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META-ANALYSIS

Duration of Breastfeeding and Risk of Overweight: A Meta-Analysis

Thomas Harder[1], Renate Bergmann[1], Gerd Kallischnigg[2], and Andreas Plagemann[1]

[1] Clinic of Obstetrics, Division of Experimental Obstetrics, Charité—University Medicine, Berlin, Germany.
[2] Epidemiology Research Group, Institute of Public Health, Technical University, Berlin, Germany.

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Observational studies suggest a longer duration of breastfeeding to be associated dose dependently with a decrease in risk of overweight in later life. The authors performed a comprehensive meta-analysis of the existing studies on duration of breastfeeding and risk of overweight. Studies were included that reported the odds ratio and 95% confidence interval (or the data to calculate them) of overweight associated with breastfeeding and that reported the duration of breastfeeding and used exclusively formula-fed subjects as the referent. Seventeen studies met the inclusion criteria. By meta-regression, the duration of breastfeeding was inversely associated with the risk of overweight (regression coefficient = 0.94, 95% confidence interval (CI): 0.89, 0.98). Categorical analysis confirmed this dose-response association (<1 month of breastfeeding: odds ratio (OR) = 1.0, 95% CI: 0.65, 1.55; 1–3 months: OR = 0.81, 95% CI: 0.74, 0.88; 4–6 months: OR = 0.76, 95% CI: 0.67, 0.86; 7–9 months: OR = 0.67, 95% CI: 0.55, 0.82; >9 months: OR = 0.68, 95% CI: 0.50, 0.91). One month of breastfeeding was associated with a 4% decrease in risk (OR = 0.96/month of breastfeeding, 95% CI: 0.94, 0.98). The definitions of overweight and age had no influence. These findings strongly support a dose-dependent association between longer duration of breastfeeding and decrease in risk of overweight.

body weight; breast feeding; meta-analysis; obesity

Abbreviations: CI, confidence interval; OR, odds ratio.

The prevalences of overweight and obesity are increasing nearly worldwide. Therefore, a high priority has been given to research strategies to prevent the development of obesity. We have published a meta-analysis (1, 2) that showed breastfeeding, compared with formula feeding, to be associated with a decreased risk of overweight. Recently, this finding was confirmed by others (3). However, neither study investigated whether a relation exists between the duration of breastfeeding and the risk of overweight. This issue is of particularly high importance since it might support the causality of this association. Furthermore, it is highly relevant to clinical practice to know whether a longer duration of breastfeeding could lead to a stronger decrease in risk of overweight in later life. Therefore, we performed a meta-analysis of the relation between the duration of breastfeeding and the risk of overweight.

Reprint requests to Dr. Thomas Harder, Clinic of Obstetrics, Division of Experimental Obstetrics, Campus Virchow-Klinikum, Charité—University Medicine Berlin, Augustenburger Platz 1, 13353 Berlin, Germany (e-mail: thomas.harder@charite.de).

MATERIALS AND METHODS

Study base

The meta-analysis was conducted according to the checklist of the Meta-analysis of Observational Studies in Epidemiology (MOOSE) group (4). We performed a literature search including the databases MEDLINE (US National Library of Medicine's database accessed through PubMed, 1966 through December 2003), CINAHL (Cumulative Index to Nursing and Allied Health Literature, 1982 through December 2003), SERFILE (bibliographic information on biomedical and health science serials, 2002–2003), and EMBASE (the Excerpta Medica database, 1989 through December 2003), using the terms breastfeeding, infant nutrition, weaning, overweight, obes* (truncated), and adipos* (truncated) in the full-text option, without language restrictions. Furthermore, a manual search was carried out on all the references cited in published original studies and in all reviews identified by the literature search (5–17). To be eligible, studies had to fulfill the following three inclusion criteria: 1) be an original report comparing breastfed subjects with exclusively formula-fed subjects (referent group) of any given age, 2) report the odds ratio and 95 percent confidence interval (or data to calculate them) of overweight or obesity associated with breastfeeding, and 3) report the duration of breastfeeding for at least one exposure group. Any definition of overweight or obesity was allowed. From review of the abstracts identified in the search, 49 articles were subjected to full review; 33 of these studies were excluded since they did not fulfill the inclusion criteria (18 studies did not provide data to calculate the odds ratio, nine studies did not use exclusively formula-fed probands as the referent, and six studies did not report the duration of breastfeeding). Details are available on request.

