

Supplementary table 1. Summary table. Breastfeeding, formula feeding and/or introduction of solids and outcome growth and overweight/obesity

Author (alphabetical order), year (ref.nr)	Study design (study name if applicable)	No. and type of included studies (SLR)/ No. of participants (cohort study)	Exposure (incl age)	Outcome (incl age)	Effect/association	Study quality	Comments
Aarts et al, 2003 (26)	Prospective cohort (one of the seven in WHO, 2002)	147 excl brf, 325 not excl brf	Excl brf 4-6 mo	Growth 0-6 mo	Growth 0-6 mo similar between excl brf infants and infants with a high rate of brf (but not excl brf)	B	Power calculation done for fertility – not growth.
Chivers et al, 2010 (27)	Prospective cohort	1330 (had mothers education and 1320 had BF category <4months or >4months)	Brf+Compl (other milk introd) ≤4months or >4months	Adiposity rebound and overweight at 14 years of age. BMI over time.	BMI consistently higher for those with BF≤4 months compared to BF > 4 months significant when adjusted for confounders. Timing of adiposity rebound lower.	B	Physical activity, sample size and power calculations not reported and by chance finding not considered.
Cole et al, 2002 (28)	Prospective cohort (Cambridge Infant Growth Study)	120 infants weighed every 4 wk from birth to 52 wk, (+at 18 mo and 24 mo)	fed breast milk (with no formula) for at least 24 wk, with solids introduced at a mean age of 15 wk	New median weight curves were constructed and compared with the British 1990 reference curves.	The British 1990 reference, reflects the growth of long-term breastfed infants only imperfectly, with mean weight falling by 0.5 SDS from 2 to 12 mo.	B	No power calculation, no details of how feeding history was collected.
de Hoog et al, 2011 (29)	Prospective cohort (ABCD-study)	2998 (Original number difficult to ascertain)	Infant feeding duration of breast-feeding: (none, ,1 mo, 1–3 mo, 4–6 mo and >6 mo); age at the introduction of formula feeding (none, ,1 mo, 1–3 mo, 4–6 mo and >6 mo); age at the introduction of complementary food (<4 mo, 4 mo, 5 mo and >5 mo).	Ethnic differences in growth during first 6 mo. weight, length and weight-for-length SDS at 6 mo minus SDS at 4 w	The growth rate was higher in almost all ethnic minorities, with b between 0·07 and 0·41 for DSDS weight and between 0·12 and 0·42 for DSDS length, compared with ethnic Dutch infants. DSDS weight-for-length was similar across groups, except for Moroccan infants (b 0·25, P,0·05) after correction for confounders. In general, exclusive breast-feeding for 4 months was associated with slower growth for all three growth measures. Feeding factors explained, to a small degree, the higher weight and length gain in African descent infants, but not the higher DSDS weight-for-length in the Moroccan population.	B	No power calculation, no definition of excl brf, do not refer to the new WHO growth curves
de Kroon et al, 2011 (30)	Prospective cohort <i>The Terneuzen Birth Cohort</i> , Netherlands	810 out of 822 58% females	Excl brf duration (only brf and formula considered) 0-15 d, 16-45, 46-74, 75-104, 105-134, 135-164, 165+ (=0, 1, 2, 3, 4, 5 and 6 mo)	BMI, body fat at 18-28 y	Sig inverse dose-response of brf-duration for BMI (β -0.13, SE 0.06), WC (β -0.39, SE 0.18) and WHR (β -0.004, SE 0.001) after correction for age, gender and confounders. More positive dietary behavior with excl brf; OR of excl brf in mo for a breakfast frequency of $\geq 5/w$ 1.15 (95% CI 1.06-1.27) and snack consumption $<2/w$ 1.15 (1.06-1.25). The direction the same for other dietary outcomes (I e	B	No power calculation, duration of excl brf does not include solids

					positive) but not significant.		
Durmus et al, 2011 (31)	Prospective cohort <i>Generation R study</i> , Netherlands	5047 out of 7295 (70%)	Brf never vs ever, Brf duration; 1) never, 2) 0-3 mo, 3-6 mo, 6-12 mo) Excl brf; 1) never, 2) partially until 4 mo, 3) exclusive until 4 mo (good definition of exclusive)	Growth rate (change is SDS in age intervals between 0-3, 3-6 and 6-12 mo) Overweight (BMI>1.1-2.3 SDS = appr adult BMI 25-30), and obesity (BMI>2.3 SDS) at 3 y	No association between brf duration and exclusivity with growth rates between 0-3 mo. Shorter brf associated with increased gain in age- and sex adjusted SDS for length, weight and BMI between 3 and 6 mo (P for trend <0.05). Similar tendencies were seen for brf exclusivity. Brf duration and exclusivity were not consistently associated with risk of OW and OB at 1, 2 and 3 y.	B	No power calculation
Gubbels et al, 2011 (32)	Prospective cohort study	1863	Breastfeeding duration in months vs. formula feeding, feeding pattern (on demand, to schedule, mixed)	Weight gain in the first year, BMI and overweight up to 4 y.	Each additional month of brf was associated with less weight gain in the first year (regression coefficient B = - 37.6 g, p < 0.001), a lower BMI z-score at age 1 (B = -0.02, p < 0.01), and a lower odds of being overweight at age 1 y (OR=0.96, p < 0.05)	B	An additional alternative recruitment group; healthy pregnant group, recruited through alternative lifestyle channel Parental reported child data on anthropometry. Sample size reported, but not study power and power calculations By chance findings not considered
Huh et al, 2010 (33)	Prospective cohort <i>Project Viva</i> , USA	847 children of 1579 eligible (54%)	Introduction of solid foods at <4, 4-5 and ≥6 mo analysed separately among infants brf for ≥4 mo (<i>breastfed</i> , n=568, 67%) or never breastfed or stopped breastfeeding <4 mo (<i>formula fed</i> , n=279, 32%)	Obesity at 3 y (BMI for age and gender ≥95 th percentile) + Subscapular and triceps skin fold thickness	Among breastfed infants timing of solid food was not associated with obesity at 3y; OR 1.1 (95% CI 0.3-4.4) Among formula-fed infants (or weaned <4 mo), intro of solids <4 mo associated with obesity (not explained by rapid early growth); OR 6.3 (2.3-6.9) Skinfold non-sig	B	Loss to follow-up 46% No power calculation No other dietary intake or physical activity accounted for. Never breastfed and brf>4 mo = one group
Ip et al, 2009 (22)	For obesity – 3 SLR and meta-analysis of good and fair quality	Study 1: >69 000 Study 2: 120 831 Study 3: 298 900 61 studies (35	2 studies ever vs never, 1 study brf ≥2mo vs never	Study 1 Overweight/obesity at 5-18 y (graded A) Study 2. (graded B) Study 3. Adiposity	A history of brf is associated with a reduced risk for obesity later in life. Observed association could reflect selective reporting and/or publication bias. Pooled adjusted OR: ever vs never Arenz 0.76 (95% CI 0.67-0.86) Owen: 0.93 (0.88-0.99) Harder: 0.96/month of brf (0.94-0.98) unadjusted	A	

		observational, 18 cohort, 7 cross-sectional, 1 case-control)		in later life(graded B)			
Kalies et al, 2005 (34)	Prospective cohort <i>LISA study group</i> , Germany	2624 out of 3097 (85%)	Duration of exclusive breastfeeding was defined as the number of months breastfed without concomitant feeding of infant's formula and classified a priori as <6 mo or ≥6 mo, and for dose-response-analysis in the categories: 0-1 mo (incl 6.8% never brf), 2-3 mo, 4-5 mo, ≥6 mo.	Elevated weight gain at 2 y (>90 th percentile for age and gender)	Excl brf <6 mo had a greater risk of elevated weight gain at 2 y; OR 1.65 (95% CI 1.17-2.30) Effect dose-dependant brf 0-1 mo; OR 1.99 (1.34-2.97)	B	No power calculation Excl brf does not consider solids
Kitsantas & Gaffney 2010 (35)	Prospective cohort	6519	Brf duration in months	Anthropometry and BMI	Normal BMI preschoolers had been breastfed longer (1.9 mo vs 1.7 mo) than overweight/obese	B	Study power not considered, power calculation not performed. By chance findings not considered
Kramer & Kakuma, 2002 (2)	Overall SLR + meta-analysis when appropriate.	Only developed countries a)4388 b)3450 c)3430 d)3455 only controlled clinical trials and observational studies.	Brf; exclusive 6 mo vs. exclusive 3-4 mo with mixed brf	Growth (weight, length, and head circumference (The aim was to examine whether or not exclusive breastfeeding for 6 mo has an impact on growth (and other outcomes))	Infants breastfed exclusively for six or more months had no observable deficits in growth: <u>a) Weight gain 3-8 mo:</u> pooled WMD of -12.45 (95% CI -23.46 to -1.44) g/mo (data id heterogeneity) <u>b)Weight gain 8-12 mo:</u> pooled WMD was -1.82 (95% CI -16.72 to +13.08) g/mo <u>c)Length gain 3-8 mo:</u> pooled analysis yielded a WMD of -0.4 (95% CI -0.7 to 0.0) mm/mo <u>d)Length gain 8-12 mo:</u> slightly but significantly higher length gain in the EBF group (WMD +0.9 (95% CI +0.3 to +1.4)) mm/mo	A	
Kramer et al, 2007a (36)	Prospective cohort (Cluster-randomized trial) The PROBIT -study	13889 of totally 17046	Duration of any brf in months, exclusive brf 3 mo or 6 mo:	Anthropometry (height, weight, head, waist, hip, mid upper arm, mid thigh) skinfold, blood pressure at 6.5 y, adiposity at 6.5 y	No significant intervention effects were observed on adiposity, stature, height, waist or hip circumference, triceps or subscapular skinfold thickness. (Note in conclusion: Previously reported beneficial effects on these outcomes may be the result of uncontrolled confounding and selection bias)	B	No power calculation for these outcomes (power calculation done on outcome gastroenteritis) The results are not validated blind but double checked with blinded methods.
Kramer et al, 2009a (37)	Prospective cohort	2951 of totally 3483 followed	Duration of any brf in months, exclusive brf	Anthropometry (height, weight;	BMI, triceps skinfold thickness, and hip circumference were higher in the EBF6 group vs	B	No power calculation for these outcomes

