ethics-HRECApply@nwu.ac.za or 018 299 1206*

The NWU-HREC would like to remain at your service and wishes you well with your study. Please do not hesitate to contact the NWU-HREC for any further enquiries or requests for assistance.

Yours sincerely,



NWU-HREC Chairperson



Head of the Faculty of Health Sciences Ethics Office for Research, Training and Support

Current details: (13218572) [illegible]
12 November 2019

File reference: 9.1.5.4.3

ANNEXURE B: NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE COHORT STUDIES

Note: A study can be given a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability.

Selection
1) Representativeness of the exposed cohort
a) Truly representative ***(one star)***
b) Somewhat representative ***(one star)***
c) Selected group
d) No description of the derivation of the cohort

2) Selection of the non-exposed cohort
a) Drawn from the same community as the exposed cohort ***(one star)***
b) Drawn from a different source
c) No description of the derivation of the non-exposed cohort

3) Ascertainment of exposure
a) Secure record (e.g., surgical record) ***(one star)***
b) Structured interview ***(one star)***
c) Written self-report
d) No description
e) Other

4) Demonstration that outcome of interest was not present at start of study
a) Yes ***(one star)***
b) No

Comparability
1) Comparability of cohorts on the basis of the design or analysis controlled for confounders
a) The study controls for age, sex and marital status ***(one star)***
b) Study controls for other factors (list) ________________________________ ***(one star)***
c) Cohorts are not comparable on the basis of the design or analysis controlled for confounders

Outcome
1) Assessment of outcome
a) Independent blind assessment ***(one star)***
b) Record linkage ***(one star)***
c) Self report
d) No description
e) Other

2) Was follow-up long enough for outcomes to occur
a) Yes ***(one star)***
b) No

Indicate the median duration of follow-up and a brief rationale for the assessment above:___________________

3) Adequacy of follow-up of cohorts
a) Complete follow up- all subject accounted for ***(one star)***
b) Subjects lost to follow up unlikely to introduce bias- number lost less than or equal to 20% or description of those lost suggested no different from those followed. ***(one star)***
c) Follow up rate less than 80% and no description of those lost
d) No statement

ANNEXURE C: NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE CASE-CONTROL STUDIES

Selection

1 Is the case definition adequate?
a) Yes, with independent validation (>1 person/record/time/process to extract information, or reference to primary record source such as x-rays or structured injury data)*
b) Yes, based on self-reports
c) No description

2 Representativeness of the cases
a) All eligible cases with outcome of interest over a defined period of time, all cases in a defined catchment area, all cases in a defined team/competition/sport, or a random sample of those cases*
b) Not satisfying requirements in part (a), or not stated.

3 Selection of controls
a) Controls were selected from the same source population as the cases*
b) controls were selected from a different source population
c) no description

4 Definition of controls
a) If cases are first occurrence of injury of interest, then it must explicitly state that controls have no history of this outcome. If cases have new (not necessarily first) occurrence of specific injury, then controls with previous occurrences of outcome of interest should not be excluded*
b) No description of injury history

Comparability

1 Comparability of cases and controls on the basis of the design or analysis
a) Study controls for previous injury*
b) Study controls for age*
Note: Cases and controls must be matched in the design and/or confounders must be adjusted for in the analysis. Alone statements of no differences between groups or that differences were not statistically significant are not sufficient.

Exposure

1 Ascertainment of exposure
a) Structured injury data (e.g. record completed by medical staff)*
b) Structured interview where blinded to case/control status*
c) Interview not blinded to case/control status
d) Written self-report or medical record (unstructured data) only
e) No description

2 Same method of ascertainment for cases and controls
a) Yes*
b) No
3Non-response rate
a) Same for both groups*
b) Non-respondents described
c) Rate different and no designation

ANNEXURE D: EXAMPLE OF MIXED EFFECT ESTIMATION OF BREASTFEEDING PRACTICES OVER THE OBSERVATION PERIOD

```
%let loc;/*location where a .CSV in a long format is retained*/

PROC IMPORT OUT= WORK.dt
          DATAFILE= "&loc"
          DBMS=CSV REPLACE;
     GETNAMES=YES;
     DATAROW=2;
RUN;

data dt;set dt;
med=arsin(percentage/100);
if year<2000 then delete;
run;

proc mixed data=dt;
class country_code;
model med=year country_code;
random country_code;
lsmeans country_code;
ods output LSMeans=estimates;
run;

data estimates;set estimates;keep country_code area CODE name prevalence prev_stder;
prevalence=sin(Estimate);
prev_stder=sin(StdErr);
if country_code="AGO" then CODE="ANG";
if country_code="BEN" then CODE="BEN";
if country_code="BWA" then CODE="BOT";
if country_code="BFA" then CODE="BUF";
if country_code="BDI" then CODE="BUR";
if country_code="CMR" then CODE="CAM";
if country_code="CAF" then CODE="CAR";
if country_code="CPV" then CODE="CAP";
if country_code="TCD" then CODE="CHA";
if country_code="COM" then CODE="COM";
if country_code="CIV" then CODE="CDI";
if country_code="COD" then CODE="ZAI";
if country_code="COG" then CODE="CNG";
if country_code="DJI" then CODE="DJI";
if country_code="ERI" then CODE="ERI";
if country_code="SWZ" then CODE="SWA";
if country_code="ETH" then CODE="ETH";
if country_code="GMB" then CODE="GAM";
if country_code="GNQ" then CODE="EQG";
if country_code="GAB" then CODE="GAB";
if country_code="GNB" then CODE="GUB";
if country_code="GHA" then CODE="GHA";
if country_code="GIN" then CODE="GIN";
if country_code="GNB" then CODE="GUB";
if country_code="KEN" then CODE="KEN";
if country_code="LSO" then CODE="LES";
if country_code="LBR" then CODE="LIB";
if country_code="MDG" then CODE="MAD";
if country_code="MWI" then CODE="MAA";
```

```
if country_code="MLI" then CODE="MAL";
if country_code="MRT" then CODE="MAU";
if country_code="MOZ" then CODE="MOZ";
if country_code="NAM" then CODE="NAM";
if country_code="NER" then CODE="NIG";
if country_code="NGA" then CODE="NIR";
if country_code="RWA" then CODE="RWA";
if country_code="STP" then CODE="STP";
if country_code="SEN" then CODE="SEN";
if country_code="SLE" then CODE="SIL";
if country_code="SOM" then CODE="SOM";
if country_code="ZAF" then CODE="SOU";
if country_code="SDN" then CODE="SUD";
if country_code="TGO" then CODE="TOG";
if country_code="TZA" then CODE="TAN";
if country_code="UGA" then CODE="UGA";
if country_code="ZMB" then CODE="ZAM";
if country_code="ZWE" then CODE="ZIM";
/*coding area*/
if CODE="SUD" then area="CA";
if country_code="AGO" then area="CA";
if country_code="CAF" then area="CA";
if country_code="CMR" then area="CA";
if country_code="COD" then area="CA";
if country_code="COG" then area="CA";
if country_code="GAB" then area="CA";
if country_code="GNQ" then area="CA";
if country_code="SUD" then area="CA";
if country_code="STP" then area="CA";
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if country_code="BDI" then area="EA";
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if country_code="DJI" then area="EA";
if country_code="ERI" then area="EA";
if country_code="ETH" then area="EA";
if country_code="KEN" then area="EA";
if country_code="MDG" then area="EA";
if country_code="MOZ" then area="EA";
if country_code="MUS" then area="EA";
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if country_code="GHA" then area="WA";
if country_code="GIN" then area="WA";
if country_code="GMB" then area="WA";
if country_code="GNB" then area="WA";
if country_code="LBR" then area="WA";
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```
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if country_code="MRT" then area="WA";
if country_code="NER" then area="WA";
if country_code="NGA" then area="WA";
if country_code="SEN" then area="WA";
if country_code="SLE" then area="WA";
if country_code="TGO" then area="WA";
/*coding Name*/
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if country_code="BEN" then name="Benin";
if country_code="BWA" then name="Botswana";
if country_code="BFA" then name="Burkina Faso";
if country_code="BDI" then name="Burundi";
if country_code="CPV" then name="Cabo Verde";
if country_code="CMR" then name="Cameroon";
if country_code="CAF" then name="Central African R.";
if country_code="TCD" then name="Chad";
if country_code="COM" then name="Comoros";
if country_code="COG" then name="Congo        ";
if country_code="CIV" then name="Côte d'Ivoire";
if country_code="COD" then name="Democratic R. Congo";
if country_code="DJI" then name="Djibouti         ";
if country_code="GNQ" then name="Equatorial Guinea";
if country_code="ERI" then name="Eritrea";
if country_code="SWZ" then name="Swaziland";
if country_code="ETH" then name="Ethiopia";
if country_code="GAB" then name="Gabon        ";
if country_code="GMB" then name="Gambia";
if country_code="GHA" then name="Ghana        ";
if country_code="GIN" then name="Guinea        ";
if country_code="GNB" then name="Guinea-Bissau";
if country_code="KEN" then name="Kenya         ";
if country_code="LSO" then name="Lesotho";
if country_code="LBR" then name="Liberia        ";
if country_code="MDG" then name="Madagascar           ";
if country_code="MWI" then name="Malawi";
if country_code="MLI" then name="Mali";
if country_code="MRT" then name="Mauritania";
if country_code="MOZ" then name="Mozambique";
if country_code="NAM" then name="Namibia";
if country_code="NER" then name="Niger";
if country_code="NGA" then name="Nigeria";
if country_code="RWA" then name="Rwanda";
if country_code="STP" then name="Sao Tome and P.";
if country_code="SEN" then name="Senegal";
if country_code="SLE" then name="Sierra Leone";
if country_code="SOM" then name="Somalia";
if country_code="ZAF" then name="South Africa";
if country_code="SDN" then name="Sudan        ";
if country_code="TGO" then name="Togo";
if country_code="UGA" then name="Uganda";
if country_code="TZA" then name="Tanzania";
if country_code="ZMB" then name="Zambia";
if country_code="ZWE" then name="Zimbabwe";
run;

/*exporting of estimates by country in STATA for further use*/
%let loc2;/*location where the STATA utputs are located*/
PROC EXPORT DATA= WORK.Estimates
        OUTFILE= "&loc2\outcome.dta"
        DBMS=STATA REPLACE;
```

RUN;

/**/

/*examples of procedures to perform the meta-analytical estimates of relative risk*/

/*installing meta function run it once*/
ssc install metan

/*making forrest plot where teta and stderr are the log natural of RR and its standard error as max between (RR-RR low CI)/1.96 and (RR up CI-RR)/1.96 and studyid is the variabe that identify the study*/
sort teta /*sorting of the RRs*/
metan teta stderr , eform randomi second(fixedi) lcols(studyid) graphregion (color(white)) textsize (150) /*example for metan*/

/*example of metaregression to evaluate source of heterogeneity*/

/*installing metareg function run it once -perform metaregression analysis to evaluate the RR in relation to a covariate-*/
ssc install metareg
metareg teta COV, wsse(stderr) graph /*example of metaregression with a generic covariate COV*/

/*example of publication bias asessment*/
/*installing metabias function run it once -perform metabias analysis evaluate the pubication bias-*/
ssc install metabias

metabias teta stderr , egger /*example of publication bias with Egger method*/

/*example of funnel plot*/

ssc install metafunnel /*installing metafunnel function run it once -perform funnel plots-*/
metafunnel teta stderr /*example for funnel plot*/

/*example of influence analysis*/
ssc install metainf /*installing metainf function run it once -perform influence analysis drop one study at the time-*/
metaninf teta stderr, label(namevar=studyid)

ANNEXURE E: SUPPORTING MATERIAL FOR THE ARTICLE

SUPPORTING MATERIAL

Text 1. Search string containing MeSH and key terms for NWU literature search.