Of the 16 original reports that met the inclusion criteria (18–33), one consisted of two independent studies (24), so that 17 studies (16 cohort studies, one case-control study) were included in this meta-analysis. From these reports, data were abstracted in duplicate, using a standardized form.

Statistical analysis

Unadjusted odds ratios and 95 percent confidence intervals were calculated directly from the data given in the articles, where possible. Otherwise, the published odds ratio and 95 percent confidence interval were used. We used three different approaches to investigate by means of meta-analytical techniques whether a relation exists between the duration of breastfeeding and the risk of overweight. First, a weighted meta-regression was performed (34), using the duration of breastfeeding as the independent variable and the weighted odds ratio for overweight in breastfed probands, compared with formula-fed subjects, as the dependent variable. Second, the pooled odds ratio for overweight in breastfed subjects was calculated separately for five predefined categories of duration of breastfeeding. Third, the pool-first method (35) was used to combine the regression coefficients obtained from the studies.

Meta-regression analysis. For meta-regression analysis, all duration-specific odds ratios had to be related to the respective duration of breastfeeding. Since the duration of breastfeeding was reported as categorical data with a certain range in the studies (e.g., 1–3 months, 4–6 months, and so on), the median of the upper and lower limits of each category was assigned to the particular estimate in each study (35). Estimates were plotted against the respective duration of breastfeeding as the independent variable. Since the scatterplot revealed a linear relation, a weighted meta-regression (34) with duration of breastfeeding as the covariate was performed (random-effects model). The regression coefficient with its 95 percent confidence interval was delogarithmized for data presentation.

Categorical analysis. A pooled odds ratio for overweight in breastfed subjects was calculated for the five separate predefined categories of duration of breastfeeding: less than 1 month, 1–3 months, 4–6 months, 7–9 months, and more than 9 months. Since the Cochrane Q-based test revealed significant heterogeneity in each case, a random-effects model was used throughout.

Trend estimation. To studies that provided data for more than two categories of duration of breastfeeding, we applied the ''pool-first method'' (35) to quantify the dose-response relation. This was possible for 11 studies (19–23, 25, 28–32). After visual inspection of the plots to ascertain model adequacy, we calculated a study-specific regression coefficient and corresponding 95 percent confidence interval for each study by use of a log-linear model. After exponentiation, the resulting odds ratio and 95 percent confidence interval for change in risk for each month of breastfeeding were pooled with a random-effects model.

Subgroup analysis. Two subgroup analyses were performed. First, we calculated separate estimates for all studies that used body mass index to measure overweight and for all that did not. Second, age-specific estimates were pooled in the predefined subgroups 0–5 years and 6 or more years by the random-effects model.

Publication bias and statistical software. Publication bias was assessed by inspection of the funnel plot and by formal testing for funnel plot asymmetry using the Begg test and the Egger test. Calculations were performed using STATA, version 8, software (Stata Corporation, College Station, Texas).

RESULTS

Study characteristics of included reports are displayed in tables 1 and 2. From the 17 studies that reported duration of breastfeeding, 14 gave data for more than one category of duration of breastfeeding, leading to 52 estimates included in the meta-regression analysis. Visual inspection of the scatterplot revealed that the relation between duration of breastfeeding and risk of overweight was linear. In the weighted meta-regression, duration of breastfeeding was significantly negatively related to risk of overweight (regression coefficient: 0.94, 95 percent confidence interval (CI): 0.89, 0.98) (figure 1).

Table 3 shows the results of categorical analysis. From 1 month of breastfeeding onward, the risk of subsequent overweight continuously decreased up to a reduction of

TABLE 1. Characteristics of the 17 studies, ordered alphabetically by first author, that are included in this meta-analysis, according to origin, design, data source, age, study size, loss to follow-up, exposure assessment method, and type of breastfeeding