	(Cluster-randomized trial) The PROBIT-study	during the first year	3 mo or 6 mo:	head-, waist-, hip-, and mid-thigh circumference; skinfold thickness) at 6.5 y	EBF3 group. Adjusted difference Excl brf 6 mo vs Excl brf 3 mo (95% CI): BMI 0.3 (0.1-0.4) Triceps skinfold (mm) 0.4 (0.03, 0.4) Hip circumference (cm) 0.6 (0.1, 1.1)		(power calculation done on outcome gastroenteritis) The results are not validated blind but double checked with blinded methods.
Kramer et al, 2011 (38)	Prospective cohort (Cluster-randomized trial) The PROBIT-study	17046	Duration of any brf in months, exclusive brf 3 mo or 6 mo:	Anthropometry (height, weight) at 6.5 y	Smaller size (especially weight for age) was strongly and statistically significantly associated with increased risks of subsequent weaning and of discontinuing exclusive breastfeeding (adjusted odds ratios = 1.2-1.6), especially between 2 and 6 months, even after adjustment for potential confounding factors and clustered measurement.	B	No attempts to standardize anthropometric measurements (because infant growth was not a major outcome of Probit). No power calculation for these outcomes (power calculation done on outcome gastroenteritis) The results are not validated blind but double checked with blinded methods.
Monasta, 2010 (23)	SLR	varies	Analysis done for duration in general, of excl and partial brf.	Age range in years for the 7 key studies (confirmed by later search to come to the conclusion): 10:2-26, 131:0.5-33, Horta:1-66, 152:0-33, 295:0-33, 294:1-64 (BMI), 301: not specified. Overweight and obesity in childhood or later in life.	10: OR 0.78 (95%CI:0.71-0.85); 131: OR 0.96 (95%CI:0.94-0.98); Horta: OR 0.78 (95%CI:0.72-0.84); 152:incl 3 SLR, weaker when adj f number of factors; 295: OR 0.86 (95%CI:0.81-0.91) – OR 0.93 (95%CI:0.88-0.99); 294:lower BMI w/BF OR 0.04 (95%CI: (0.05) – (-0.02)); 301: OR 0.75 (95%CI:0.71-0.79).	B	Publication bias not assessed, some characteristics not included) and methodology of dietary intake not exact
Moorcroft, 2011 (24)	SLR. 24 papers were included in the SLR (1 RCT, re-analysis of data from 2 RCTs, 20 cohort studies and 1 case-control study).	Reported number in 24 studies : 80 – 3768	Introduction of solids between 12-20 weeks	Overweight and obesity in childhood 6mo – 3years	Conclusion: No clear association. Though of the 27 observations in Table 2 there is an association between early introduction of solid and later weight in 10 observations and none in the rest. The reverse is never seen.	B	Publication bias not assessed, some characteristics not included, 8 (RQ hard, studies not designed for RQ), conflict of interest not stated for included studies

Oddy et al, 2006 (39)	Birth cohort, <i>Second Perth Infant Feeding Study (PIFSI II)</i> , Perth, Australia	587 of 870 contacted (68%) and of 1068 eligible (55 %)	Duration of full breastfeeding: <4 wk vs \geq 4 wk (also considered as continuous variable), and age regular infant formula feeding commenced	Growth, overweight (>85 th percentile of weight/length)	By 52 wk, infants who had been fully brf for at least 4 wk were lighter (9731 g vs 10138 g; $P=0.041$) and shorter (73.7 cm vs 75.6 cm; $P=0.001$) than infants who had received infant formula by 4 wk. These results were stronger for boys and for babies less than 3500 g at birth. Overweight infants were more likely to have been given formula feeds at an earlier age (Kaplan Meier Log Rank Test = 6.70; $P=0.001$) than normal weight infants.	B	No power calculations.
Rebhan et al, 2009 (40)	Prospective cohort	1901	Brf exclusively for > or =6 months (group A), fully/exclusively > or =4 months, but not exclusively > or =6 months (group B); infants not breastfed/breastfed <4 months (group C)	Parents reported weight and length 1st day of life, age of 3-10 days, 4-6 weeks, 3-4 mo, and 6-7 mo	The application of the World Health Organization (WHO)-child growth standards showed lower weight-for-length z-scores in first days of life in group C versus groups A and B, whereas in months 6/7 group C showed the highest scores.	B	Some important confounders not included, only 9 mo follow-up, no power calculations
Rzehak et al, 2009 (41)	Prospective cohort	7643	Full-brf at least 4 mo	Weight, length, BMI	The difference in the velocity of weight gain for breastfed vs. other children is -18 g/month in the first 3 month, -93 g/month between month 3 and 6, -14 g/month between month 6 and 12 and -3 g/month beyond the 24th month. Infants fully-breastfed gain less weight, but grow equally in length in the first 12 months of life versus mixed or formula-fed children. Velocities in length are not different between breastfed and non-breastfed children. Over time, a slightly lower risk (difference < 2%) of being overweight was estimated for breastfed children. The protective effect of breastfeeding on becoming overweight is related to its weight-velocity-modifying-effect in early infancy.	B	2 groups based on family history of allergy, breastfeeding definition= at least 4 mo, no total duration and no definition of full breastfeeding (=exclusive?)
Scholtens et al, 2007 (42)	Prospective cohort	2347	Breastfeeding duration and diet and lifestyle factors at 7 y	Overweight as BMI (height, weight) at 1 y and 7 y	Compared with nonbreastfed children, children breastfed for >16 weeks had a lower BMI at 1 year of age, after adjustment for confounders (beta = -0.22, 95% confidence interval: -0.39, -0.06). The association between breastfeeding and BMI between 1 and 7 years of age was negligible, while a high BMI at 1 year of age was strongly associated with a high BMI between 1 and 7 years of age in the same model. These findings suggest that the lower BMI and lower risk of overweight among breastfed children later in life are already achieved at 1 year of age.	B	No power calculations, no identification of confounders
Scholtens et	Prospective	2043	Breastfeeding	Overweight as BMI	Breastfeeding for >16 weeks was significantly	A	

al, 2008 (43)	cohort		duration and diet and lifestyle factors at 7 y	(height, weight) at 8 y	associated with a lower overweight risk at 8 years (adjusted odds ratio: 0.67, 95% confidence interval: 0.47-0.97), and the association hardly changed after adjustment for diet (adjusted odds ratio: 0.71, 95% confidence interval: 0.49-1.03).		
Van Rossem et al, 2010 (44)	Prospective cohort study	884 mother-infant pair of 2128 women who delivered a live infant, 1579 were eligible for a 3-y follow-up, after 1244 loss to follow-up and excluded, the study sample was 884	Brf the first 6 mo of life, 4 categories: “never brf”, “any brf for less than 6 mo”, “partial brf for 6 mo”, “full brf for 6 mo”. (solids or liquids other than breast milk and formula not considered) In addition, a continuous duration of Brf (to 12 mo)	At 3 y: age- and sex-specific BMI z score, the sum of subscapular and triceps skinfold thicknesses (SS+TR) (a measurement of subcutaneous adiposity) and obesity. Obesity defined as BMI for age and sex $\geq 95^{\text{th}}$ percentile	At 3 y of age, adj BMI z-score of fully brf at 6 mo was 0.17 (95% CI: -0.43, 0.09) units lower than never brf. After additional adjustment for infant weight change, the estimate for BMI z-score was attenuated (-0.03, 95% CI: -0.27, 0.20), and estimates for SS + TR modestly attenuated (from -1.48 mm (95% CI: -2.52, -0.44) to -1.16 mm (95% CI: -2.18, -0.14), and for the odds of being obese from 0.21 (95% CI: 0.07, 0.68) to 0.29 (95% CI: 0.08, 1.05). For each month a child was brf until the age of 6 mo, the decrement in BMI z score was 0.04 units (95% CI: -0.07, -0.01) and the decrement in SS + TR was 0.19 mm (95% CI: -0.31, -0.07) and the odds of being obese was reduced by 8% (95% CI: -2% to -18%)	B	Loss to follow-up >30%. Sample size reported, but not study power and power calculations. By chance findings not considered
WHO, 2002 (25)	Prospective cohort (7 country) Analysis done for n=1252	7 countries with 500-700/country Data from the World Health Organization Multinational Study of Breast-feeding and Lactational Amenorrhea on infants living in generally favorable environments were used.	Differential timing and content of complementary food	Growth 0-32 w (8 mo)	Postnatal growth appears to not be sensitive to differential timing. Type or frequency of introduction of complementary foods in healthy infants living in environments without major economic constraints and low rates of illness. Based on the relatively small effects found, even though significant, the authors concluded that the results did not provide evidence of benefit or risk related to growth because of timing of giving complementary foods nor to differential types and frequencies of complementary foods between 4-6 months of age in healthy infants living in environments without major economic restraints and low rates of illness.	B	Power calculation done for fertility – not growth. 7 of 9 participating countries not compatible with Nordic population

- WHO Multicentre Growth Reference Study Group, 2006 (45). Primary growth data and related information were gathered from 8440 healthy breastfed infants and young children from widely diverse ethnic backgrounds and cultural settings (i.e. Brazil, Ghana, India, Norway, Oman and USA). The study resulted in new growth charts showing slower growth of the breastfed infants from about two-three months of age compared to previous international growth charts of infants given formula and other food.
- Horta et al; WHO, 2007 (21). States that the risk for overweight/obesity in childhood and adolescence was 20 % (1-9 y) - 30 % (9-19 y) lower among breastfed subjects compared with non-breastfed. Difference for >19 y was not significant. Pooled OR (95% CI) 0.79 (0.71 to 0.87), 0.69 (0.60 to 0.80) and 0.88 (0.74 to 1.04), respectively.