Text 2. Example search string containing MeSH terms for Medline database search.

Text 3. Number of identified papers for each database from NWU literature search.

Text 4. Meta-regression for the Mortality risk vs. Exclusive breastfeeding

Table 1. NOS-score for case-control and cohort studies.

Figure 1. Funnel plot for publication bias with respect to exclusive breastfeeding.

Figure 2. Funnel plot for publication bias with respect to breastfeeding initiation.

Text 1. Search String containing MeSH and key terms for NWU literature search.

[(Neonate; Neonat*; Neonatal; Infant; Child; Perinatal) OR (“Under five year”) AND (Exclusive breastfeeding; Breastfed; Breastfeeding; Breast milk; Human milk) AND (Partially breastfed; Partial breastfeeding; Predominantly breastfed; Never breastfed) AND (Mortality; Survival; Death; Under five mortality; Infant mortality; Neonatal death; Neonatal mortality; Perinatal mortality; Perinatal death)]

Text 2. Example search string containing MeSH terms for Medline database search.

((((Neonate OR Neonates OR Neonatal OR Infant OR Infants OR Child OR Children OR Perinatal OR "under five") AND (Exclusive breastfed OR "Exclusive breastfeeding" OR Breastfed OR Breastfeeding OR "Breast milk" OR "Human milk" OR "Early initiation" OR "Timely initiation")) AND ("Partially breastfed" OR "Partial breastfeeding" OR "Predominantly breastfed" OR "Predominant breastfeeding" OR "Never breastfed")) AND (Mortality OR Survival OR Death OR "Under five mortality" OR "Infant mortality" OR "Neonatal death"))

Text 3. Number of identified papers for each database from NWU literature search

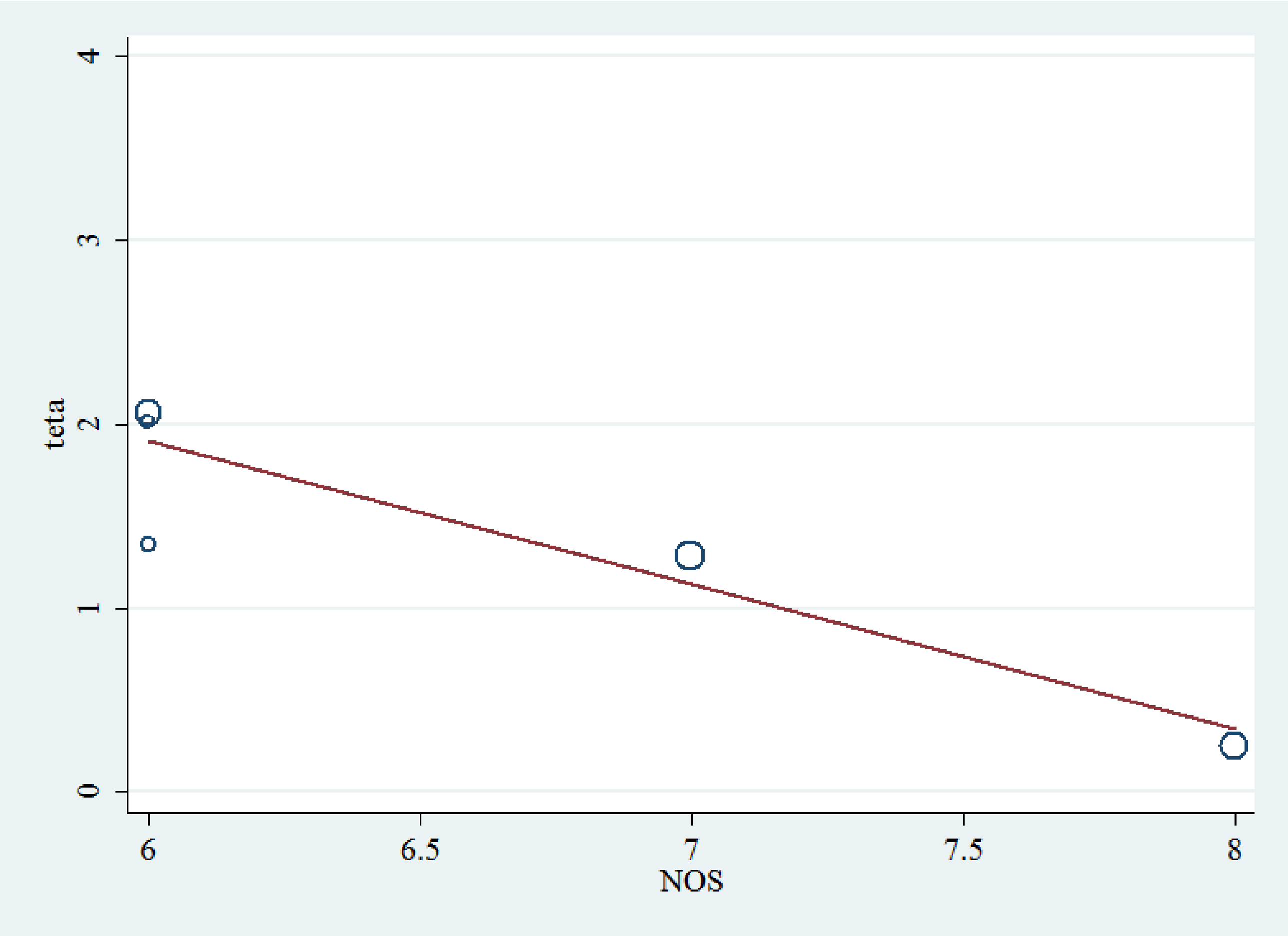
Database included	**Records obtained**
EbscoHost Academic Search Complete	890
CINAHL with Full Text	260
Health Source: Nursing/Academic Edition	204
SocINDEX with Full Text	88
Environment Complete	80
MEDLINE	78
Science Citation Index	75
Business Source Complete	52
SPORTDiscus with Full Text	47
MasterFILE Premier	43
EconLit with Full Text	31
Social Sciences Citation Index	31
Directory of Open Access Journals	23
APA PsycInfo	11
Springer Nature Journals	10
Health Source - Consumer Edition	9
GreenFILE	8
ScienceDirect	8
SciELO	6
APA PsycArticles	5
Communication Source	5
Atla Religion Database with AtlaSerials	3
Business Insights: Essentials	3
JSTOR Journals	3
Scopus®	1
Total	1958

Academic journals, peer reviewed included in search for all languages.

Text 4. Meta-regression for the Mortality risk vs. Exclusive breastfeeding

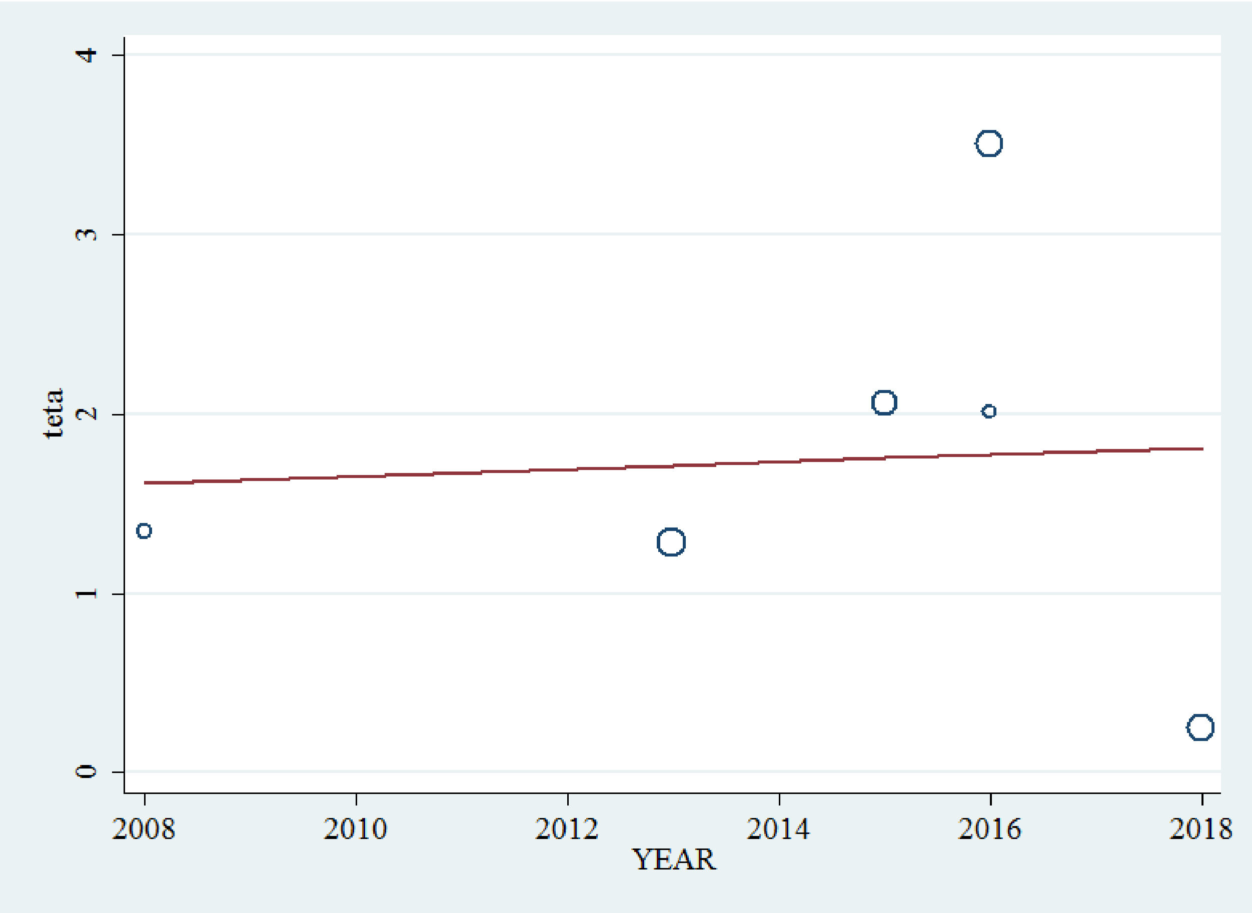
NEW CASTLE OTTAWA SCALE

```
Meta-regression                                      Number of obs  =        5
REML estimate of between-study variance              tau2           =   .01898
% residual variation due to heterogeneity            I-squared_res  =   30.48%
Proportion of between-study variance explained       Adj R-squared  =   96.13%
With Knapp-Hartung modification
------------------------------------------------------------------------------
        teta |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         nos |  -.7824431   .1654548    -4.73   0.018    -1.308994   -.2558921
       _cons |   6.603224   1.132887     5.83   0.010     2.997871    10.20858
------------------------------------------------------------------------------
```