Reference	Origin	Study design	Data source	Age	Study size (final no.)	Lost to follow-up (%)	Exposure assessment	Type of breastfeeding
Armstrong et al. (18)	Great Britain	Cohort	Survey	3–4 years	32,200	38	Records	Exclusive
Czajka-Narins and Jung (19)	United States	Cohort	Hospital	2 years	409	Not reported	Records	Partial
Dubois et al. (20)	Canada	Case-control	Hospital	4–9 months	89	Not reported	Questionnaire	Partial
Gillman et al. (21)	United States	Cohort	Survey	9–14 years	15,341	55.1	Questionnaire	Partial
Hediger et al. (22)	United States	Cohort	Survey	3–5 years	2,685	18	Questionnaire	Partial
Langnäse et al. (23)	Germany	Cohort	Hospital	1, 2, and 5–7 years	1,326	48	Not reported	Not reported
Liese et al. (I) (24)	Germany	Cohort	Survey	9–10 years	1,046	48	Questionnaire	Partial
Liese et al. (II) (24)	Germany	Cohort	Survey	9–10 years	1,062	47	Questionnaire	Partial
O'Callaghan et al. (25)	Australia	Cohort	Hospital	4–6 years	4,062	45	Questionnaire	Not reported
Parsons et al. (26)	Great Britain	Cohort	Survey	33 years	11,407	27	Not reported	Partial
Poulton and Williams (27)	New Zealand	Cohort	Hospital	3, 5, 7, 9, 11, 13, 15, 18, 21, and 26 years	695–939	9.5–33	Not reported	Partial
Richter (28)	German Democratic Republic	Cohort	Survey	6–7 years	2,385	Not reported	Not reported	Not reported
Thorogood et al. (29)	Great Britain	Cohort	Hospital	1 year	66	59	Records	Not reported
Toschke et al. (30)	Czechoslovakia	Cohort	Survey	6–14 years	33,768	2	Questionnaire	Partial
Von Kries et al. (31)	Germany	Cohort	Survey	5–6 years	10,240	23	Questionnaire	Exclusive
Wadsworth et al. (32)	Great Britain	Cohort	Survey	6 years	3,731	Not reported	Not reported	Not reported
Yeung et al. (33)	Canada	Cohort	Survey	1, 3, 5, and 6 months	316	23	Not reported	Partial

more than 30 percent, reaching a plateau at 9 months of breastfeeding.

Figure 2 shows the forest plot with odds ratio and 95 percent confidence interval and the pooled estimate for the reduction in risk of overweight for each month of breastfeeding, calculated from trend analysis by a random-effects model. Each month of breastfeeding was found to be associated with a 4 percent decrease in risk (odds ratio (OR) = 0.96/month of breastfeeding, 95 percent CI: 0.94, 0.98). A fixed-effects model revealed a similar pooled odds ratio and a nearly identical 95 percent confidence interval (OR = 0.96, 95 percent CI: 0.95, 0.98).

In only two of these studies (22, 31) was the influence of the duration of exclusive breastfeeding analyzed. The pooled odds ratio for risk of overweight per month of exclusive breastfeeding was 0.94 (95 percent CI: 0.89, 0.99; random-effects model).

Subgroup analyses revealed that the definition of overweight influenced the estimate only slightly. In studies that used body mass index to define overweight, the pooled odds ratio was 0.96 (95 percent CI: 0.94, 0.98) for eight studies, while the odds ratio was 0.93 (95 percent CI: 0.87, 0.99) for the three studies that used another measure to define overweight or obesity. Similarly, the age at examination had only a marginal influence on the magnitude of the effect of duration of breastfeeding on risk of overweight. The pooled odds ratio from all five studies investigating probands up to or including 5 years of age was 0.97 (95 percent CI: 0.94, 0.99), while in older subjects aged 6 or more years, it was 0.96 (95 percent CI: 0.93, 0.99) for six studies. No evidence of publication bias was observed, as indicated by a symmetric funnel plot (not shown) and a nonsignificant Begg test ($p = 0.64$) and Egger test ($p = 0.77$).

TABLE 2. Characteristics of the 17 studies, ordered alphabetically by first author, that are included in this meta-analysis, according to duration of breastfeeding, outcome assessment, definition of overweight/obesity, and confounders