- SACN, 2011 (20). Infants who are not breastfed are more likely to be obese in later life. Strategies that promote, protect and support exclusive breastfeeding for a round the first 6 months of an infant's life should be enhanced, and should recognize the benefits for long-term health.

Supplementary table 2. Summary table. Breastfeeding, formula feeding and/or introduction of solids and outcome blood pressure

Author (alphabetical order), year (ref.nr)	Study design (study name if applicable)	No. and type of included studies (SLR)/ No. of participants (cohort study)	Exposure (incl age)	Outcome (incl age)	Effect/association	Study quality	Comments
de Jonge et al, 2010 (46)	Prospective study (<i>Generation R-study</i>)	807-845 of 1071 (75-79%)	Brf; 1) never, 2) partially, 3) exclusive for >=4 mo (good definition of exclusive)	Left cardiac structures and blood pressure at 2 y	No differences in cardiac structures and blood pressure at 2 y observed between breastfed and non-breastfed children. Duration and exclusivity of brf not consistently associated with outcomes.	B	No power calculation
Ip et al, 2009 (22)	2 meta-analysis of a total of 26 studies of various design (13 studies included in both meta-analysis). Both studies graded B.	Total 37 266 subjects Martin 2005: Meta-analysis of 15 studies (Observations within 2RCTs, 8 prospective cohorts, 1 retrospective cohort, and 4 cross-sectional studies) Owen, 2003: Meta-analysis of 24 studies (Observations within 1RCT, 12 cross-sectional, and 11 cohort studies)	Breastfeeding vs formula feeding in infancy	Systolic and diastolic blood pressure at 1-60 y/1-71 y	An association between a history of breastfeeding during infancy and a small reduction in adult blood pressure, but the clinical or public health implication of the finding is unclear. SBP -1.4 (-2.2, -0.6) and -1.10 (-1.8, -0.4) respectively DBP -0.5 (-0.9, -0.04) and -0.36 (-0.79, 0.08) respectively	A	Although both analyses had moderate methodological quality and reported similar findings, the authors had different appraisals of the public health importance of the small reduction in systolic blood pressure.
Kramer et al, 2007a (36)	Prospective cohort (Cluster-randomized trial) The PROBIT-study	13889 of totally 17046	Duration of any brf in months, exclusive brf 3 mo or 6 mo:	Blood pressure at 6.5 y	No significant differences in blood pressure between those exclusively brf for 3 mo vs 6 mo	B	No power calculation for these outcomes (power calculation done on outcome gastroenteritis) The results are not validated blind but double checked with blinded methods.
Kramer et al, 2009a (37)	Prospective cohort	2951 of totally 3483 followed	Duration of any brf in months, exclusive brf	Blood pressure at 6.5 y	No significant differences in blood pressure between those exclusively brf for 3 mo vs 6 mo	B	No power calculation for these outcomes

	(Cluster-randomized trial) The PROBIT-study	during the first year	3 mo or 6 mo:				(power calculation done on outcome gastroenteritis) The results are not validated blind but double checked with blinded methods.
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- Horta et al; WHO, 2007 (21). Subjects who were breastfed experienced lower mean systolic blood pressure. The difference was statistically significant, but the magnitude was relatively modest (decreased by slightly more than 1 mmHg).
- SACN, 2011 (20). conclude that infants who are breastfed tend to have slightly lower blood pressure although there is inconsistent evidence that breastfeeding influences subsequent cardiovascular mortality Strategies that promote, protect and support exclusive breastfeeding for a round the first 6 months of an infant's life should be enhanced, and should recognize the benefits for long-term health.

Supplementary table 3. Summary table. Breastfeeding, formula feeding and/or introduction of solids and outcome serum cholesterol

Author (alphabetical order), year (ref.nr)	Study design (study name if applicable)	No. and type of included studies (SLR)/ No. of participants (cohort study)	Exposure (incl age)	Outcome (incl age)	Effect/association	Study quality	Comments
Ip et al, 2009 (22)	One meta-analysis (graded C) of 27 cohort and 13 cross-sectional studies	10 681 subjects (5 829 breastfed and 4 852 formula-fed) Infancy (<1 y, 26 studies), childhood/adolescence (1-16 y, 17 studies) and/or adulthood (17-65 y, 9 studies).	Breastfeeding vs no breastfeeding	Cholesterol levels in infancy (<1 y), childhood/adolescence (1-16 y) and adulthood (17-65 y)	In 25 of 26 observations, infants who were breastfed reported higher mean total cholesterol levels compared with infants who were formula-fed. The overall mean difference was +24.75 mg/dL (95% CI 18.95 to 30.55). In 16 of 17 observations, the mean total cholesterol levels in children or adolescents who were breastfed in their infancy were similar to those who were formula-fed. The overall mean difference was 0.0 mg/dL (95% CI -2.7 to 2.7 mg/dL). Lower mean total cholesterol levels in adults who were breastfed in their infancy compared with those who were formula-fed in their infancy were reported in seven of nine observations. The overall mean difference was -6.96 mg/dL (95% CI -2.32 to -11.6 mg/dL).	A	Ip et al state that no conclusions can be drawn about the evidence based on this meta-analysis since it was graded C (due to data based on individuals with a wide age range, gender and other confounders were not explicitly analysed, detailed information (e.g. fasting or not fasting) on the collection of specimen for cholesterol testing not included.
Owen et al, 2008 (47)	Overall SLR + meta-analysis	17498 (12890 bfr, 4608 formula-fed)	Brf (ever) and formula fed	Total cholesterol concentration	Mean total blood cholesterol was lower ($P = 0.037$) among those ever breastfed than among those fed formula milk (mean difference: -0.04 mmol/L; 95% CI: -0.08, 0.00 mmol/L). The difference in cholesterol between infant feeding groups was larger ($P = 0.005$) and more consistent in 7 studies that analyzed "exclusive" feeding patterns (-0.15 mmol/L; -0.23, -0.06 mmol/L) than in 10 studies that analyzed nonexclusive feeding patterns (-0.01 mmol/L; -0.06, 0.03 mmol/L). Adjustment for potential confounders including socioeconomic position, body mass index, and smoking status in adult life had minimal effect on these estimates.	A	

- Horta et al; WHO, 2007 (21). Adults who had been breastfed experienced lower total cholesterol compared with non-breastfed. The difference was statistically significant, but the magnitude was relatively modest (mean difference: -0.18; 95% CI: -0.30 to -0.06 mmol/L).
- SACN, 2011 (20). Infants who are breastfed tend to have slightly lower total serum cholesterol concentrations in adult life although there is inconsistent evidence that breastfeeding influences subsequent cardiovascular mortality. Strategies that promote, protect and support exclusive breastfeeding for about the first 6 months of an infant's life should be enhanced, and should recognize the benefits for long-term health.

Supplementary table 4. Summary table. Breastfeeding, formula feeding and/or introduction of solids and outcome diabetes type 1 (T1DM) and type 2 (T2DM)

Author (alphabetical order), year (ref.nr)	Study design (study name if applicable)	No. and type of included studies (SLR)/ No. of participants (cohort study)	Exposure (incl age)	Outcome (incl age)	Effect/association	Study quality	Comments
Couper et al, 2009 (49)	Prospective cohort	548, of which 17 had more than 1 first degree relative with T1DM	Weight gain; Brf; Exclusive and Total 0 month, >0-3 months, >3months. Age of intro cow's milk, gluten, non-gluten. Breast-fed at intro of cereals and cow's milk.	Islet autoimmunity (higher risk of later development of T1DM in later life)	The study showed no effect of breast-feeding or other diet variables, but being above average in weight in early life, especially the first 2 years, increase the risk of islet cell autoimmunity in children with first degree relative with type 1 diabetes Weight gain as weight z score predicted hazard ratio=1.43 (95% CI:1.10-1.84), and BMI z score hazard ratio=1.29(95CI:1.01-1.67). The risk among those with z score >0 larger than <0. Also weight and BMI z score at 2 years as well as change from birth to 2 years predicted risk of islet autoimmunity. The authors point out the interaction between the diet and weight gain, including that formula-fed infants gain more weight from 3 months of age compared to breastfed infants (2 refs: 20,21). They also discuss that it is not possible to reconcile variable findings of infant diet effects on the development of islet autoimmunity (7 refs: 11-17), such as early introduction of cow's milk and cereals, by an overriding risk of weight gain (3 refs: 12-14).	B	Physical activity, sample size and power calculations not reported and by chance finding not considered. Unfortunately there were significant missing data in the diet records restricting the power of the analysis and as noted by the authors, an effect could have been missed. A limitation of the study is the outcome measure of islet autoimmunity rather than type 1 diabetes.
Ip et al, 2009 (22)	Overall SLR + meta-analysis when appropriate. For T1DM – 2 SLR and meta-analysis graded B + 4 studies graded B + 2 graded C	9 447 cases and 38 957 controls	Study 1. Ever vs never Study 2. >=3 mo vs <3 mo	T1DM	Two meta-analysis of fair quality including a total of 17 case-control studies reported OR 1.23 (95% CI 1.12-1.35) and 1.43 (1.15-1.77) respectively for the risk of T1DM if breastfed <3 mo vs >=3 mo. 5 of 6 later published studies reported similar results. However, these were retrospective case-control studies. Comparison of ORs between studies with long-term recall of brf-data and those more recent showed significant differences in T1DM risk only with long-term retrospective data.	A	
Ip et al, 2009 (22)	1 high-quality meta-analysis (Owen 2006,	76 744 subjects	Ever vs never breastfed in pooled analysis of seven	T2DM in later life	Pooled adjusted OR 0.61 (95% CI 0.44-0.85) for those breastfed compared with formula fed. 3 of the 7 studies had information about important	A	

