

Early life course factors, early childhood caries and oral health related quality of life among five-year-olds-a prospective and intergenerational study from Eastern Uganda

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To my parents: Mr. and Mrs. Turyamwijuka.

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Abbreviations

DAGs	Directed Acyclic Graphs
DMFT/dmft [lower case])	Decayed missing filled teeth (adult [capital letters]/ children [lower case])
DMFS/dmfs	Decayed missing filled surfaces
EBF	Exclusive breastfeeding
ECOHIS	Early childhood oral health impact scale
GNI	Gross national income
GDP	Gross domestic product
MI	Motivational interviewing
OHRQOL	Oral health related quality of life
PROMISE-EBF	Promoting infant health and nutrition in sub-Saharan Africa: Safety and efficacy of exclusive breastfeeding promotion in the era of HIV
SES	Socio-economic status
WHO	World Health Organisation

Scientific environment

The work comprising this thesis was conducted from 2012 -2016 at the Department of Clinical Dentistry, University of Bergen, Norway and the Centre for International Health, University of Bergen, Norway.

Professor Anne Nordrehaug Åstrøm was the main supervisor. The co-supervisors were Dr Lars Thore Fadnes and Dr Isaac Okullo.

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Summary

Background: The Early childhood caries, ECC, literature considering children in low income countries is limited to a few cross-sectional studies. Longitudinal studies using causal diagrams (DAGs) with intergenerational empirical data are missing in the dental literature.

Aim: To estimate the effects of an exclusive breastfeeding, EBF, intervention in pregnant mothers on ECC in her offspring, the prevalence of ECC and the effect of early life course factors on ECC and OHRQOL of 5- year-old children and their caretakers in Mbale, Eastern Uganda.

Methods: This study is based on data from a birth cohort of mother-child pairs emanating from the PROMISE-EBF trial (ClinicalTrials.gov no: NCT00397150). In 2011, at a 5-year follow-up of the birth cohort, 417 mother-child pairs participated in face to face interviews and underwent full mouth dental examinations at a household level. ECC and mother's caries experience was recorded according to the World Health Organization's criteria. Information about early life course factors, such as feeding habits, breastfeeding, parental characteristics and socio-economic status, SES, was assessed at the recruitment-, 3-, 6-, 12-, 24- weeks, 2- years and 5-years follow-up interviews with mothers or caretakers.

Results: The prevalence of ECC in 5- year-old children was 39%, whereas mean dmft was 1.5 (standard deviation [SD] 2.9) and 1.7 (SD 2.9) in the intervention and control groups, respectively (Study I). Utilising DAGs, EBF was a protective causal factor of ECC from analyses involving three multivariable models (Study II). Study III revealed that caretaker's caries experience was positively associated with the ECC of their children and ECC was positively associated with poor OHRQOL in children and their families.

Conclusion: Using a birth cohort design, this thesis provides evidence of early life course factors as possible causal factors of ECC. Consistent with a life course model, the hypothesis of intergenerational association in caries experience and OHRQOL between mothers and their 5- year-old offspring was supported.

Consequences: Further work using intervention studies involving early life-course risk factors of ECC is needed to inform oral health promotion policy in Uganda.

List of publications

1. Birungi N, Fadnes LT, Okullo I, Kasangaki A, Nankabirwa V, Ndeezi G, Tumwine JK, Tylleskär T, Lie SA, Åstrøm AN. Effect of Breastfeeding Promotion on Early Childhood Caries and Breastfeeding Duration among 5 Year Old Children in Eastern Uganda: A Cluster Randomized Trial. PLoS ONE 2015; 10(5): e0125352.
2. Birungi N, Fadnes LT, Kasangaki A, Nankabirwa V, Okullo A, Lie SA, Tumwine JK, Åstrøm AN, for the PROMISE-EBF study group. Assessing causal effects of early life course factors on early childhood caries in 5-year-old Ugandan children using directed acyclic graphs (DAGs): A prospective cohort study. Manuscript.
3. Nancy Birungi, Lars Thore Fadnes, Victoria Nankabirwa, James Kashugyera, Tumwine, Anne Nordrehaug Åstrøm, for the PROMISE-EBF study group. Associations of caretaker characteristics with early childhood caries and oral health related quality of life: a prospective two generation study. Submitted for publication.

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Definitions

Early childhood caries	The presence of one or more decayed (non cavitated or cavitated lesions), missing (due to caries), and filled teeth in any primary tooth in a child 71 months or younger
Exclusive breastfeeding	The practice of giving breast milk only and no other liquids, except drops or syrups with vitamins, mineral supplements or medicines
Motivational interviewing	Is a patient-centred treatment that focuses on building intrinsic motivation for change by exploring and resolving ambivalence.
Anticipatory guidance	Is a pro-active developmentally based counselling technique that focusses on the needs of a child at a particular stage in life

1.Introduction

1.1 Early childhood caries-definition

The concept of early childhood caries (ECC) refers to the presence of one or more decayed (non-cavitated or cavitated lesions), missing (due to caries), and filled teeth in any primary tooth in a child 71 months or younger (1). This term was adopted to facilitate efforts to standardise case definitions of reporting caries in the primary dentition and to reflect the multifactorial aetiological nature of ECC (2, 3). In this thesis, ECC implies dental caries in the primary dentition assessed on fully erupted teeth according to the World Health Organization criteria (4) and recorded at cavity level in terms of decayed, missed and filled teeth (dmft).

1.2 Prevalence, distribution and development of ECC across time in high-, middle- and low income countries

ECC is one of the most common childhood diseases, described as a public health problem, globally (5, 6) According to the Global Burden of Disease, GBD, 2010 study, untreated caries in deciduous teeth constituted the 10th most prevalent condition worldwide, affecting 9% of the global population (7). Major findings from an ecological study of 1-5-year-old children conducted between 2012 and 2013, involving nine countries (Morocco, Cambodia, Greece, India, Indonesia, Kenya, Myanmar, Vietnam, and the Philippines) showed a generally high prevalence with inequalities in the distribution of ECC (8). The overall prevalence of ECC (dmft>0) was 52% with a mean of decayed, missed and filled teeth (dmft) of 8.9. The lowest prevalence of ECC was observed in Greece (19%), and the highest prevalence was found in the Philippines (98%). Regarding the decayed, filled teeth component dft,

the lowest mean value was found in Kenya (3.7) and the highest mean value was observed in the Philippines (12.3) (8). In high income countries, there has been a reduction in the prevalence of ECC during the twentieth century, although ECC remains an important problem in subgroups of the populations (9, 10). According to findings from the United States, there has been a decline in dental caries in the primary dentition of preschool children from 24% in 1988 to 23% in 2012 (11). Notably, however, the proportion of affected surfaces may be shifting from less untreated (dt) to more restored dental surfaces (ft) and dental caries disparities by poverty has remained in preschool children (3). In Scandinavia, studies have indicated that the decline in caries started in the late sixties and early seventies (12). Amongst 5-year-old children, 60%, 61%, 40%, 63% and 72% were reported to be caries free in 1991-1992 in Finland, Denmark, Iceland (Reykjavik), Norway and Sweden, respectively (13). Masumo (14), summarized studies considering the prevalence of ECC in high, middle and low income countries, published during the period between 2006 and 2012. Among the low and middle income countries covered in his review, China had the highest prevalence of ECC (71%) among 36-71-month-old children while the lowest prevalence was observed among Iranian children aged 12-36 months (35-26 %). Among the high income countries covered by Masumo's review, the caries prevalence was highest in Germany (45%) among 60-72 month-olds and lowest in the United States (3%) among 12-36-month-olds (15).

Table 1 summarises the prevalence ($dmft > 0$) and extent (mean $dmft/dmfs$) of ECC in high income countries provided by studies using the WHO criteria and published between 2010 and 2016. The highest prevalence (80%) was observed in a convenient sample from an Indian tribal community in the United States while the lowest prevalence (3%) was observed in a representative study of 18-24-month-old children in Iburi, Japan. It should be noted that 4 of the studies reviewed in Table 1 are based on country representative samples of children (Hong Kong, UAE and Lithuania) (16-19).

Table1. Studies from high** income countries published between 2010 and 2016 showing ECC prevalence (dmft>0) and extent (mean dmft) assessed according to the WHO criteria

1stauthor (reference)	Year	Country	Age months	Sample size	Mean dmft/dmfs* ±SD	dmft>0 %
Hoffmeister (20)	2016	Chile	24 to 48	2987		20
Warren (21)	2015	United States	36	232	9.6*	80
Grund (22)	2015	Germany	71	496	0.9±2.0	26
Schroth (23)	2015	Canada	<71	319	3.9±5.0	52
Baggio (24)	2015	Switzerland	36 to 71	856		25
Gussy (25)	2015	Australia	18-36	467		8-23
Nakayama (26)	2015	Japan	18 to 23	1,675	0.1	3
Kowash (18)	2015	UAE	< 71	176	10.9	
Ghazal (27)	2015	United States	36	90		66
Braun (28)	2015	United States	50	928	21.5±19.9*	89
Batliner (29)	2014	United States	36 to 71	981	21.3±20.0*	
Nobile (30)	2014	Italy	36 to 71	515	2.7	19
Congui (31)	2014	Italy	18 to 60	544		16
Han (32)	2014	Korea	<71	1,214		48
Naidu (33)	2013	Trinidad	36 to 71	251		29
Sagheri (34)	2013	Ireland	48	337	0.49±1.4	
Mantonanaki (35)	2013	Greece	71	605		17
Deichsel (36)	2012	Germany	13 to 36	661	0.2	5
Chu CH (16)	2012	Hong Kong	63	700	2.2	49
Strömberg (37)	2012	Sweden	36 to 71	10,927		11
Pieper (38)	2012	Germany	71 to 84	1082	1.9	45
Barford (39)	2012	Denmark	36	594	0.3	8
Wong (17)	2011	Hong Kong	48	1261	1.5±3.0	20
Dogar (40)	2011	Australia	24 to 48	253		40
Al-Mutawa (41)	2010	Kuwait	48-71	1277	3.7±6.9- 4.8±9.6	32-24
Al-Jewair (42)	2010	Canada	< 71	833		5
Schroth (43)	2010	Canada	<72	66	2.8±4.0	53
Slabsinskiene (19)	2010	Lithuania	36	950	2.1±0.1	51

**High income country 2016 fiscal year World Bank classification: GNI per capita ≥ \$12,736
<http://data.worldbank.org/about/country-and-lending-groups>

Table 2 summarises the prevalence (dmft>0) and extent (mean dmft/dmfs) of ECC in low- and middle income countries reported by studies using the WHO criteria and published during 2010-2016. Of these studies, 22 were based on representative samples of populations within the country's populations (44-66), three on country representative samples (67-69) and the rest on convenient or selected samples. As shown, Bosnia and Herzegovina had the highest prevalence and severity (83%, 6.8) among 36-71-month-old children. Earlier studies have shown that Kenya has the highest prevalence of ECC in East Africa among 37-71-month-olds in 2010, amounting to 60%. In Tanzania, the prevalence of ECC was 3.7% in 2012 and 30% in 2010. More recently, Ugandan studies from the capital city Kampala, have shown relatively stable estimates of ECC amounting to 17.6% and 18.1% among 6-36-month-olds in 2012 and 2014, respectively.

Table 2 Studies from middle and low income countries** published between 2010 and 2016 showing ECC prevalence (dmft>0) and extent (mean dmft) assessed according to the WHO criteria

1st author (Reference)	Year	Country	Age (months)	Sample	Mean dmft	dmft>0 %
Sacic (69)	2016	Bosnia & Herzegovina	36-71	165	6.8	83
Gopal (44)	2016	India		477	2.4±1.5	27
Zhang (67)	2016	China	12 - 72	pooled		65
Moimaz (70)	2015	Brazil	0-36	768		17
Folayam (45)	2015	Nigeria	6 - 71	497		7
Khanh (71)	2015	Vietnam	12-72	593		74
Stephen (46)	2015	India	18 -71	2771		16
Kuriakose (47)	2015	India	<60	1329		54
Olatosi (48)	2015	Nigeria	6 -71	302	0.73	21
Sarathong (72)	2015	Thailand	36 and71	344		44-56
Turton (73)	2015	Cambodia	0 - 72	362		66
Corrêa-Faria (49)	2015	Brazil	24 - 71	387		34
Iyun (50)	2014	Nigeria	36 -71	540	0.65±1.5	24
Wulaerhan (51)	2014	China	36 -71	670	5.0±3.8	74
Lui (52)	2014	China	71	726	3.0	62
Ferraz (53)	2014	Brazil	71	540		50
Lui (52)	2014	China	71	745	3.0	62
Perera (74)	2014	Sri Lanka	36 - 60	285	1.8	48
dos Santos (75)	2014	Brazil	43.2	320		20
Masumo (76)	2014	Uganda	6 -36	816		18
Ramos-Jorge (55)	2014	Brazil	36-71	451		51
Prakasha (56)	2013	India	36-71	2000	2.0±3.0	48
Dogan (77)	2013	Turkey	8 - 60	3171	0.63±1.8	17
Bagherein (57)	2013	Iran	30 - 70	400	8.4±11.2	55
Corrêa-Faria (78)	2013	Brazil	36-71	593		54
Pattanaporn (58)	2013	Thailand	36 and71	350		36-78
Gaidhane (59)	2013	India	24 -71	330		32
Sankeshwari (60)	2013	India	36-71	1250		63
Martins-Junior (61)	2013	Brazil	24-71	638	2.9±4.0	52
Singh (79)	2012	India	36-71	712	1.9±3.3	40
Masumo (80)	2012	Uganda	6-36	816		18
Masumo (80)	2012	Tanzania	6-36	1221		4
Qadri (81)	2012	Syria	36-71	400	4.3±4.2	70
Parisotto (82)	2012	Brazil	36 - 48	351	1.9±3.9	40
Subramaniam (83)	2012	India	8-48	1500	0.9	28
Retnakumari (84)	2012	India	12-36	350		51
Kumarihamy (85)	2011	Sri Lanka	12-24	422	2.0	32
Ozer (86)	2011	Turkey	36-71	226	2.9	47
Tusek (87)	2011	Serbia	13-64			31
Chedid (88)	2011	Lebanon	< 48	99		75
Sufia (62)	2011	Pakistan	36 - 71	700	1.9±3.3	41
Begzati (68)	2010	Kosovo	24-72	1237	10.6	18
Begzati (63)	2010	Kosovo	12 -72	1008	11±3.6	17
Rwakatema (65)	2010	Tanzania		372	0.95±0.41	30
Senesombath (64)	2010	Laos	36 -47	400	5.5±4.3	82
Njoroge (66)	2010	Kenya	36 to 71	356	2.5±2.3	60

** Middle and low income countries 2016 fiscal year World Bank classification: GNI per capita <12,736. <http://data.worldbank.org/about/country-and-lending-groups>

According to a report from the World Health Organization (WHO), the prevalence of dental caries experience among 12-year-old school children in middle- and low income countries has been low until recent years, but is now tending to increase (89). In contrast, a decline in the prevalence of children's caries experience has been observed in most high income countries during the past 40 years although the prevalence of untreated caries is still not fully understood. In 2010 untreated caries in deciduous teeth was the 10th most prevalent health condition affecting 621 million children worldwide (90). Globally, considering untreated caries in deciduous teeth, the age-standardized prevalence and 95% confidence intervals were 8.9 (8.6–9.2) in 1990 and 8.8 (8.5–9.1) in 2010. In 1990, the age-standardized prevalence of untreated caries varied from 5.8 (5.1–6.6) in Australia to 10.8 (9.8–11.8) in high income Asia-Pacific. The corresponding estimates in 2010 were 6.5 (6.0–7.0) in western Europe and 10.4 (9.6–11.2) in Southeast Asia (90). In Sub-Saharan African countries, the age-standardized prevalence of untreated caries in deciduous teeth varied from 7.8 (7.1–8.5) to 7.9 (7.2–8.8) between 1990 and 2010. The significant decline in children's caries experience has been highest in countries with the greatest economic and social development. No significant improvement has occurred in children's caries experience in countries with low levels of human and economic development (5).

1.3 Within country socio-economic distribution of ECC

Globally, there is overwhelming evidence that the burden of dental caries, including ECC, discriminates according to social indicators (e.g. education, socio-economic status, SES) and thus ECC has been recognised as a marker of social inequality (89, 91-94). Social inequality is characterised by an existence of unequal opportunities, access and distribution of goods between various social groups of the society. In high income countries, the burden of ECC tends to be polarised towards the socio-economically disadvantaged groups- and towards minority groups (95). According to recent data from the United States obtained in 2011-2012 (11), the caries prevalence was higher for Hispanic (46%) and non-Hispanic black (44%) children compared

with non-Hispanic white children (31%) aged 2–8 years. Moreover, non-Hispanic Asian children presented with a lower caries prevalence (36%) compared with Hispanic children (46%), but were not different from non-Hispanic white or non-Hispanic black children (11). In Scotland, the percentage with $d_3mft > 0$ (British Association of the Study of Community Dentistry, BASCD criteria), was calculated for 5-year-old children between 1993 and 2003, suggesting that a high level of caries persisted among children from deprived areas. Among the most affluent, the $d_3mft > 0$ was 35% in 1993 and 30% in 2003 while among the least affluent, it was 81% and 70%, respectively (96). A retrospective cohort study from British Columbia, carried out in 2006–2007, involving 4- and 6-year old kindergarten children revealed that caries rates declined across the survey years for all SES groups investigated (97). However, caries experience varied from 49.2% in low SES neighbourhoods and 37.3% in moderate-level SES communities to 30.5% in high SES areas (97). A recent study from Switzerland revealed that disadvantaged children aged 36–71 months were more likely than their less disadvantaged peers to present with ECC (24). In Scandinavia, similar disparities have been reported according to parental education and marital status (98, 99). Minority groups in high income countries have been reported to have a high caries burden as well (9, 100–102). In general, the middle income countries show a similar socio-economic gradient as the high income countries, children with a lower SES tend to have higher ECC prevalence than their higher SES counterparts (103–105).

A social gradient in the prevalence of ECC has also been observed within low income countries. However, this gradient is not as uniform in direction as the gradient in the high- and middle income countries where socially disadvantaged children (children from lower socioeconomic backgrounds, having parents of low education, from single parent families and with immigrant status) consistently have worse oral health than their higher socioeconomic counterparts. In a Tanzanian cross-sectional study

involving adolescents with a mean age of 13.5 years, the less poor households presented more frequently than the poor households with $DMFT > 0$, great treatment needs and poor oral hygiene (106). In another Tanzanian study involving younger children (6-36 months), the influence of socioeconomic factors on ECC was not significant (80). In a Nigerian study, although not statistically significant, there was a tendency of higher ECC prevalence in children of higher SES compared to children of lower SES (48). A study from Uganda, involving 3-5-year-old children, reported higher odds of having $dmft > 0$ among children with less-well educated mothers. In another Ugandan study involving 6-36 months old children, families with low SES had the highest odds of reporting poor child oral health status (107). According to the literature reviewed above, significant variation in children's caries experience according to social indicators exists within countries globally.

1.4 Conceptual models and factors influencing ECC

Evidently, the susceptibility to- and development of ECC is influenced by numerous factors. Thus, ECC is labelled a multifactorial disease (108-110). According to the model by Fischer Owens (111), factors that influence the ECC prevalence/incidence occur at the individual-, family- and community level (Figure 1). The individual level includes among others; saliva properties, immunity, genetic factors, tooth quality, sugar consumption and oral hygiene behaviour. The family level includes maternal oral health, maternal knowledge and attitudes towards oral health, parental education and SES, while the community level includes neighbourhood SES, poverty, area disparities in community water fluoridation. Factors at the different levels interact via complex mechanisms to contribute to the occurrence of ECC (111). Petersen's risk factor model (91), proposes that events leading to adverse health outcomes can be both proximal and distal in their relation to the outcome; proximal factors that are acting directly or indirectly on diseases, while distal factors are acting via a number intermediary, more proximal factors. In the unifying model by Seow (112), maternal characteristics, the socio-environmental and child's risk factors specifically involved in the occurrence of ECC have been connected. In line with these theoretical models,

several systematic reviews and critical summaries have identified risk factors of ECC (108, 113, 114). According to these reviews, family education, socio-economic disadvantage and sugar consumption have been identified as respectively, major distal upstream- and proximal individual risk factors of ECC at the population level (115).