Reference	Duration of breastfeeding	Outcome assessment	Definition of overweight and obesity	Confounders
Armstrong et al. (18)	6–8 weeks	MS*	Obesity: BMI* > 95th percentile; severe obesity: BMI > 98th percentile	Sex, birth weight, and socioeconomic status
Czajka-Narins and Jung (19)	2–4, 5–7, 8–10, and 11–18 months	MS	Overweight: BMI > 18.5 kg/m^2	None
Dubois et al. (20)	<1, 1–3, and >3 months	MS	Obesity: >90th percentile of weight/age	None
Gillman et al. (21)	<1, 1–3, 4–6, 7–9, and >9 months	SR*	Risk of overweight: BMI = 85th–95th percentile; overweight: BMI > 95th percentile†	Age, sex, Tanner stage, television, physical activity, eating habits, weight cycling, concerns to gain weight, birth order, household income, daily energy intake, maternal body mass index, birth weight, and maternal smoking
Hediger et al. (22)	≤2, 3–5, 6–8, and ≥9 months	MS	Risk of overweight: BMI = 85th–94th percentile; overweight: BMI > 95th percentile	Birth weight, ethnicity, age, sex, maternal body mass index, and age at introduction of solid food
Langnäse et al. (23)	≤6 and >6 months	MS	Overweight: BMI > 90th percentile	None
Liese et al. (I) (24)	<6 and 6–12 months (exclusive breastfeeding: <2, 2–4, and 5–6 months)	MS	Overweight: BMI > 90th percentile	Age, sex, city, nationality, socioeconomic status, and smoking
Liese et al. (II) (24)	<6 and 6–12 months (exclusive breastfeeding: <2, 2–4, and 5–6 months)	MS	Overweight: BMI > 90th percentile	Age, sex, city, nationality, socioeconomic status, and smoking
O'Callaghan et al. (25)	≤2 weeks, 3–6 weeks, 7 weeks–3 months, 4–5 months, and ≥6 months	MS	Moderate obesity: BMI = 85th–94th percentile; marked obesity: BMI > 94th percentile	Birth weight, sex, small for gestational age, eating problems, and sleeplessness
Parsons et al. (26)	>1 month	MS	Obesity: BMI > 30 kg/m^2	Maternal body mass index, social class, and maternal smoking
Poulton and Williams (27)	≤6 and >6 months	NR*	Overweight: 3–15 years: percentiles (not further specified); >15 years: BMI > 25 kg/m^2	Sex, birth weight, maternal education, and maternal and paternal overweight
Richter (28)	<3, 3–6, and ≥7 months	MS	Overweight: weight > 120%	None
Thorogood et al. (29)	<1, 1–2, 3–4, 5–6, and >6 months	MS	Overweight: weight/50th percentile of weight divided by length/50th percentile of length >110%	None
Toschke et al. (30)	<1, 2–3, 4–6, and >6 months	MS	Overweight: BMI > 90th percentile; obesity: BMI > 97th percentile	Parental education, parental obesity, maternal smoking, birth weight of >4,000 g, daily television watching of >1 hour, sport outside school, and siblings
Von Kries et al. (31)	≤2, 3–5, 6–12, and >12 months	MS	Overweight: BMI > 90th percentile; obesity: BMI > 97th percentile	Parental education, maternal smoking during pregnancy, birth weight of <2,500 g, own bedroom, and consumes butter more than 3 times per week
Wadsworth et al. (32)	≤2, 3–4, 5–10, and >10 months	NR	Overweight: BMI > 90th percentile; obesity: BMI > 97th percentile	Socioeconomic status during childhood, birth weight of >2,500 g, no. of persons per room at 2 years, and fat consumption at 4 years
Yeung et al. (33)	≥2 months	MS	Obesity: weight/length > 95th percentile	None

* MS, weight and height were measured by investigators; BMI, body mass index; SR, weight and height were self-reported by probands; NR, not reported.

† Unadjusted data are reported only for "overweight," not for "at risk for overweight."