	including 7 studies) No single studies afterwards		studies		confounders. These 3 studies concluded that adjustment did not alter crude estimate, Ip et al don't feel confident that all potential confounders has been ruled out.		
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- Horta et al; WHO, 2007 (21). The prevalence of type-2 diabetes was lower among breastfed subjects. All effects were statistically significant, but for some outcomes their magnitude was relatively modest.
- COT/SACN, 2011 (50). *JOINT STATEMENT. Timing of introduction of gluten into the infant diet.* SACN and COT do not consider the evidence sufficient to support EFSA's conclusion on the introduction of gluten into the infant diet no later than 6 completed months of age with the aim of reducing the risk of subsequent development of T1DM.
- SACN, 2011 (20). Infants who are not breastfed are at greater risk of type 2 diabetes. Strategies that promote, protect and support exclusive breastfeeding for a round the first 6 months of an infant's life should be enhanced, and should recognize the benefits for long-term health.

Supplementary table 5. Summary table. Breastfeeding, formula feeding and/or introduction of solids and outcome acute otitis media (AOM), gastrointestinal infection and lower respiratory infection (LRI)

Author (alphabetical order), year (ref.nr)	Study design (study name if applicable)	No. and type of included studies (SLR)/ No. of participants (cohort study)	Exposure (incl age)	Outcome (incl age)	Effect/association	Study quality	Comments
Duijts et al, 2009 (51)	SLR	GI: 40 518 (8 out of 21 studies about gastrointestinal infection) LRI: 60 377 (16 out of 21 studies about LRI) 21 studies (case-control, follow-up or randomized control trials)	Brf; (various definitions)	The included studies varies between 0-30 days and 0-24 months	GI: 6 out of 8 studies suggested brf had a protective effect, and the size varied according to duration and exclusiveness of brf. LRI: 13 out of 16 studies concluded brf had a protective effect Five studies combined duration and exclusiveness of breastfeeding. All those studies observed a protective dose/duration-response effect on gastrointestinal or respiratory tract infections. These studies strongly suggest that breastfeeding protects infants against overall infections, gastrointestinal and respiratory tract infections in industrialized countries.	B	Discusses publication bias, but no calculation. No description of the methodology used to assess dietary intake.
Duijts et al, 2010 (52)	Prospective cohort <i>Generation R study</i> , Netherlands	4 164 of 7 893 (53%)	Brf; 1) never (12.8%), 2) partial for <4 mo, not thereafter (29.2%), 3) partial 4-6 mo (28.8%), 4) excl 4 mo, partial thereafter (25.7%), 6) excl for 6 mo (1.4%) Good definition of exclusive brf. Partial = breastmilk + formula and/or solids	Infectious disease <1 y (serious cold, ear or throat infection, pneumonia, bronchitis, gastrointestinal tract infection) NOTE: in results they only mention infections in the upper respiratory (URTI), lower respiratory (LRTI) and gastrointestinal tracts (GI)	Compared with never breastfed, those excl brf 4 mo + partially thereafter had lower risk of URTI, LRTI and GI until 6 mo (adj OR 0.65 (95% CI 0.51-0.83), 0.50 (0.32-0.79) and 0.41 (0.26-0.64), respectively), and of LRTI between 7-12 mo (adjOR 0.46 (0.31-0.69)). Similar tendencies were observed for infants excl brf for 6 mo or longer. Partial brf, even for 6 mo, did not result in sig lower risks.	B	No power calculation
Fisk et al, 2011 (53)	Birth cohort	1764	Duration of brf the first and second 6 mo of infancy; never brf, <1 mo, 1-3 mo, 4+ mo, 4-6 mo, 7-11 mo, 12+ mo	6 and 12 mo: Infections 0-6 and 6-12 mo: Ear infections 1 or more times (reported doctor-	No sign associations between duration of brf and prevalence of ear infection: 0-6 mo of infancy: Adj RR (per month increase in brf): 0.93 (0.85-1.02) Second 6 mo of infancy: Adj RR (per month increase in brf): 1.00 (0.97-1.03)	B	Sample size reported (<i>large sample size</i>), but not study power and power calculations. By chance findings

			Adj for age of intro solid foods	diagnosed infection). Gastrointestinal morbidity (reported infections): 1 or more bouts of diarrhoea lasting 2+ days, 1 or more bouts of vomiting lasting 2+ days	Sign associations between duration of brf and prevalence of diarrhoea: 0-6 mo of infancy: Adj RR (per month increase in brf): 0.88 (0.83-0.92), p trend <0.001 Second 6 mo of infancy: Adj RR (per month increase in brf): 0.97 (0.95-0.99), p trend=0.002 Adj RR for brf ≥6 mo vs “never brf” for diarrhoea 0-6 mo: 0.43 (0.30-0.61) Sign associations between duration of brf and prevalence of vomiting: 0-6 mo of infancy: Adj RR (per month increase in brf): 0.92 (0.86-0.99), p trend=0.02 Second 6 mo of infancy: Adj RR (per month increase in brf): 0.97 (0.95-1.00), p trend=0.05 Adj RR for brf ≥6 mo vs “never brf” for vomiting 0-6 mo: 0.60 (0.39-0.92) Wheezing: Sign associations between duration of brf and prevalence of chest wheezing/whistling: 0-6 mo of infancy: Adj RR (per month increase in brf): 0.96 (0.93-1.00), p trend=0.05 Second 6 mo of infancy: Adj RR (per month increase in brf): 0.98 (0.96-1.00), p trend=0.04 Adj RR for brf ≥6 mo vs “never brf” for wheezing/whistling 0-6 mo: 0.67 (0.51-0.87) LRI: Sign associations between duration of brf and prevalence of lower respiratory tract infections: 0-6 mo of infancy: Adj RR (per month increase in brf): 0.94 (0.89-0.99), p trend=0.02 Second 6 mo of infancy: Adj RR (per month increase in brf): 0.98 (0.95-1.01), p trend=0.2 Adj RR for brf ≥6 mo vs “never brf” for lower respiratory tract infections 0-6 mo: 0.65 (0.43-0.96)		not considered
Ip et al, 2009 (22)	AOM: Meta-analysis of 5 cohort-studies reporting OR or RR of AOM comparing any definition of brf duration to exclusive formula feeding (all printed before 2000). GI: 1 meta-	AOM: Varying in the different included studies (ca 300 – ca 15000, most a few thousands). GI: 12 prospective cohorts totaling 5473 subjects, 2 retrospective cohort studies totaling 504 subjects and 2 case-control	AOM: GI: Breastfeeding. Only 4 of 16 studies had clear definitions on feeding practices. For the final analysis infant feeding was dichotomized into 2 groups; exclusive brf and partial/mixed feeding or exclusive artificial feeding. LRI: Excl brf vs no breastfeeding	AOM GI: “Any illness associated with vomiting, change in consistency or frequency of stools, or isolation of known enteropathic bacterial or viral agent” LRI: Hospitalization secondary to lower respiratory tract disease	AOM: Breastfeeding was associated with significant reduction in AOM. Pooled adjusted OR of risk for AOM when comparing ever brf with never brf was 0.77 (95% CI 0.64-0.91). Excl brf for 3 or 6 mo compared with never brf pooled adjusted OR was 0.50 (0.36-0.70). 3 studies not included in meta-analysis due to no group exclusively formula fed. They showed no effect of brf when comparing < or > 13w of brf, but sig risk reduction when comparing brf for >4 or >6 mo vs <4 or <6 mo GI: Results were conflicting. 9/16 studies saw protective effect of brf. Majority of studies suffered from methodological flaws. Not possible to pool	A	