Life course epidemiology emphasises the importance of events or insults present or absent throughout life that predispose or protect from chronic disease (116). ECC has been described as a chronic disease and by its definition captures an individual's disease history; summary of one's past experience. Also, ECC predicts future disease in the subsequent permanent dentition (117-119). Therefore, the life course approach to chronic disease epidemiology can be applicable to explore risk factors of ECC. According to the critical period model, events or risks occurring at a particular period (foetal stage, infancy, early childhood) have lasting effects on health regardless of later risk exposures (120). In contrast, the accumulation of risk model recognises that exposures at different stages along the life course may build up to increase the risk of outcomes (116). A longitudinal study using data from a birth cohort in New Zealand assessed parental SES as an early life course predictor of oral health outcomes in adulthood (121). It was observed that parental SES and their oral health related beliefs were associated with participants' oral beliefs at later life stages (121). Similarly and in accordance with the accumulation risk model, a birth cohort from Brazil showed that adolescents who were consistently poor (born and grew up in poverty) had a worse pattern of dental caries than their counterparts who were never poor (122). Also in agreement with the accumulation of risk hypothesis, studies have revealed that the higher the sugar consumption along the life course, the higher the dental caries increment (123). Children who were born and grew up in poverty presented with a poorer profile of tooth brushing habits than their socioeconomically better-off counterparts (122).

The mineral composition of human milk renders it vital for growth and development of oral tissues (124). Also, the immunological and mineral content of human milk are important in the progression or impediment of the carious process (125). Taking into account the life course perspective, infant diets and feeding practices including exclusive breastfeeding, EBF, and breastfeeding duration constitute early life exposures of ECC. Breastfeeding practices have been categorised differently in the literature; for instance nocturnal breastfeeding, ‘ad-libidum’ nocturnal breastfeeding, prolonged breastfeeding (differing durations) and EBF (126). Some studies have indicated that nocturnal breastfeeding (26, 127, 128) and prolonged breastfeeding (129-136) associate positively with ECC development, while others have not found clear associations (85, 137-141). A challenge with this research is that different definitions of breastfeeding practices and ECC have been used across various studies. This research is further complicated by the various methodologies employed in the measurement of key variables. Systematic reviews have raised concerns about the quality of evidence in terms of the different definitions of breastfeeding and ECC as well as the length of exposures (126, 142). Due to weak methodology and lack of a consistent and strong association between breastfeeding and ECC, these systematic reviews have been inconclusive (126). More recently, however, two meta-analyses have found that breastfeeding in infancy may protect against dental caries during childhood (143, 144).

As evidenced in the literature, biological, behavioural, socio-economic and psychological conditions experienced during early life influence oral health in later life stages (121-123, 129, 145-149). Most of this evidence stems from high- and middle income countries. In addition, most of the studies have assessed the oral health influence of the early life factors, focusing adolescents and adults. Few life-course studies have been concerned with ECC as an outcome, covering the developmental stage of preschool children. The bulk of studies from low income countries are cross-sectional, thus lacking the appropriate longitudinal design. A limitation of all observational studies, both cross-sectional and longitudinal, is that both risk exposures and ECC are socially patterned - thus differences between women who breastfeed and those who do not may confound the observed associations.

Moreover, observational studies make it difficult to decide whether the association of risk factors with ECC are causal or have alternative explanations. Table 3 provides a summary of literature reviews considering determinants of ECC from low-, middle-, and high income countries, published during the period 2010 - 2016. Meta-analyses and systematic reviews regarding breastfeeding and bottle-feeding have concluded that breastfeeding can prevent dental caries during infancy and early childhood (143, 144). Individual factors such as level of Mutans streptococci and oral health behaviours were identified as risk indicators of ECC in two of the systematic reviews (150, 151). Also, intermediate factors such as maternal influence and upstream factors like SES status has also been identified as risk factors for ECC (113, 114).

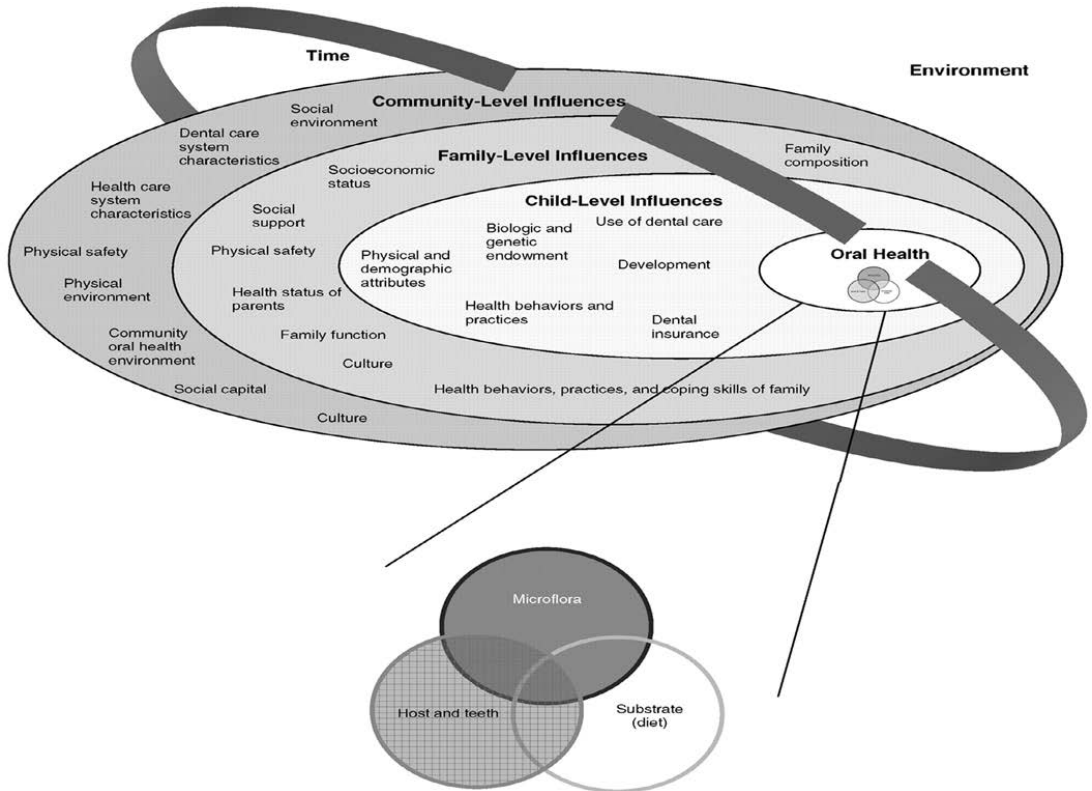


Figure 1. The multidimensional conceptual framework for ECC as discussed by Fisher and co-workers 1997

Table 3 Literature reviews published between 2010 and 2016 focusing on factors (proximal and distal) influencing ECC from high, middle and low income countries, () number of studies included.

Author/year Reference	Review type	Study designs included (No)	Country Classification*(No)	Exposure definition	Outcome	Main conclusion
Tham /2015 (144)	systematic review & meta-analysis	nested cohort within RCT's (6) cohort(8) and cross sectional (46)	low income (8), high/middle income (55)	breastfeeding	dental caries	Breastfeeding in infancy may protect against dental caries
Avilla /2015 (143)	systematic review & meta-analysis	cross sectional (5), case control (1), cohort (1)	middle income (5), and high income(2)	1. bottle feeding 2. breastfeeding	dental caries in primary dentition	The scientific evidence indicated that breastfeeding can protect against ECC
Leong /2012 (151)	systematic review	1. longitudinal (3), cross-sectional (4) 2. RCT (6), longitudinal (4), cross-sectional (3)	middle income (5) and high income (9)	1. acquisition and colonisation of oral bacteria 2. risk and/or protective factors in infants (0-12 months)	ECC	Factors occurring during the first year of life affect ECC experience. Maternal factors influence bacterial acquisition, whereas colonisation was mediated by oral health behaviours and practices and feeding habits.
Parriso/2010 (150)	systematic review	cross-sectional (14), longitudinal (2)	low income (1), middle income (7), high income (8)	Mutans streptococcus	ECC	Mutans streptococci levels are a strong risk indicator for ECC.
Congui /2014 (113)	systematic review	longitudinal (2), ecological (1) cross-sectional (8)	low, middle and high income (1) middle (3), and high (3).	background factors	ECC	The most crucial factors involved in ECC development are the SES of the family and the role played by the parents/caregivers as the main source of attitude toward oral care and values
Distal factors						
Leong 2012 (same as above) (151)	systematic review	1. longitudinal (3), cross-sectional (4) 2. RCT (6), longitudinal (4), cross-sectional (3)	middle income (5), and high income (9)	1. acquisition and colonisation of oral bacteria 2. risk and/or protective factors in infants (0-12 months).	ECC	Maternal factors influence bacterial acquisition, whereas colonization was mediated by oral health behaviours and practices and feeding habits.
Hooley 2012 (114)	systematic review	cross-sectional (47), longitudinal (7), case control (1)	low income (1), middle income (21), high income (33)	parental influence	dental caries (0-6 yrs.)	Collaboration between psychologists and dentists may accelerate the identification and understanding of the mechanisms that underlie risk associated with ECC.

1.5 Perspectives on the concept of risk factors of ECC and causal considerations

Longitudinal studies are essential for identification of risk factors of ECC, whereas cross-sectional studies may provide information on ECC risk indicators (108). The seminal work of Rose (152), discussing determinants of individual cases and determinants of prevalence and incidence rates in populations, provides an important distinction in the understanding of disease occurrence. This implies that risk factors are not necessarily fully transferable to individual cases and can often not be reliably predicted for individuals (115). Divaris (115) reviewed available tools and approaches to predict ECC and notified a misconception in defining ECC as a person condition rather than a condition occurring at the enamel-biofilm interface of the tooth surface level. Moreover, as population derived risk factors or determinants are conceptually different from the causes of individual disease, he notified the fallacy in applying population level parameters to individuals, labelled “privatization of risk” (152). Thus, risk factors associated with ECC prevalence and incidence in large population studies are seldom good predictors of individual case occurrence. Early life-course factors of ECC identified in the articles of this thesis are in accordance with a population perspective, using a prospective cohort- and a randomised controlled trial design.

Recently it has been expressed that the translation of the evidence of ECC risk factors into meaningful action and improvements of oral health for individuals and populations has been incomplete and slow (153). Understanding the association between early life-course factors and ECC is an essential prerequisite for the planning and implementation of oral health care and preventive programs. However, the presence of associations or correlations does not always imply causation. A challenge in observational research is to assess whether a correlation may be due to a causal association, chance or is biased by confounding. In randomised controlled trials, the observed differences are to a limited degree affected by systematic bias making the causal interpretations less complicated. They may be interpreted as effect measures

since the randomisation process contributes to relatively exposed and unexposed groups that are exchangeable (154). In contrast, with observational studies, in principle the exposed and unexposed are not exchangeable, and thus could be biased by confounding, that is an extraneous factor associated with both the exposure and the outcome. Confounding variables are usually adjusted for when known in multiple variable statistical analyses or by stratification-although it is commonly unclear which confounding variables to collect and adjust for in the statistical analyses. Inappropriate adjustment of confounding variables can lead to confounding and bias of results (155).

Causation can be defined in counterfactual terms as “*had the exposure differed, the outcome would differ*” (156). As the outcome under the counterfactual condition is often unknown, researchers make causal inferences at individual or population levels. Another way to assess whether observational studies detect true effects is to compare observational versus randomised controlled trial results on the same question (157), with some studies showing good agreement (158).

In the field of health sciences research, different approaches to causal modelling have been suggested such as graphical models for example causal diagrams or directed acyclic graphs (DAGs), potential- outcome (counterfactual) models, sufficient-component cause models and structural equation models (SEM) (159). These approaches provide complementary perspectives and can be employed together to improve causal interpretations of statistical results (159).

A DAG is a visual representation of causal relationships believed to exist between variables of interest, including the exposure, outcome and potential confounding variables (160). In the DAG, an arrow connecting two variables indicates causation and variables with no direct causal association are left unconnected. DAGs are neither bi-directional nor undirected and therefore consist of single-headed arrows

(160). They are also acyclic, meaning that a series of arrows between sequential variables should not lead back to the original variable. The presence of open backdoor paths in a DAG may result in spurious associations unless these paths are blocked by adjustment of confounding variables. Backdoor paths are paths leading to the outcome from the exposure by the tail end of an arrow (160). The presence of a collider variable on a path blocks it. A collider variable is a common effect of two variables on a specific path. DAGs can illustrate qualitative population assumptions and sources of bias not easily seen with other causal model approaches. Unlike the SEM approach, the graphical theory does not require parametric assumptions such as linearity (159). Several causal models are available, and the structural causal model provides unification of the language of counterfactuals, structural equations and causal graphs (161).

1.6 Effects of early interventions to prevent ECC

According to the life course approach, the prenatal- and immediate postnatal periods provide opportunities for early interventions to promote maternal and child oral health. The importance of oral health interventions during pregnancy is endorsed by professional associations due to high rates of maternal periodontal disease observed during pregnancy that has potentially negative implications for birth outcomes, which in turn may have harmful consequences for the future oral health situation of the offspring (162). Interventions during pregnancy with the aim of promoting healthy feeding practices like EBF; have been conducted with good effects (163-167). Based on a common risk factor approach (168), reduction in ECC development has been measured as a secondary outcome of interventions whose primary aim was to promote healthy feeding practices in children (169-172).

Few oral health interventions have been conducted during the critical period of pregnancy (173). Vamos (172) presented a recent systematic review considering oral health interventions among pregnant women, covering experimental and non-experimental designs and focusing the outcomes of maternal knowledge, attitudes, beliefs and self-reported compliance concerning oral health. Most of the studies

covered by this review showed significant improvements on maternal knowledge related to child's oral health (173). Vague descriptions of the interventions provided and a general lack of long-term oral health outcomes (e.g. caries situation among offspring) make it difficult to interpret the link between intervention components and outcomes as well as to decide about the effectiveness of interventions during pregnancy. However, interventions utilising motivational interviewing (MI) and anticipatory guidance involving parents have shown promising results with respect to reduction of ECC and improved clinical compliance with recommended fluoride treatment regimens (174-177).

Table 5 highlights ECC interventions conducted during pregnancy and or early childhood, utilising MI, anticipatory guidance and training in infant feeding guidelines. As depicted, an anticipatory guidance intervention significantly reduced the incidence of severe ECC and in later follow-ups the severity of caries was lowered in the test group, although not significantly (174, 178). Of the studies utilising MI, one study showed lower caries prevalence in the test group, while the other study reported improved cognitions among mothers as well as self-reported cleaning of their children's teeth (179, 180). The infant feeding intervention from Brazil did not show statistically significant results though the incidence of ECC was lower in the intervention group (170).

Table 4 Review of studies published after 2007 reporting early life interventions during pregnancy and or in early childhood utilising motivational interviewing, anticipatory guidance and training in infant feeding guidelines

Author year	Purpose	Target group	Study design & allocation	Content of intervention	Main findings
Plutzer 2008 (174)	To test the efficacy of an oral health promotion programme for the parents of infants, starting during pregnancy	Nulliparous women, most in the 5th -7th months of pregnancy from Adelaide, South Australia	Cluster randomised trial test n= 327 control n=322	-Three rounds of printed information applied in the form of anticipatory guidance (during pregnancy, at 6 and 12 months)	-The incidence of S-ECC in the test group was 1.7% and in the control group 9.6% ($p < 0.001$).
Harrison 2012 (179)	1.Reduce the prevalence of dental caries in young Cree children 2.Comparisons of differences in mothers' dental health knowledge, personal dental practices, and child-rearing practices	Canadian Cree women who had recently given birth or between the 12 th and 34 weeks of pregnancy	Cluster randomised trial Test n=131 Control n=141	MI (one counselling session during pregnancy and up to 6 more sessions postnatally until the child's 2 nd birthday)	-Caries prevalence was 76% in the control group and 65% in the treatment group. The group difference was not statistically significant -There was a substantial benefit of the intervention in controlling for a higher severity of disease.No significant effect of the intervention on self-reported maternal oral health behaviours was demonstrated. -Dental-health-related child quality of life was slightly different between groups.
Plutzer 2012 (178)	To assess whether the effect of providing mothers with guidance during pregnancy and when the child was 6 and 12 would be sustained at 6-7 years of age	Children, whose mothers had been enrolled in a RCT during pregnancy and a comparison group of similar school children, from Adelaide, South Australia	Cluster randomised trial test n=97 control n=91 comparison group=62	Three rounds of printed information applied in the form of anticipatory guidance (during pregnancy, at 6 and 12 months)	-33% of children in the trial had caries compared with 42% in the comparison group -All measures of caries severity were lower, but not significantly so, in the intervention than in the control group. -Children in the comparison group of school children had more severe caries than those in the trial and in the intervention group especially. -Children in both randomized groups suffered significantly less toothache than those in the comparison group
Chaffee 2013 (170)	To estimate the caries impact of providing training in infant feeding guidelines to workers	All pregnant women with scheduled clinic in the municipality of Porto Alegre, Brazil	Cluster randomised trial Test n=237 Control n=221	-Ten Steps recommendations and strategies for incorporation into maternal consultations -Posters to and pamphlets	-There was no statistically significant reduction in ECC (52.3% intervention vs. 57.0% control) .
Makvandi 2015 (180)	Evaluate the impact of an oral health intervention with mothers of 1-2 years old children.	Mothers of 1-2 year old children in day care from Hamadan (western Iran)	Cluster randomised trial Test n= 45 control n= 45	-MI (3 sessions), a booklet, and mobile phone text-message reminders	-Effective moderately in improving cognitions and self-reported cleaning children's teeth.

1.7 Psycho-social consequences of ECC-Oral health related quality of life

Based on the paradigm shift towards a patient-centred, bio-psychosocial approach to oral health care, oral health related quality of life (OHRQOL) has become important in oral health research. OHRQOL is a multidimensional construct that includes a subjective evaluation of individuals' oral health, functional wellbeing, emotional wellbeing, expectations and satisfaction with care and sense of self (181).

ECC impacts on the quality of life of children and their families by interfering, among other things, with childhood development, nutritional status, self-esteem, learning ability and psychological conditions of the family (182-185). Numerous scales exist in the literature that measure OHRQOL for specific diseases and age groups (186). The dynamic nature of child growth and development regarding cognition, facial and dental changes present challenges in the measurement of their OHRQOL. Some of the instruments developed for children use the parents' /caretakers' responses on behalf of the child while others use the child's account (187). Indeed, discordance has been observed in ratings of children's quality of life when either the children respond for themselves or the caregivers respond on behalf of their children (188). However, depending on aspects like the type of measure, the age of the child, there are strong arguments to use caregivers response on behalf of the child or the child's own account (189, 190).

The early childhood oral health impact scale (ECOHIS) utilises parental responses in the name of the child (191). It comprises of a child impact section (CIS) with nine items and the family impact section (FIS) with four items. The items of CIS include four descriptive domains; symptoms, function, psychological, self-image, or social interaction while the items in the FIS include family distress and function domains. The original English version has been translated and adapted in several languages (192-200). A shortened and culturally modified version of the ECOHIS has shown

satisfactory psychometric properties when used with preschool children in Uganda (182). Although the OHRQOL status of the child has been demonstrated to be a consequence of ECC and other oral health conditions (201-204), this relationship is still less well understood in low income countries.