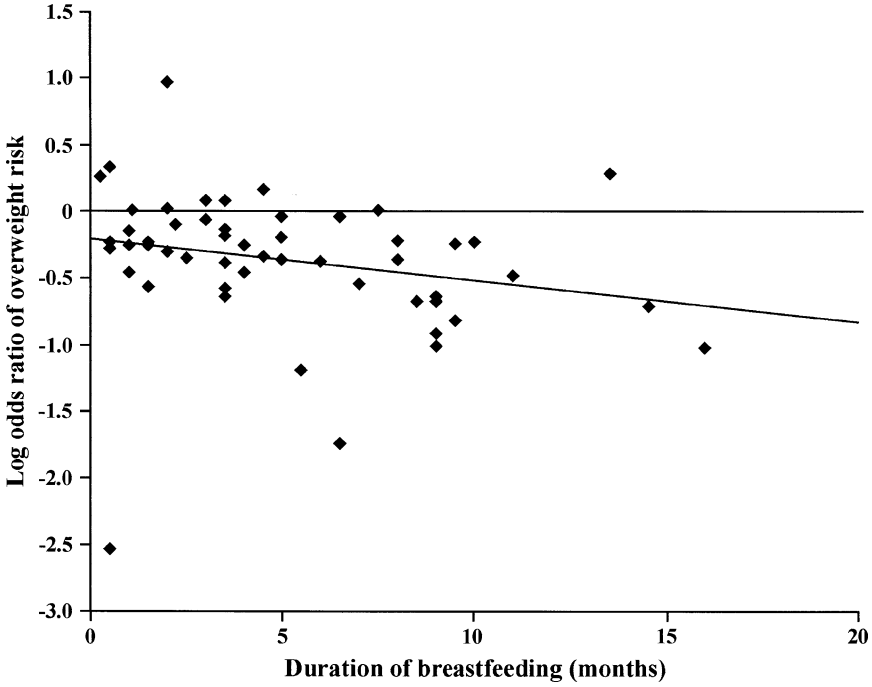

FIGURE 1. Scatterplot and meta-regression line of log odds ratio of risk of overweight/obesity associated with breastfeeding, according to duration of breastfeeding. A total of 17 studies provided 52 estimates of duration of breastfeeding and overweight. Weighted meta-regression revealed a significant inverse linear relation between the duration of breastfeeding and the risk of overweight (regression coefficient = 0.94, 95% confidence interval: 0.89, 0.98).

DISCUSSION

Using three different techniques, we show that a longer duration of breastfeeding is associated with a larger decrease in risk of overweight. Each of the three methods used in our study has its own advantages and limitations. Meta-regression analysis is known to be highly flexible with regard to the shape of the dose-response relation (34). However, the duration-specific estimates from one study are not completely independent from each other as they have the same referent category in each case, which could bias the result. This disadvantage can be at least partly overcome by the use of separate categories of duration of breastfeeding. However, because of the smaller sample sizes in some of the categories, the power of the statistical analysis might be limited. The ''pool-first method'' (35) is highly flexible with regard to the shape of the dose-response-relation, and it ensures complete independence of all included estimates. However, as a minimum of three categories is needed to calculate the study-specific regression coefficient in the log-linear model, in the case of our meta-analysis, the use of this technique had to be restricted to studies from which study-specific regression coefficients could be calculated. Nevertheless, in essence, all three methods came to the same result of an inverse linear association between duration of breastfeeding and risk of overweight in later life. However, it has to be considered that all studies performed until now on breastfeeding and risk of overweight are secondary analyses of health surveys or of studies designed primarily to answer different questions.

One major methodological problem to overcome in a meta-analysis of breastfeeding and risk of overweight is the change of the definition of overweight over time. Following the proposal of the Meta-analysis of Observational

TABLE 3. Duration of breastfeeding and risk of overweight: categorial analysis (random-effects model)

	Duration of breastfeeding				
	<1 month	1–3 months	4–6 months	7–9 months	>9 months
No. of duration-specific study estimates	5	14	15	11	7
Odds ratio for overweight	1.0	0.81	0.76	0.67	0.68
95% confidence interval	0.65, 1.55	0.74, 0.88	0.67, 0.86	0.55, 0.82	0.50, 0.91