	analysis of 16 studies (14 cohort and 2 case-control) graded B. No further studies afterwards. LRI: 1 meta-analysis of 7 cohort studies. No further single studies.	studies with 311 pairs of subjects. LRI: 7 cohort studies, total 3201 breastfed and 1324 non-breastfed subjects.			the adjusted relative measures found in the studies. Summary crude OR for the 14 cohort studies were 0.36 (95% CI 0.32-0.41, heterogeneity, $p<0.01$), and for the 2 case-control studies 0.54 (0.36-0.41, heterogeneity, $p=0.35$). Just before Ip was sent to the publishers they were told about a new study (our nr 306, Quigley), a case-control study (167 cases and 137 controls) showed that infants who were breastfeeding had a reduced risk of diarrhea compared to infants not breastfeeding (adjusted OR 0.36, 95% CI 0.18-0.74). LRI: Summary relative risk RR 0.28 (95% CI 0.14-0.54) of hospitalization due to LRTI <1 y in those excl brf 4 mo or more compared with formula fed.		
Kramer & Kakuma, 2002 (+later updates) (2)	Overall SLR + meta-analysis when appropriate.	AOM: 3762 GI: 3482 LRI: 510 only controlled clinical trials and observational studies.	Brf; exclusive 6 mo vs. exclusive 3-4 mo with mixed brf	AOM: One or more episodes of otitis media in first 12 mo. GI: One or more episodes of gastrointestinal infections in first 12 mo LRI: One or more episodes of lower respiratory tract infections in first 12 mo	Exclusive 6 mo vs. exclusive 3-4 mo with mixed brf afterwards AOM: varying results: episodes)."Duncan 1993 and Kramer 2000a both found a slightly elevated risk for one or more episodes of otitis media (pooled RR 1.28; 95% CI 1.04 to 1.57) but Duncan 1993 found a nonsignificant reduction in risk for frequent otitis media (RR 0.81; 95% CI 0.43 to 1.52) GI: RR 0.67; 95% CI 0.46 to 0.97" LRI: Oddy 1999, Kramer 2000a: no reduced risk (pooled RR 0.91; 95% CI 0.82 to 1.02)	A	
Landonenou et al, 2010 (54)	Prospective study	926	Duration of brf in weeks (exclusive vs. partial)	All infectious (incl. otitis media, acute respiratory infection, gastroenteritis, urinary tract infection, conjunctivitis, thrush) at 1, 3, 6, 9 and 12 mo	All infectious diseases treated as one outcome. Prolonged exclusive breastfeeding was associated with fewer infectious episodes ($r(s)=-0.07$, $p=0.019$) and fewer admissions to hospital for infection ($r(s)=-0.06$, $p=0.037$) in the first year of life. Partial breastfeeding was not related to protective effect. AOM: Infants exclusively breastfed for 6 months presented with fewer infectious episodes than their partially breastfed or non-breastfed peers and this protective effect persisted after adjustment for potential confounders for AOM (OR 0.37, 95% CI 0.13 to 1.05). ARI (OR 0.58, 95% CI 0.36 to 0.92), and thrush (OR 0.14, 95% CI 0.02 to 1.02).	B	No power calculation
Rebhan et al, 2009 (40)	Prospective cohort	1901	Brf exclusively for > or =6 months (group	Retrospective questionnaire at age	In multivariate analysis > or =6 months of exclusive breastfeeding reduced significantly the	B	Some important confounders not

			A), fully/exclusively > or =4 months, but not exclusively > or =6 months (group B); infants not breastfed/breastfed <4 months (group C)	of 9 mo (How often during last 9 mo child suffer GI infections diagnosed by physician)	risk for > or =1 episode of gastrointestinal infection(s) during months 1-9 compared to no/<4 months breastfeeding (adjusted odds ratio [OR]: 0.60; 95% confidence interval [CI]: 0.44-0.82).		included, only 9 mo follow-up, no power calculations
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Supplementary table 6. Summary table. Breastfeeding, formula feeding and/or introduction of solids and outcome cancer

Author, year	Study design (study name if applicable)	No. and type of included studies (SLR)/ No. of participants (cohort study)	Exposure (incl age)	Outcome (incl age)	Effect/association	Study quality	Comments
Ip et al, 2009 (22)	SLR Includes 1 SLR (Guise 2005) + 2 meta-analysis (Kwan 2004, + Ip made a meta-analysis of 3 studies included in Guise, 2 A, 1B)	3266 subjects with ALL, number of controls unclear one SLR and two one meta-analysis (both only including case-control studies)	Short (≤ 6 mo) vs long (> 6 mo) breastfeeding.	Acute lymphocytic leukemia (ALL) Acute myelogenous leukemia (AML)	There is an association between a history of breastfeeding of at least 6 months and a reduction in the risk of both ALL and AML. Ip meta-analysis: Brf ≤ 6 mo vs never brf: ALL OR 0.91. 95% CI 0.83-1.00), Brf > 6 mo vs never brf: ALL OR 0.80. 95% CI 0.71-0.91) Kwan meta-analysis: Brf ≤ 6 mo vs never brf: OR 0.88. 95% CI 0.80-0.96) Brf > 6 mo vs never brf: OR 0.76. 95% CI 0.68-0.84). Ip et al conclude that there is association between a history of breastfeeding of at least 6 months duration and a reduction in the risk of both ALL and AML.	A	
Martin et al, 2005a (55)	Cohort-study + Metaanalysis	26 included; 2 cohort/nested case-control, 24 case-control	Ever or exclusive brf vs never brf, various durations of brf, separate meta-analysis of prolonged brf > 6 -8 mo vs never brf, 2 studies examined exclusive brf vs never brf.	Childhood cancers (all cancers and specific cancers)	Lower risks associated with having been breast-fed: 9% (95% CI 5 2–16%) for acute lymphoblastic leukemia, 24% (3–40%) for Hodgkin's disease 41% (22–56%) for neuroblastoma, with little between-study heterogeneity. The estimates for Hodgkin's disease and neuroblastoma, however, were driven by single studies. There was little evidence that breast-feeding was associated with acute nonlymphoblastic leukemia, non-Hodgkin's lymphoma, central nervous system cancers, malignant germ cell tumors, juvenile bone tumors, or other solid cancers. In conclusion, ever having been breast-fed was inversely associated with acute lymphoblastic leukemia, Hodgkin's disease and neuroblastoma in childhood, but noncausal explanations are possible. Even if causal, the public health importance of these associations may be small. The author's estimates suggest that increasing breast-feeding from 50% to 100% would prevent at most 5% of cases of childhood acute leukemia or lymphoma.	C	No duplicate study selection and data extraction. 85 % of studies relied on long-term recall, only 8% examined breastfeeding exclusivity and control response rates were under 80% in over half. Included due to few studies with outcome cancer.

Martin et al, 2005b (56)	SLR + meta-analysis (+ cohort study with the Boyd Orr cohort consisted of 4999 subjects who were originally surveyed in 1937 – 39, when they were 0 – 19 years of age)	14 included; 11 case-control, 3 cohort/nested case-control studies + Boyd Orr cohort	Ever or exclusive brf vs never brf, various durations of brf, separate meta-analyses comparing any or exclusive brf of > 6 mo with never brf were undertaken	Adult cancer (all cancers and specific cancers)	No association between breast-feeding and breast cancer (regardless of menopausal status) (relative risk [RR] = 0.94, 95% CI = 0.85 to 1.04). However, breast-fed women had a reduced risk of premenopausal breast cancer (RR = 0.88, 95% CI = 0.79 to 0.98) but not of postmenopausal breast cancer (RR = 1.00, 95% CI = 0.86 to 1.16). Conclusion: Ever having been breast-fed was not associated with overall breast cancer risk, although the meta-analysis revealed a reduced risk of premenopausal breast cancer in women who had been breast-fed.	C	No duplicate study selection and data extraction. (Stated that one author extracted the data on two separate occasions to check the consistency of data extraction), infant feeding was assessed in adulthood for most studies included Included due to few studies with outcome cancer.
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Supplementary table 7. Summary table. Breastfeeding, formula feeding and/or introduction of solids and outcome atopic disease

Author (alphabetical order), year (ref.nr)	Study design (study name if applicable)	No. and type of included studies (SLR)/ No. of participants (cohort study)	Exposure (incl age)	Outcome (incl age)	Effect/association	Study quality	Comments
Alm et al, 2009 (65)	Prospective cohort (but food data retrospective)	4921 (60.2% of selected population)	Current patterns of food introduction (to assess risk factors for eczema)	Eczema at 1 y	Intro fish <9 mo OR 0.76 (0.62-0.94), p=0.009. No effect of brf duration. Maternal eczema OR1.54 (1.30-1.84), sibling w eczema OR 1.87 (1.50-2.33), cow's milk allergy OR 3.64 (2.35-5.64), having a bird in the home OR 0.35 (0.17-0.75)	B	No power calculation. Excl brf wrongly defined (no cow's milk protein introduced). Gender not given. Food data collected retrospectively 6 and 12 mo
Bergmann et al, 2002 (58)	Prospective cohort	1314 of a birth cohort of 7609	Duration of any breastfeeding. Brf <1 week and no brf combined.	Prevalence of atopic eczema during the first 7 y	Brf was carried out longer if at least one parent had eczema. Prevalence of eczema during first 7 y increased with each additional month of brf OR 1.03 (95% CI 1.00-1.06), with a history of parental eczema (OR 2.06 (1.38-3.08), and if other atopic signs and symptoms appeared, especially specific sensitization (1.53; 1.25-1.88), and asthma (1.41; 1.07-1.85). Conclusion. Parental eczema is the major risk factor, but longer duration of brf also increase the risk. Although brf should be recommended for all infants, it does not prevent eczema in children with a genetic risk.	B	No power calculation. Brf only as total duration. No consideration of other feeding. 92% breastfed at maternity ward, but 2% received glucose solution and 49% formula in addition (13% hydrolyzed)
Elliott et al, 2008 (59)	Prospective cohort (ALSPAC)	13 978. Brf data from 12 623-12 706 and outcome data from 51-79%	Brf never-ever, Brf duration never, <1 mo, 1-3 mo, 3-6 mo and 6+ mo Excl brf duration never brf, excl brf <4 mo, excl brf ≥4 mo	Atopy at 7 y (skin prick test)	No consistent evidence for either a deleterious effect or a protective effect of breastfeeding on later risk of allergic disease, even when their mothers are asthmatic. Neither reverse causation nor low to follow-up appears to have materially biased the results. OR for atopy 1.12 (95% CI 0.92-1.35) at 7-8 y	B	No power calculation, no definition excl brf
Giwerzman et al, 2010 (60)	High-risk birth cohort (born to mothers with a history of asthma)	321 411 included in the cohort, 321 after exclusion	First: Duration of exclusive breastfeeding. Second: influence of the fatty acid composition of	Eczema (and wheezy disorders, see table 2m)	Exclusive brf significantly increased the risk of eczema adjusted for demographics, filaggrin variants, parents' eczema and pets at home (N=306; RR 2.09; 95% CI 1.15-3.80; P=0.016). (Only duration of exclusive breastfeeding is included, not of any brf.)	B	No definition of exclusive breastfeeding, no particulars of dietary assessment tool reported. Unclear if