1.8 Justification of the studies presented in this thesis

According to some previous studies, the burden of ECC is high among Ugandan preschool children (76, 80, 205). Due to methodological challenges associated with previous studies and considering replication as an important principle in scientific investigation, estimation of the prevalence of ECC and identification of early life course ECC risk factors in preschool children are considered to be important. A life course approach to children's oral health considers both intra-and inter-generational (i.e. how oral health and associated factors of one generation relates to those of the next generation) risk factors of ECC. Research into the nature and extent of intergenerational transmission of oral health has been asked for to enhance identification of individuals and families at risk and ensure that groups with the greatest need receive preventive measures (206). Intergenerational studies, considering the association between mother's dental caries status and the ECC status and OHRQOL of her offspring have not been conducted in Uganda. Moreover, there is a lack of experience with the use of causal frameworks in dental research (207). A review of the literature considering the influence of early life feeding practices on ECC revealed that sub-Saharan Africa was underrepresented compared to other regions (208). In Uganda, the studies involving risk factors of ECC have been cross-sectional in design. Cross-sectional studies can generate hypotheses about the causal relationship between early life-course factors and later ECC development. These hypotheses can only be confirmed in prospective longitudinal cohort studies. There is a lack of longitudinal evidence, especially from low income settings.

2.Aims

Focusing 5-year-old children and their caretakers in Mbale, Eastern Uganda, this study aimed to estimate; the effects of an EBF intervention in pregnant mothers on ECC in her offspring, the prevalence of ECC, and the effect of early life course factors on ECC and oral health related quality of life.

Three specific objectives outlined below were used to achieve the main aim of this thesis.

2.1 Specific objectives

Paper I- Assuming that EBF promotion may change the general health and oral health focus of the caretakers; it could impact on children's subsequent health and oral health, including duration of breastfeeding and feeding patterns as well as ECC. This study assessed the effect of promoting EBF for six months on ECC and breastfeeding duration assessed at 5-year follow-up of children enrolled at birth to the PROMISE-EBF trial in Uganda.

Paper II- This study aimed to estimate the effect of distal and proximal early life-course factors on early childhood caries (ECC) in 5-year old Ugandan children particularly focusing the estimation of the effect of EBF on ECC using directed acyclic graphs (DAGs)

Paper III-To examine whether caretakers' caries experience was associated with ECC of their 5-year- old children in households in Uganda and to investigate whether children's and caretaker's caries experience was associated with OHRQOL of children and their families after adjusting for possible confounding factors related to socio-demographics and parental attributes. It was hypothesised that children's ECC

associated positively with the caries experience of their caretakers. Also, it was hypothesised that children's and caretaker's caries experience would affect the oral quality of life of 5- year- old children and their families.

3. MATERIALS AND METHODS

3.1 Study Area

The papers comprising this thesis utilise data from a cohort of children, and their caretakers that participated in a multicentre community-based cluster randomised trial (PROMISE-EBF, ClinicalTrials.gov no: NCT00397150) conducted from 2006 to 2008 and with follow-ups until 2011 (167). The trial took place in 3 countries; Burkina Faso, Uganda and South Africa. This thesis focuses on the Ugandan site, conducted in Mbale district, Eastern Uganda.

Uganda is located in East Africa bordered on the east by Kenya, the west by the Democratic Republic of Congo, the north by South Sudan and in the south by Tanzania and Lake Victoria. According to the latest housing and national population census, the population of Uganda is estimated to be about 34.6 million with an annual growth rate of 3% between 2002 and 2014 (209). The majority of the Ugandan population lives in rural areas (75%) (209). Uganda is administratively divided into districts that are further divided into counties or municipalities, sub-counties and villages at the lowest level. According to the 2016 fiscal year the World Bank analytical classification based estimates of gross national income (GNI) per capita, classified Uganda as a low income country with a GNI of \$1,045 or less (210). The third dose of the pentavalent vaccine (DPT3) is used as one of the core indicators to measure coverage and quality of health care in Uganda. DPT3 coverage was 93% in 2013/14-above the annual target of 83% (211).

Mbale is one of 112 districts in Uganda, located in the Eastern region at the foothills of Mt Elgon. Mbale has a population of about 488,000 inhabitants. The majority of the population are subsistence farmers. Lumasaaba is the predominant local language

spoken in the area. Mbale is administratively divided into seven sub-counties. Mbale municipality is the district centre and has approximately ten percent of the district population. Bungokho sub-county; a rural area surrounds Mbale Municipality.

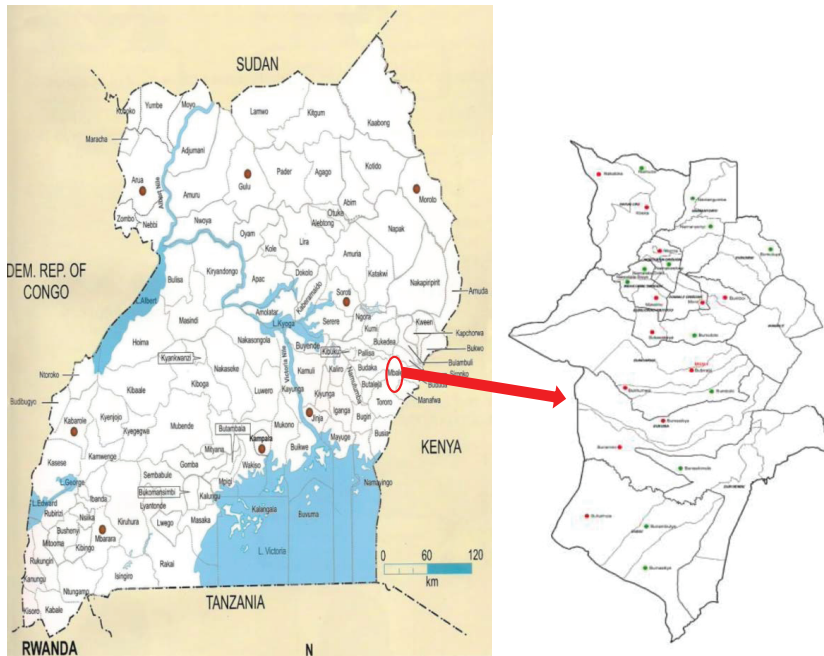


Figure 2 Map of Uganda and neighbouring countries with Mbale district (red circle) and enlarged to the right. The selected study clusters within Mbale district are indicated by coloured dots. The green and red dots represent the intervention and control clusters, respectively.

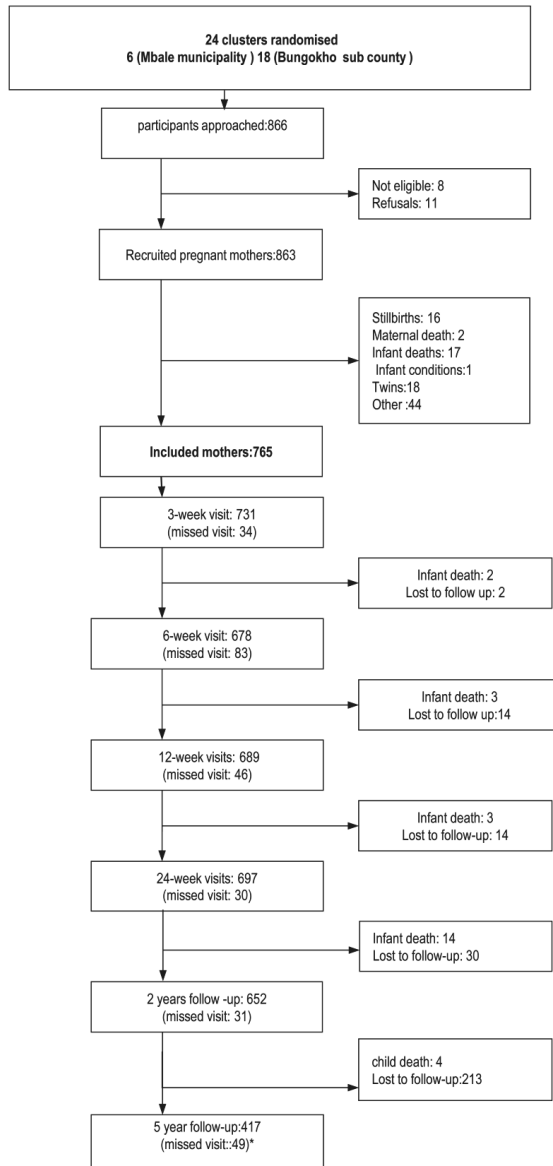
3.2 PROMISE EBF – a cluster randomised behavioural intervention trial

The PROMISE-EBF trial was a multicentre community-based cluster randomised behavioural intervention involving households from the two largest sub-counties in Mbale; Mbale municipality and Bungokho. Twenty-four clusters consisting of 1-2 villages were selected based on information provided on social services and infrastructure characteristics according to proximity to roads and water sources (Figure 2). Eighteen of the clusters were located in Bungokho and six in Mbale

municipality. The PROMISE EBF aimed to assess the effect of individual home-based peer- counselling on EBF six months after birth. Between January 2006 and August 2008, participants were recruited into the study by a designated community recruiter. Eligibility criteria for participation were a pregnant woman of 7-months gestational age or more, intention to continue residing in the study area and consenting to participate. A mother who had given birth to a baby less than one-week old was also eligible for recruitment. Exclusion criteria were a woman who did not intend to breastfeed her child, multiple deliveries/pregnancies and infants with birth deformities/defects like cleft palate and cleft lip that hindered breastfeeding. Of the 866 women approached in the PROMISE -EBF trial, 864 (97%) met the eligibility criteria. A further 98 participants were excluded due to twin births, still births, infant conditions, maternal and infant deaths and other reasons (Figure 3). A total of 765 mother- infant pairs were finally included in the study. The unit of randomization were clusters consisting of 1-2 villages with an average of 1000 inhabitants corresponding to a birth rate of approximately 35 per cluster. Twenty-four clusters were stratified into urban-rural and allocated randomly with a ratio 1:1 to intervention and control groups. Women in the intervention groups received home-based individual peer counselling to support EBF for six months from lay counsellors in 5 visits. The intervention comprised of one prenatal counselling visit and additional visits at the first, fourth, seventh and tenth week after delivery carried out at household level by trained counsellors. The control group received standard care provided by the public health services. The primary outcome of the PROMISE-EBF trial was the prevalence of EBF and diarrhoea reported by mothers of infants aged 12 and 24 weeks.

3.3 Birth cohort study- follow-up visits from the PROMISE EBF

Between 2006 and 2011, follow-up visits from the PROMISE EBF were carried out by research assistants at household level at three weeks, six weeks, 12 weeks, 24 weeks, two years and five years post-delivery (Figure 3). These visits by research assistants were independent of the visits by local counsellors. The papers of this thesis are based on information from 417 mother/caretaker-child pairs provided at the recruitment interview and the six follow-up visits of the birth cohort study. In June 2011, the last 5-year follow-up study was carried out household level. Original recruiters or local council chairpersons guided the research team to the households with the help of tracking sheets containing names of the participants enrolled in the trial five years earlier. Of the 765 included participants, 26 children had died, 273 were lost to follow-up and 49 missed the follow-up visit (Figure 3).



*not available for oral examination

Figure 3. The cohort flow diagram

3.4 Interviews

For papers I, II and III, information from the recruitment interview and six follow-up visits was utilised (Table 5). Trained research assistants conducted face to face interviews with the mother at the household level. The interviews were completed at recruitment, at the 3-, 6-, 12-, and 24 weeks visits and follow-ups at 2- and 5-years of age. At the 5- year follow -up, in instances where the mother was not available, the interview was conducted with the child's caretaker. The interview schedules were constructed in English and translated into Lumasaaba, the local language which is commonly spoken in Mbale. At the recruitment interview questions were asked about the mother's characteristics, pregnancy history, breastfeeding experience, breastfeeding intentions, SES, household activities, employment, use of clinic/medical services and previous child mortality. At the 3-, 6-, 12-, and 24 weeks follow- up visits, mothers were interviewed on infant breastfeeding initiation and infant feeding habits.

At the 2 year follow- up, information concerning breastfeeding, food recalls, health behaviours (vaccination, bed net usage, health service utilisation) and morbidity was obtained, whereas the 5-year follow-up interview included questions pertaining to child (breastfeeding, food recalls, bed net usage, morbidity, general hygiene, injury and oral health) and the mother (oral health) (Appendix I). Also, at the 5-year follow-up, there was an oral health interview regarding the mother's perception of the child- and family oral health related quality of life, perceived child and own oral health and general health. The oral health related quality of life (OHRQOL) of the family and child was assessed as part of the oral health questions. The OHRQOL was evaluated using a modified version of the Early Childhood Oral Health Impact Scale (ECOHis) (191) (Appendix 1)

3.5 Anthropometry

Nutrition status was assessed using anthropometric assessments carried out at all interviews at the household level. The measurements were carried out in line with the guidelines from the WHO (212). At the 3, 6, 12, 24 weeks ‘Baby /infant/adult Length- height measuring system SET 2’ and infant weight scale spring type from UNICEF supplies was used. The Length was measured to the nearest 0.1cm and weight recorded the nearest 0.1kg. At the 5-year follow-up, ‘Shorr’ height measuring boards provided by UNICEF supplies Uganda for standing height recorded to the nearest 0.5cm were used. The weight of the children was done using portable analogue Seca scales recorded to the nearest 1kg. Validity exercises were carried out once during the five months of the 5-year follow-up.

3.6 Oral examination

Both the mother/caretaker and children underwent a full-mouth clinical oral examination, conducted at household level by qualified dentists. Under natural light and with the child’s head tilted in the upward direction, the oral examination was performed using a disposable explorer probe and mirror. Regarding the mothers/caretakers, the oral examination was performed with the participant sitting and face head tilted in the upward direction while the examiner standing or sitting behind them examined their teeth using a disposable explorer probe and mirror.

Teeth were inspected for dental caries according to criteria described by the World Health Organization with deviations concerning the examining probe (4). Dental caries was scored present when there was a visible cavitation of the tooth surface. Dental caries was recorded using the decayed, missing and filled teeth index (dmft) for the primary dentition and the DMFT index for the caretakers. The participants who needed dental treatment were referred for dental treatment to health facilities.

Table 5 provides an overview of the design, exposure measurements and outcomes of the three papers in this thesis.

A test-retest examination was conducted to assess inter- and intra-rater agreement after 2 weeks, involving 22 mother-child pairs who were not part of the study but who had the same demographic characteristics as the study participants.

Table 5 Study design, main exposure(s) and outcome(s) in Papers I-III

Paper	Study design	Main exposure (assessment time points)	Outcome at 5-year follow-up
Paper I	Cluster randomised trial	-EBF promotion (24 th week post-partum)	-ECC
Paper II	Prospective cohort	-Marital status (recruitment interview) -SES (recruitment interview) -Marital status (recruitment) -EBF (24 weeks post-partum) -Breastfeeding duration (2-and 5 years follow- up) -Stunting (5-years follow-up) -Tooth hygiene (5-year follow-up) -Sugar consumption (5-year follow-up) -Dental attendance (5-year follow-up) -Self-reported general health status (5-year follow-up)	-ECC
Paper III	Prospective cohort	-SES (recruitment interview) -ECC (5-year follow-up) -caretaker caries status (5-year follow-up)	-OHRQOL(ECOHIS) -ECC

3.7 Data Management

For the follow-up visits prior to the 5-year follow-up-, data was entered into hand held computers with the software Epihandy (www.epihandy.com). The Data was synchronised daily to a server. During the 5-year follow-up, the research assistants checked the data for errors and missing information and the entries were done using the Epi-data program (<http://www.epidata.dk/>), that had quality checks in case of incorrect or illogical entry. Double data entry was done to ensure that unmatched data was corrected from the original questionnaires.

3.8 Causal framework

Following Hernan and Robins (213, 214), the underlying causal relationships between ECC and the early life course factors considered in Paper II were visualised using causal diagrams/DAGs. As briefly outlined in the introduction, DAGs are sets of arrows that characterise causal and temporal relationships between variables with specified effect directions (155). In a causal path, the exposures (for instance sugar consumption), connect to the outcome (ECC) by a head to tail connection, depicting the existence but not the strength of a causal relationship. Alternative paths between the exposure and outcome, known as ‘backdoor paths’ were ‘blocked’ or closed to avoid spurious causal associations. Blocking in casual diagram terminology refers to the adjustment of variables that keep the back door path open. In summary, proximal individual- and family-level covariates; nutrition status (individual), breastfeeding duration (individual) EBF (individual), sugar consumption (family-level) and tooth hygiene (family-level) were assumed to have direct effects on ECC, whereas the effect of more distal family-level covariates; SES, maternal education status, and marital status were assumed to be mediated through the proximal variables. Additionally, unmeasured variables; enamel hypoplasia and cariogenic bacteria were included in the DAG for the purpose of giving a clearer picture of the causal mechanisms. Three probable statistical models based on three DAGs were used in the analysis.

3.9 Statistical analysis

The statistical package Stata IC version 13 was used for analysis. The prevalence and severity of ECC were reported using proportions and means respectively. Comparisons of groups were performed using test statistics. Statistical significance was placed at $p < 0.05$. Negative binomial regression was utilised in univariate and

multivariable analysis to estimate effect measures together with inferential statistics with 95% confidence intervals (CI). Incidence rate ratios (IRR) were used as the effect measure with negative binomial regression analysis (Paper I, II and III). Due to the majority of the children presenting with no ECC, the zero values were increased and thus a zero-inflated negative binomial regression was used for analysis for paper I

The goodness of fit of the negative binomial regression versus the zero-inflated negative binomial regression models was tested using the Vuong's test. Also, linear regression and the Kaplan-Meier analyses were used in Paper I to compare breastfeeding duration across trial arms and to describe time to cessation of breastfeeding respectively. Principal component analysis (PCA) was utilised as a data reduction tool in Paper II, and multiple correspondence analyses were used to construct the socioeconomic index used in papers; I, II and III.

In all the crude and adjusted analyses, the cluster effect (due to the cluster being used as the primary sampling unit and also due to the clustered randomization) was considered to adjust the confidence intervals of the estimates and thus avoid overestimating the precision of those estimates (215). To adjust for potential loss to follow-up, an inverse probability weighting method (IPW), was applied (216). First, a categorical variable capturing having missing or not missing data regarding the outcome variable ("ECC-missingness variable") was constructed. In a second step, probit regression was used to assess the probability of being followed-up, using the 'missingness' variable as dependent variable and variables associated with loss to follow-up (SES, place of residence, education) as independent variables. Next, the probability of being followed-up was used to predict scores for the observed participants, and the inverse of the predicted scores was used to weight the observed participants. Children followed-up (observed for the outcome variable-ECC) that were similar to those lost to follow-up were weighted-up in the analysis. The median (interquartile range, IQR) for the weights was 1.8 (1.7-2.0). Table 6 summarises the statistical tests and methods used in papers I, II and III of this thesis.

Table 6 Statistical methods used in Papers I-III

Statistic measure or method used	Paper I	Paper II	Paper III
Means	+	+	+
Proportions	+	+	
Chi-square	+	+	+
t-test	+	+	
Kappa	+	+	+
Cronbach's alpha		+	+
Young's test	+		
Principal components analysis (PCA)		+	
Survival analysis-Kaplan Meier curve	+		
Inverse probability weighting	+	+	+
Linear regression	+		
Negative binomial regression	+	+	+
Zero-inflated negative binomial regression	+		

3.10 Ethical issues

An informed consent form was signed by each of the participants that could write. For those who could not write 'X' was used to indicate consent.

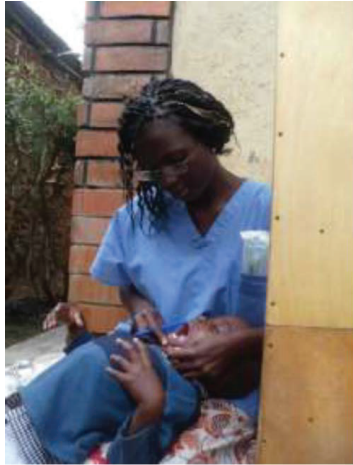
Ethical clearance was obtained from Makerere University School of Medicine, Research and Ethics Committee (SOMREC), the Uganda National Council for Science and Technology. PROMISE-EBF also received ethical clearance from Regional Committees for Medical and Health Research Ethics, Western Norway – REK-VEST (05/8197).