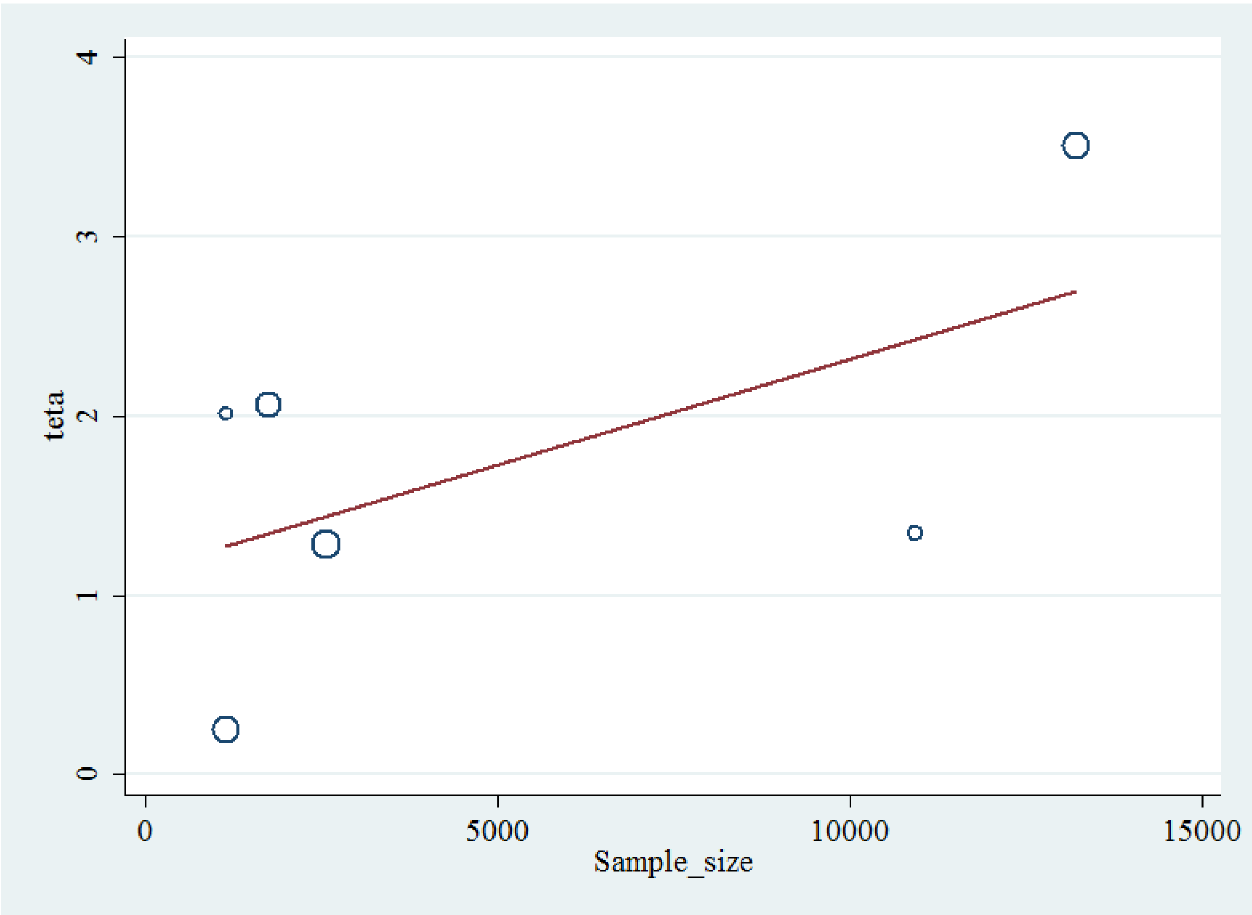
PUBLICATION YEAR

```
Meta-regression                                        Number of obs  =        6
REML estimate of between-study variance                tau2           =    1.436
% residual variation due to heterogeneity              I-squared_res  =   97.00%
Proportion of between-study variance explained         Adj R-squared  = -24.66%
With Knapp-Hartung modification
------------------------------------------------------------------------------
        teta |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        year |    .019809   .1577807     0.13   0.906    -.4182603    .4578784
       _cons |  -38.15988   317.8277    -0.12   0.910     -920.591    844.2712
------------------------------------------------------------------------------
```



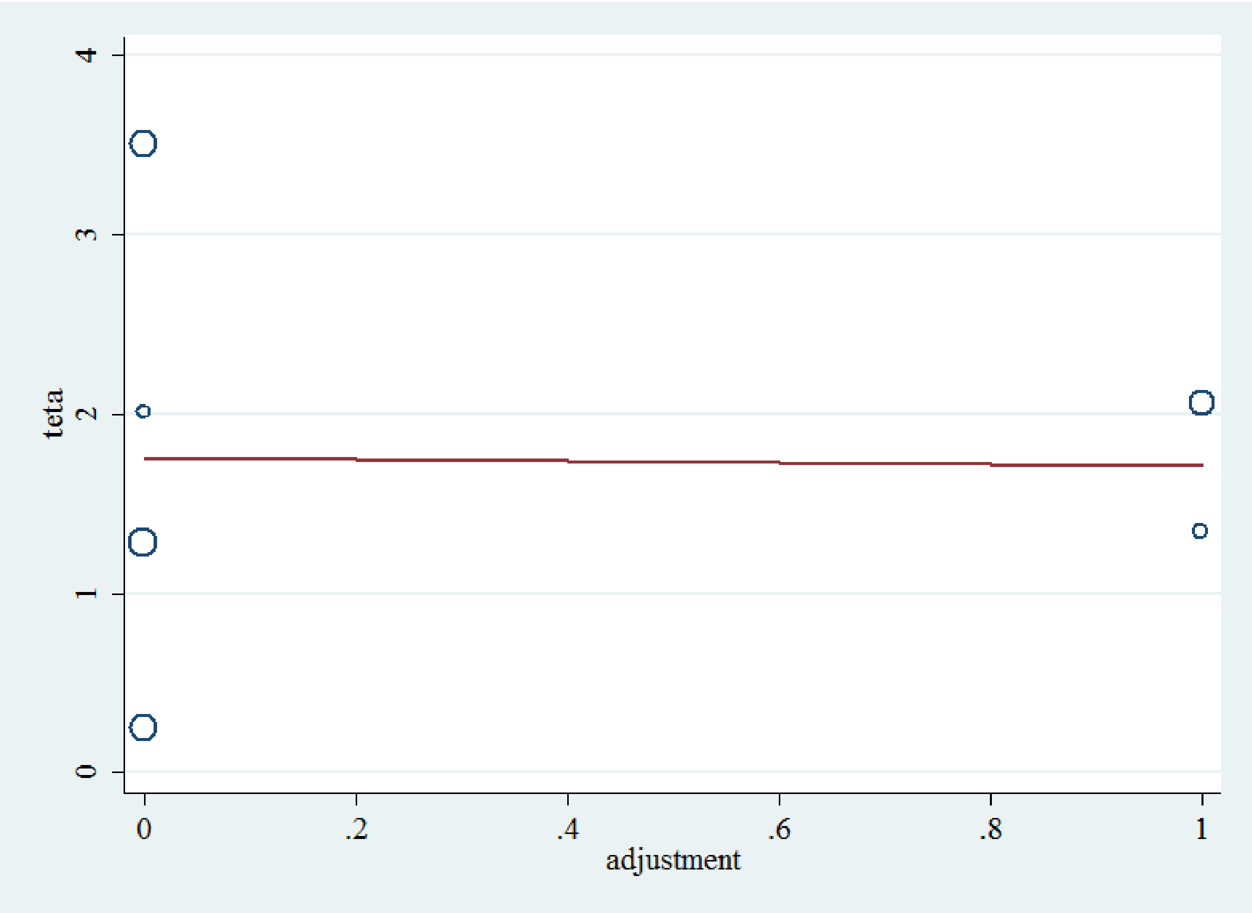
SAMPLE SIZE

```
Meta-regression                                      Number of obs  =       6
REML estimate of between-study variance              tau2           =   .9104
% residual variation due to heterogeneity            I-squared_res  =  93.21%
Proportion of between-study variance explained       Adj R-squared  =  20.95%
With Knapp-Hartung modification
------------------------------------------------------------------------------
        teta |      Coef.   Std. Err.       t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
 sample_size |   .0001181   .0000813     1.45   0.220    -.0001076    .0003437
       _cons |   1.136836   .5811948     1.96   0.122    -.4768198    2.750491
------------------------------------------------------------------------------
```



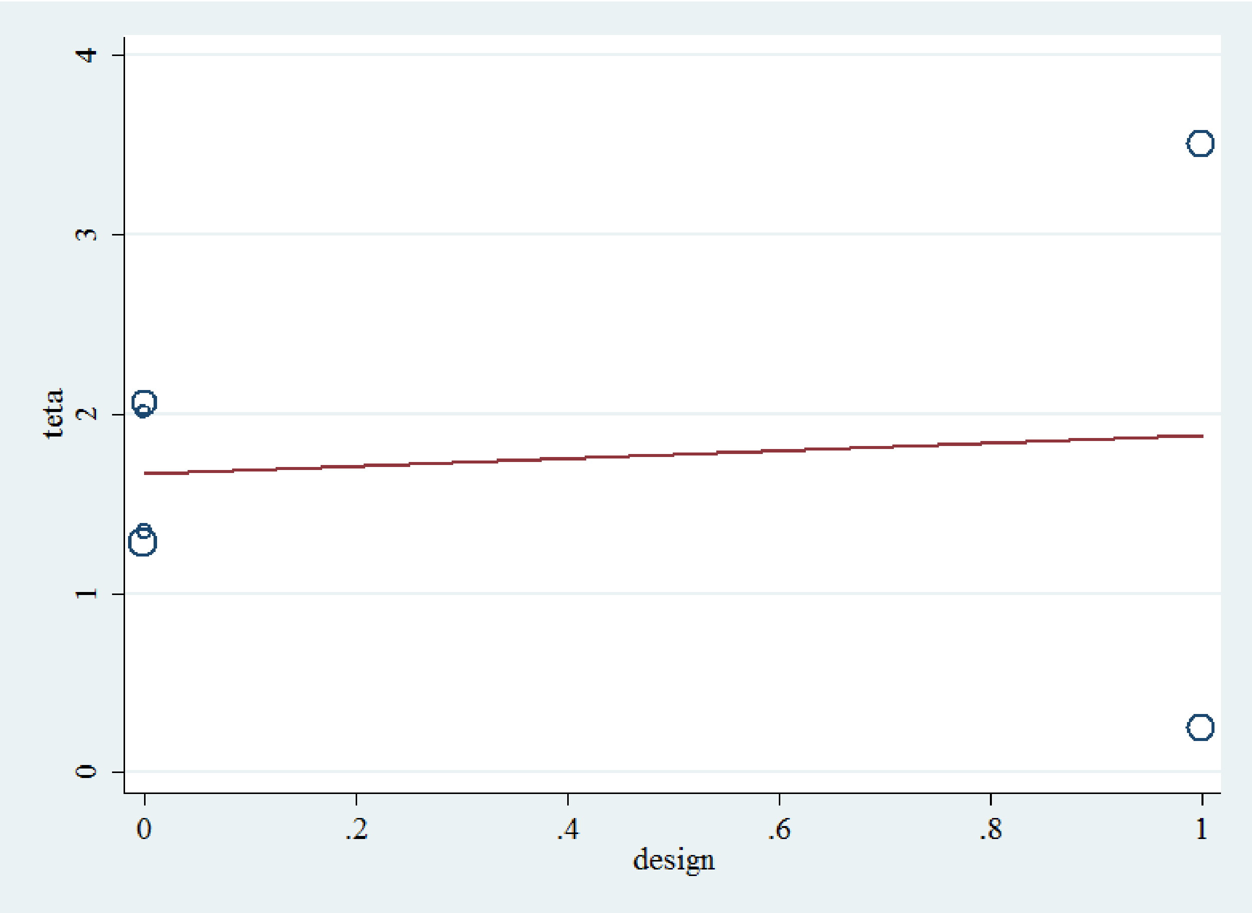
ADJUSTMENT POOR = 1

```
Meta-regression                                       Number of obs  =        6
REML estimate of between-study variance               tau2           =    1.444
% residual variation due to heterogeneity             I-squared_res  =   96.99%
Proportion of between-study variance explained        Adj R-squared  = -25.39%
With Knapp-Hartung modification
------------------------------------------------------------------------------
        teta |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
  adjustment |  -.0511422   1.067085    -0.05   0.964    -3.013844     2.91156
       _cons |   1.759568   .6140503     2.87   0.046     .0546913    3.464445
------------------------------------------------------------------------------
```



STUDY DESIGN COHORT = 0, CASE_CONTROL = 1

```
Meta-regression                                        Number of obs  =        6
REML estimate of between-study variance                tau2           =    1.434
% residual variation due to heterogeneity              I-squared_res  =   96.96%
Proportion of between-study variance explained         Adj R-squared  =  -24.53%
With Knapp-Hartung modification
------------------------------------------------------------------------------
        teta |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      design |   .2083048   1.057275     0.20   0.853    -2.727162    3.143772
       _cons |   1.671979   .6157429     2.72   0.053    -.0375971    3.381556
------------------------------------------------------------------------------
```




```
Code for metaregression (function metareg stata)
metareg teta covariate, wsse(stde) graph
where teta = log(RR estimate; base exp(1))
```

stde = standard error of teta computed as: di/1.96 where di = max ((log (upper 95% confidence interval bound)-log (RRi)); (log (RRi)-log (lower 95% bound)))

Table 1. NOS-score for case-control and cohort studies.