			mother's milk on the risk from breastfeeding		Analysed the effect from duration of exclusive brf before disease onset on the disease risk.		duration of exclusive breastfeeding is really duration of any breastfeeding. Sample size reported, but not study power and power calculations. By chance findings not considered
Ip et al, 2009 (22)	1 meta-analysis of 18 prospective cohort studies (Our study nr 102 Gdalevich, rated A). No further updates.	10 prospective studies included, sample size 17-991. Total of 4 158 participants.	Excl brf >3 mo	Atopy. Mean follow-up time 4.5 y	OR 0.58 (95% CI 0.41-0.92) when comparing excl brf > or <3 mo in children with a family history of atopy. When separating those with short follow-up (<2y) and those with longer OR were 0.74 (0.61-0.90) and 0.78 (0.62-0.99) respectively.	A	
Kramer et al, 2007b (61)	Prospective cohort (Cluster-randomized trial) The PROBIT - study	13889	Duration of any brf in months, exclusive brf 3 mo or 6 mo:	Allergy and asthma: At 6.5 y ISAAC questionnaire and skin prick test	The experimental group had no reduction in risks of allergic symptoms and diagnoses or positive skin prick tests. In fact, after exclusion of six sites (three experimental and three control) with suspiciously high rates of positive skin prick tests, risks were significantly increased in the experimental group for four of the five antigens.	B	No power calculation for these outcomes (power calculation done on outcome gastroenteritis) The results are not validated blind but double checked with blinded methods..
Kramer et al, 2009a (37)	Prospective cohort (Cluster-randomized trial) The PROBIT - study	2951 of totally 3483 followed during the first year	Duration of any brf in months, exclusive brf 3 mo or 6 mo:	Atopic symptoms, skin-prick tests	No significant differences in atopic outcomes between the EBF3 and EBF6 groups.	B	No power calculation for these outcomes (power calculation done on outcome gastroenteritis) The results are not validated blind but double checked with blinded methods.
Kramer et al, 2009b (62)	Prospective cohort (Cluster-randomized trial) The PROBIT - study	13889	Duration of any brf in months, exclusive brf 3 mo or 6 mo:	Allergy symptoms at 1,3, 6, 9 and 12 mo and at 6.5 yr ISAAC questionnaire	Maternal postnatal smoking was associated with wheezing and hayfever symptoms, while the duration of exclusive breastfeeding was not protective against any of the studied outcomes. The risk factors for allergic symptoms were similar in children with positive skin-prick tests to those in the overall cohort.	B	No power calculation for these outcomes (power calculation done on outcome gastroenteritis) The results are not validated blind but double checked with blinded methods.
Silvers 2009 (63)	NZ Astma and allergy cohort	1105 Recruitment	Exclusive BF, Any BF and Additional BF –	Eczema; Atopy (skin-prick test)	Breastfeeding was not associated with eczema or atopy at 15 months	B	Power calculation described.

	study, Christchurch and Wellington	before birth =>from birth – 15 months Prospective Questionnaire at birth, 3, 6 and 15 months	alla as continous variables				Note – other food was not taken into account.
Snijders et al, 2008 (66)	Prospective cohort study	2558 infants included of 2834 enrolled at birth.	Age at first intro (0-3 mo, 4-6 mo, 7-9 mo, > 9 mo) of cow milk products; defined as artificial formulas, raw/pasteurized milk, porridge, dairy products and yoghurts. Age of intro of other food products (eg, fruit mash) (3 mo, 4-6 mo, after 7 mo. Brf duration included as confounder (never, 0-3 mo, 4-6, 7-9, > 9 mo)	Atopic manifestations in the first 2 y of life; Eczema (parental questionnaire), atopic dermatitis (AD) (according to UK Working Party Criteria), recurrent wheeze, any sensitization, sensitization against cow milk, hen egg, peanut(venous blood samples at 2 y)	More delay in both intro of cow milk products and other food products was associated with a higher risk for eczema. No association between intro of cow milk products and AD, however more delay in other food products was associated with higher risk for AD. A delayed intro of other food products was associated with an increased risk for atopic sensitization. Exclusion of infants with early symptoms of eczema and recurrent wheeze (to avoid reverse causation) did not essentially change the results.	B	An additional alternative recruitment group; healthy pregnant group, recruited through alternative lifestyle channels Sample size reported, but not study power and power calculations. By chance findings not considered
Tarini et al, 2006 (64)	SLR	Reported numbers in 13 studies: 79-1265	Early introduction of solid foods (before age 4 mo)	Allergic disease; Eczema, Asthma or wheezing, Food allergy, Allergic rhinitis, pollen allergy, animal dander allergy, any allergic disease	Early solid feeding may increase the risk of eczema. However, there are little data supporting an association between early solid feeding and other allergic conditions. 5 of 9 studies found a positive association between early solid feeding and eczema, with persistence of the association for 10 y in one study. 4 studies found no association. One study found an association between early solid feeding and pollen allergy. No strong evidence to support the association between early solid feeding and the development of persistent asthma, persistent food allergy, allergic rhinitis or animal dander allergy.	B	Publication bias not assessed
Yang et al, 2009 (57)	SLR + meta-analysis	Total 34227 (27 study populations) (varying between 42-15430)	Brf., duration at least 3 months, exclusive brf (no other milk products, solids etc added to infants diet in first 3 mo) + never brf or brf < 3 mo	Atopic dermatitis during childhood (follow-up varying between 1 y to 7 y)	Summary OR 0.89 (95% CI 0.76-1.04) – for the effect of exclusive brf on the risk of AD Pooled OR for study populations with atopic heredity was 0.78 (95% CI 0.58-1.05) No strong evidence of protective effect of exclusive brf for at least 3 mo against AD	B	Discusses publication bias, but no calculation. Several characteristics of included studies reported, but not all. Characteristics of excluded papers not given,

Zutavern et al, 2008 (67)	Prospective cohort	2073	Feeding history at 6 mo (solid food introduction)	Skin and allergic symptoms 6 y	A delayed introduction of solids (past 4 or 6 months) was not associated with decreased odds for asthma, allergic rhinitis, or sensitization against food or inhalant allergens at 6 years of age. On the contrary, food sensitization was more frequent in children who were introduced to solids later. There was no protective effect of a late introduction of solids or a less diverse diet within the first 4 months of life.	B	Original cohort was 3097/ Reasons for lower response rate was not reported No power calculations
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- Greer et al; AAP, 2008 (16). Evidence that breastfeeding for at least 4 mo, compared with feeding formula made with intact cow milk protein, prevents or delays the occurrence of atopic dermatitis, cow milk allergy, and wheezing in early childhood. Little evidence that delaying the timing of the intro of complementary foods beyond 4 to 6 months prevents the occurrence of atopic disease. At present, insufficient data to document a protective effect of any dietary intervention beyond 4 to 6 months for the development of atopic disease.
- Swedish Paediatric Society, 2010 (68). Breastfeeding give some protection against infection-induced airway symptoms of asthma type, but breastfeeding has not been proven to decrease the risk of atopy and allergies.

Supplementary table 8. Summary table. Breastfeeding, formula feeding and/or introduction of solids and outcome asthma

Author (alphabetical order), year (ref.nr)	Study design (study name if applicable)	No. and type of included studies (SLR)/ No. of participants (cohort study)	Exposure (incl age)	Outcome (incl age)	Effect/association	Study quality	Comments
Elliott et al, 2008 (59)	Prospective cohort (ALSPAC)	13 978. Brf data from 12 623-12 706 and outcome data from 51-79%	Brf never-ever, Brf duration never, <1 mo, 1-3 mo, 3-6 mo and 6+ mo Excl brf duration never brf, excl brf <4 mo, excl brf ≥4 mo	Wheeze at 3 y and 7.5 y (self-report) Asthma 7.5 y (self report) Lung function at 8 y	No consistent evidence for either a deleterious effect or a protective effect of breastfeeding on later risk of allergic disease, even when their mothers are asthmatic. Neither reverse causation nor low to follow-up appears to have materially biased the results. OR for wheeze in the first 3 y; 0.98 (95% CI 0.79-1.22) OR for bronchial hyper responsiveness at 7-8 y; 1.07 (0.82-1.40)	B	No power calculation, no definition excl brf
Fredriksson et al, 2007 (69)	Population-based cohort	1933	Breastfeeding duration; 0-3 mo, 4-6 mo, 7-9 mo, 10-12 mo and 12 mo or longer	Asthma as primary outcome Chronic respiratory symptoms as secondary outcomes	U-shaped relation between brf and the outcomes. For some of the results, we're not sure whether it is exclusive or any breastfeeding. Lowest prevalence of asthma with brf 4-9 mo and with brf 7-9 mo for persistent wheezing, cough and phlegm. Significant adj OR for asthma of 1.03 (95% CI: 1.00, 1.05) per one-month increase in brf duration from 4-6 mo. The risk of persistent wheezing increased 12 % per month from 7-9 mo to shorter brf duration and 5 % per month to longer brf duration. The risk of persistent cough increased 8% per month from 7-9 mo to shorter brf duration and 4 % per month to longer brf duration. The risk of persistent phlegm increased 8 % and 4 % per month for decrease and increase in brf duration, respectively.	B	Sample size reported (<i>large sample size</i>), but not study power and power calculations. By chance findings not considered
Giwerzman et al, 2010 (60)	High-risk birth cohort (born to mothers with a history of asthma)	321 411 included in the cohort, 321 after exclusion	First: Duration of exclusive breastfeeding. Second: influence of the fatty acid composition of mother's milk on the risk from breastfeeding	Wheezy disorders	Excl brf significantly reduced the risk of wheezy episodes (RR 0.67; 95% CI 0.48-0.96; P = 0.021) and of severe wheezy exacerbation (RR 0.16; 95% CI 0.03-1.01; P = 0.051). <i>(Only duration of exclusive breastfeeding is included, not of any brf.)</i> Analysed the effect from duration of exclusive brf before disease onset on the disease risk	B	No definition of exclusive breastfeeding, no particulars of dietary assessment tool reported. Unclear if duration of exclusive breastfeeding is really duration of any breastfeeding.