Data collection interview at the household in Mbale 2011. Photo by Lars T Fadnes



Anthropometry height measurement at the household in Mbale 2011. Photo by Lars T Fadnes



Oral clinical examination at household in Mbale 2011 Photo by Lars T Fadnes

4.RESULTS

4.1 Reliability

The results of the calibration process, comparing the dmft scores for each tooth between two examiners revealed a median kappa for inter-rater agreement of 0.92 with an interquartile range (IQR) of 0.62–1. The median kappa (IQR) for the intra-rater agreement was 0.80 (0.64–1). The corresponding values for the caretakers' DMFT were 0.91 (0.67–1) and 0.83 (0.77–1), respectively.

4.2 Paper I

Effect of breastfeeding promotion on early childhood caries and breastfeeding duration among 5-year-old children in Eastern Uganda A cluster randomized trial

In this paper, the ECC prevalence outcome was examined in 417 children at the 5-years follow-up from post-partum. It was hypothesised that children of mothers randomly assigned to receive breastfeeding promotion would have children with less ECC prevalence than children of mothers randomly assigned to usual prenatal care. This study aimed to assess the effect of promoting EBF for 6 months on ECC and breastfeeding duration assessed at 5-year follow-up in children enrolled at birth to the PROMISE EBF trial in Uganda.

Children of mothers in the intervention and control group presented with a median age (IQR) of 4.6 years (4.2–5.2) and 4.4 years (4.1–5.1), respectively. The child sex distribution in the arms was balanced, with 50.2 % males in the intervention and 49.5% in the control group. At baseline, the intervention and control group differed with respect to socio economic status, presence of electricity in household, source of water and place of birth. The loss-to-follow-up at the 5-year follow-up was significantly different in the trial arms regarding SES. Differences in loss to follow-up between the trial arms were adjusted using inverse probability weights. The mean

dmft (standard deviation [SD]) was 1.5 (2.9) and 1.7 (2.9) in the intervention and control arms, respectively. The corresponding prevalence of ECC was 38% and 41%. The mean dmft (SD) among the males was the same in both trial arms 1.6 (2.9) while among the females it was slightly different, with mean (SD) of 1.5 (2.7) and 1.8 (2.7) in the intervention and control arms, respectively. The tooth specific pattern of ECC was similar in both trial arms. The upper jaw central incisors and the lower jaw molar teeth were most frequently affected by ECC. Negative binomial regression analysis adjusting for social economic variables and taking clustering effect into account showed an IRR of 0.92 (95% CI 0.67–1.27)

The effect of EBF promotion on breastfeeding duration has not been documented and commented on further in this thesis since it was assessed as a secondary outcome in paper I.

4.3 Paper II

Assessing causal effects of early life course factors on early childhood caries in 5-year-old Ugandan children using directed acyclic graphs (DAGs): A prospective cohort study

This study aimed to estimate the effect of distal and proximal early life-course factors on ECC in 5-year old Ugandan children particularly focusing the estimation of the effect of EBF on ECC using DAGs. A causal model approach in terms of Directed Acyclic Graphs (DAGs) was used to identify confounding variables to be adjusted for in the final multivariable regression models. The analytical sample involved 417 children. The mean dmft (SD) in the total group was 1.6 (2.9) with no filled teeth component. The corresponding prevalence of ECC was 39%. The children who were socio-economically better off and who were their mother's first child were significantly less likely to have responses at the 5-year follow-up.

The causal approach analyses utilised three probable models based on DAGs; 1-3 (Figure 4a-c). The plausibility of direct paths between variables in the DAGs was informed by theoretical conceptual frameworks and empirical evidence (see attached paper II). Figure 4a shows the DAG for Model 1 with assumed direct (causal) effects on ECC from EBF, breastfeeding duration, tooth hygiene, sugar consumption, and anthropometric status. Alternative ‘back door’ paths (i.e. $EBF \leftarrow \text{marital status} \leftarrow \text{maternal education} \rightarrow \text{wealth index} \rightarrow \text{dental attendance} \leftarrow \text{ECC}$, $EBF \leftarrow \text{sugar consumption} \rightarrow \text{cariogenic bacteria} \rightarrow \text{ECC}$ and $EBF \leftarrow \text{anthropometric status} \rightarrow \text{enamel hypoplasia} \rightarrow \text{cariogenic bacteria} \rightarrow \text{ECC}$.) were defined and needed to be blocked to avoid spurious associations. Visiting a dentist (measured by dental attendance) in the Ugandan setting is a problem-based practice (where people tend to seek dentists when they have oral symptoms and pain) making it an effect rather than a precursor of ECC as evidenced by the literature (217, 218). In the path; $EBF \leftarrow \text{marital status} \leftarrow \text{maternal education} \rightarrow \text{wealth index} \rightarrow \text{dental attendance} \leftarrow \text{ECC}$ -dental attendance was identified as a collider variable, blocking the path, thus making it unnecessary to include variables along the path as confounders in the final regression analysis. Model 1 based on DAG 1 included the following variables; EBF, breastfeeding duration, tooth hygiene, sugar consumption and anthropometric status. In this analysis, EBF for 24 weeks was indicated as a causal protective effect of ECC with IRR (95% CI) of 0.65 (0.46–0.93).

In model 2, based on DAG 2; (Figure 4b) the causal path from ECC to anthropometric status was assumed to be more plausible than the causal path from anthropometric status to ECC as it has been shown in the literature that ECC has consequences for children’s nutritional status (219, 220). Both dental attendance and anthropometric status were colliders in DAG 2 Therefore the remaining open backdoor paths were; $EBF \leftarrow \text{marital status} \leftarrow \text{breastfeeding duration} \rightarrow \text{cariogenic bacteria} \rightarrow \text{ECC}$, $EBF \leftarrow \text{wealth index} \rightarrow \text{tooth hygiene} \rightarrow \text{cariogenic bacteria} \rightarrow \text{ECC}$ and $EBF \leftarrow \text{wealth index} \rightarrow \text{sugar consumption} \rightarrow \text{cariogenic bacteria} \rightarrow \text{ECC}$. Thus, the direct paths to ECC consisted of breastfeeding duration, EBF, sugar consumption and tooth hygiene which constituted the final analytical model. Model 2 did not show any other substantial effects on ECC other than those demonstrated in model 1.

In Model 3 based on DAG 3; (Figure 4c), an additional direct path from dental attendance to cariogenic bacteria and from cariogenic bacteria to ECC was assumed to be plausible which opened previously closed backdoor paths for flow of association i.e. (EBF← marital status ← maternal education →wealth index → dental attendance →cariogenic bacteria →ECC). Thus in addition to the direct paths to ECC from sugar consumption, tooth hygiene, breastfeeding duration and EBF, the variables from the opened back door paths (dental attendance, wealth assets index, maternal education and marital status) were included in the analytical model. The results revealed that EBF and having both parents living together had protective effects on ECC. The corresponding IRRs (95% CIs) were 0.64 (0.44–0.91) and 0.43 (0.21–0.87), respectively.

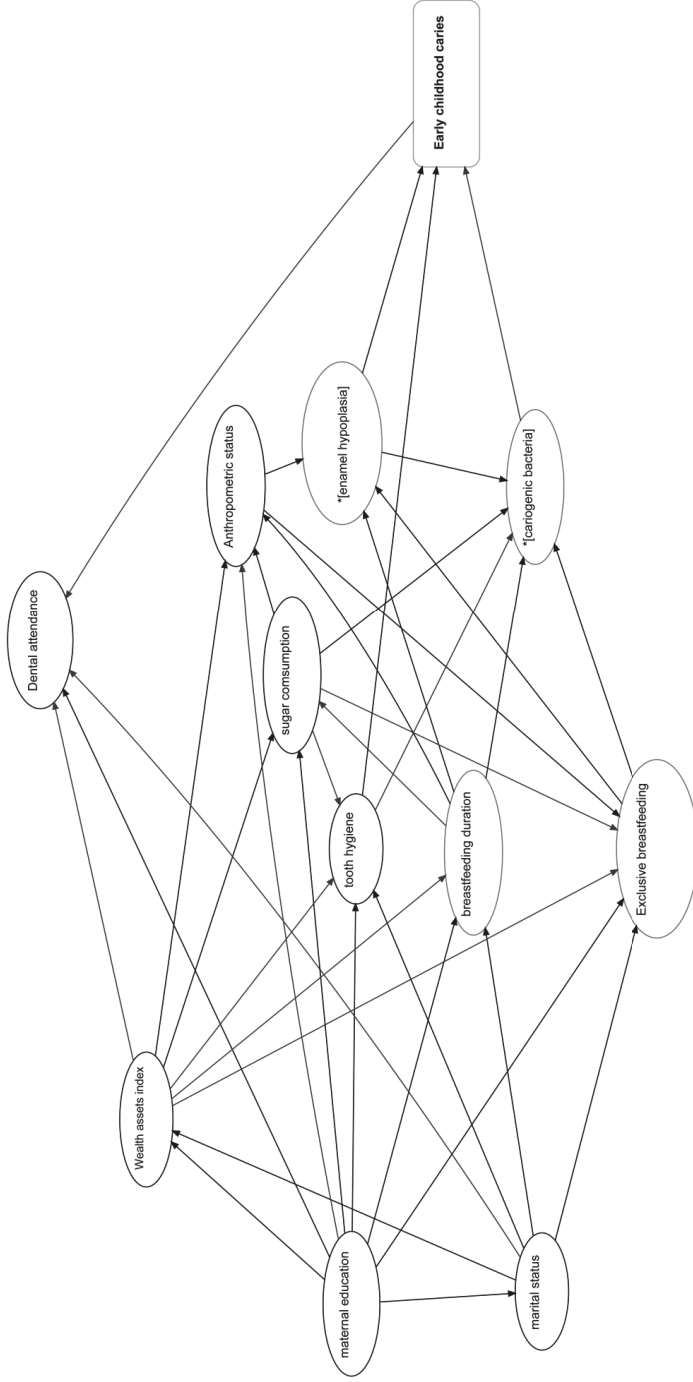


Figure 4a-DAG 1

*Indicates unmeasured variable

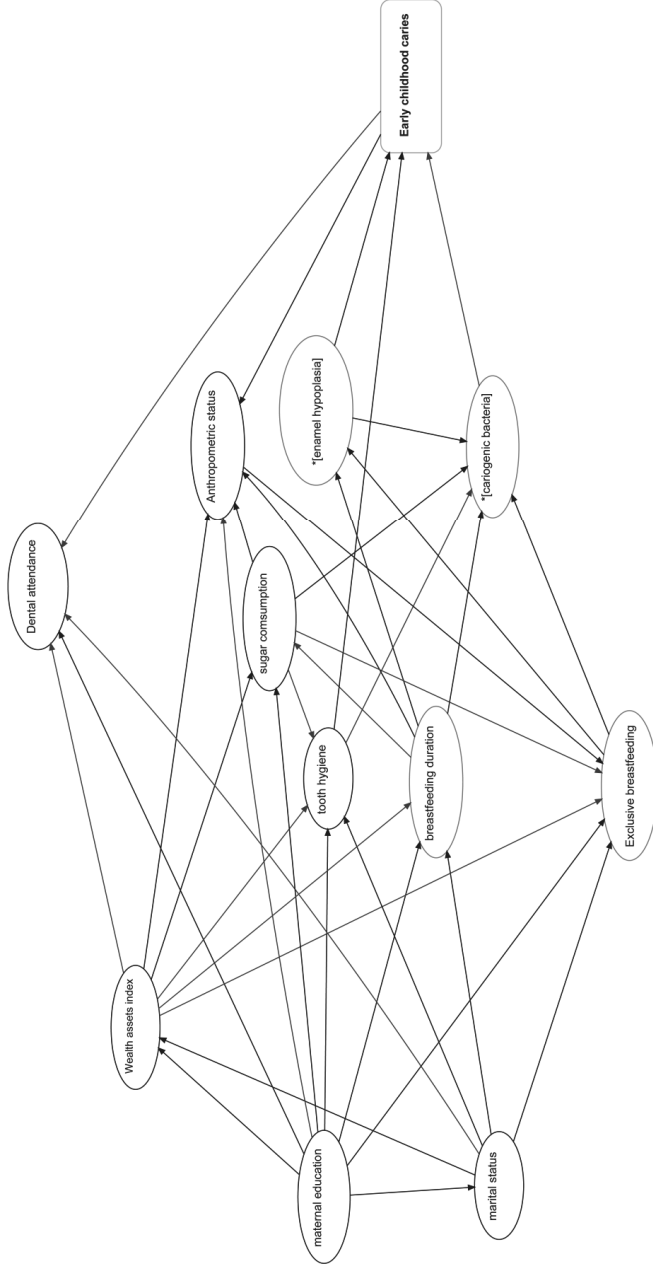


Figure 4b-DAG 2

*Indicates unmeasured variable

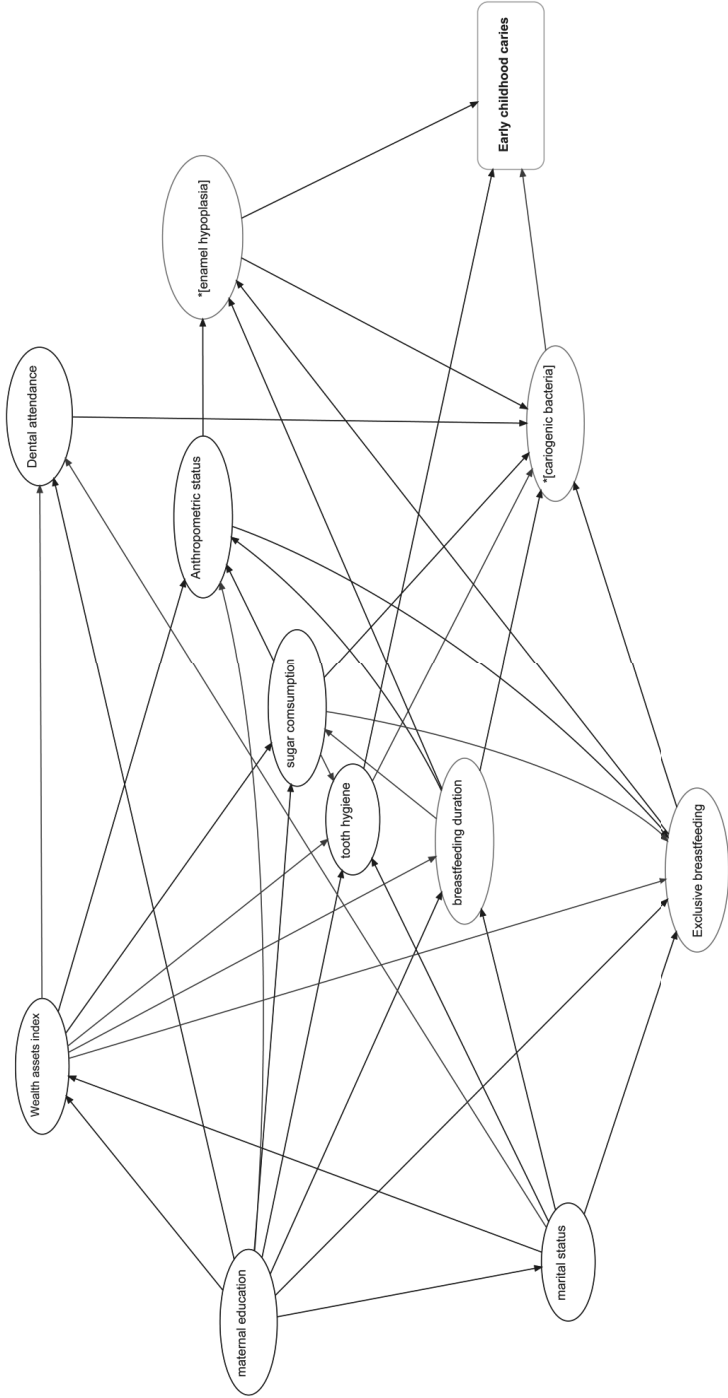


Figure 4c-DAG 3

*Indicates unmeasured variable

4.4 Paper III

Caretaker's caries experience and its association with early childhood caries and children's oral health related quality of life: a prospective two generation study

This study examined whether caretaker's caries experience was associated with ECC of their 5-year-old offspring. Whether children's and caretaker's caries experience associated with OHRQOL in children and their families was also investigated. It was hypothesised that children's ECC associated positively with the caries experience of their caretakers and that children's and caretaker's caries experience would influence OHRQOL in children and their families.

Of the 417 caretakers investigated, 97% were females. The mean age (SD) of the caretakers was 3.1 (7.8). Slightly over half of the caretakers had achieved at least primary education (55%). Most of the caretakers were married or cohabitating (94%). The prevalence of dental caries was 63% among the caretakers, with a mean DMFT (SD) of 2.5 (3.5). The prevalence of child- and family oral health related quality of life impacts (ECOHIS score >0) was 23.5% and 8.7%, respectively. The corresponding figure for the total OHRQOL score was 24.2%. The respective Cronbach's alpha coefficients were 0.91, 0.89, and 0.92 respectively.

Negative binomial regression analysis revealed that caretaker's caries experience was positively associated with that of their offspring (IRR 2.0, [95% CI] 1.3–3.0).

Children's caries experience (IRR 1.8, [95% CI] 1.2–3.0), but not caries experience of caretakers, was associated with OHRQOL impacts. Caretakers who perceived child's oral health to be good were less likely to report OHRQOL impacts (IRR 0.20, [95% CI] 0.12–0.35).

5. DISCUSSION

This section discusses the findings of Paper I-III with reference to their respective aims and implications for public oral health in early childhood. Methodological issues are examined in detail in the separate papers. Additional methodological considerations are discussed as an initial part of section 5.

5.1 Comments on the cluster randomized behavioural intervention study design

The clusters (made up of 1-2 villages) for the randomised controlled trial were selected based on information provided on social services and infrastructure characteristics according to proximity to roads and water sources. This means that the generalisability/external validity of the findings of this thesis is limited to populations in similar social and demographic areas. In the initial PROMISE-EBF study, the sample size of pregnant mothers was calculated based on the power needed to detect differences in the primary outcomes; EBF and diarrhoea at 3months-follow-up from birth. The idea behind calculating a sample size is to ensure an adequate number of participants to maximise the chances of observing a real intervention effect if it is there and to be reasonably sure that a negative finding implies that there is no important difference (221). Type II errors may occur if the statistical analyses are conducted with a sample having inadequate statistical power. Despite a large sample size, there is the possibility that the present study was underpowered to detect a small but real difference in the measured ECC outcome. Thus, in the 5-year follow-up of the PROMISE EBF, lack of statistically significant difference between intervention and control arms regarding ECC as reported in Paper I, could have been attributed to weak power in the analyses as the sample size was not calculated to detect such differences. Nonetheless, the confidence intervals reported for the effects were fairly precise, suggesting that the study sample available was not insufficiently powered and thus type II errors were not likely. Because the mothers involved were aware of their allocation status, contamination between study groups was a possibility.

Therefore, corridors were allowed between intervention and control clusters to act as buffer areas to minimise this possible contamination contributing to diluting any possible differences between groups due to the intervention. Also, any measurement error in continuous outcome variables would tend to add to the residual variance and thus may have decreased the power.

The individual participants of the PROMISE- EBF trial were randomised according to the villages where they lived (clusters consisting of 1-2 villages). Since individuals within the same villages (clusters) are more similar than individuals between different villages or clusters, the observations of each participating mother were not recognised to be statistically independent. Thus, the efficiency of the sample was less than the total number of individual participants in all clusters would imply (222). This cluster effect has been adjusted for across the thesis papers using marginal methods with robust variance estimation to avoid overestimation of the precision of the confidence intervals and thus making incorrect inferences. Thus, the confidence limits were widened by accounting for the clustering of the intervention although the cluster specific effects in terms of intra-class correlation coefficients were small. It may be that breastfeeding promotion had a shorter term effect on children's caries development that was no longer present at 5-year follow-up. In general, studies with clustered designs have been poorly handled in the dental research literature. In a study reporting on the quality of 23 cluster randomised trials, few studies had accounted appropriately for the cluster design in sample size calculation and the statistical analyses (223-225).