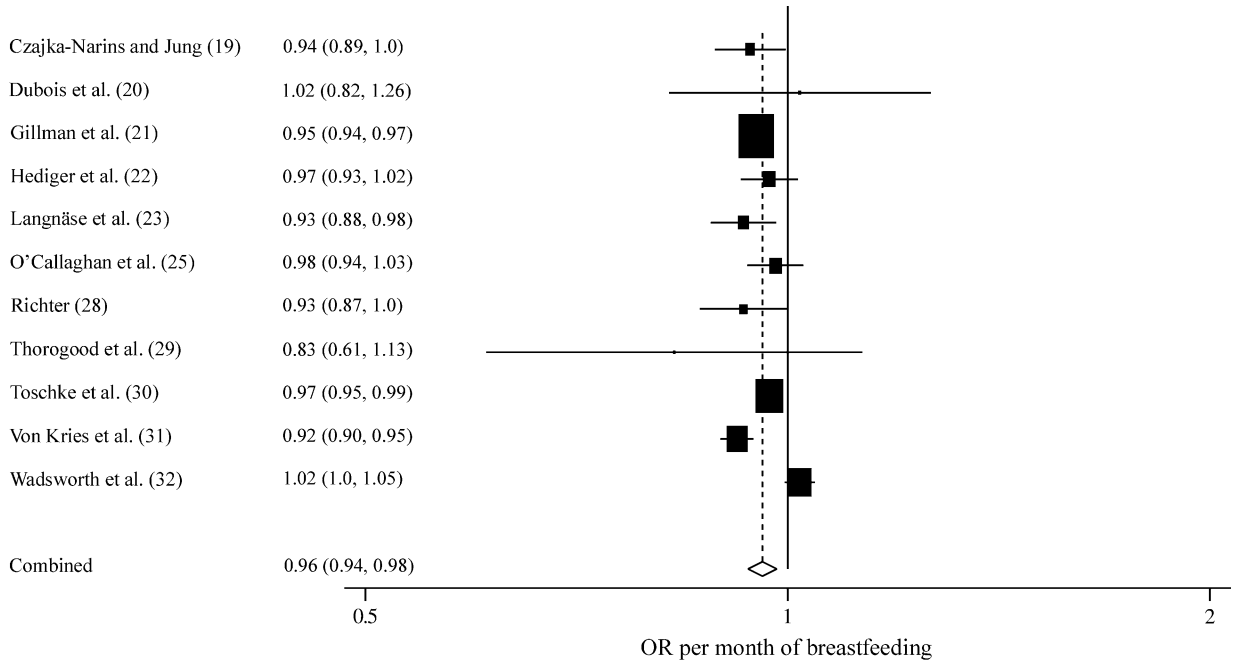

FIGURE 2. Odds ratios (with corresponding 95% confidence intervals in parentheses) for overweight, per month of breastfeeding. Studies are ordered alphabetically by first author. The pooled or "combined" odds ratio (OR) was calculated by a random-effects model.

Studies in Epidemiology group (4), we included any definition of overweight and investigated the possible consequences of this strategy by subgroup analysis. In fact, the definition of overweight had only a minor impact on the pooled estimate.

Eight of the studies (18, 22, 24–27, 31, 32) gave duration-specific, confounder-adjusted estimates, some only for subsets of the data. Because of this small sample size and considering the fact that the type and number of confounders differed largely among these studies, we did not calculate a pooled estimate of the confounder-adjusted odds ratio. Remarkably, only three (19, 21, 22) of the 17 studies gave some basic information on ethnicity, mostly by declaring a "mixed" ethnic background of the population. Therefore, it is unclear to date whether the effect of breastfeeding on risk of overweight is restricted to certain ethnic groups and might be confounded by social class. Taken together, a statistically based decision on the role of confounding could not be derived from the data here. However, Savitz (36) has postulated that, in general, the existence of a dose-response relation reduces the likelihood of an association to be completely due to confounding, since increasingly implausible scenarios are required for the exposure-confounder association to exaggerate the dose-response gradient.

The mechanisms by which breastfeeding affects the risk of overweight are still unclear. Breastfeeding results in a lower body weight gain during the critical neonatal period, obviously caused by a lower mean caloric intake in breastfed infants, compared with formula-fed neonates (37). A lower body weight gain during neonatal life has been shown to lead to decreased risk of obesity in adolescence and adulthood (38). In animal experiments, the kind of neonatal nutrition was shown to influence the development of neuroendocrine circuits in the mediobasal hypothalamus that regulates appetite control and body weight, with long-term consequences for risk of obesity (for review, refer to reference 39). These mechanisms might also explain why a longer duration of breastfeeding is associated with a stronger decrease in risk of overweight in later life.

In summary, we found that the duration of breastfeeding is inversely and linearly associated with the risk of overweight. The risk of overweight was reduced by 4 percent for each month of breastfeeding. This effect lasted up to a duration of breastfeeding of 9 months and was independent of the definition of overweight and age at follow-up. Even if interpreted as being of relatively small size, this association, if causal, might be of importance for the general population. Since the majority of studies analyzed here used partially breastfed subjects, it might be concluded that, beyond exclusive breastfeeding, also longer partial breastfeeding up to 9 months leads to a greater decrease in risk of overweight in later life, which might be considered in future clinical recommendations.

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