							Sample size reported, but not study power and power calculations. By chance findings not considered
Ip et al, 2009 (22)	1 meta-analysis of 12 prospective cohort studies (Our study nr 103 Gdalevich, rated A) + 3 new studies (our studies nr 32, 197 and 406 – all rated B)	Meta-analysis included 12 prospective cohorts totaling 8183 term infants followed for a mean of 4.1 y. 3 new studies sample size 1037-4964 with 0-31% drop-out	Brf >3 mo compared with not breastfed	Asthma	Breastfeeding for ≥3 mo associated with reduced risk of asthma compared to not breastfed in children without family history (OR 0.73, 95% CI 0.59-0.92). This association also found in subjects <10 y of age with a family history.	A	NOTE one study not included in Ip's meta-analysis due to lack of arm with brf>3 mo. This study (Sears, 2002 were not among our studies) reported an increased risk in asthma with increased duration of breastfeeding in those with maternal history of asthma.
Karmaus et al, 2008 (70)	Prospective cohort <i>The Isle of Wight Birth Cohort Study</i> , UK	1456 of 1536 children born (95%) 1360 (86%) remaining at 10 y	The triad of maternal prenatal smoking, any brf ≥3 mo, recurrent lower respiratory tract infection (RLRTI)	Childhood asthma	Of the 3 risk factors RLRTI seemed to be the most important. Brf ≥3 mo attenuated the effects of both RLRTI and smoking on asthma	B	No power calculation
Kramer & Kakuma, 2002 (2)	Overall SLR + meta-analysis when appropriate.	3993 (wheezing) 552 (asthma) only controlled clinical trials and observational studies.	Brf; exclusive 6 mo vs. exclusive 3-4 mo with mixed brf	2 or more wheezing in first 12 months	wheezing in the EBF group (pooled RR 0.79; 95% CI 0.49 to 1.28) Risk of asthma at five to six years (pooled RR was 0.91; 95% CI 0.61 to 1.36).	A	
Kramer et al, 2007b (61)	Prospective cohort (Cluster-randomized trial) The PROBIT - study.	13889	Duration of any brf in months, exclusive brf 3 mo or 6 mo:	Allergy and asthma: At 6.5 y ISAAC questionnaire and skin prick test	There was no reduction in the risk of asthma (hay fever, or eczema) at age 6.5 years when comparing the intervention with the control areas. This does not support the view that prolonged or exclusive breastfeeding has a protective effect on asthma or allergy.	B	No power calculation for these outcomes (power calculation done on outcome gastroenteritis) The results are not validated blind but double checked with blinded methods.
Kramer et al, 2009b (62)	Prospective cohort (Cluster-randomized trial)	13889	Duration of any brf in months, exclusive brf 3 mo or 6 mo:	Allergy symptoms at 1,3, 6, 9 and 12 mo and at 6.5 yr ISAAC questionnaire	Maternal postnatal smoking was associated with wheezing and hayfever symptoms, while the duration of exclusive breastfeeding was not protective against any of the studied outcomes. The risk factors for allergic symptoms were similar in	B	No power calculation for these outcomes (power calculation done on outcome gastroenteritis)

	The PROBIT - study				children with positive skin-prick tests to those in the overall cohort.		The results are not validated blind but double checked with blinded methods.
Kull 2010 (71)	Stockholm, Sweden (BAMSE)	Birth cohort, N=4089, this follow-up N=3825	Duration of any brf in months, exclusive brf 4 mo vs. partial	Outcomes at 1, 2, 4 and 8 y Heridity for allergy (physician-diagnosed); asthma (at least 4 episodes of wheezing during last 12 mo), IgE antibodies	80% excl breastfed during first 4 mo, mean duration 5.1 mo (SD 2.5 mo). At 8 years, excl breastfeeding for at least 4 months reduced risk for asthma, adj OR 0.63; 95% CI, 0.50-0.78 compared w breastfeeding <4 mo, especially when combiuned with sensitization; excl brf for at least 4 mo reduced the risk of allergic asthma (adj OR 0.59; 95% CI, 0.37-0.93), but not of non-allergic asthma (adj OR, 1.18; 95% CI, 0.56-2.48).	B	Power calculation originally made for asthma
Midodzi et al, 2010 (72)	Prospective cohort	N=13 546 To this study: N=8499 complete baseline data and no prior asthma and biological parent as the person most knowledgeable	Prenatal problems, Cesarean delivery, low birth weight, breastfeeding and wheezing, allergy, infection, daycare	Physician diagnosed asthma at 2-5 yrs	Breastfeeding decreased the incidence of asthma Breastfeeding > 3 months HR: 0.82 (95% CI: 0.69-0.97)	B	Breastfeeding not a major subject in the study. (< 50% of original sample incl).
Scholtens et al, 2009 (73)	Prospective cohort (PIAMA)	3115	Data on breast feeding and asthma were collected by questionnaires 1-8 y	At 8 years, specific immunoglobulin E (IgE) to airborne allergens and bronchial responsiveness were measured.	Breast feeding (>16 weeks vs no breast feeding) was significantly associated with a lower asthma prevalence from 3 to 8 years of age, in children of both non-allergic and allergic mothers. OR=0.57 (95% CI:0.41-0.80), this was also significant stratified in children of both non-allergic fathers (OR=0.62 (95%CI:0.40-0.94)) and mothers (OR=0.52 (95% CI:0.34-0.78)) and children with allergic fathers (OR=0.51 (95%CI:0.30-0.86)). It did not reach significance for children with allergic mothers probably because of the low number of children in the group. Breast feeding was not associated with bronchial hyper-responsiveness. No interaction between breast feeding and gender, maternal allergy or paternal allergy was observed in any of the associations. Breast feeding is associated with a lower asthma risk in children until 8 years of age without evidence of attenuation and regardless of the family history of allergy.	B	No power calculations, no identification of confounders
Silvers 2009	NZ Astma and	1105	Exclusive BF, Any	Doctor diagnosed	Breastfeeding significantly reduced the risk of	B	Power calculation

(63)	allergy cohort study, Christchurch and Wellington	Recruitment before birth =>from birth – 15 months Prospective Questionnaire at birth, 3, 6 and 15 months	BF and Additional BF – all as continuous variables	astma; Wheezing; Inhaler use	adverse respiratory outcomes at 15 months. After adjustment for confounders, each month of excl breastfeeding reduced risk of doctor-diagnosed asthma by 20% (odds ratio 0.80, 95% CI 0.71 to 0.90), wheezing -12% (0.88, 0.82 to 0.94) and inhaler use -14% (0.86, 0.78 to 0.93) The median duration of exclusive breastfeeding was 1.4 months [interquartile range (IQR) 0–4] and of any breastfeeding was 9.0 months (IQR 4–13). Duration of exclusive breastfeeding was a stronger determinant of respiratory outcomes than the duration of any breastfeeding.		described. Note – other food was not taken into account.
Snijders et al, 2008 (66)	Prospective cohort study	2558 infants included of 2834 enrolled at birth.	Age at first intro (0-3 mo, 4-6 mo, 7-9 mo, > 9 mo) of cow milk products; defined as artificial formulas, raw/pasteurized milk, porridge, dairy products and yoghurts. Age of intro of other food products (eg, fruit mash) (3 mo, 4-6 mo, after 7 mo. Brf duration included as confounder (never, 0-3 mo, 4-6, 7-9, > 9 mo).	Recurrent wheeze in the first 2 y of life	A delayed intro of other food products showed higher risk for recurrent wheeze. Longer brf duration (7-9 mo) showed a reduced risk for recurrent wheeze. The risk for recurrent wheeze for brf > 9 mo tended in the same direction. Exclusion of infants with early symptoms of eczema and recurrent wheeze (to avoid reverse causation) did not essentially change the results.	B	An additional alternative recruitment group; healthy pregnant group, recruited through alternative lifestyle channels Sample size reported, but not study power and power calculations. By chance findings not considered
Tarini et al, 2006 (64)	SLR	Reported numbers in 7 studies: 79-1265	Early introduction of solid foods (before age 4 mo)	Asthma or wheezing (and other allergic disease (see table 21)	No strong evidence to support the association between early solid feeding and the development of persistent asthma. One case-control study found a positive association with asthma. 3 cohort studies found no significant relationship with asthma by 4, 5 or 7 y. 3 cohort studies found no significant association with episodes of wheezing,, while 1 found a positive association.	B	Publication bias not assessed
Zutavern et al, 2008 (67)	Prospective cohort	2073	Feeding history at 6 mo (solid food introduction)	Skin and allergic symptoms 6 y	A delayed introduction of solids (past 4 or 6 months) was not associated with decreased odds for asthma, allergic rhinitis, or sensitization against food or inhalant allergens at 6 years of age. On the contrary, food sensitization was more frequent in children who were introduced to solids later.	B	Original cohort was 3097/ Reasons for lower response rate was not reported No power calculations

					There was no protective effect of a late introduction of solids or a less diverse diet within the first 4 months of life.		
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- Greer et al; AAP, 2008 (16). Evidence that breastfeeding for at least 4 mo, compared with feeding formula made with intact cow milk protein, prevents or delays the occurrence of atopic dermatitis, cow milk allergy, and wheezing in early childhood. Little evidence that delaying the timing of the intro of complementary foods beyond 4 to 6 mo prevents the occurrence of atopic disease. At present, insufficient data to document a protective effect of any dietary intervention beyond 4 to 6 mo for the development of atopic disease.
- Swedish Paediatric Society, 2010 (68). Breastfeeding give some protection against infection-induced airway symptoms of asthma type, but breastfeeding has not been proven to decrease the risk of allergies.