All the participants assigned to intervention and control groups should be available for analysis for the randomisation process to be successful. Hence, it was crucial to monitor loss to follow-up across time and exclusion of individuals across the groups. Differences between intervention and control groups after the initial group assignment that are not random, or group differences that occur due to loss to follow-

up may induce confounding and selection biases, thereby affecting the internal validity of the study. In Paper I, confounding was minimised by the stringent random allocation procedure which produced intervention and control groups with generally similar baseline characteristics. However, at baseline, some group differences with respect to participants' SES were still observed that paralleled group differences in SES (single parents and primipara) found at the 5-year follow-up. Analysing only the complete cases as an option for dealing with missing cases would have induced bias since missing had not occurred randomly. Multiple imputation and full-likelihood methods are other post data collection techniques for dealing with missing data (216). In this thesis, IPW was used to account for losses to follow-up. As discussed by Seaman, in comparison to multiple imputation, IPW is less technically sophisticated and more easily interpretable (216).

5.2 Comments on the birth cohort study design

From a life-course perspective, a prospective birth cohort is the appropriate epidemiological design to evaluate any impact of early life exposures on the subsequent development of ECC as issues regarding whether the exposure or outcome comes first or last are not a concern (226). In Paper II and III, exposures pertaining to the children and their caretakers were measured at the recruitment stage and early follow-ups enabling valid assessment of early life course factors on ECC and oral health related quality of life (Table 5).

A major limitation of observational cohort studies is that unmeasured or residual confounding may have created spurious associations. In spite of efforts to limit confounding biases inadequate adjustment for factors that predict both exposures and outcomes in this present study remains an alternative explanation for the observed associations (227). The multifactorial nature of ECC and use of observational study designs for Paper II and III implied that the possibility of confounding bias needed to be addressed. Confounding bias in this thesis was dealt with by use of a random allocation design, DAGS, and multivariable regression methods. The DAGs enabled qualitative visual assessment of confounder selection in the Ugandan context based

on a priori knowledge and evidence in the literature. Using visual graphical models as an adjunct to the negative binomial regression improved the estimation of possible causal effects of the early life course factors on ECC (228). This is because DAGs can visually illustrate population assumptions and sources of bias (159). The DAGs used to identify the effects of early life course factors of ECC proposed three models (Paper II). Having more than one causal framework is plausible given the multidimensional nature of the risk factors of ECC (111). Multiple causal structures are unavoidable and realistic when dealing with observational data. Thus, having more than one causal structure leading to different conclusions on confounding is plausible albeit the causal assumptions should be stated explicitly (213).

Selection bias is another important inherent threat to internal validity in any cohort study (226). In this study, measures were put into place during the field work stage at the 5-year follow-up to minimise further loss to follow-up (Figure 3). This included prior meetings with the initial recruiters from the clusters to increase the ability to locate households belonging to the cohort. Efforts were made to optimise follow-up and increase the number of participants reached including multiple visits when participants were unavailable. In addition, a post-survey data collection, analysis technique to adjust for loss to follow-up, the inverse probability weighting, was implemented in each paper of this thesis. Also, in the present study, selection bias could occur if the SES of some participants changed across time in terms of upward or downward mobility of SES. This is less likely, however, considering the relatively short follow-up period of 5-years in this cohort study.

5.3 Comments on measurement issues

Several aspects contribute to the overall quality of an epidemiological study. To ensure good quality of the data collections during the for 5-year follow -up, the

research assistants and dentists, underwent training, calibration exercises and were continuously supervised and monitored during the field work. Also blinding of the dental examiners and research assistants as to whether the participants belonged to intervention or control groups minimised the possibility of measurement bias. Thus, anticipated sources of information- and other measurement biases due to social desirability, selective recall, over- and underreporting and misclassification of clinical observations were probably limited to a reasonable degree (229). In addition, the interview schedules were translated into Lumasaaba, the local language in Mbale, administered in face to face interviews with caretakers to compensate for difficulties in interpretation that caregivers may suffer. The interview schedule was also piloted before use in the field to ensure appropriateness of concepts and questions and this content validity. The data entry programme used -EpiData (<http://www.epidata.dk>) had inbuilt quality checks. Therefore, extreme or illogical values could not be entered into the database. Double data entry helped to sort out any errors through cross-checking the case record forms in the event of mismatches or errors.

In Paper III, a modified version of the Child impact scale, (CIS), of the ECOHIS instrument was utilised with the child impact section having four of its original nine items that were considered appropriate for the Ugandan socio-cultural context. Removing items from the CIS was deemed necessary during a previous testing of the psychometric properties of the ECOHIS scale among caregivers and preschool children in Uganda (182). The modification of the Ugandan version of this scale hampers comparability of the findings obtained in Paper III. However, the internal consistency reliability of the modified scale showed a Cronbach's alpha above 0.70 which is classified as excellent (230). The results provided in Paper III corroborates findings from a study using the same modified version of the ECOHIS scale in Kampala, the capital of Uganda (182). All participating caretakers completed the modified ECOHIS scale adding support to the face validity of its Lumasaaba version.

A clear description of the measurement procedure is often lacking although it has been shown that there is a correlation between quality of reporting and the actual

conduct and design of a study (231). Standardisation of working methods is needed to ensure repeatability, comparability and validity of the results (232). The definition of ECC used in this study followed the WHO issued guidelines (with deviations with regards to the probe used) yielding rather basic and relevant information with simple methods under field conditions (4). Other standardisation criteria for assessing dental caries are also available, such as The British Association for the Study of Community Dentistry (BASCD) (233) as well as the recently developed International Caries Detection and Assessment System (ICDAS) (234). However, as no radiographs or artificial light sources were available to guide the dental examination, the WHO method was deemed most appropriate for the present study. Due to lack of equipment, early enamel caries lesions could have been overlooked (235). Therefore, due to the fact that the detection threshold applied was at the cavity level, misclassification regarding ECC status was plausible and could lead to underestimation of the true ECC prevalence. The dentists were trained and calibrated to limit the possibility of misclassification. Results from the inter- observer and intra-observer assessments of dental examiners using Kappa statistics indicated an acceptable reliability according to interpretation suggested by Landis and Koch (236).

5.4 Comments on the main findings

Contrary to what was hypothesised in Paper I, women who were randomly assigned to a behavioural intervention to promote EBF for six months did not present with children having less ECC prevalence than mothers in the control group at the 5-year follow-up. Notably, the PROMISE-EBF behavioural intervention did not explicitly involve an oral health component. However, it was assumed that the EBF intervention would change the general health- and oral health attitudes of the caretakers with further positive consequences for subsequent health and oral health of their offspring. In view of the common risk factor approach, this was a plausible

assumption (168). Several studies from various settings have studied tertiary outcomes from cohorts nested within trials aimed at different primary outcomes to investigate effects on behaviours and clinical outcomes with some reporting positive findings (163, 237) and others not (169, 171). Acknowledging the array of various factors contributing to the determination of oral health, it is not surprising that the effect of oral health interventions has been limited and still constitutes a challenge (177). Existing effective strategies for ECC include risk assessment, brushing with fluoride toothpaste, fluoride varnish application and certain behavioural interventions affecting preventive self-care practices (10). However, also when fluoride varnish was applied in combination with behavioural interventions – there has been a lack of effect when it comes to reduced caries incidence (238, 239). Although caries research of the last years reflects a more thorough understanding of the associated risk factors, caries still seems to be resistant to any preventive intervention. The proceedings of the 2014 ECC conference (10), encompassing evidence-based reviews on the state of science regarding ECC epidemiology, aetiology, prevention and disease management, maintains that there is a lack of high-quality evidence from randomised controlled trials as to what are the most effective means to prevent and manage ECC, particularly when it comes to children younger than six years.

A substantial proportion of the Ugandan children investigated, 39%, presented with caries experience ($dmft > 0$) at 5-years follow-up from birth. These estimates are similar to those of a previous study from Uganda that reported a prevalence of 42% among the 5-year-olds (205). In Uganda, more recent studies using comparative measurement methodology (WHO) have focussed on younger children aged 6-18 months, and the prevalence has been reported to be about 18% (76, 80).

Neighbouring East African countries have reported a lower prevalence of ECC. In Tanzania among 6-18 months old caries prevalence was limited to only 4% (80). Due to differences in age groups and differences in exposure to fluoride in drinking water being high in some parts of Tanzania, the Tanzanian and Uganda studies of preschool children are not entirely comparable. The high ECC burden and unmet need for oral care (percentage of $dmft$ that was untreated caries) may be indicative that ECC constitutes a public health problem in Uganda. Population- and individually based

strategies, such as community water fluoridation and use of fluoridated toothpaste vary according to geographic areas and at the individual level and could at least partly explain the distribution of ECC prevalence across East African countries. More recently, sugar has been emphasised as one of the most important risk factors for dental caries (240, 241). According to the latest Ugandan population census, there has been an increase in urbanisation- which parallels increased consumption of more added sugars without being followed by a matching scale-up of oral health promotion activities (242). This could be another plausible explanation for high ECC experience demonstrated in rural districts of Uganda such as Mbale.

According to Paper II, EBF for 24 weeks associated negatively with ECC across the three models based on the postulated DAGs. The findings of Paper II are difficult to compare with previous studies since any breastfeeding and not EBF has been the measure of breastfeeding utilised in those studies (80). Nevertheless, a previous study from Uganda was inconclusive about the effect of breastfeeding (80). In support of the findings in Paper II, meta-analyses including studies using various measures of breastfeeding finally concluded that breastfeeding can be protective of ECC in infancy (143, 144). The possible mechanism for this protective effect could be found in the early pre-eruptive developmental stages. As the process of amelogenesis requires optimal calcium deposition into the enamel matrix, EBF may be an important supply of calcium for the infants (243). Since enamel development of the primary teeth is completed during the first year of life, malnutrition, during the neonatal period is a plausible cause of developmental enamel defects in the primary dentition, such as hypoplasia (244). In the neighbouring country of Uganda, Tanzania, the prevalence of hypoplasia in primary teeth is high, and has been estimated to 33% and the prevalence has been demonstrated to be increased in prematurely born children (14). Enamel hypoplasia provides a more cariogenic environmental niche and less protective enamel and defects that include hypo

mineralisation might increase susceptibility to demineralisation (245). It has been observed that children with enamel hypoplasia are more likely to experience ECC (246-248). These studies suggested intermediate pathways involving malnutrition. Moreover, it has been found that poor nutrition increases the likelihood of dental caries (249) as well as enamel hypoplasia (248). Furthermore, eruption times may be affected by increasing or decreasing susceptibility of dentition to acid attack depending on whether eruption or exfoliation is delayed (245, 249).

In Paper III, intergenerational factors, such as caregivers' caries experience and marital status were positively associated with ECC. A possible explanation is that caregivers' oral health situation reflects their oral health related behaviours and attitudes, which in turn influence the oral health condition of their children. The role of the family for caries in sibling has been the focus of researchers for several decades. Using random effects regression models, recent studies of Norwegian siblings identified a fairly strong family effect with large between family variability in the range of 13-29%, thus confirming the importance of the family as an arena where children's oral health is formed (250). With regard to marital status, the association with ECC may be linked to lower household income, family stress and reduced attentional resources (114). According to Paper III, maternal education and SES were not associated with ECC. In Uganda, less educated mothers have been reported to be more likely to have children with caries (205). The point estimates for SES in the present study was in the expected direction (the least poor having less caries), although not significant. This contrasts the previous literature as the socio-demographic gradient of ECC has been demonstrated in a plethora of studies (91-97, 103).

As demonstrated in Paper III, OHRQOL was associated with ECC as well as caregiver's perception of child's oral health situation. The association between the reported impacts and parental perception was in the expected direction, caregiver's of children with less ECC experience were less likely to report oral impacts. These results highlight that OHRQOL measures are associated with both clinical and self-report measures. The results are in line with those of a previous study from East

Africa demonstrating a positive association between toothache and OHRQOL and good internal consistency of the modified ECOHIS instrument (182).

5.5 Comments on research implications for oral health care among children

Identification of early life course factors of ECC within a birth cohort design provides an opportunity to make inferences about possible causal relationships, which again is important when it comes to the planning, implementation and evaluation of oral health care programs focusing preschool children and their caretakers. The significance of early life-course factors, the high prevalence of ECC at the age of five years, the importance of parents and the family in caries development of children as well as the consequences of ECC for children's and families OHRQOL suggest that early intervention should be put into the context of primary health care in Uganda. It has been recommended by several professional organisations that all children have their preventive dental visit during their first year of life and that information about caries preventive measures is important for parents and caretakers of young children. Previous evidence from cross-sectional surveys conducted in Uganda can be strengthened by the findings from the randomised intervention and prospective cohort studies included in this thesis despite limitations in terms of a single assessment of ECC at the 5-years follow-up from birth and inadequate information concerning exposure to fluoride. The results from Paper I and II indicate a protective effect of EBF that may be further investigated by longitudinal studies as well as in carefully designed intervention studies encompassing an oral health component. An intervention study similar to that in paper I but including oral health promotional aspects demonstrated a beneficial effect (172).

6. Conclusion

Using a birth cohort design, this thesis provides evidence of early life-course factors as possible important causal factors of ECC. Consistent with a life-course model, the hypothesis of intergenerational association in caries experience and OHRQOL between mothers and their 5-year-old offspring was supported.

- The prevalence of ECC among 5-year-olds in Mbale is substantial and EBF for 24 weeks is an important early life protective factor. Despite this, the promotion of EBF did not have any significant protective effect of ECC this finding corroborates evidence that behavioural interventions such as PROMISE-EBF have tended to be more successful in modifying attitudinal and behavioural outcomes than in the reduction of disease incidence.
- Other established predictors of ECC such as sugar consumption and SES were not significant in this work, and further instigation of those risk factors in low-income country settings is necessary.
- Graphical causal inference approaches are applicable to empirical oral health data, thereby adding to the scanty oral health research literature using these methods. Further use of causal inference approaches may help understand the risk factors of ECC based upon which appropriate interventions need to be designed and implemented.
- Intra-generational association in oral health was supported using clinical and self-reported measures. Further work in this area could assist in understanding the mechanisms behind this relationship in these settings.

7. Future perspectives

The re-emergence of sugar as a risk factor that plays a pivotal role in the establishment of dental caries makes it an important risk factor to consider in the assessment of dental caries. That said, the role of early life feeding practices, including sugar consumption should be taken into account when designing programmes or interventions. The measures of assessment for sugar consumption need to be standardised especially for low income settings.

Because of the conflicting direction of association of the influence SES with ECC in some middle and low income countries, it is necessary for to further investigate this relationship, particularly how sugar consumption is related across the socio-economic gradient.

There is a plethora of literature involving prevention strategies for ECC from high income and some middle income countries in the literature in contrast to low income countries mostly sub-Saharan Africa. Strategies such as motivational interviewing, MI, have had promising results regarding health- and oral-health related behaviours of significance for ECC. Little of the research findings emanating from sub-Saharan Africa has been translated into interventions and assessed to inform policy. In view of the common risk factor approach, this knowledge gap could be reduced by designing multidisciplinary interventions encompassing key areas of paediatric health. Such multidisciplinary strategies could also be assessed for cost effectiveness.

8. References

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9. ORIGINAL PAPERS.

RESEARCH ARTICLE

Effect of Breastfeeding Promotion on Early Childhood Caries and Breastfeeding Duration among 5 Year Old Children in Eastern Uganda: A Cluster Randomized Trial

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Abstract

Background

Although several studies have shown short term health benefits of exclusive breastfeeding (EBF), its long term consequences have not been studied extensively in low-income contexts. This study assessed the impact of an EBF promotion initiative for 6 months on early childhood caries (ECC) and breastfeeding duration in children aged 5 years in Mbale, Eastern Uganda.

Methods

Participants were recruited from the Ugandan site of the PROMISE- EBF cluster randomised trial (ClinicalTrials.gov no: [NCT00397150](https://clinicaltrials.gov/ct2/show/study/NCT00397150)). A total of 765 pregnant women from 24 clusters were included in the ratio 1:1 to receive peer counselled promotion of EBF as the intervention or standard of care. At the 5 year follow-up, ECC was recorded under field conditions using the World Health Organization's decayed missing filled tooth (dmft) index. Adjusted negative binomial and linear regression were used in the analysis.

Results

Mean breastfeeding duration in the intervention and control groups (n=417) were 21.8 (CI 20.7–22.9) and 21.3(CI 20.7–21.9) months, respectively. The mean dmft was 1.5 (standard deviation [SD] 2.9) and 1.7 (SD 2.9) in the intervention and control groups, respectively. Corresponding prevalence estimates of ECC were 38% and 41%. Negative binomial regression analysis adjusted for cluster effects and loss-to-follow-up by inverse probability

data collection and analysis, decision to publish, or preparation of the manuscript.

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weights (IPW) showed an incidence-rate ratio (IRR) of 0.91 (95% CI 0.65–1.2). Comparing the effect of the trial arm on breastfeeding duration showed a difference in months of 0.48 (-0.72 to 1.7).

Conclusion

PROMISE EBF trial did not impact on early childhood caries or breastfeeding duration at 5 years of age. This study contributes to the body of evidence that promotion of exclusive breastfeeding does not raise oral health concerns. However, the high burden of caries calls for efforts to improve the oral health condition in this setting.

Trial Registration

ClinicalTrials.gov [NCT00397150](https://clinicaltrials.gov/ct2/show/study/NCT00397150)

Introduction

Exclusive breastfeeding (EBF), that is giving the baby no solids or liquids besides breast milk, other than vitamins and medication has been considered to be one of the most effective preventive strategies to reduce infant mortality in developed and low income countries [1–5]. With respect to optimal duration of exclusive breastfeeding, a Cochrane review concluded that EBF for six months has advantages over EBF for three to four months such as reduced risk of gastrointestinal infection and more rapid maternal weight-loss after birth [6]. Another Cochrane review concluded that additional lay support for breastfeeding mothers was effective in prolonging EBF, whereas the effect on duration of any breastfeeding was uncertain [7]. A review focusing on breastfeeding promotion by peer counsellors and summarizing the small amount of evidence from Africa, revealed improvements in terms of breastfeeding initiation, duration and exclusivity [8]. Although several studies have shown some short term health benefits of exclusive breastfeeding promotion, its long-term consequences have rarely been studied in low-income contexts. Little is known about the long term effects of exclusive breastfeeding promotion on early childhood caries (ECC) and duration of any breastfeeding, particularly in non-occidental cultural settings [9,10].

Early childhood caries denotes any form of caries (cavitated or not) occurring in the primary dentition of children 71 months or younger [11,12]. ECC is one of the most prevalent chronic childhood diseases having extensive quality of life implications for the child as well as the child's family [13–16]. Previous studies from Uganda have reported a caries prevalence of 18% in 6–36 months old children [17]. A study conducted in Kampala, the capital city of Uganda, involving preschool children aged 3, 4 and 5 years revealed caries prevalence of respectively, 45%, 59% and 65% indicating that ECC is a significant problem among preschool children in this country [18]. There is conflicting evidence as to how breastfeeding impacts on ECC with some studies reporting a positive, some a negative- and others no relationship between breastfeeding and ECC [19–21]. Iida et al. [22] concluded that infant breastfeeding and its duration whether overall, full or exclusive was not associated with any increased risk of ECC. In Japanese 3- year- old children, however, breastfeeding for 18 months or longer was associated with increased prevalence of dental caries [23]. Prolonged duration of breastfeeding above 1 year and nocturnal breastfeeding has been associated with ECC development [24]. Evidence suggests that teeth are susceptible to caries shortly after tooth eruption and prior to final maturation

which may indicate that EBF practices during the first six months could be important for oral health—potentially as a risk factor [25]. Evidence of a beneficial or harmful effect of breastfeeding on ECC has been provided mainly by observational studies and thus could be attributed to methodological limitations [26]. According to systematic reviews on the relationship between breastfeeding and dental caries in children, only three studies had moderately appropriate design, but were without uniform definition of EBF [10,27]. However, the Belarussian EBF promotion intervention designed as a cluster randomised trial to promote exclusive- and prolonged breastfeeding showed no significant effect on ECC at 6.5 years follow-up [28]. The feeding patterns in this Belarussian population of mothers are quite different from what is commonly practiced in several low-income countries in Sub-Saharan Africa, including Uganda [29]. Assigning some participants to a breastfeeding arm and others to a non-breastfeeding arm would be unethical, so a trial studying the effect of promotion of EBF provides a good opportunity to study the effect of this intervention on ECC.