Rater 1									
Cohort									
Study	**Selection 1**	**Selection 2**	**Selection 3**	**Selection 4**	**Comparability 1**	**Outcome 1**	**Outcome 2**	**Outcome 3**	**Score**
Biks et al., 2015	1	1	1	1	1	0	1	0	6
Orsido et al., 2019	1	1	1	1	1	1	0	1	7
Edmond et al., 2008	1	1	1	1	1	0	1	0	6
Edmond et al., 2006	1	1	1	1	1	0	1	0	6
WHO Study team (Ghana)	1	1	1	1	1	1	1	0	7
WHO Study team (Senegal)	1	1	1	1	1	0	1	0	6
Mengesha et al., 2016	1	1	1	1	0	1	0	1	6
Neovita., 2016	1	1	1	1	1	1	0	1	7
Rollins et al., 2013	1	1	1	1	1	0	1	1	7
Edmond et al., 2007	1	1	1	1	1	0	1	0	6
Bahl et al., 2005	1	1	1	1	1	1	1	0	7
Case-control									
Study	**Selection 1**	**Selection 2**	**Selection 3**	**Selection 4**	**Comparability 1**	**Evaluation 1**	**Evaluation 2**	**Evaluation 3**	**Score**
Girma et al., 2011	1	1	1	1	1	1	1	0	7
Shifa et al., 2015	1	1	1	1	1	1	1	1	8
WHO team, 2000 (Gambia)	1	1	1	1	1	0	1	0	6

Rater 2									
Cohort									
Study	**Selection 1**	**Selection 2**	**Selection 3**	**Selection 4**	**Comparability 1**	**Outcome 1**	**Outcome 2**	**Outcome 3**	**score**
Biks et al., 2015	1	1	1	1	1	0	1	0	6
Orsido et al., 2019	1	1	1	1	0	1	0	1	6
Edmond et al., 2008	1	1	1	1	1	0	1	1	7
Edmond et al., 2006	1	1	1	1	1	0	1	1	7
WHO Study team (Ghana)	1	1	1	1	1	1	1	1	8
WHO Study team (Senegal)	1	1	1	1	0	1	1	0	6
Mengesha et al., 2016	1	1	1	1	0	1	0	1	6
Neovita., 2016	1	1	1	1	1	1	0	1	7
Rollins et al., 2013	1	1	1	1	1	0	1	1	7
Edmond et al., 2007	1	1	1	1	1	0	1	0	6
Bahl et al., 2005	1	1	1	1	1	1	1	0	7
Case-control									
Study	**Selection 1**	**Selection 2**	**Selection 3**	**Selection 4**	**Comparability 1**	**Evaluation 1**	**Evaluation 2**	**Evaluation 3**	**score**
Girma et al., 2011	1	1	1	1	1	1	1	0	7
Shifa et al., 2015	1	1	1	1	1	1	1	1	8
WHO team, 2000 (Gambia)	1	1	1	1	1	0	1	0	6

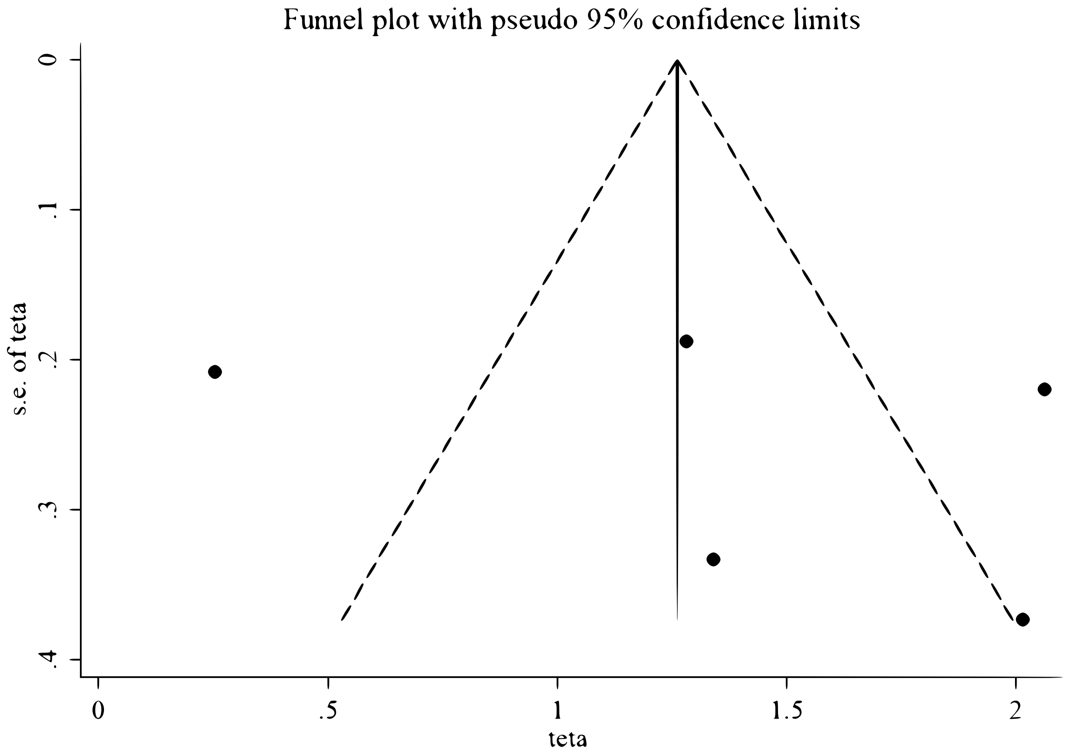


Figure 1. Funnel plot for publication bias with respect to exclusive breastfeeding.

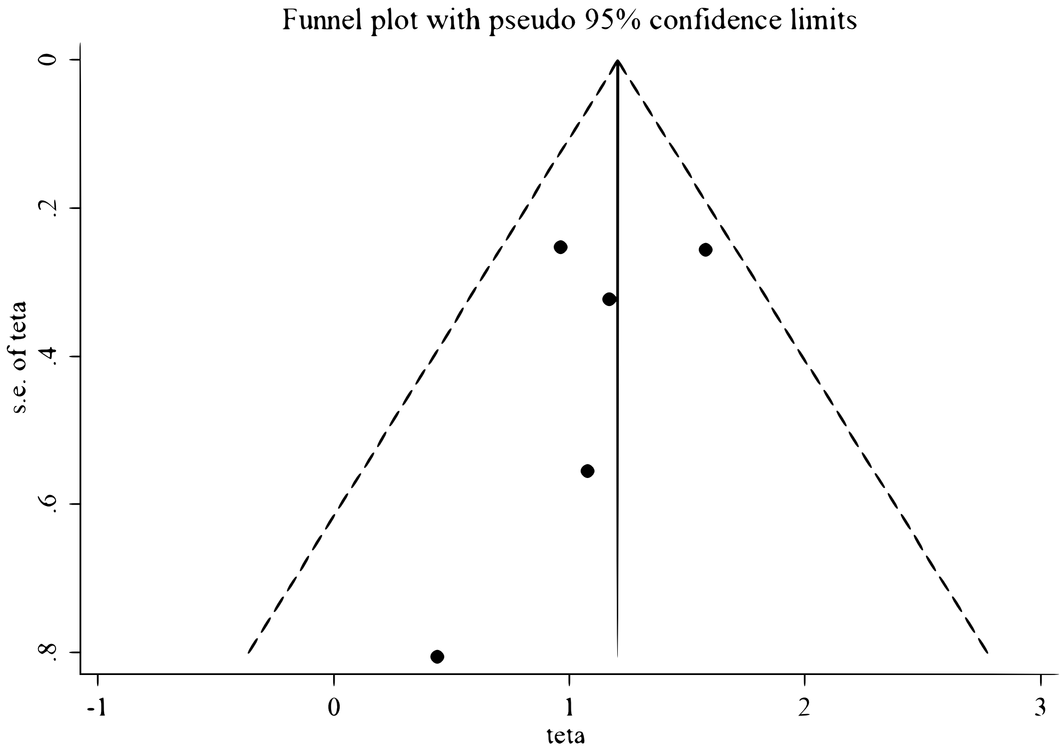


Figure 2. Funnel plot for publication bias with respect to breastfeeding initiation.

ANNEXURE F: PUBLISHED ARTICLE BY EUROPEAN JOURNAL OF PEDIATRICS

European Journal of Pediatrics
https://doi.org/10.1007/s00431-020-03721-5

REVIEW

Impact of breastfeeding on mortality in sub-Saharan Africa: a systematic review, meta-analysis, and cost-evaluation

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Abstract

Sub-Saharan Africa has lower breastfeeding rates compared to other low- and middle-income countries, and globally holds the highest under-five mortality rates. The aims of this study were to estimate mortality risk for inappropriate breastfeeding, prevalence of breastfeeding, population attributable fraction, and the economic impact of breastfeeding on child mortality, in sub-Saharan Africa. The systematic review included databases from Medline and CINAHL. Meta-analysis of mortality risk estimates was conducted using random effect methods. The prevalence of breastfeeding in Sub-Saharan African countries was determined using UNICEF's database. Population attributable fraction was derived from the prevalence and relative risk data. The cost attributable to child deaths in relation to inappropriate breastfeeding was calculated using the World Health Statistics data. The pooled relative mortality risk to any kind of infant feeding compared to exclusive and early breastfeeding initiation were 5.71 (95%CI: 2.14, 15.23) and 3.3 (95%CI: 2.49, 4.46), respectively. The overall exclusive and early initiation of breastfeeding prevalence were 35%(95%CI: 32%;37%) and 47%(95%CI: 44%;50%), respectively. The population attributable fraction for non-exclusive and late breastfeeding initiation breastfeeding were 75.7% and 55.3%, respectively. The non-health gross domestic product loss resulted in about 19.5 USB$.

Conclusion: Public health interventions should prioritize appropriate breastfeeding practices to decrease the under-five mortality burden and its related costs in sub-Saharan Africa.

What is Known:
- *Globally, sub-Saharan Africa holds the highest under five mortality rates and still has lower breastfeeding rates compared to other low- and middle-income countries.*
- *There is a significant association between child mortality and inappropriate breastfeeding practices.*

What is New:
- *A five-fold and three-fold increased risks for under-five mortality were estimated with regard to non-exclusive breastfeeding and delayed breastfeeding initiation, respectively.*
- *55–75% of under-five deaths can be attributable to inappropriate breastfeeding practices and at least part of them could be potentially prevented with breastfeeding promotion interventions, saving a non-health gross domestic product loss of 19.5 USB$.*

Keywords Child · Mortality · Breastfeeding · Prevalence · Public health · Africa South of the Sahara

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Abbreviations

BFHI	Baby-friendly hospital initiative
EBF	Exclusive breastfeeding
EIBF	Early initiation of breastfeeding
GDP	Gross domestic product
HIV	Human immunodeficiency virus
ICC	Intraclass correlation coefficient
MeSH	Medical subject headings
NHGDPL	Non-health gross domestic product loss attributable to child deaths
NOS	Newcastle–Ottawa scale
PAF	Population attributable fraction
PMTCT	Prevention of mother to child transmission
PRISMA	Preferred reporting items of systematic reviews and meta-analysis
U5MR	Under-five mortality rate
UNICEF	United Nations Children's Fund
USB$	United States billion dollars
US$	United States dollars
WHO	World Health Organization

Introduction

Globally, from 1990 to 2015, child mortality was estimated to have claimed the lives of 236.3 million children before their fifth birthday [1]. The Sustainable Development Goal in 2015 set its target for 2030 to an under-five mortality rate (U5MR) of 25 or fewer deaths per 1000 live births [2]. Currently, sub-Saharan Africa holds the highest U5MR of 83.1 deaths per 1000 live births [1].