Supplementary table 9. Summary table. Breastfeeding, formula feeding and/or introduction of solids and outcome IQ, neurodevelopmental outcomes

Author (alphabetical order), year (ref.nr)	Study design (study name if applicable)	No. and type of included studies (SLR)/ No. of participants (cohort study)	Exposure (incl age)	Outcome (incl age)	Effect/association	Study quality	Comments
Ip et al, 2009 (22)	1 SLR rated A and 2 SLR rated B + 8 new cohort studies (1 A, 6 B and 1 C)	Jain 40 publications (30 birth cohorts, 5 RCT, 5 school registry, 3 case-control) from 1929-2001. Drane 24 studies from 1966-1998. 3 rd SLR 11 studies 1978-1995 8 new studies including 44-3380 term subjects.	Brf; Most studies did not differentiate between exclusive and partial brf. All definitions of exclusive brf accepted, but conclusions qualified with respect to the definitions used	cognitive performance,	Little or no evidence for an association between breastfeeding in infancy and cognitive performance in childhood.	A	
Jedrychowski et al, 2012 (77)	Prospective cohort (Poland)	469 (314 excl brf, 154 complementary fed at 3 mo)	Exclusive brf vs complementary feeding. NOTE: the authors differentiate between exclusive ≥ 3 mo, 4-6 mo and >6 mo. Seems unlikely that 119 (25) is excl brf >6 mo	Neurodevelopment over a 7-y follow-up Bayley Mental Scales of Infant Development-second edition (BSID-II) at 1-3 y, Weschler intelligence test for children (WISC-R) at 6 and 7 y	Children breastfed exclusively for up to 3 months had intelligence quotients (IQs) that were on average 2.1 points higher compared to the others (95% confidence interval (CI), 0.24-3.9); children breastfed for 4-6 months scored higher by 2.6 points (95% CI, 0.87-4.27); and the benefit for children breastfed even longer (>6 months) increased by 3.8 points (95% CI, 2.11-5.45). The authors conclude that results of the study support the WHO expert recommendations on exclusive breastfeeding for 6 months; moreover, they provide evidence that even a shorter duration of exclusive breastfeeding in early infancy produces beneficial effects on the cognitive development of children.	B	No power calculation. Exclusive breastfeeding is defined in accordance with WHO, but it is unclear whether it is actually used in practice. It seems unlikely that 119 (25%) is exclusively breastfed >6 mo. Complementary feeding is defined as never breastfed or mixed fed the first 3 mo.
Kramer et al, 2008 (76)	Prospective cohort (Cluster-randomized)	13889	Duration of any brf in months, exclusive brf 3 mo or 6 mo Comparison between	IQ at age 6.5 y	The experimental area had higher means on all of the Wechsler Abbreviated Scales of Intelligence measures, with cluster-adjusted mean differences (95% confidence intervals) of +7.5 (+0.8 to +14.3)	B	no power calculation

	trial) The PROBIT -study		the experimental area and the control area		for verbal IQ, +2.9 (-3.3 to +9.1) for performance IQ, and +5.9 (-1.0 to +12.8) for full-scale IQ. Teachers' academic ratings were significantly higher in the experimental group for both reading and writing.		
Kramer et al, 2009a (37)	Prospective cohort (Cluster-randomized trial) The PROBIT -study.	2951 of totally 3483 followed during the first year	Duration of any brf in months, exclusive brf 3 mo or 6 mo: Comparison between EBF3 and EBF6	IQ and teacher and parents' ratings at 6.5 y	No significant differences between the EBF3 and EBF6 groups on Wechsler Abbreviated Scales of Intelligence measures, or teacher's ratings on those that had started school.	B	No power calculation for these outcomes (power calculation done on outcome gastroenteritis (mentioned in paper 180)) The results are not validated blind but double checked with blinded methods.
Oken et al, 2008 (79)	Prospective cohort	25 446 with all prior data – (90% of eligible ?) (/of 28 277 had 18 month postpart interview/of 50 276 initial interview + FFQ in pregn/92 676 liveborn singletons/of 101 042 pregnancies '97-'02)	BF categories: < BF duration: <1mon, 2-3, 4-6, 7-9, >10 months	18 mo (and 6 mo) developmental milestones	Breastfed 2-3, 4-6, and > 6months showed all higher motor developmental milestones in comparison to BF < 1 month. Breastfed > 6months showed higher social or cognitive developmental milestones in comparison to BF < 1 month. Breastfed 2-3, 4-6, and > 6months showed all higher TOTAL developmental milestones in comparison to BF < 1 month	B	Only breastfeeding duration, only size at birth, no power calculations, study power and sample size not considered– BUT very many participants included
Whitehouse et al, 2011 (80)	Longitudinal cohort study of women and their children	1195 1976 followed up at 10 y and with complete brf data and 1195 of these with language data at 10 y. Cohort of 2868	Duration of predominately brf: “never brf”, “brf predominately for <4mo, “brf predominately for 4-6 mo”, “brf predominately for >6 mo” (Predominately brf presumed to occur up to intro of other milk than breast milk. Definition did not preclude solids). Similar 4 categories of duration of any brf	Language ability test at 10-y (also at 5 y) using the Peabody Picture Vocabulary Test - Revised; PPVT-R	Predominately brf for >6 mo had a mean PPVT-R score (language ability test score) that was 4.04 points higher than those never brf. This compared with an increase of 3.56 points at 5 y. A dose-response relationship was found: those predominately brf for <4 mo had higher language scores than those never brf (regression coefficient (b) = 2.71), while the effect was stronger for predominately brf for 4-6 mo (b=3.83) and stronger still for predominately brf for >6 mo (b=4.04).	B	Sample size reported, but not study power and power calculations. By chance findings not considered

Zhou et al, 2007 (81)	Prospective cohort	303	Brf	IQ at 4 y	There was no association between the duration of breast-feeding and IQ of the children. The expected IQ of a child at 4 y of age who was breast-fed for 6 mo was only 0.2 point (95% confidence interval -0.8 to 1.2) higher than that of a child who had never been breast-fed.	B	Breastfeeding was asked at 6 mo and 4 yr of age No power calculations
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- Horta et al; WHO, 2007 (21). Subjects who were breastfed showed higher performance in intelligence tests. All effects were statistically significant, but for some outcomes their magnitude was relatively modest.

Supplementary table 10. Summary table. Breastfeeding, formula feeding and/or introduction of solids and outcome celiac disease

Author (alphabetical order), year (ref.nr)	Study design (study name if applicable)	No. and type of included studies (SLR)/ No. of participants (cohort study)	Exposure (incl age)	Outcome (incl age)	Effect/association	Study quality	Comments
Akobeng et al, 2006 (83)	SLR + meta-analysis	Total 1131 cases (varying between 7-491) + 3493 controls (varying between 73-1949)	Brf; various definitions (different durations or medians were used in the different primary studies) and therefore not combined)	Celiac disease (varying between 2 y and 15 y in the 6 studies included)	Being breastfed at introduction of gluten decreased the risk of getting celiac disease (pooled OR 0.48, 95% CI 0.40-0.59) Not clear whether brf delays onset of CD or provides permanent protection	A	Characteristics of excluded papers not given, conflict of interest only stated for the authors not the included studies. The SLR only included studies based on histologically confirmed coeliac disease, but the primary studies compared different durations of breastfeeding and exact timing of introduction and amount of gluten consumed was not given.

- ESPGHAN (2008) (19) consider it prudent to introduce gluten in small amount while the infant is still breast-fed and to avoid both early (<4 months) and late (>7 months) introduction of gluten.
- EFSA, 2009 (17) state that present available data support the belief that gluten containing foods should be introduced not later than 6 months of age, preferably while still breastfeeding.
- COT/SACN, 2011 (50). *JOINT STATEMENT. Timing of introduction of gluten into the infant diet.* SACN and COT do not consider the evidence sufficient to support EFSA's conclusion on the introduction of gluten into the infant diet no later than 6 completed months of age with the aim of reducing the risk of subsequent development of celiac disease.

Supplementary table 11. Summary table. Breastfeeding, formula feeding and/or introduction of solids and outcome inflammatory bowel disease (IBD)

Author (alphabetical order), year (ref.nr)	Study design (study name if applicable)	No. and type of included studies (SLR)/ No. of participants (cohort study)	Exposure (incl age)	Outcome (incl age)	Effect/association	Study quality	Comments
Klement et al, 2004 (84)	SLR	17 studies included, but only 4 studies for Crohns disease and 4 studies for ulcerative colitis were of high quality. 27-713 cases and 98-713 controls/study (Ulcerative colitis) 24-1396 cases and 90-1396 controls/study (Crohns)	Brf; (various definitions)	Inflammatory bowel disease (Ulcerative colitis and/or Chron disease)	Breastfeeding had a statistically significant protective role against ulcerative colitis and an even greater role against Crohn disease Pooled OR for Crohns disease 0.67 (95% CI 0.52-0.86) Pooled OR for ulcerative colitis 0.77 (0.61-0.96) If only the studies of good quality are included pooled OR are; 0.45 (0.26-0.79) for Crohns disease and 0.56 (0.38-0.81) for ulcerative colitis.	A	Most of the included studies relied on long recall for the breastfeeding data. Only two had data from infancy, but then only breastfeeding at maternity ward. However, breastfeeding was only documented as ever-never, and this kind of recall from mothers tend to be accurate. Age of subjects: appr. ¼ >18 y, ¼ <18 y, ¼ = mix, ¼ =?