Assuming that EBF promotion may change the general health and oral health focus of the caretakers, it could impact on children's subsequent health and oral health, including duration of breastfeeding and feeding patterns as well as early childhood caries. Thus, this study assessed the effect of promoting EBF for 6 months on ECC and breastfeeding duration assessed at 5 year follow-up in children enrolled at birth to the PROMISE EBF trial in Uganda.

Subjects and Methods

The protocol for this trial and supporting CONSORT checklist are available as supporting information; see [S1 Checklist](#) and [S1 Protocol](#).

Study setting

The present study is a five year follow-up of caretaker-children pairs of the Ugandan site of the PROMISE-EBF trial (ClinicalTrials.gov no: [NCT00397150](#)) conducted in 2011 in Mbale district, Eastern Uganda [30]. This district has a literacy rate of 75% and 60% among males and females, respectively [31]. The fluoride concentration in drinking water is not monitored and may vary across the different geographical regions.

Study design

PROMISE-EBF was a multicentre community based cluster-randomised behavioural intervention trial conducted in sub Saharan Africa between January 2006 and June 2008. The aim of this intervention was to assess the effect of individual home-based peer counselling to promote exclusive breastfeeding for 6 months after birth. The unit of randomization were clusters made up of 1–2 villages with an average of 1000 inhabitants corresponding to a birth rate of approximately 35 per cluster. A total of 24 clusters were stratified into urban and rural and allocated at random (computer generated with an allocation ration 1:1) to intervention and control groups. Women in the intervention group received home based individual peer counselling to support EBF for 6 months from lay counsellors in terms of information and encouragement in 5 visits. One visit was prenatal and the other visits were in the first, fourth, seventh and tenth week post-delivery. The control group received standard care from the public health services. The primary outcome of this trial was prevalence of EBF and diarrhoea reported by mothers of infants aged 12- and 24 weeks. Detailed information about PROMISE-EBF has been published previously [5,32].

The PROMISE-EBF study involved 765 healthy mother-infant breastfeeding pairs and resulted in two child cohorts from the intervention and control groups that differed substantially with respect to the prevalence of EBF at 24 weeks of infant's age. (59% versus 12%) [5]. The visits and follow-ups were carried out at household level in the 24 clusters between 2006–2011

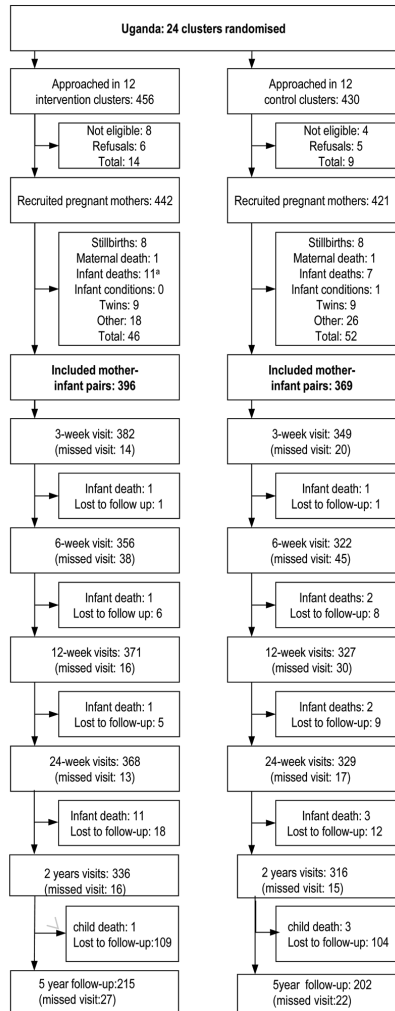


Fig 1. Flowchart. ^aSome had more than one inclusion criteria.

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including in the intervention and control groups respectively; 336 and 316 mother-child pairs from the 2-year follow-up and, 215 and 202 mother-child pairs in the 5-year follow-up (Fig 1). A proportion was lost-to-follow-up due to relocation or not being at home when approached for two to three home visits.

Primary and secondary outcomes

The primary outcome of this study is the prevalence of ECC assessed by the decayed missing filled teeth (dmft) index at the five year follow-up.

The secondary outcome of this study is the duration of any breastfeeding.

Interview with mothers at the 5-year follow-up visit

Research assistants conducted structured interviews with mothers/ caretakers in their local language Lumasaba. The interview included questions regarding socio-demographic characteristics, general health, breastfeeding, nutrition, food security, morbidity, oral health and oral health related quality of life (OHRQoL). Breastfeeding duration was assessed by mothers recall at 2- and 5 years follow-up. The questions; did you breastfeed, are you still breastfeeding and for how long did you breastfeed were used to evaluate breastfeeding duration at all interview visits. Multiple correspondence analyses was used to construct a socio-economic index categorised into wealth quintiles and based on ownership of assets such as furniture and household characteristics including electricity, type of water source, roof material and toilet type from the recruitment interview. Multiple correspondence analysis is analogous to principal component analysis for categorical data [33].

Clinical oral examination of children at the 5-year follow-up visit

A full mouth clinical oral examination was carried out at household level by two trained and calibrated dentists (NB and AK). Children were examined following the WHO guidelines under field conditions [34]. Children were placed with their face in upward direction facing natural light, with the clinician standing or sitting at the backside using a mirror and probe for oral examination. ECC was assessed on fully erupted teeth using the decayed, missing filled teeth index (dmft) [34]. A tooth was recorded as decayed if it was visually cavitated or if on probing, the probe stuck into the suspected tooth surface. A missing tooth was qualified as missing due to extraction when this was confirmed by the caretaker. Further confirmation was sought if caries was the reason for extraction. The primary outcome variable; ECC, was constructed from the dmft index. In the present analysis ECC was used as a count variable and also dichotomised. The count variable was a sum score of decayed, missed and filled teeth in child's mouth. The count variable was dichotomised into: $dmft > 0$ denoted presence or prevalence of ECC and $dmft = 0$ denoted absence of ECC. The interviewers and dentists were aware of the children's involvement in the PROMISE-EBF trial but were blinded with respect to their group allocation. Duplicate oral examinations were carried out by dental surgeons (NB and AK), involving 22 children considered to be representative of the trial participants based on age and site of residence.

Reliability measurement

Un-weighted Cohen's Kappa was used to assess inter-rater reliability by comparing the dmft score for each tooth across two examiners. Intra-rater reliability was assessed by comparing the dmft score for each examiner across a time interval of two weeks. The observed median Kappa for inter-rater agreement amounted to 0.92 with an interquartile range (IQR) of (0.63–1). The intra-rater agreement revealed a median Kappa of 0.80 IQR (0.64–1).

Data cleaning and statistical analysis

Double data entry was carried out. The statistical package Stata IC version 13 was used for data analysis. Analyses of the sample characteristics were performed using frequency tables, means and proportions. Due to overdispersed and skewed count data, with about half of the cases presenting with $dmft = 0$, the standard negative binomial regression was used. In a parallel analysis, a two-step zero inflated negative binomial regression model was employed in order to

predict a zero or non-zero ECC outcome in the first step of analysis using logit link. In the second step, the effect of the intervention on the non-zero ECC outcomes was estimated. The goodness fit of standard negative binomial model was compared with the goodness of fit of the zero inflated one using the Vuong's test. Incidence rate ratios (IRRs) and 95% confidence intervals (CIs) were used to assess the effect of breastfeeding promotion on ECC experience whilst adjusting for the cluster design. Linear regression for continuous normally distributed data was conducted to compare any breastfeeding duration between the trial arms. Breastfeeding recall at 2- and 5 years follow-up was assessed using survival analysis for time related data and described using a Kaplan Meier plot. To adjust for potential differences in loss-to-follow-up between the trial arms, an inverse-probability weights method was applied. A probit regression analysis was conducted to assess background factors which were associated with lost to follow-up (socio-economic status, level of education and residence in rural/urban area). This probability was then used to calculate the inverse probability weight by calculating the inverse of predicted scores for being lost to follow-up. These weights were included in the regression models (using the `pweight` command). The median of the weights was 1.8 (IQR 1.7–2.0); i.e. children who were available for oral examination were weighted slightly up in the analysis to represent a median 1.8 children at baseline.

Ethics

Ethical approval for the study was granted by Makerere University Medical School Research Ethics Committee, the Uganda National Council for Science and Technology and Regional Committees for Medical and Health Research Ethics, Western Norway (05/8197). Consent was given at the individual level by participants after cluster randomization. As a first step, verbal consents were obtained from the pregnant women as to whether or not she wanted to be visited by a data collector for more information about the trial. In a second step, written consent was given after comprehensive information about the trial procedures up to the last follow-up. At the 5-year follow-up, the caretakers gave assent for their children. Signed or thumb-printed informed consent was obtained from each mother prior to study participation. The consent procedure was approved by the ethical committees.

Results

Of the 417 children examined, 208 were boys and 209 girls, with an almost balanced sex distribution across the trial arms. The median age was 4.5 (IQR 4.2–5.2) years. At baseline the intervention and control group differed to some extent with respect to socio-economic status (including electricity in the house, water source) and place of birth (Table 1). The socio-demographic differences at the five year follow-up paralleled those seen at baseline (randomization) with significant differences in the socio-economic status and place of birth categories (Table 2). Continuous data did not differ by allocation status at baseline and 5year follow-up. Loss to follow-up in the 5-year follow-up was slightly more likely among those who were primipara, single, widowed, separated or divorced (Table 2).

The prevalence of children with caries in the intervention and control arm was 38% and 41%, respectively. The corresponding mean dmft was 1.5 (SD 2.9) and 1.7 (SD 2.9), respectively (Table 3). Mean dmft for boys was 1.6 in both trial arms, whereas for girls the mean dmft was 1.5 (2.7) and 1.8 (2.9) in intervention and control arm, respectively (Table 3).

As shown in Fig 2, the tooth specific pattern of ECC was similar across trial arms. Maxillary (upper jaw) central incisors and mandibular (lower jaw) molar teeth were most frequently affected by ECC in the intervention and the control arm. In the upper jaw, the mean dmft for the central incisors (teeth 51, 61) were highest in the intervention arm, whereas the mean dmft for

Table 1. Baseline characteristics at randomisation.

	Intervention	Control
Categorical data		
Eligible mother infant pairs(n)	396	369
Marital status		
Married	244(62%)	234(64%)
Cohabiting	119(30%)	104(28%)
Single, widowed, separated, or divorced	29(7%)	28(68%)
Socio-economic status quintile		
1(poorest)	91(23%)	62(17%)
2	97(24%)	86(23%)
3	76(19%)	49(13%)
4	71(18%)	84(23%)
5(least poor)	61(15%)	88(24%)
Electricity in house		
Yes	53(14%)	70(19%)
Toilet		
None or open	84(25%)	59(18%)
Pit or ventilated improved pit	245(72%)	266(81%)
Flush	10(3%)	3(<1%)
Parity		
Primipara	81(21%)	85 (23%)
Multipara	311(79%)	281 (77%)
Previous child death		
Yes	109(36%)	80(29%)
Attendance of antenatal (index child)		
Yes	272(72%)	274(78%)
Place of birth (index child)		
Out of facility	208(55%)	146(42%)
Facility	173(45%)	205(58%)
Continuous Data Median (IQR)		
Maternal Age		
Years	25(20–30)	24(20–30)
Maternal Education		
Years	6(4–8)	6(5–9)
Maternal Body Mass index		
At 6 weeks (kg/m ²)	22(20–24)	22(20–24)

IQR- Interquartile range, kg/m²- kilogram per square metre.

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the molar teeth (teeth 55, 54) were highest in the control group. In the lower jaw, the mean dmft for the molar teeth (teeth 74, 75) were highest in the control group.

Mean breastfeeding duration was 21.8 (CI 20.7–22.9) months in the intervention and 21.3 (CI 20.7–21.9) months in the control arm (Table 3) (Fig 3).

Linear regression, adjusted for cluster effect revealed no statistically significant relationship between breastfeeding duration and the trial arms with a month's difference of 0.48 (CI -0.72 to 1.7) (not shown in Table).

The negative binomial regression, with robust variance estimates adjusted for clustering, showed no significant difference between the trial arms with respect to total dmft and dmft in

Table 2. Background characteristics at 5 years follow-up and among that lost- to-follow-up.

	Intervention % (n)	Control % (n)	Lost to follow-up in intervention % (n)	Lost to follow-up in Control % (n)
Categorical data				
Eligible mother pairs	54.3(215)	54.7(202)	45.7(181)	45.3(167)
Marital status				
Married, cohabiting	92.5(197)	95.5(193)	92.7(166)	88.5(146)*
Single, widowed, separated or divorced	7.5(16)	4.5(9)	7.3(13)	11.5(19)
Social economic status quintile				
1 (poorest)	70.7(152)	58.6(119)*	61.9(112)	47.3(79)
2 (least poor)	29.3(63)	41.4(84)	38.1(69)	52.7(88)
Electricity in house				
Yes	12.7(27)	16.6(33)	14.6(26)	22.8(37)
Toilet				
None or open	25.4(46)	22.3(41)	24.0(38)	12.5(18)
Pit or ventilated improved pit/Flush	74.6 (135)	77.7 (143)	76.0 (120)	87.5(126)
Parity				
Primipara	16.6(35)	20.9(42)	27.8(50)*	28.8(46)
Multipara	83.4(176)	79.1(159)	72.2(130)	71.2(114)
Previous child death				
Yes	34.3(61)	32.7(52)	37.2(48)	23.7(28)
Attendance of antenatal (index child)				
Yes	70.4(145)	79.4(154)	74.7(127)	76.0(120)
Place of birth (index child)				
Out of facility	58.1(122)	39.9(77)*	50.3(86)	43.7(69)
Facility	41.9 (88)	60.1(116)	49.7(85)	56.3(89)
Child sex				
Male	50.2(108)	49.5(100)	51.4(92)	52.4(87)
Female	49.8(107)	50.5(102)	48.6(87)	47.6(79)
Continuous data median (IQR)				
Maternal Age				
Years	26(21–30)	25(25–31)	24(20–28)	23(20–28)
Maternal Education				
Years	6(4–7)	6(4–9)	6(4–8)	7(5–9)
Maternal Body Mass index				
At 6 weeks (kg/m ²)	22(20–24)	22(20–24)	22(20–23)	23(20–23)
Child Age				
Years	4.6(4.2–5.2)	4.4(4.1–5.1)	4.5(4.1–5.0)	4.1(3.9–5.0)

*p<0.05 IQR—interquartile range, kg/m²- kilogram square metre.

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anterior maxillary teeth. Compared to the control arm, the incidence rate ratio of having ECC in the intervention arm was 0.91 (CI 0.65–1.26). The corresponding ratio for ECC in anterior maxillary teeth was 1.31 (CI 0.84–2.31). The estimates adjusted for site and socio-economic status were similar to the unadjusted ones with IRRs of 0.92 (CI 0.67–1.27) and 1.42 (0.88–2.31) respectively (Table 4). Zero inflated negative binomial analyses revealed essentially the same estimates as the negative binomial regression model (S1 Table).

Table 3. Mean early childhood caries in total dentition and anterior maxillary teeth, mean breastfeeding duration and proportion of early childhood caries at 5 years follow-up in intervention (n = 215) and control group (n = 202).

	n	Intervention		Control	
		Mean(SD)	Median (IQR)	Mean (SD)	Median(IQR)
ECC in all dentition					
Boys	208	1.6 (3.2)	0 (0–2)	1.6 (2.9)	0 (0–2)
Girls	209	1.5 (2.7)	0 (0–2)	1.8 (2.9)	0 (0–2)
Overall sample	417	1.5 (2.9)	0 (0–2)	1.7 (2.9)	0 (0–2)
ECC in anterior maxillary teeth					
Boys	208	0.54 (1.2)	0 (0–0)	0.34 (1.1)	0 (0–0)
Girls	209	0.51 (1.3)	0 (0–0)	0.43 (1.2)	0 (0–0)
Overall sample	417	0.53 (1.3)	0 (0–0)	0.38 (1.1)	0 (0–0)
Mean breastfeeding duration in months	n	Mean (SD)		Mean (SD)	
	417	21.8 (6.5)		21.3 (6.2)	
Proportion of ECC > 0		% (n)		% (n)	
		38 (81)		41 (83)	

ECC-Early childhood caries, SD-standard deviation, n-number, IQR- Interquartile range.

doi:10.1371/journal.pone.0125352.t003

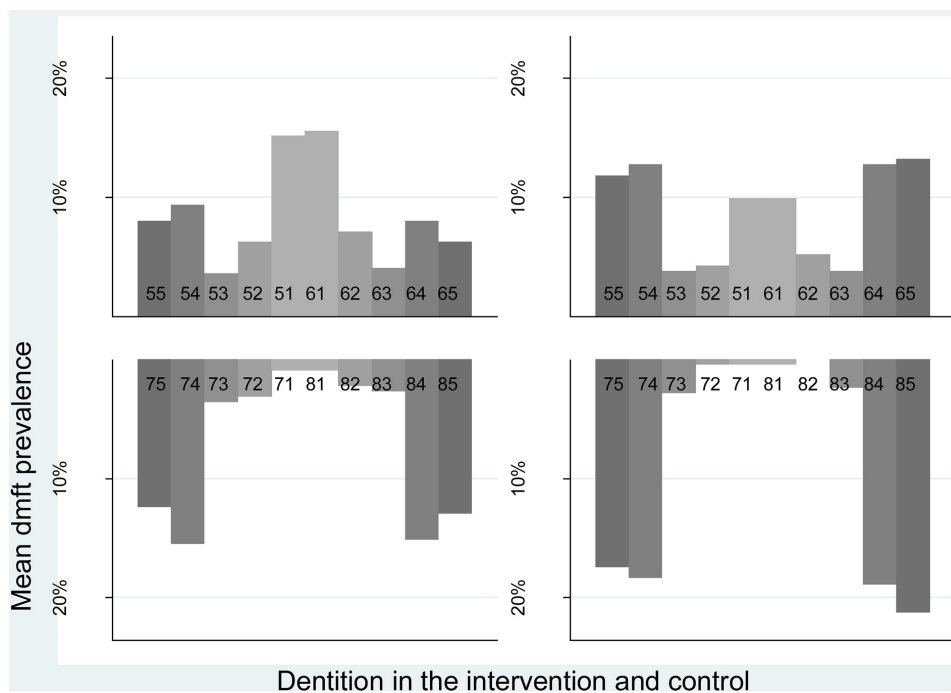


Fig 2. Mean caries (dmft) prevalence distribution by tooth type (numbered) in maxilla (upper figures) and mandible (lower figures) in intervention (left figures) and control group (right figures).

doi:10.1371/journal.pone.0125352.g002

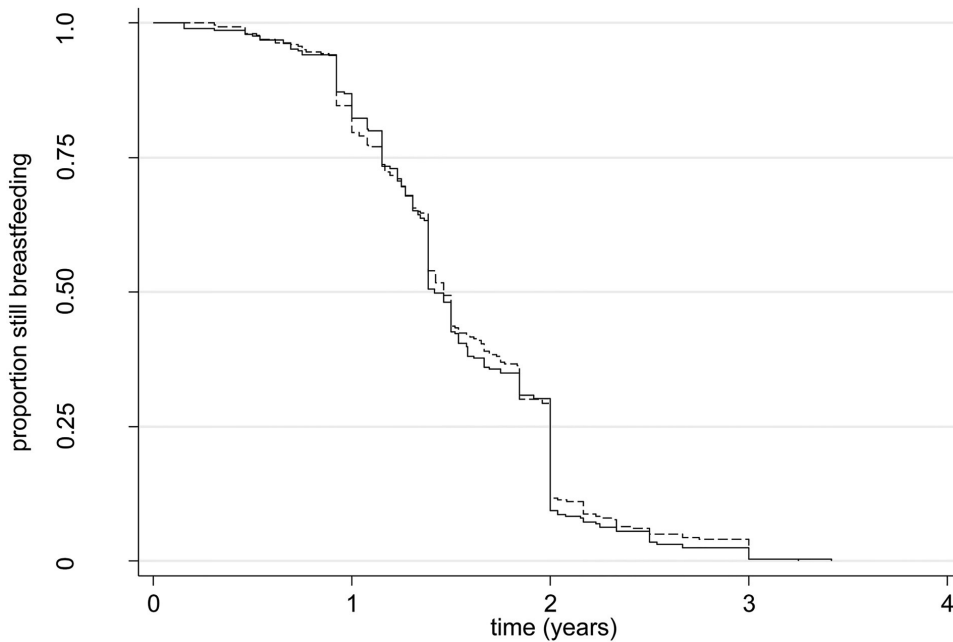


Fig 3. Kaplan-Meier plot showing breastfeeding duration in years. * Dashed line indicates intervention group; complete line indicates control group.