The nutritional status of children is one of the main modifiable risk factors for under-five mortality [3–7]. The World Health Organization (WHO) and United Nations Children's Fund (UNICEF) strongly recommend early initiation of breastfeeding (EIBF) and exclusive breastfeeding (EBF) during the first 6 months of life for the widely acknowledged health and nutritional benefits [8].

In recent years, a large improvement in EBF prevalence was observed in sub-Saharan Africa. The prevalence more than doubled in West and Central Africa (from 12% in 1995 to 28% in 2015) and increased from 35 to 47% in East and Southern Africa [1]. Despite these improvements, sub-Saharan Africa still has lower EBF rates (35%) when compared to low- and middle-income countries (39%) [9].

Several systematic reviews and meta-analyses investigated the association of appropriate breastfeeding practices and child mortality [10–16]. However, none have specifically focused on the sub-Saharan Africa region. Furthermore, there is a gap of knowledge regarding the economic impact of breastfeeding practices in relation to child mortality in sub-Saharan Africa.

Therefore, the primary aim of this study was to perform a systematic review and meta-analysis of the association between breastfeeding practices (particularly EBF and EIBF) and the risk of mortality in children under 5 years in sub-Saharan Africa. A second aim was to evaluate how improved breastfeeding practices may reduce the economic impact attributable to U5MR in sub-Saharan Africa.

Materials and methods

Eligibility criteria of included studies for systematic review and meta-analysis

The literature search was conducted on observational studies published from 01 January 2000 to 31 May 2019, with no language restrictions used. Eligible papers were included if they reported an estimate for breastfeeding practices (EBF, EIBF, continued breastfeeding, any breastfeeding vs other inappropriate breastfeeding practices) and all-cause in children under 5 years of age in sub-Saharan Africa. The eligibility criteria for the meta-analysis were limited to studies reporting estimates for strength of association (with 95% CI) between EBF and/or EIBF and all-cause mortality in children under 5 years of age in sub-Saharan Africa. EBF was defined by the proportion of infants aged 0–5 months of age who are fed exclusively with breast milk and EIBF as the proportion of children who were put to the breast within the first hour after birth, respectively [17].

Data sources

The literature search was conducted by searching electronic databases and scanning through reference lists of the included studies and relevant systematic reviews and meta-analyses. Medical subject headings (MeSH) and key terms (Supporting material: Text 1) were used to define the search and the North-West University library search engine (powered by EBSCO*host*) was used to identify existing evidence. Databases such as MEDLINE and CINAHL were included in the search engine (Supporting material: Text 3).

Study selection and quality assessment

The paper selection was conducted independently by two investigators following the preferred reporting items of systematic reviews and meta-analysis (PRISMA) guidelines [18]. The titles and the abstracts of the citations retrieved by the searches were screened for relevance (CP, HA). The investigators independently checked the full papers for eligibility (CP, HA). The quality assessment was conducted independently by the same investigators using the Newcastle–Ottawa scale (NOS) [19]. Agreement between the two investigators was reported using Cohen's K, intraclass correlation coefficient (ICC), and percentage of agreement. Thereafter, the data (author; year published; country; number of subjects in study; number of deaths; persons year of follow-up; exposure of feeding (per age group); estimate risk for all-cause mortality including HR, OR, RR (95%CI); other specific mortality outcome (only if reported); covariates) from eligible studies were extracted independently by the two investigators. Disagreements were resolved by consensus and a third author (CR) was consulted if no agreement could be reached.

Statistical analysis

We conducted a meta-analysis to estimate relative risk of mortality due to non-EBF and delayed breastfeeding initiation. Afterwards, we estimated EBF and EIBF prevalence in sub-Saharan Africa. Then, prevalence and all relative risk estimates (OR, RR, and HR) were merged to provide population attributable risks. Finally, population attributable risk was used, along with data on sub-Saharan Africa population structure gross domestic product, and health cost to estimate how improved breastfeeding practices may reduce the economic impact attributable to U5MR in sub-Saharan Africa.

Meta-analytic estimates

Meta-analysis of mortality relative risk estimates was determined by random and fixed effect methods. Heterogeneity was evaluated using the Cochrane Q test and the I^2 statistic. Stratification, study exclusion, and meta-regression analyses were conducted to identify sources of heterogeneity. A sensitivity analysis was also performed considering only the most reliable prospective studies. Publication bias was assessed by funnel plot visual inspection and the Egger's test [20]. Influence analyses were conducted excluding one study at a time.

Breastfeeding prevalence in sub-Saharan Africa

Breastfeeding prevalence (EBF and EIBF) in sub-Saharan African countries was estimated during the period 2000–2018 using data from the UNICEF database [21]. A mixed model having the arcsine of the breastfeeding prevalence as outcome and random intercept by country was used to estimate marginal least squared means and 95% confidence limits by country. Breastfeeding prevalence by country was computed by retro-transformed sin values and meta-analyzed by a fixed effect model having country under-five median population during the period 2000–2018 as weight variable. Prevalence estimates by regions were compared using a linear meta-regression approach.

Population attributable risk estimates

The relative risk for mortality and the prevalence of population at risk (complementary to breastfeeding practice prevalence) were merged, resulting in the population attributable fraction (PAF = (Pr (RR-1))/((Pr (RR-1)) + 1) where Pr is the prevalence of the population at risk and RR is the estimate of the relative risk of mortality.

Assessment of breastfeeding mortality costs

Non-health gross domestic product loss (NHGDPL) attributable to child deaths was undertaken as proposed by Kirigia et al. [22] (based on World Health Statistics 2015).

$$\mathrm{NHGDPL_{area}} = \sum_{\mathrm{i}}^{\mathrm{n}}\sum_{\mathrm{t}}^{\mathrm{k}} \frac{1}{(1+r^{\mathrm{t}})} \Delta\mathrm{GDP_i Mort_i}$$

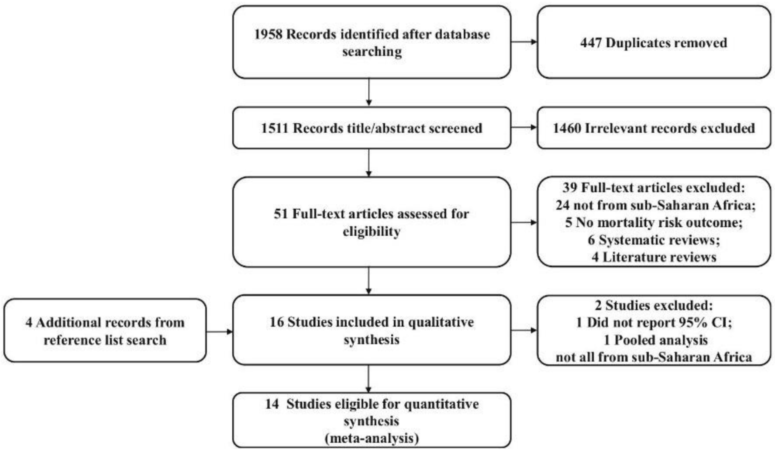
where i represents i-th country in a region, n the total number of countries within a region, t the t-th year of life loss, k the total number of working years lost (difference between the retirement age (assumed 65) and the age at starting work (assumed 20)); $\Delta\mathrm{GDP_i}$ the difference between the per-capita gross domestic product (GDP) and the per-capita health expenditure of the i-th country; r the discount rate ($r = 3\%$) which takes into account the variation of the economic productivity during the working period. Finally, $\mathrm{Mort_i}$ represents the number of child deaths from that given country and it was estimated considering the median under-five mortality attributable to inappropriate breastfeeding practices by country during the period 2000–2018. This element was calculated multiplying the total under-five deaths by country with the proportion of under-five deaths due to inappropriate breastfeeding practices. We assumed that 15% of the total under-five child deaths are attributable to poor breastfeeding practices dividing the worldwide 800,000 child deaths attributable to poor breastfeeding practices observed in 2017 by the 5.5 million under-five child deaths that occurred in the same year [1]. The NHGDPL preventable by proper breastfeeding practices was computed multiplying deaths by the PAF. The NHGDPL was reported as US billion dollars (USB$).

Results

Systematic review

The initial literature search yielded 1511 after the removal of duplicates. After title and abstracts screening, 51 records were assessed for eligibility. After the exclusion of 39 full text articles (Fig. 1), 16 studies were included in the qualitative synthesis [23–37]. Two of these studies were not eligible to be retained for the meta-analysis. One study did not report the

Fig. 1 Flow chart of paper selection



95% confidence intervals [24] and the other study conducted a pooled analysis which included a country from Peru, outside sub-Saharan Africa [23] (Fig. 1). Of the 16 studies included for qualitative synthesis, nine were prospective studies [23, 26–29, 32, 34–36], two were retrospective studies [31, 37], and four were surveys [24, 30, 33, 38]. The quality of the studies according to the NOS score ranged between a minimum of six points to a maximum of eight points out of nine, with a median of seven points. Agreement between the two investigators rating the study quality was satisfactory (Cohen $K = 0.52$, ICC = 0.82, agreement = 73%). Study characteristics are reported in Table 1. The relative risk estimates for non-EBF vs EBF ranged from 3.6 (95%CI: 2.5, 5.2) [36] to 33.3 (95% CI: 25, 50) [26]. The relative risk estimates for predominant breastfeeding and partial breastfeeding vs EBF ranged from 0.94 (95% CI: 0.41, 3.45) [37] to 1.46 (95% CI: 0.75, 2.86) [23] and from 0.80 (95% CI: 0.14, 4.61) [28] to 3.82 (95% CI: 1.99, 7.34) [29], respectively. The median number of adjusting factors among studies was seven and only four studies reported less than five factors [25, 33–35]. Two of these studies did not report any adjusting factors [33, 34].

Mortality risk in relation to exclusive breastfeeding and early initiation of breastfeeding and their population attributable fractions

Mortality risk in association with any kind of infant feeding compared to EBF was 5.71 (95% CI: 2.14, 15.23) and relevant heterogeneity was observed ($I^2 = 96.3\%$; $P_{\text{Cochrane-test}} < .001$) (Fig. 4). Here, the exclusion of the study from Motsa et al. [37] reduced the between-study heterogeneity the most ($I^2 = 90.2\%$; $P_{\text{Cochrane-test}} < 0.01$). Further heterogeneity reduction was obtained when applying meta-regression considering NOS score, $I^2 = 35\%$. Delayed compared to early breastfeeding initiation increased the relative mortality risk to 3.33 (95% CI: 2.49, 4.46), with no heterogeneity ($I^2 = 0\%$, $P_{\text{Cochrane test}} = .406$). According to this sensitivity analysis, the RR estimate for mortality due to non-EBF and delayed breastfeeding initiation would have been 4.21 (95% CI: 1.5, 12.2) and 3.19 (95% CI: 1.6, 6.34), which overlap with the initial estimates of 5.71 (95% CI: 2.14, 15.23) and 3.33 (95% CI: 2.49, 4.46), respectively. According to funnel plot visual inspection (Supporting: Figs. 1 and 2) and the Egger test, no indication of publication bias was observed ($P_{\text{Egger}} > 0.1$).