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Discussion

Although the PROMISE-EBF trial had a substantial impact on breastfeeding exclusivity, the intervention had no effect on breastfeeding duration as reported by mothers at the 2- and 5- year-follow-up visits. Thus, this study found no significant differences in ECC and breastfeeding duration, corresponding to the null hypothesis. However, several studies may not identify true differences (type II errors).

Table 4. Incidence rate ratios (IRR) with 95% confidence intervals (CI) for early childhood caries (ECC) in all dentition and in anterior maxillary teeth in intervention and control groups (n = 417), both unadjusted (except for clustering) and adjusted negative binomial regression models.

	ECC in all dentition IRR(95%CI)	ECC anterior maxillary teeth IRR(95%CI)
Unadjusted		
Intervention	0.91(0.65–1.23)	1.39(0.84–2.31)
Control	1	1
Adjusted*		
Intervention	0.92(0.67–1.27)	1.42(0.88–2.31)
Control	1	1

* adjusted for site of residence and socio-economic status in addition to clustering.

doi:10.1371/journal.pone.0125352.t004

Whereas 59% and 12% of mothers in the intervention and control arm reported exclusive breastfeeding at 24 weeks follow-up, mean duration of any breastfeeding at 5 year follow-up was 21.8 and 21.3 months in the intervention and control groups respectively. These results are close to the WHO recommendations of complementary feeding for at least two years [1,2] and corroborate estimates of previous studies from East African countries with mean number of months having breastfed reported to be in the range from 13.0–19.6 months [4]. The lack of effect on duration of any breastfeeding might be related to the fact that the current cultural practice in Uganda, represented by the control arm, is not far from the recommendations in terms of total duration of breastfeeding [2].

Previous studies of observational design have reported a positive association between ECC and breastfeeding [35–37]. However, the present PROMISE-EBF trial using home-based exclusive breastfeeding promotion by peer counsellors provided to mothers during the first weeks after birth, did not show any impact on ECC across early childhood. The present results are in line with a similarly designed study in a different setting in Belarus [28]. They are also accordant with another western study focusing caries reduction as an outcome of peer led social support for recommended breastfeeding practices [38]. Although the large Belarusian trial led to potentially clinically important increase in exclusive and total breastfeeding duration, the trial was found to be without any effects on ECC in children at the 6 5-years follow-up visit. It is evident that intervention strategies, such as PROMISE EBF, have been more successful in modifying behavioural and attitudinal outcomes such as parents' cognition and feeding practices and less successful in reducing incidence of dental caries [28,39]. In contrast to the present results, a recently conducted Brazilian study reported that early home based dietary counselling during infancy, including exclusive breastfeeding for 6 months, actually reduced caries incidence and severity at 4 years of age in this low-income setting [40]. Notably, the specific effect of exclusive breastfeeding promotion in that study was difficult to assess as feeding practices was only a part of the intervention packages.

Despite the absence of any intervention effect in the present study, substantial proportions of the participating children presented with ECC at 5 years of age, amounting to 38% and 41% in the intervention and control arm, respectively. These rates are consistent with previously recorded estimates among preschool children in Uganda [18]. Carious lesions were not evenly distributed across teeth, being most prevalent in the upper incisors and the lower molars and less prevalent in the lower incisors, thus reflecting the pattern of eruption. Consistent caries patterns have been reported previously in a similar population and socio-cultural setting [17,18]. Information about the prevalence of ECC in the paediatric population of sub-Saharan Africa is scarce and the Mbale region, eastern Uganda has been surveyed to a very limited extent. The results regarding ECC prevalence and distribution reflect an unmet need for dental care, suggesting that ECC constitutes a public health problem in the area investigated. A high prevalence of ECC as observed in the present study of Ugandan preschool children, may be attributed to low levels of fluoride in drinking water, lack of wide spread use of fluoridated toothpaste and to the ongoing nutrition transition in the region. The nutrition transition implies risk factors for health and oral health such as the adoption of diet high in fat and commercialised sugar products. [41]

A number of strengths and limitations of the present study merit consideration. An important strength was the randomized trial design utilised that minimised the risk of confounding. However, the PROMISE-EBF intervention was designed to assess changes in exclusive breastfeeding during the first 6 months and not to compare duration of breastfeeding or ECC at 5 year follow-up. The extent of losses to follow-up, typical of long-term trials in resource poor settings, reduced the analytical sample for its ability to differentiate smaller intervention effects. Nevertheless, post-hoc power calculations showed that the power of this study was satisfactory

in terms of assessing duration of breastfeeding and ECC. The substantial loss-to-follow-up was largely due to relocation of the families to unknown addresses. This high mobility of the studied population could have contributed to potential group differences in the intervention and control arms and potentially to a selection bias. Checking baseline characteristics of socio-economic and educational factors between those followed-up and those lost-to-follow-up at 5 years suggests that there is a slightly higher loss of those most educated and of the socio-economically least poor. Thus, compared to individuals retained in the cohort, individuals lost to follow-up tended to be advantaged in terms of socio-economic status. However, the loss to follow-up was rather balanced between the trial arms, making it less probable that bias due to non-response has seriously affected the present effect estimates. Adjusting for loss-to-follow-up with inverse probability sample weights, IPW, taking socio-economy, years of education of the mother and site of residence into account did not change the results (only second decimal changes). It is thus not likely that loss-to-follow-up biased the findings substantially.

To protect against measurement bias interviewers and dentists at the 5 year follow-up were blinded to the allocation status of the participants and had not been involved in the previous follow-ups. However, without x-ray examination, enamel caries or white spot lesions may have been overlooked or misclassified leading to an underestimation of ECC prevalence. To limit such misclassification, the dental recorders were trained on the relevant examination and they were calibrated. Both examiners were experienced dental surgeons, practicing clinical dental work at the time of the study. The acceptable levels of inter- and intra-rater reliability measures [42] obtained suggests that misclassification, being a threat to the internal validity of the clinical registration may not be a substantial problem in this study. On the other hand and since it was impossible to fully blind participants, social desirable responses may have been given and mothers in the intervention arm may have reported healthier practice just to please the research staff. If the tendency of social desirable answers with respect to breastfeeding duration differed across study groups, this may have constituted a source of differential misclassification providing a biased estimate of the observed association. However, the fact that the intervention group did not report a longer duration of breastfeeding than the control arm could suggest that this may not be a substantial problem. Some studies focusing on breastfeeding have shown that recall tends to deteriorate with increasing time, when mothers are asked about breastfeeding duration, the reports become increasingly inaccurate with increasing time since cessation [43,44]. As we assessed duration of breastfeeding both at a follow-up visit at 2 years and at 5 years, the time difference between the first of these visits and the time when many stopped breastfeeding was short, which probably limited recall difficulties. Lenore et al. [45] showed that infant feeding data collected within 18 months after the event can be used in epidemiological studies. Thus the 2 year recall breastfeeding in addition to the 5 year recall data could have enhanced the validity of mothers' recall.

It is probable that respondents could have had preference for rounded and approximated answers (digit preference) for breastfeeding duration. This might have decreased the precision of the breastfeeding duration. There is a tendency to digit preference for example 2, 2.5 and 3 years among those who breastfed the longest and had not stopped breastfeeding at the 2 years visit. Still, it is less likely to be systematic differences between the groups. A Brazilian study [43], showed that mothers of higher social-economic status were more likely than their lower socio-economic counterparts to overestimate breastfeeding duration. With respect to the present study, the control group had more participants with high socio-economic status than the intervention group indicating a source of differential misclassification. However, adjusting socio-economic status in the multiple variable regression analysis did not lead to substantial change of the estimates.

Some would argue that using zero-inflated negative binomial regression analysis could be preferred to negative binomial regression analysis. A parallel analysis using this model showed similar results and thus did not change the conclusion of the study.

Conclusion

The PROMISE EBF trial did not impact on early childhood caries or breastfeeding duration at 5 years of age. This study contributes to the body of evidence that promotion of exclusive breastfeeding does not raise oral health concerns. However, the high burden of caries calls for efforts to improve the oral health condition in this setting.

Supporting Information

S1 Checklist.

(PDF)

S1 File. Web appendix 2011.

(PDF)

S2 File. Histogram and box plot for early childhood caries.

(PDF)

S1 Protocol. PROMISE-EBF study protocol.

(PDF)

S1 Table. Results for zero inflated negative binomial regression.

(PDF)

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Author Contributions

Conceived and designed the experiments: NB LTF AK VN IO GN JKT TT ÅNA. Performed the experiments: NB LTF AK VN IO GN JKT ÅNA. Wrote the paper: NB LTF AK VN SAL IO GN JKT TT ÅNA.

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APPENDIX I

Questionnaire for 5 years follow-up on the PROMISE EBF study 2011

-----Introduction-----

DC1 Data collector Interviewer's Code (responsible) #
 1=MOMU 2=DONA 3=STNA
 4=OLWA 5=PEKA 6=EDMA-
 7=NABI 8=Other interviewer

DC1b specify data collector _____

ID Unique Subject Identifier (USI) #####

idate Date of interview:
 Date/month/year <dd/mm/yyyy>

itime Time of interview (hh.mm): ##.##

GPSLong GPS coordinates
 GPS Longitude ###.###

GPSLat GPS Latitude ###.###

GPSAlt GPS Altitude ###.###

site urban/rural ##
 51 Mbale Municipality
 52 Bungokho

moved The mother has moved after the last (18 months) interview? # 0=No, 1=Yes

diswhere Where has the mother moved?
 District, specify _____

vilwhere Village or city, specify _____

cellphon Do you have any cell phone numbers #####
 that could reach the mother?

revisit Planned revisit (optional) _____

-----Initial questions about the mother - infant pair -----

mofchild She is the mother of the child # 0=No, 1=Yes

checkprom Was the child included in the PROMISE EBF study? # 0=No, 1=Yes, 9=Don't know
 I.e. asking questions about feeding of children
 and was born around 4-5 years ago?

death Is the child dead? # 0=No, 1=Yes, 9=Don't know
 IF YES: verbal autopsy form:
 Verbal Autopsy Standards - Ascertaining and attributing causes of death -
 International standard verbal autopsy questionnaires - WHO 4w-14yrs.pdf

matdeath The mother is dead # 0=No, 1=Yes, 9=Don't know
 away The mother is away for other reasons # 0=No, 1=Yes, 9=Don't know

childname Write down the name of the child
 that was born around 4 years ago _____

kgarten Has \$name\$ started in nursery school or kindergarten? # 0=No, 1=Yes, 9=Don't know

mowork What is the mother's present main occupation? #
 1=Peasant/farmer 2=Petty trade
 3=Commercial farmer
 4=Shop keeper 5=Student
 6=Casual labourer
 7=Salary work 9=Other

-----Infant Feeding Recalls -----

everBF Did you ever breastfeed \${name}\$? # 0=No, 1=Yes, 9=Don't know

stillBF Do you still breastfeed \${name}\$? # 0=No, 1=Yes, 9=Don't know

BFlastda From the time you woke up yesterday morning till you woke up this morning did you breastfeed \${name}\$? # 0=No, 1=Yes, 9=Don't know
For how long did you breastfeed \${name}\$?

BFmonths ## months
If don't know (try to probe more, if still don't know, use coding 99)

whystop What was your main reason for stopping to breastfeed/not breastfeed your \$name\$? #
1=Child grown too big for breast
2=Work or school related
3=Lactation problems
4=Illness, other than 3
5=Child not growing well
6=Not enough breast milk
7=Advice from others
8=New pregnancy
9=Other

BFchange Have counselling that you got regarding breastfeeding changed the way that you have fed \$name\$? # 0=No, 1=Yes, 2=did not get any counselling, 9=Don't know
(If no, skip next question)

durchange How have the counselling changed your infant feeding practices? Change in duration? # 0=No, 1=Breastfeeding longer duration, 2=Breastfeeding shorter duration, 9=Don't know

freqchange Change in frequency? # 0=No, 1=Breastfeeding more frequently, 2=Breastfeeding less frequently, 9=Don't know

excchange Change in exclusivity? # 0=No, 1=giving more breastmilk and less of other foods, 2=giving less breast milk and more of other foods, 9=Don't know

foodsep Does \$name\$ get food cooked separately? # 0=No only adult/family food, 1=Yes food cooked separately, 2=Both, 9=Don't know

-----Food recall -----

Now I am going to ask you questions which are related to what \$name\$ is eating:
How often does \$name\$ drink and eat the following items? Use the same codes for this section:
0=No, never
1=Yes, less than weekly,
2=1-3 times/week
3=4-6 times/week,
4=daily,
9=Don't know

fjuice Fruit juice #

swbev Other sweetened beverages (including soda, baalafu etc) #

tea Tea with milk #

cowsmilk Milk (Cow's, goat's, condensed or powdered) #

dairy Other dairy product like yoghurt, cheese and cream #

porridge Porridge or cereals (including sorghum, soya and millet) #

bread Bread or chapatti (pan cakes) #

matooke Matooke (mashed banana) #

posho Posho (maize stew) #

yams Yams #

cassava Cassava #

potatoes Sweet potatoes or Irish potatoes #

beans Beans or peas #

gnuts Ground nuts (including paste and sauce) #

veggr Green leafy vegetables (including greens) #

othveg Other vegetables #

fruits Fruits (including pinapples, passion fruit, mango, etc) #

eggs	Eggs	#
meat	Meat (including chicken)	#
fish	Fish	#
brew	Beer or brew	#
oil	Oil or butter	#
othfood	Other	#
foodsp	specify food	_____

----- Family's food situation -----

How often during the last month last month... Use same codes for this section
 0=No, never,
 1=Rarely (1-2 days last month)
 2=Sometimes (3-10 days/month)
 3=Often (10+ days per month)

fsec1	Did you worry that your household would not have enough food? (last month)	#
fsec2	Were you or any household member not able to eat the kinds of foods you preferred because of a lack of resources? (last month)	#
fsec3	Did you or any household member eat a limited variety of foods due to a lack of resources?	#
fsec4	Did you or any household member eat food that you preferred not to eat because a lack of resources to obtain other types of food?	#
fsec5	Did you or any household member eat a smaller meal than you felt you needed because there was not enough food?	#
fsec6	Did you or any other household member eat fewer meals in a day because there was not enough food?	#
fsec7	Was there ever no food at all in your household because there were not resources to get more?	#
fsec8	Did you or any household member go to sleep at night hungry because there was not enough food?	#
fsec9	Did you or any household member go a whole day without eating anything because there was not enough food?	#

-----Bed Net -----

samebed	Does \$name\$ usually sleep in your bed?	# 0=No, 1=Yes, 9=Don't know
bednet	Is \$name\$ covered by a bed net at night?	# 0=No, 1=Yes, 9=Don't know
treatnet	If yes, is it an insecticide treated bed net?	# 0=No, 1=Yes, 9=Don't know

-----Self-rated health -----

Now I am going to ask you questions which are related to \$name\$'s health:

genhealt	In general how healthy would you say that your \$name\$ is compared to other children?	# 1=Not very healthy, 2=Quite healthy, 3=very healthy
----------	--	---

-----Diarrhoea 2-week recall-----

diar2w1	During the last two weeks (including last day), did \${name}\$ have diarrhoea?	# 0=No, 1=Yes, 9=Don't know
diar2w2	The day \${name}\$ had most loose or watery stools, how many loose or watery stools did \${name}\$ pass?	## times
diar2w3	Did any of the stools contain blood?	# 0=No, 1=Yes, 9=Don't know
diar2w4	Were the stools of different consistency than before \${name}\$ fell ill with diarrhoea?	# 0=No, 1=Yes, 9=Don't know
diar2w5	Did the illness interfere with \${name}\$'s ability to drink or eat?	# 0=No, 1=Yes, 9=Don't know
diar2w6	Did you seek treatment for this?	# 0=No, 1=Yes, 9=Don't know
diar2w7	If yes, where did you go?	# 1=Relatives and friends, 2=Traditional healer, 3=Pharmacy, 4=Government health facility 5=Private health facility, 9=Other
diar2w8	How many days did the diarrhoea last? /	## days

How many days has the diarrhoea lasted?

diar2w9 During the period of illness, did you feed \$name\$ more often, more seldom than or just as often as before the illness started? # 0=Did not change feeding frequency, 1=more seldom, 2=more often 4=Child did not want eat food (Select only 1 - ONE!)

----- Recall on persistent diarrhoea -----

diarper1 Since the last visit (child was around 2 years of age), has \${name}\$ had diarrhoea that lasted 2 weeks or longer? # 0=No, 1=Yes, 9=Don't know
diarper2 Would you please tell me approximately how long the last episode has lasted? ## weeks (if don't know put 99)

diarper3 Did you seek treatment for this? # 0=No, 1=Yes, 9=Don't know
diarper4 Where did you go? # 1=Relatives and friends, 2=Traditional healer, 3=Pharmacy, 4=Government health facility, 5=Private health facility, 9=Other

----- Pneumonia 2-week recall -----

During the last two weeks (including last day), did \${name}\$ have cough, fast breathing or difficult breathing?

pneu2w1 Cough # 0=No, 1=Yes, 9=Don't know

pneu2w2 Fast breathing # 0=No, 1=Yes, 9=Don't know

pneu2w3 Difficult breathing # 0=No, 1=Yes, 9=Don't know

pneu2w4 Did the illness interfere with \${name}\$'s ability to drink or eat? # 0=No, 1=Yes, 9=Don't know

pneu2w5 Did you seek treatment for this? # 0=No, 1=Yes, 9=Don't know

pneu2w6 Where did you go? # 1=Relatives and friends, 2=Traditional healer, 3=Pharmacy, 4=Government health facility, 5=Private health facility, 9=Other

pneu2w7 During the period of illness did you feed \$name\$ more often or less often than before the illness started? # 0=Did not change feeding frequency, 1=more seldom, 2=more often 3=Child did not want eat food (Select only 1 - ONE!)

----- Malaria 1 year recall -----

malaria1 During the past year, did \$name\$ have any episodes of fever? # 0=No, 1=Yes, 9=Don't know

malaria2 During the past year, did \$name\$ have any episodes of chills and rigors? # 0=No, 1=Yes, 9=Don't know
(if no to both 1 & 2, skip the rest of the malaria section)

malaria3 How many episodes of fever and or chills and rigors ## times
has \$name\$ had in the past year (estimate if uncertain)?

malaria4 For any of these episodes, did \$name\$ have convulsions that lasted more than 5 minutes? # 0=No, 1=Yes, 9=Don't know

malaria5 How many times has \$name\$ had fever with convulsions lasting more than 5 minutes? ## times

malaria6 How many of these episodes were confirmed as malaria by health workers or in a health facility? ## times

malaria7 Did you seek treatment for any of these episodes? # 0=No, 1=Yes, 9=Don't know

malaria8 If yes, where did you go for the first episode? # 1=Relatives and friends, 2=Traditional healer, 3=Pharmacy,

		4=Government health facility 5=Private health facility, 9=Other
malaria9	If yes, where did you go for the second episode?	# 1=Relatives and friends, 2=Traditional healer, 3=Pharmacy, 4=Government health facility 5=Private health facility, 9=Other
malaria10	If yes, where did you go for the third episode?	# 1=Relatives and friends, 2=Traditional healer, 3=Pharmacy, 4=Government health facility 5=Private health facility, 9=Other
malaria11	Did \$name\$ receive a blood transfusion?	# 0=No, 1=Yes, 9=Don't know
malaria12	What kind of medicines have you used as treatment during the last year?	# 1=Fansidar 2=Co-Artem or other artemisini 3=Mefloquine/lariam or malaron 4=Quinine, 5=Chloroquine, 6=Septtrin/bactrim 8=Cholaramphenicol or Amoxycil 9=other or don't know

-----Malaria 2 week recall-----

malaria13	During the past 2 weeks, did \$name\$ have any episodes of fever?	# 0=No, 1=Yes, 9=Don't know
malaria14	During the past week, did \$name\$ have any episodes of chills and rigors?	# 0=No, 1=Yes, 9=Don't know
malaria15	How many episodes of fever and or chills and rigors has \$name\$ had in the past weeks (estimate if uncertain)?	## times
malaria16	For any of these episodes, did \$name\$ have convulsions that lasted more than 5 minutes?	# 0=No, 1=Yes, 9=Don't know
malaria17	How many times has \$name\$ had fever with convulsions lasting more than 5 minutes?	## times
malaria18	How many of these episodes were confirmed as malaria by health workers or in a health facility?	## times
malaria19	Did you seek treatment for any of these episodes?	# 0=No, 1=Yes, 9=Don't know
malaria20	If yes, where did you go?	# 1=Relatives and friends, 2=Traditional healer, 3=Pharmacy, 4=Government health facility 5=Private health facility, 9=Other
malaria21	Did \$name\$ receive a blood transfusion?	# 0=No, 1=Yes, 9=Don't know

-----helminths 1 year recall-----

helm1	During the past year, was \$name\$ given deworming medicines [mebendazole, albendazole, praziquantel, ivermectin, DEC etc]?	# 0=No, 1=Yes, 9=Don't know
helm2	If yes, how many times? (estimate if uncertain)	## times
helm3	Is there an available health card for \$name\$?	# 0=No, 1=Yes, 9=Don't know
helm4	Information about deworming in health card:	
helm5a	Deworming (has \$name\$ been given deworming medicines): Has it been given?	# 0=No, 1=Yes, 9=Don't know
helm5b	Number of times	## times
helm5c	Dated in health card?	# 0=No, 1=Yes, 9=Don't know
helm5d	Last date from health card	<dd/mm/yyyy>

-----Injuries -----

injur1 Since birth has your child ever had an injury? # 0=No, 1=Yes, 9=Don't know

Which injury/injuries did the child have?

injur2a Fracture # 0=No, 1=Yes, 9=Don't know

injur2b Tear of the skin # 0=No, 1=Yes, 9=Don't know

injur2c Bruises # 0=No, 1=Yes, 9=Don't know

injur2d Injury of internal organs # 0=No, 1=Yes, 9=Don't know

injur2e Cuts # 0=No, 1=Yes, 9=Don't know

injur2f Traffic accident # 0=No, 1=Yes, 9=Don't know

injur2g Loss of teeth # 0=No, 1=Yes, 9=Don't know

injur2h Burns # 0=No, 1=Yes, 9=Don't know

injur2i Other, specify

What was the cause of the injury/injuries?

injur3a Burning # 0=No, 1=Yes, 9=Don't know

injur3b Poisoning # 0=No, 1=Yes, 9=Don't know

injur3c Animal bites # 0=No, 1=Yes, 9=Don't know

injur3d Cuts # 0=No, 1=Yes, 9=Don't know

injur3e Fall # 0=No, 1=Yes, 9=Don't know

injur3f Traffic accident # 0=No, 1=Yes, 9=Don't know

injur3g Assault # 0=No, 1=Yes, 9=Don't know

injur3h Battering # 0=No, 1=Yes, 9=Don't know

injur3i Sexual abuse # 0=No, 1=Yes, 9=Don't know

injur3j Other, specify

(skip those of the following which are not relevant)

injur4 What agent burnt the child? # 1. Kerosene, 2. Hot water, 3. Acid burn, 4. Petroleum, 5. Candle, 6. Bush fire, 7. Burning house, 8. Other

injur5 What poison did the child take? # 1. Medicine, 2. Paraffin, 3. Alcohol, 4. Mushrooms, 5. Other

injur6 Where did the animal that bit find the child? # 1. In the garden, 2. Inside the house 3. Compound, 4. Other

injur7 Which part of the body was bitten by the animal? # 1. Lower limbs, 2. Foot, 3. Arms, 4. Hands, 5. Trunk, 6. Head

injur8 What instrument caused the cuts? # 1. Razor blade, 2. Knife, 3. Panga, 4. Hoe, 5. Axe, 6. Other

injur9 What assistance did the child receive for the injuries? # 1. First aid at home, 2. First aid at a health centre 3. Admitted to a health unit 4. Treated by a traditional healer, 5. Other

injur10 What was the outcome after the injury/injuries? # 1. Recovered fully, 2. Recovered with some disability, 3. Still sick, 4. Died, 5. Other, 6. Don't know

Has your child ever had any of the following surgical procedures?

injur11a Injections # 0=No, 1=Yes, 9=Don't know

injur11b Taking off blood samples # 0=No, 1=Yes, 9=Don't know

injur11c False teeth extraction # 0=No, 1=Yes, 9=Don't know

injur11d Ear perceiving # 0=No, 1=Yes, 9=Don't know

injur11e Circumcision # 0=No, 1=Yes, 9=Don't know

injur11f Scarification # 0=No, 1=Yes, 9=Don't know

injur11g Incision and drainage # 0=No, 1=Yes, 9=Don't know

injur11h Surgical toilet and suture # 0=No, 1=Yes, 9=Don't know

-----Disabilities -----

disab1 Compared with other children, did <name> have any serious # 0=No, 1=Yes, 9=Don't know
delay in sitting, standing, or walking?

disab2 Compared with other children, does <name> have difficulty # 0=No, 1=Yes, 9=Don't know
seeing, either in the daytime or at night?

disab3 Does <name> appear to have difficulty hearing? # 0=No, 1=Yes, 9=Don't know

disab4 When you tell <name> to do something, does he/she seem # 0=No, 1=Yes, 9=Don't know
to understand what you are saying?

disab5 Does <name> have difficulty in walking or moving his/her arms # 0=No, 1=Yes, 9=Don't know
or does he/she have weakness and/or stiffness in the arms or legs?

disab6 Does <name> sometimes have fits, become rigid, or lose # 0=No, 1=Yes, 9=Don't know
consciousness?

disab7 Does <name> learn to do things like other children his/her # 0=No, 1=Yes, 9=Don't know
age?
disab8 Does <name> speak at all (can he/she make himself/herself # 0=No, 1=Yes, 9=Don't know
understood in words; can he/she say any recognizable words)?
disab9 Is <name>'s speech in any way different from normal? # 0=No, 1=Yes, 9=Don't know
disab10 Compared with other children his/her age, does <name> # 0=No, 1=Yes, 9=Don't know
appear in any way mentally backward, dull or slow?

-----Hospitalisation-----

hosp1 Since birth has \$(name)\$ ever been admitted to hospital? # 0=No, 1=Yes, 9=Don't know
hosp2 How many times has \$(name)\$ been admitted #
to hospital? ## times
hosp3 Was \$name\$ admitted to a hospital or health clinic # 0=No, 1=Yes, 9=Don't know
during the last 3 months?
hosp4 Was this the nearest health unit? # 0=No, 1=Yes, 9=Don't know
hosp5 Why did you go there? # 1=Services better in chosen
facility
2=Easier transport
3=More affordable
4=I wanted to go to the bigges
hospital I can afford
5=I do not trust the people at
the nearest health unit
9=Other
hosp5s Other, specify

-----Hygiene-----

When do you usually wash hands? Use the same code for all
0=Never/rarely
1=Sometimes
2=Usually/Normally
3=Always
hygiene1 Before cooking? #
hygiene2 Before eating? #
hygiene3 Before feeding \$name\$? #
hygiene4 After visiting the toilet? #
hygiene5 Does \$name\$ wash his/her hands before eating? #
hygiene6 Does \$name\$ wash his/her hands after visiting toilet? #
hygiene7 So you use soap when you wash your hands? #
hygiene8 Do you wash \$(name)\$'s hands with soap? #

-----Oral health survey questionnaire-----

Child's oral hygiene behavior and dental attendance

OR1 Before today - have you ever taken your child # 0=No, 1=Yes, 9=Don't know
to a dentist/dental therapist for a check up?
OR2 What is used to clean your child's teeth? # 1=Tooth brush,
2=Chewing stick
3=Cloth
4=Finger
5=Other
OR3 Who usually brushes your child's teeth? # 1=Child, 2=Parent
3=Someone else
4=Teeth not brushed
OR4 How often are the child's teeth cleaned / brushed? # 0=Never,
1=less than once a day
2=Once a day, 3=Twice a day
4=More than twice a day

Questions on Psychosocial and dental disease.

OR5 Has \$(name)\$ ever had toothache? # 0=No, 1=Yes, 9=Don't know
OR6 Has \$(name)\$ ever had swollen and bleeding gums? # 0=No, 1=Yes, 9=Don't know
(Ever seen blood in the child's mouth or when he/she
spits after brushing)
OR7 Has \$(name)\$ ever cried because of pain in the mouth? # 0=No, 1=Yes, 9=Don't know

OR8 Has \${name}\$ ever failed to sleep because of pain in the mouth? # 0=No, 1=Yes, 9=Don't know

OR9 Has \${name}\$ ever refused to eat because of pain in the mouth? # 0=No, 1=Yes, 9=Don't know

OR10 Has \${name}\$ ever refused to play because of pain in the mouth? # 0=No, 1=Yes, 9=Don't know

OR11 Did \${name}\$ experience any symptoms during his/her teeth eruption? # 0=No, 1=Yes, 9=Don't know

OR12 If yes, which of the following symptoms? ## 1=Gum swelling, 2=Gum irritation, 3=Fever, 4=Sleep disturbance, 5=Loss of appetite, 6=Diarrhoea, 7=Increase salivation/drooling, 8=Coughing, 9=Vomiting, 10=Convulsions

SECTION F: Family Impact Scale

Use the same codes for questions below:
 0=Never, 1=Once/twice
 3=Sometimes, 4=Often
 5=Almost daily

OR13 How often have you or the other parent taken time off work due to \${name}'s\$ oral (gum/teeth) problem. #

OR14 How often have your child required more attention from you or the other parent due to \${name}'s\$ oral problems. #

OR15 How often have you or the other parent had less time for yourself due to \${name}'s\$ oral problems? #

OR16 How often has your own sleep and the sleep of the other parent been disturbed due to \${name}'s\$ problem with mouth and teeth? #

OR17 How often have ordinary family activities been disturbed due to child's mouth/teeth problems? #

OR18 Have you or other parent been upset by the child's mouth/teeth problems? #

OR19 Have you or other parent felt guilty about the child's mouth/teeth problems? #

OR20 Has \${name}'s\$ pain in the mouth ever caused disagreement or conflict in the family? #

OR21 Has the teeth problems of \${name}\$ ever caused financial loss/difficulties for the family? #

OR22 I general how would you describe the oral health condition of your child? # 1=good, 2=neither good or bad, 3=bad

OR23 Has your child used sweetened cough syrup for a longer period? # 0=No, 1=Yes,

-----Adult oral health survey questionnaire-----

01 Do you brush your teeth? # 0=No, 1=Yes, 9=Don't know

02 If yes to 1, what device do you use? # 1=Plastic tooth brush, 2=Chewing stick, 3=Other

03 How often do you brush? # 0=never, 1=Occasionally, 2=Once a day, 3=More than once a day

04 Do you use toothpaste when brushing your teeth? # 0=No, 1=Yes, 9=Don't know

05 If yes to 4, which toothpaste do you use? _____

06 If no to 4, what alternative substance do you use? _____

DIETARY HABITS

07 Do you eat or take sugared snacks? # 0=No, 1=Yes, 9=Don't know

08 How often? # 0=never, 1=Occasionally

2=Once a day
3=More than once a day

09a Mention the snacks you often take
Cakes # 0=No, 1=Yes, 9=Don't know
09b Ice cream # 0=No, 1=Yes, 9=Don't know
09c Biscuits # 0=No, 1=Yes, 9=Don't know
09d Chocolates # 0=No, 1=Yes, 9=Don't know
09e Others, specify

010 Do you take sugared drinks? # 0=No, 1=Yes, 9=Don't know

011 How often? # 0=never
1=Occasionally
2=Once a day
3=More than once a day

012 Which sugared drinks do you usually take?

-----SUBJECTIVE MEASURES OF ORAL AND GENERAL HEALTH-----

013 Percieved general health status # 1=Very poor, 2=Poor
3=Fair, 4=Good, 5=Very good

014 Perceived oral health status # 1=Very poor, 2=Poor
3=Fair, 4=Good, 5=Very good

015 During the previous 6 months have you had pain from gums? # 0=No, 1=Yes, 9=Don't know

016 During the previous 6 months have you had toothache? # 0=No, 1=Yes, 9=Don't know
3=To some extent,
4=Considerably
5=A great deal

017 Perceived need for dental treatment # 1=Not at all, 2=Very little
3=To some extent,
4=Considerably
5=A great deal

018 Perceived dental pain in mouth in past six months # 0=No, 1=Yes, not severe
2=Yes, severe,
3=Yes, very severe

-----Prevalence of oral impacts on daily performances-----

During the past six months, has problems related to your mouth affected any of the following daily activities?

019 Eating food # 0=No, 1=Yes, 9=Don't know
020 Speaking # 0=No, 1=Yes, 9=Don't know
021 Cleaning your teeth and dentures # 0=No, 1=Yes, 9=Don't know
022 Doing light physical activities # 0=No, 1=Yes, 9=Don't know
023 Going out # 0=No, 1=Yes, 9=Don't know
024 Sleeping # 0=No, 1=Yes, 9=Don't know
025 Relaxing # 0=No, 1=Yes, 9=Don't know
026 Smiling, laughing without embarrassment # 0=No, 1=Yes, 9=Don't know
027 Emotional state;becoming easily upset # 0=No, 1=Yes, 9=Don't know
028 Enjoying the contact of other people # 0=No, 1=Yes, 9=Don't know
029 Carrying out main role or work # 0=No, 1=Yes, 9=Don't know

030 Any other impact (specify)

-----Antropometry and clinical examination -----

weight5y	Child's weight (kg)	##.# kg
height5y	Child's height (cm)	###.# cm
oedema	Does the child have pretibial oedema (feet/legs)?		# 0=No, 1=Yes, 9=Don't know
spleen	Palpation of spleen (est. centimetres below the ribs)	## cm
comments	Any comments: (Optional)	
		
		
		

WHO ORAL HEALTH ASSESSMENT FORM (1997)

Country.....

Leave blank (1) <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> (4)	Year Month (5) <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> (8)	Day (9) <input type="text"/> <input type="text"/> (10)	Identification number (11) <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> (14)	Examiner <input type="text"/> (15)	Original/duplicate <input type="text"/> (16)
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GENERAL INFORMATION		OTHER DATA (specify and provide codes)	
Name		<input type="text"/> (29)	
Date of birth	(17) <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> (20)	Occupation	<input type="text"/> (25)
Age in years	(21) <input type="text"/> <input type="text"/> (22)	Geographical location	(26) <input type="text"/> <input type="text"/> (27)
Sex (M = 1, F = 2)	<input type="text"/> (23)	Location type:	<input type="text"/> (28)
Ethnic group	<input type="text"/> (24)	1 = Urban	
		2 = Periurban	
		3 = Rural	
		CONTRAINDICATION TO EXAMINATION	
		Reason:	
		<input type="text"/> (31)	
		0 = No	
		1 = Yes	

CLINICAL ASSESSMENT	
<p>EXTRA-ORAL EXAMINATION</p> <p>0 = Normal extra-oral appearance</p> <p>1 = Ulceration, sores, erosions, fissures (head, neck, limbs)</p> <p>2 = Ulceration, sores, erosions, fissures (nose, cheeks, chin)</p> <p>3 = Ulceration, sores, erosions, fissures (commissures) <input type="text"/> (32)</p> <p>4 = Ulceration, sores, erosions, fissures (vermillion border)</p> <p>5 = Cancrum oris</p> <p>6 = Abnormalities of upper and lower lips</p> <p>7 = Enlarged lymph nodes (head, neck)</p> <p>8 = Other swellings of face and jaws</p> <p>9 = Not recorded</p>	<p>TEMPOROMANDIBULAR JOINT ASSESSMENT</p> <p>SYMPTOMS</p> <p>0 = No</p> <p>1 = Yes</p> <p>9 = Not recorded</p> <p><input type="text"/> (33)</p> <p>SIGNS</p> <p>0 = No</p> <p>1 = Yes</p> <p>9 = Not recorded</p> <p>Clicking <input type="text"/> (34)</p> <p>Tenderness (on palpation) <input type="text"/> (35)</p> <p>Reduced jaw mobility (< 30 mm opening) <input type="text"/> (36)</p>

ORAL MUCOSA	
<p>CONDITION</p> <p>0 = No abnormal condition</p> <p>1 = Malignant tumour (oral cancer)</p> <p>2 = Leukoplakia</p> <p>3 = Lichen planus</p> <p>4 = Ulceration (aphthous, herpetic, traumatic)</p> <p>5 = Acute necrotizing gingivitis</p> <p>6 = Candidiasis</p> <p>7 = Abscess</p> <p>8 = Other condition (specify if possible)</p> <p>9 = Not recorded</p>	<p>LOCATION</p> <p>0 = Vermillion border</p> <p>1 = Commissures</p> <p>2 = Lips</p> <p>3 = Sulci</p> <p>4 = Buccal mucosa</p> <p>5 = Floor of mouth</p> <p>6 = Tongue</p> <p>7 = Hard and/or soft palate</p> <p>8 = Alveolar ridges/gingiva</p> <p>9 = Not recorded</p>
(37) <input type="text"/> <input type="text"/> (40)	
(38) <input type="text"/> <input type="text"/> (41)	
(39) <input type="text"/> <input type="text"/> (42)	

<p>ENAMEL OPACITIES/HYPOPLASIA</p> <p>Permanent teeth</p> <p>0 = Normal</p> <p>1 = Demarcated opacity</p> <p>2 = Diffuse opacity</p> <p>3 = Hypoplasia</p> <p>4 = Other defects</p> <p>5 = Demarcated and diffuse opacities</p> <p>6 = Demarcated opacity and hypoplasia</p> <p>7 = Diffuse opacity and hypoplasia</p> <p>8 = All three conditions</p> <p>9 = Not recorded</p>	<p>DENTAL FLUOROSIS</p> <p>0 = Normal</p> <p>1 = Questionable</p> <p>2 = Very mild</p> <p>3 = Mild</p> <p>4 = Moderate</p> <p>5 = Severe</p> <p>8 = Excluded</p> <p>9 = Not recorded</p>										
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46	36										

<p>COMMUNITY PERIODONTAL INDEX (CPI)</p> <p>0 = Healthy</p> <p>1 = Bleeding</p> <p>2 = Calculus</p> <p>3* = Pocket 4-5 mm (black band on probe partially visible)</p> <p>4* = Pocket 6 mm or more (black band on probe not visible)</p> <p>X = Excluded sextant</p> <p>9 = Not recorded</p>	<p>LOSS OF ATTACHMENT*</p> <p>0 = 0-3 mm</p> <p>1 = 4-5 mm (cementoamel junction (CEJ) within black band)</p> <p>2 = 6-8 mm (CEJ between upper limit of black band and 8.5-mm ring)</p> <p>3 = 9-11 mm (CEJ between 8.5-mm and 11.5-mm rings)</p> <p>4 = 12 mm or more (CEJ beyond 11.5-mm ring)</p> <p>X = Excluded sextant</p> <p>9 = Not recorded</p>								
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* Not recorded under 15 years of age

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