Prevalence of exclusive breastfeeding and early initiation of breastfeeding in sub-Saharan Africa

We estimated an EBF prevalence in Sub-Saharan African countries of 34% (95% CI: 32%, 37%) during the period 2000–2018 (Fig. 2), with a large variability among the countries (5% in Chad to 86% in Rwanda). When considering different regions, we observed the highest EBF prevalence of 50% in East Africa (95%CI: 47%, 54%, $I^2 = 94.3\%$). EBF prevalences were 40% (95% CI: 33%, 47%, $I^2 = 81.9\%$), 29% (95% CI: 23%, 36%, $I^2 = 91.1\%$) and 22% (95% CI: 18%, 26%, $I^2 = 89.7\%$) in Southern Africa, Central Africa, and West Africa, respectively. Overall difference between regions was non-significant ($P = 0.068$), East Africa had statistically significantly higher EBF prevalence compared to Southern Africa ($P = 0.029$), Central Africa ($P = 0.034$), and West Africa ($P = 0.043$).

EIBF prevalence was 47% (95% CI: 44%, 50%) (Fig. 3). Also, EIBF prevalence had a large range of variability among countries ranging from 26% (Somalia) to 87% (Eritrea). Southern Africa had the highest EIBF prevalence (60% (95% CI: 51%, 70%, $I^2 = 33.6\%$). East Africa, Central Africa, and West Africa had a prevalence of 59% (95% CI:

Table 1 Characteristics of included studies for the systematic review of breastfeeding practices and child mortality

Author, year	Country	Sample	Exposure (age-group)	Mortality	Covariates	NOS
Prospective studies						
Bahl et al. (2005)[b]	Ghana, India and Peru	N: 9424 D: 104 P-year: 3264	EBF VS. PRE (6–26 w) PBF VS. PRE NBF VS. PRE	HR_{EBF}: 1.46 (0.75;2.86) HR_{EBF-DS}: 1.36 (0.37;5.03) HR_{PBF}: 2.46 (1.44;4.18) HR_{PBF-DS}: 3.37 (1.46;7.75) $HR_{PBF-ALRI-S}$: 3.57 (0.93;13.7) HR_{NBF}: 10.5 (5.0;22.0) HR_{NBF-DS}: 8.96 (2.56;31.4) $HR_{NBF-ALRI-S}$: 32.7 (6.82;157.2)	Infant's weight at enrolment, sex, twin status, birth order, [e] education, place of delivery, household water supply	7
Biks et al. (2015)	Ethiopia	N: 1752 D: 130 P-year: 1473	NEBF VS. EBF (< 1 y) EI > 1 d VS. EI < 1 h EI 1–24 h VS. EI < 1 h	RR_{NEBF}: 7.86 (5.11;12.10) RR_{EI}: 2.96 (1.76;4.96) RR_{EI}: 4.84 (2.94;7.99)	Nutrition factors, environmental factors, behavioural factors, residential factor, [e] biological factors, SES	6
Edmond et al. (2006)	Ghana	N: 10,947 D: 268 P-year: 10,947	PRE VS. EBF (< 28 d) PBF VS. EBF EI 1–24 h VS. EI < 1 h EI > 1 d VS. EI < 1 h	HR_{PRE}: 1.30 (0.90;1.87) HR_{PBF}: 3.82 (1.99;7.34) HR_{EI}: 1.43 (0.88;2.31) HR_{EI}: 2.88 (1.87;4.42)	Parity, [e] age, [e] income, place of delivery, gender, gestational age, number of antenatal visits, place of birth, birth attendant, infant health at birth, infant health at the time of interview, [e] health at the time of delivery, household water supply, neonatal size at birth	6
Edmond et al. (2007)	Ghana	N: 10,942 D: 140 P-year: 840	PRE VS. EBF (< 28 d) PBF VS. EBF EI > 1 d VS. EI < 1 d	OR_{PRE}: 0.97 (0.45;2.04) OR_{PRE-IS}: 1.45 (0.90;2.34) OR_{PBF}: 0.80 (0.14;4.61) OR_{PBF-IS}: 5.73 (2.75;11.91) OR_{EI}: 1.63 (0.85;3.11) OR_{EI-IS}: 2.61 (1.68;4.04)	[e] education, [e] income, sanitation, overcrowding, antenatal care, delivery attendant, site of delivery, [e] ethnicity, [e] age, parity, [e] perinatal health, sex, gestational age, neonatal perinatal health, other breastfeeding practices, household water supply, neonatal size at birth, congenital abnormalities	6
Edmond et al. (2008)	Ghana	N: 11,751 D: 320 P-year: 901	PRE VS. EBF (< 28 d) EI > 1 d VS. EI < 1 d	HR_{PRE}: 1.05 (0.25;4.38) HR_{EI}: 2.94 (1.00;8.73)	[e] education, sanitation, site of delivery, [e] age, [f] age, [e] perinatal health, multiple births, gender, EI, infant perinatal health, pre-lacteal feeding	6
Mengesha et al. (2016)	Ethiopia	N: 1152 D: 68 P-year: 75	NEBF VS. EBF (< 28 d)	HR_{NEBF}: 7.5 (3.77;15.60)	[e]	6
Neovita (2016)	Ghana	N: 22,995	(1 to < 3 m) EI 2–23 h VS. EI < 1 h	RR_{EI}: 2.22 (1.51;3.26)	Sex, study site, birth weight, singleton babies, [e] age, [e] education, parity, skilled birth attendant, caesarean section, wealth quartile	7

Table 1 (continued)

Author, year	Country	Sample	Exposure (age-group)	Mortality	Covariates	NOS
		D: 699 P-year: 11,4-98	EI > 1 d VS. EI < 1 h (3 to < 6 m) EI 2–23 h VS. EI < 1 h EI > 1 d VS. EI < 1 h	RR_{EI}: 2.37 (0.73;7.73) RR_{EI}: 1.54 (1.05;2.27) RR_{EI}: 1.84 (0.57;5.93)		
Neovita (2016)	Tanzania	N: 31,9-99 D: 1112 P-year: 63,9-98	(1 to < 3 m) EI 2–23 h VS. EI < 1 h EI > 1 d VS. EI < 1 h (3 to < 6 m) EI 2–23 h VS. EI < 1 h EI > 1 d VS. EI < 1 h	RR_{EI}: 1.05 (0.66;1.66) RR_{EI}: 1.39 (0.34;5.56) RR_{EI}: 1.41(0.92;2-.16) RR_{EI}: 0.66(0.41;6-.66)	Sex, study site, birth weight, singleton babies, [e] age, [e] education, parity, skilled birth attendant, caesarean section, wealth quartile	7
Orsido et al. (2019)	Ethiopia	N: 964 D: 159 P-year: 16	EI > 1 h VS. EI < 1 h (< 28 d)	RR_{EI}: 2.62 (1.60;4.30)	[e] and neonatal factors, neonatal illness, service-related factors	7
Rollins et al. (2013)	South Africa	N: 2589 D: 101 P-year: 2589	PBF VS. EBF (0–12 m) NEBF VS. EBF	HR_{PBF}: 2.6 (1.9;3.8) HR_{NEBF}: 3.6 (2.5;5.2)	Sex, age, HIV status, water source, [f] age, enrolment clinic, [e] education	7
WHO team (2000)[a]	Ghana Senegal	N: 1099 D: 33 N: 3534 D: 425	NBF VS. BF (< 23 m) NBF VS. BF (< 23 m)	RR_{NBF}: 7.9 (1.2;53.2) RR_{NBF}: 2.0 (1.4;3.1)	[e] education, age-group	7 6
Retrospective studies						
Girma et al. (2011)	Ethiopia	N: 296 D: 74	nBF VS. eBF (< 5 y)	OR_{nBF}: 13.21 (3.28;53.16)	Ethnicity, religion, parity, floor materials of the house, [f] age, eBF, vaccination history, wealth quintile	7
Shifa et al. (2018)	Ethiopia	N: 1143 D: [c]	nBF VS. eBF (< 5 y) PRE VS. EBF PBF VS. EBF EI > 1 h VS. EI < 1 h nBF VS. eBF (< 1 y) PRE VS. EBF PBF VS. EBF EI > 1 h VS. EI < 1 h	HR_{eBF}: 8.09 (4.08;16.05) HR_{PRE}: 0.94 (0.38;2.29) HR_{PBF}: 1.29 (0.86;1.94) HR_{EI}: 1.55 (0.95;2.51) HR_{eBF}: 14.19 (5.51;36.50) HR_{PRE}: 1.19 (0.41;3.45) HR_{PBF}: 0.91 (0.54;1.51) HR_{EI}: 1.43 (0.80;2.59)	Sex, [c] education, wealth index, husband's occupation, marital status of mother, first breastfeeding started, breastfeeding status within 6 months of age, eBF, bottle feeding, timing of first bath, anything applied to umbilical wound	8
WHO team (2000)[a]	Gambia	N: 431 D: 202	NBF VS. BF (< 23 m)	OR_{NBF}: 0.9 (0.3;2.6)	[e] age, age-group	6
Surveys						
Ettarh and Kimani (2012)	Kenya	N: 16,1-62	CBF 6-12 m VS. BF < 6 m (< 5 y)	HR_{CBF}: 0.55 (0.20;1.48)	Place of residence, [c] age, [c] education, sex, birth order, household wealth quintile, place of delivery, province, duration of	–

Table 1 (continued)

Author, year	Country	Sample	Exposure (age-group)	Mortality	Covariates	NOS
		D: [c]	CBF > 12 m VS. BF (< 6 m)	HR_{CBF}: 0.13 (0.02;0.84)	breastfeeding, postnatal visit at 2 months; place of residence x breastfeeding duration	
Kayode et al. (2012)	Nigeria	N: 28,6-47 D: 3201	CBF 6–12 m VS. NBF (< 5 y) CBF > 12 m VS. NBF	OR_{CBF}: 0.27 (0.24;0.30) OR_{CBF}: 0.10 (0.08;0.11)	[c]	–
Lindstrom et al. (2015)[b]	Ethiopia	N: 9173 D: [c]	nBF (0 m) nBF (1–11 m) BF 11 m (1–4 y) BF 23 m (1–4 y) BF 35 m (1–4 y) BF 47 m (1–4 y)	OR_{nBF}: 115.35 [d] OR_{nBF}: 2.85 OR_{BF}: 1.81 OR_{BF}: 1.5 OR_{BF}: 2.0 OR_{BF}: 7.9	SES, environmental factors, [e] education, [e] age, [f] age, multiple births, sex	–
Motsa et al. (2016)	Swaziland Lesotho, Zambia and Zimbabwe	N: 13,2-18 D: 677	EBF VS. NBF (< 1 y) PBF VS. NBF (< 1 y)	HR_{EBF}: 33.3 (25; 50) HR_{PBF}: 25 (25; 33.3)	[e] demographic, environmental factors and SES, infant's bio-demographic variables	–

N number of subjects, *D* number of deaths, *P year* persons year of follow-up, *EBF* exclusive breastfeeding, *PRE* predominant breastfeeding, *w* week/s, *PBF* partial breastfeeding, *NBF* not breastfeeding, *HR* hazard ratio, *DS* diarrhea specific, *ALRI-S* acute lower respiratory infection-specific, *NEBF* not EBF, *y* year/s, *d* day/s, *h* hours/s, *EI* early initiation of breastfeeding, *RR* relative risk, *SES* socio-economic status, *OR* odds ratio, *IS* infection specific, *m* month/s, *nBF* never breastfed, *eBF* ever breastfed, *BF* breastfeeding, *CBF* continued breastfeeding

[a] Stratified by country

[b] Not eligible for meta-analysis

[c] Not reported

[d] Confidence intervals not reported

[e] Maternal

[f] Paternal

54%, 64%, I^2 = 79.8%), 43%(95% CI: 35%, 51%, I^2 = 70.8%), and 35% (95% CI: 30%, 41%, I^2 = 73.2%), respectively. The overall difference between regions was strongly significant ($P < 0.001$), with significant differences between early breastfeeding prevalence of Central Africa and West Africa ($P < 0.001$) and East Africa ($P = 0.004$), respectively, West Africa and East Africa ($P = 0.003$), as well as East Africa and South Africa ($P < 0.001$). Also, the difference between EIBF prevalence in West Africa and in South Africa was statistically significant ($P = 0.031$) (Fig. 4).

Population attributable fraction and breastfeeding mortality costs

Finally, we estimated that the PAF for non-EBF was 75.7% in sub-Saharan Africa, ranging from 70.2% in East Africa to 77% in West Africa. The PAF for late breastfeeding initiation was 55.3% in sub-Saharan Africa, ranging from 48.2% in Southern Africa to 60.2% in West Africa (Table 2). The NHGDPL attributable to under-five child deaths was 130 USB$. The NHGDPL attributable to inappropriate breastfeeding practices resulted in about 19.5 USB$. When considering deaths avoidable by EBF and early breastfeeding initiation, the NHGDPL would be 8.3 and 8.4 USB$ in sub-Saharan Africa, respectively (Table 3).

Discussion

We reported that a five-fold increased risk for mortality was observed with suboptimal breastfeeding practices. The overall prevalences for EBF and EIBF were 34% and 47%, respectively. The PAF for non-EBF and for late breastfeeding initiation were 75.7% and 55.3%, respectively. Finally, the total NHGDPL attributable to under-five child deaths and inappropriate breastfeeding practices were calculated to be 130 USB$ and 19.5 USB$, respectively.

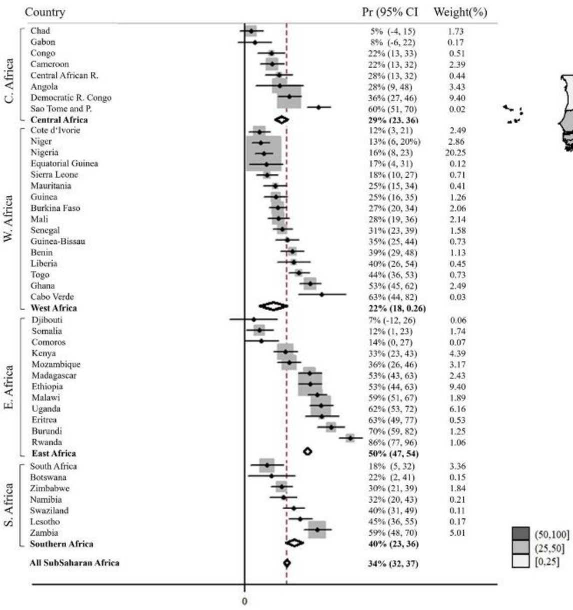


Fig. 2 Exclusive breastfeeding prevalence in sub-Saharan Africa

Our results agree with previous systematic reviews and meta-analysis of breastfeeding practices and mortality in sub-Saharan Africa [10–16]. We confirm that breastfeeding is a cost-effective intervention with potential to prevent child deaths [39]. Feeding colostrum during EIBF and practicing EBF may protect against infections, such as sepsis, acute

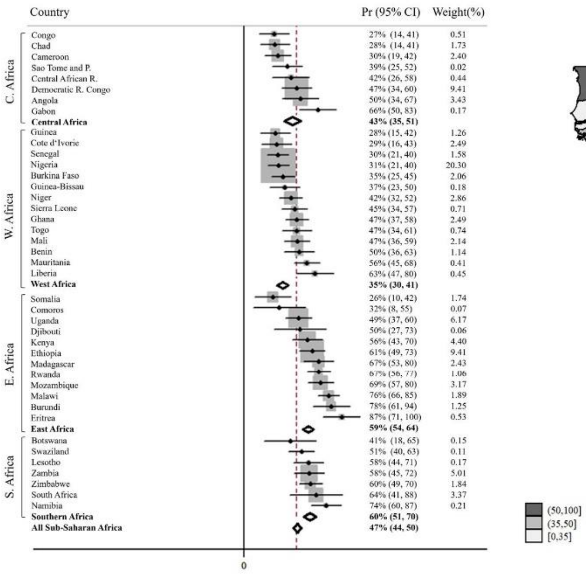


Fig. 3 Early initiation of breastfeeding prevalence in sub-Saharan Africa

Fig. 4 Meta-analysis of breastfeeding practices in relation to mortality risk

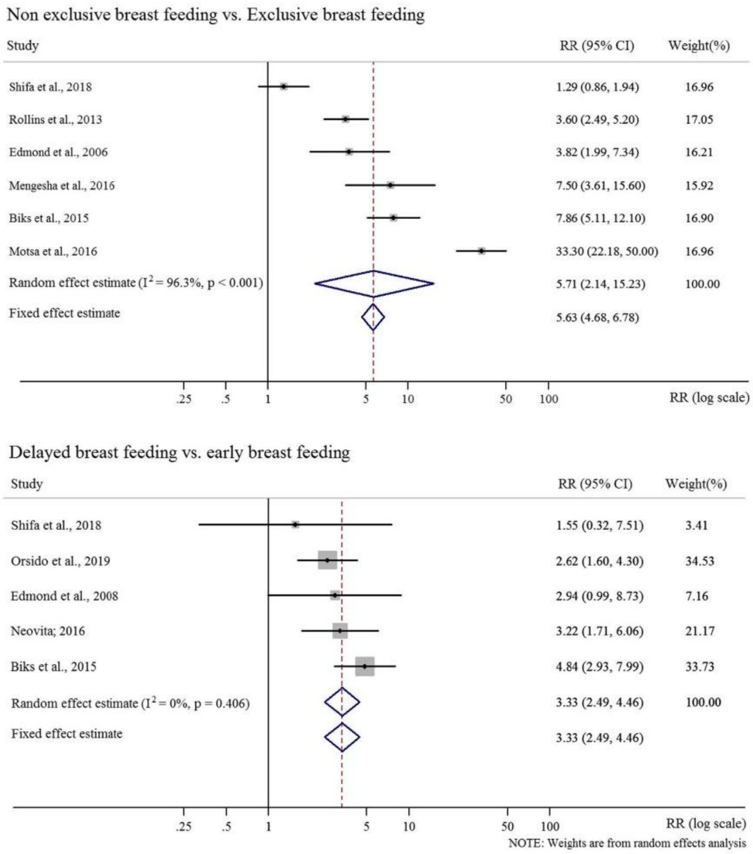


Table 2 Population at risk and population attributable fraction for mortality attributable to breastfeeding practices

Area	Pp[a] risk (95% CIs)	RR[b] (95% CIs)	PAF (95% CIs)
Non-EBF vs. EBF			
Sub Saharan Africa	66% (63%; 68%)	5.71 (2.14, 15.23)	75.7% (42, 91)
Central Africa	71% (64%; 77%)		77.0% (42, 92)
West Africa	78% (74%; 82%)		78.6% (46, 92)
East Africa	50% (46%; 53%)		70.2% (34, 88)
Southern Africa	60% (53%; 67%)		73.9% (38, 91)
Late breastfeeding initiation vs. Early breastfeeding initiation			
Sub Saharan Africa	53% (50%; 56%)	3.33 (2.49, 4.46)	55.3% (45; 66)
Central Africa	57% (49%; 65%)		57.0% (48; 69)
West Africa	65% (59%; 70%)		60.2% (61; 71)
East Africa	41% (36%; 46%)		48.9% (30; 61)
Southern Africa	40% (30%; 49%)		48.2% (25; 63)

PAF population attributable fraction PAF = Pp (RR-1)/(Pp (RR-1) + 1)

[a] Population at risk derived from meta-analytical estimate of prevalence by area UNICEF 2000–2018

[b] Relative risk of mortality derived from meta-analytical estimate of relative risk estimates from included studies

Table 3 Economic gross domestic product loss attributable to child mortality in Sub-Saharan Africa

Area	All causes (USB$)[a]	Any type BF (USB$)[b]	Exclusive BF (USB$)[c]	Early initiation BF (USB$)[d]
Sub-Saharan Africa	129.973	16.753	8.359	8.394
Central Africa	29.117	3.754	1.876	1.878
West Africa	72.836	8.753	4.405	4.348
East Africa	9.321	1.456	0.742	0.714
Southern Africa	18.699	2.789	1.336	1.453

USB$ billions of US dollars, *BF* breastfeeding

[a] Economic loss due to child mortality for all cause

[b] Economic loss due to child mortality for inappropriate breastfeeding

[c] Economic loss due to child mortality for non-exclusive breastfeeding

[d] Economic loss due to child mortality for delayed breastfeeding initiation

respiratory tract infection, meningitis, omphalitis, and diarrhea, which are the main causes of child deaths in developing countries [40]. According to a systematic review and meta-analysis, peer counselling as a community intervention reduces the risk of non-EBF significantly, especially in low- and middle-income countries [41]. However, some education interventions have not proven effective in reducing mortality [42]. Adherence to the baby-friendly hospital initiative (BFHI) *Ten Steps* has been proven to have a positive impact on short- and long-term breastfeeding outcomes. Community support interventions are part of the step 10 of the BFHI and appear to be essential for sustaining breastfeeding impacts of BFHI in the longer term [43]. Therefore, emphasis ought to be placed on encouraging mothers to deliver in a health institution [44], together with continued support of breastfeeding through community interventions [43].

In the present study, a large variability among studies was observed for mortality risk estimates for exclusive breastfeeding. This large variability could be better understood for example considering the study of Shifa et al. [37] which provided the lower RR estimate and the study of Biks et al. [26] which provided the higher RR estimate. These two studies were both performed in Ethiopia and in rural areas but were located in the South and North-western regions, respectively, which are completely different from a geographic viewpoint. The study from Shifa et al. [37] was conducted in a pluvial area while the study from Biks et al. [26] was conducted in a desert area with different rates of exclusive breastfeeding of 50% and 80%, respectively. Notably and as reported by the authors, the large food availability in the southern area may have influenced both exclusive breastfeeding and child mortality.

The overall EBF prevalence for infants under 6 months in sub-Saharan Africa was estimated to be poor (34%) compared to the 2025 WHO target of at least 50%. Our estimated prevalence of EBF among infants younger than 6 months was consistent with the results by Cai et al. [9], who reported a prevalence of 35% of EBF in Africa in 2010. We also estimated that the prevalence of EIBF was just below 50%. This result is confirmed by the WHO Global Survey, which reported that the prevalence of EIBF is approximately 50% in many low- and middle-income countries [45]. However, this survey was conducted more than 10 years ago (2004–2005) in Africa, which indicates the poor improvement of EIBF in sub-Saharan Africa, specifically.

In the present work, large variability was observed between individual sub-Sahara African countries and regions for both EBF and EIBF prevalence. This variability can be explained by the multiple factors associated with breastfeeding practices [46], or the risk of bias, which may have occurred through the retrospective evaluation methods used by UNICEF's database [47]. Another factor may have been the existing disparities towards adopting the WHO guidelines from 1997 to 1998 [48] to 2006 [49] for feeding with respect to the postnatal prevention of mother to child transmission (PMTCT) of human immunodeficiency virus (HIV). The infant feeding guidelines in 1997–1998 [48] and 2001 [50] created a huge policy shift towards the promotion of replacement feeding and the distribution of free infant formula to HIV positive women enrolled in the PMTCT programmes [51]. As new evidence was emerging, the updated 2006 guidelines emphasized EBF among HIV positive mothers after the risks of childhood infections, malnutrition associated with replacement feeding, and higher HIV-free survival rate among exclusively breastfed than among replacement fed infants were reported [49].

According to the population at risk and the mortality risk, we estimated that about 55–75% of child deaths are due to inappropriate breastfeeding practices among affected children, and that a proportion of those deaths is avoidable if the prevalence of appropriate breastfeeding practices would improve in sub-Saharan Africa. Moreover, we estimated that child mortality due to inappropriate breastfeeding practices results in a loss of GDP of about 19.5 USB$. Thus, if EBF and EIBF prevalence would grow, this cost would potentially be reduced, with child deaths avoided, to approximately 8.4 and 7 USB$, respectively. The present cost analysis is in agreement with previous reports [22] and results in an immediate and remarkable economic saving that will be maintained in the long term.

It was reported that the cost of a community intervention aimed to improve EBF practice in South Africa would be in the range of 200–300 US$ per woman [52]. Such an intervention for improving breastfeeding would result in a total cost of 1.1 USB$ across sub-Saharan Africa if it was applied extensively, that is, to all mothers who experienced a child death in the last year. Notably, this cost represents approximately 6% of the overall GDP loss due to child mortality in relation to poor breastfeeding practices [53, 54].

Our work has limitations. Due to missing information, we limited our analysis to EBF and EIBF. It would have been of interest to consider other exposures as well, such as mixed feeding and timing of breastfeeding initiation. Another weakness of our work is that we provided results for sub-Saharan Africa as a whole, while a country-specific evaluation of breastfeeding practices impact may be of greater interest for practitioners. Finally, we pooled different RR estimates such as HR, RR, and odds ratio, including one estimate from a survey, which could have generated bias. On the other hand, a sensitivity analysis was performed considering only the most reliable prospective studies, which overlapped with the initial RR estimates.

This study is unique because it integrates epidemiological, public health, and economic data providing novel information regarding how improved breastfeeding practices may impact sub-Saharan African society. In addition, breastfeeding prevalence, U5MR, child population, and costs were obtained from reliable population-based surveys. It is not merely speculation that sub-Saharan Africa would greatly benefit by an extensive plan of interventions aimed to improve beneficial breastfeeding practices. Public health interventions aimed to improve EBF and EIBF may prevent 55% to 75% of lives lost due to inappropriate breastfeeding practices, saving more than 10 USB$.

Authors' contribution CP and CR conceptualized and designed the study and data collection instruments and drafted the initial manuscript. CP and HA collected data and CR carried out the initial analyses. HA, JG, and SK contributed to the acquisition, analysis, or interpretation of data reviewed and revised the manuscript critically for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Compliance with ethical statements

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors and is approved for ethical clearance by the North-West University Health Research Ethics Committee (NWU-00974-19-A1).

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ANNEXURE G: AUTHOR GUIDELINES FOR THE ARTICLE

Instructions for Authors

Types of papers

Editorials

Reviews – (non-)invited with a maximum of 3000 words or 4-5 pages.

Original Articles – with a maximum of 3000 words or 4-5 pages.

Short communication - have a limited length (1500 words), one table and/or figure and not more than 12 references. The authors should bring new information and insights from basic research or clinical experience while concentrating on some aspects of diseases and disorders such as etiology and pathophysiology, diagnostic tools, innovative treatments, genotype-phenotype correlation, etc.

Correspondence - with a maximum of 300 words, relate to previously published papers and discuss some aspects of the paper at stake of which the authors are invited to write a reply that is published together with the letter.

Clinical Algorithm – (non-)invited with a maximum of 2000 words or 3-4 pages and less than 12 references. Personal experience/eminence opinion. Including algorithms, tables and up-to-date references.

Editorial Procedure

Authors are obliged to provide names, addresses and institutions of at least 4 possible, internationally well-known reviewers with indication of their expertise / merits and scientific accomplishment; it is discouraged to list more than 1 local (from the same country) reviewer because of possible conflicts of interest.

Manuscript Submission

Manuscript Submission

Submission of a manuscript implies: that the work described has not been published before; that it is not under consideration for publication anywhere else; that its publication has been approved by all co-authors, if any, as well as by the responsible authorities – tacitly or explicitly – at the institute where the work has been carried out. The publisher will not be held legally responsible should there be any claims for compensation.

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Please ensure you provide all relevant editable source files. Failing to submit these source files might cause unnecessary delays in the review and production process.

Please note:

The authors are requested to include a list with their submission stating the individual contributions to the paper. – This information is mandatory for all submissions.

The e-mail addresses of all authors need to be provided with the submission.

Title Page

The title page should include:

- The first and last name(s) of all author(s) with their e-mail addresses
- A concise and informative title
- The affiliation(s) and address(es) of the author(s)
- The e-mail address, telephone and fax numbers of the corresponding author

Please note:

The author's names should be followed by neither their titles nor their affiliation.

Affiliations should be marked by numerals after the names and be listed in a footnote.

Abstract

Please provide an abstract with a maximum of 200 words. The abstract should not contain any undefined abbreviations or references. The abstract of each manuscript needs to reflect the essential message of the article, including the results of the quantitative data as well as a sound conclusion. The abstract should not be structured but should end with “Conclusion: …” (Conclusion written in italics) followed by the concluding sentence written with regular fonts.

Keywords

Please provide 4 to 6 keywords which can be used for indexing purposes.

Give a list of Abbreviations in alphabetical order.

"What is Known – What is New" (Authors Summary)

Please indicate for the fast reader "What is Known" and explain "What is New" and please note that this part will be judged by the reviewers and will be printed in the Journal. The size of this section is limited to four 600 characters (bullet list).

The “What is known / What is new” section is not required for EAP Statements.

Text

Text Formatting

Manuscripts should be submitted in Word.

Use a normal, plain font (e.g., 10-point Times Roman) for text.

Use italics for emphasis.

Use the automatic page numbering function to number the pages.

Do not use field functions.

Use tab stops or other commands for indents, not the space bar.

Use the table function, not spreadsheets, to make tables.

Use the equation editor or MathType for equations.

Save your file in docx format (Word 2007 or higher) or doc format (older Word versions).

Manuscripts with mathematical content can also be submitted in LaTeX.

LaTeX macro package (Download zip, 188 kB)

Headings

Please use no more than three levels of displayed headings.

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Abbreviations should be defined at first mention and used consistently thereafter.

Footnotes

Footnotes can be used to give additional information, which may include the citation of a reference included in the reference list. They should not consist solely of a reference citation, and they should never include the bibliographic details of a reference. They should also not contain any figures or tables.

Footnotes to the text are numbered consecutively; those to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data). Footnotes to the title or the authors of the article are not given reference symbols.

Always use footnotes instead of endnotes.

Acknowledgments

Acknowledgments of people, grants, funds, etc. should be placed in a separate section on the title page. The names of funding organizations should be written in full.

Please note:

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Please apply consecutive numbering to all your manuscript lines. Please write the numbers next to the line on the left margin. Do not count each page individually but rather keep counting up across all pages of the manuscript.

Authors should write as briefly and clearly as possible and arrange the manuscript logically:

• Title page

• Abstract

• List of Abbreviations in alphabetical order

• Introduction (to be kept short)

• Materials and methods

• Patients' medical reports

• Results

• Discussion

• References

• Tables

• Figure legends

Scientific style

Eponyms

Eponyms should be used in their non possessive form (e.g., Marfan syndrome, Crohn disease, and not Looser's zone).

SI units

SI units are preferred, but not mandatory. Whatever units are adopted, consistency within a paper is essential.

If SI units are used, it is appreciated if non-SI units (mg, ml etc.) or a conversion factor are provided as well.

References

Citation

Reference citations in the text should be identified by numbers in square brackets. Some examples:

1. Negotiation research spans many disciplines [3].

2. This result was later contradicted by Becker and Seligman [5].

3. This effect has been widely studied [1-3, 7].

Reference list

The list of references should only include works that are cited in the text and that have been published or accepted for publication. Personal communications and unpublished works should only be mentioned in the text. Do not use footnotes or endnotes as a substitute for a reference list.

The entries in the list should be numbered consecutively.

Journal article

Gamelin FX, Baquet G, Berthoin S, Thevenet D, Nourry C, Nottin S, Bosquet L (2009) Effect of high intensity intermittent training on heart rate variability in prepubescent children. Eur J Appl Physiol 105:731-738. https://doi.org/10.1007/s00421-008-0955-8

Ideally, the names of all authors should be provided, but the usage of “et al” in long author lists will also be accepted:

Smith J, Jones M Jr, Houghton L et al (1999) Future of health insurance. N Engl J Med 965:325–329

Article by DOI

Slifka MK, Whitton JL (2000) Clinical implications of dysregulated cytokine production. J Mol Med. https://doi.org/10.1007/s001090000086

Book

South J, Blass B (2001) The future of modern genomics. Blackwell, London

Book chapter

Brown B, Aaron M (2001) The politics of nature. In: Smith J (ed) The rise of modern genomics, 3rd edn. Wiley, New York, pp 230-257

Online document

Cartwright J (2007) Big stars have weather too. IOP Publishing PhysicsWeb. http://physicsweb.org/articles/news/11/6/16/1. Accessed 26 June 2007

Dissertation

Trent JW (1975) Experimental acute renal failure. Dissertation, University of California

Always use the standard abbreviation of a journal's name according to the ISSN List of Title Word Abbreviations, see

ISSN.org LTWA

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Please note:

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All tables are to be numbered using Arabic numerals.

Tables should always be cited in text in consecutive numerical order.

For each table, please supply a table caption (title) explaining the components of the table.

Identify any previously published material by giving the original source in the form of a reference at the end of the table caption.

Footnotes to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data) and included beneath the table body.

Artwork and Illustrations Guidelines

Electronic Figure Submission

Supply all figures electronically.

Indicate what graphics program was used to create the artwork.

For vector graphics, the preferred format is EPS; for halftones, please use TIFF format. MSOffice files are also acceptable.

Vector graphics containing fonts must have the fonts embedded in the files.

Name your figure files with "Fig" and the figure number, e.g., Fig1.eps.

Line Art

Definition: Black and white graphic with no shading.

Do not use faint lines and/or lettering and check that all lines and lettering within the figures are legible at final size.

All lines should be at least 0.1 mm (0.3 pt) wide.

Scanned line drawings and line drawings in bitmap format should have a minimum resolution of 1200 dpi.

Vector graphics containing fonts must have the fonts embedded in the files.

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Definition: Photographs, drawings, or paintings with fine shading, etc.

If any magnification is used in the photographs, indicate this by using scale bars within the figures themselves.

Halftones should have a minimum resolution of 300 dpi.

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Definition: a combination of halftone and line art, e.g., halftones containing line drawing, extensive lettering, color diagrams, etc.

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Color art is free of charge for online publication.

If black and white will be shown in the print version, make sure that the main information will still be visible. Many colors are not distinguishable from one another when converted to black and white. A simple way to check this is to make a xerographic copy to see if the necessary distinctions between the different colors are still apparent.

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Avoid effects such as shading, outline letters, etc.

Do not include titles or captions within your illustrations.

Figure Numbering

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Figures should always be cited in text in consecutive numerical order.

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Each figure should have a concise caption describing accurately what the figure depicts. Include the captions in the text file of the manuscript, not in the figure file.

Figure captions begin with the term Fig. in bold type, followed by the figure number, also in bold type.

No punctuation is to be included after the number, nor is any punctuation to be placed at the end of the caption.

Identify all elements found in the figure in the figure caption; and use boxes, circles, etc., as coordinate points in graphs.

Identify previously published material by giving the original source in the form of a reference citation at the end of the figure caption.

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