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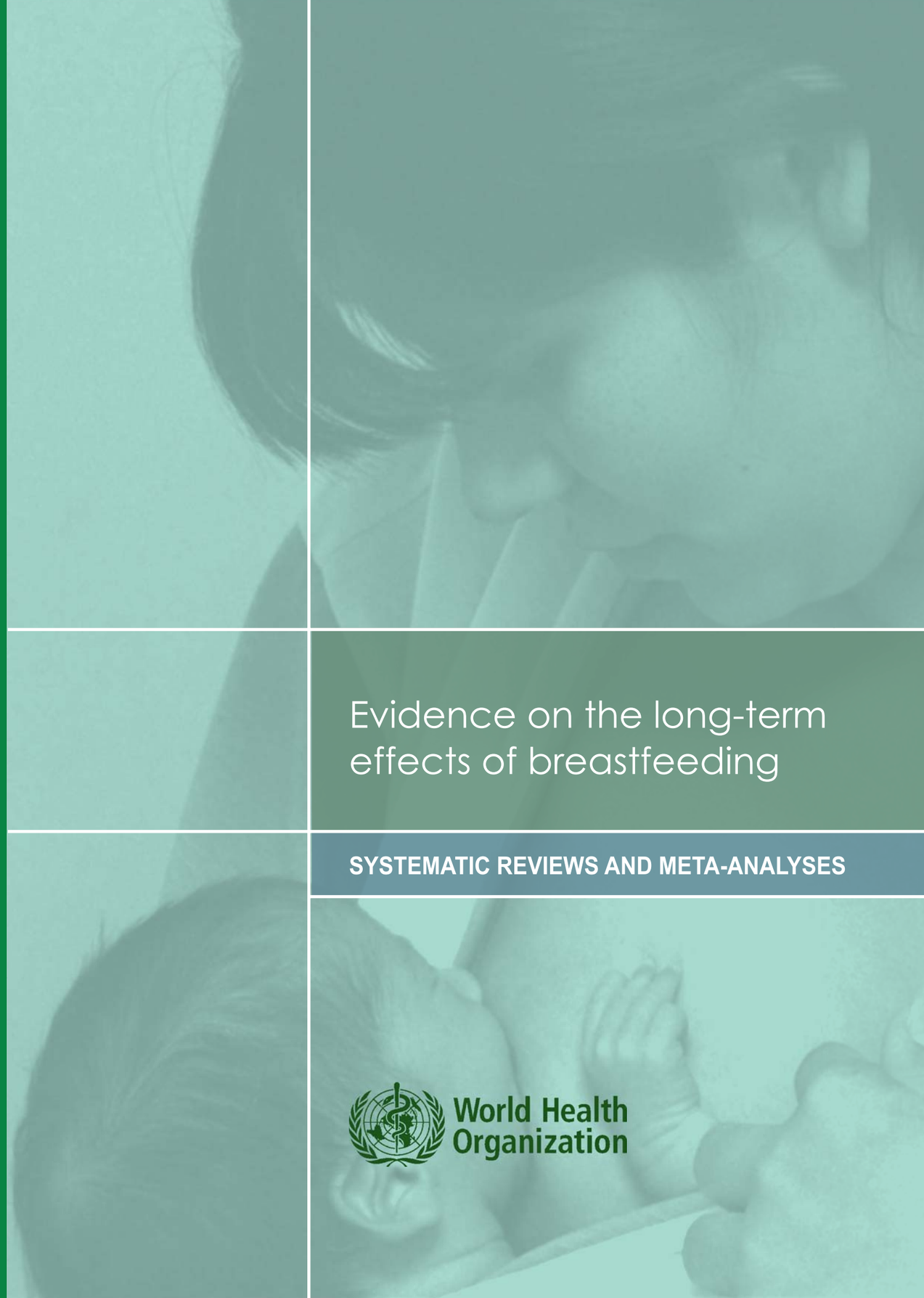
EVIDENCE ON THE LONG-TERM EFFECTS OF BREASTFEEDING: SYSTEMATIC REVIEWS AND META-ANALYSES WHO



Evidence on the long-term effects of breastfeeding

SYSTEMATIC REVIEWS AND META-ANALYSES

World Health Organization

Evidence on the long-term effects of breastfeeding

SYSTEMATIC REVIEWS AND META-ANALYSES

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Executive summary

Background: Breastfeeding presents clear short-term benefits for child health, mainly protection against morbidity and mortality from infectious diseases. On the other hand, there is some controversy on the long-term consequences of breastfeeding. Whereas some studies reported that breastfed subjects present a higher level of school achievement and performance in intelligence tests, as well as lower blood pressure, lower total cholesterol and a lower prevalence of overweight and obesity, others have failed to detect such associations.

Objectives: The primary objective of this series of systematic reviews was to assess the effects of breastfeeding on blood pressure, diabetes and related indicators, serum cholesterol, overweight and obesity, and intellectual performance.

Search strategy: Two independent literature searches were conducted at the World Health Organization in Geneva, Switzerland, and at the University of Pelotas in Brazil, comprising the MEDLINE (1966 to March 2006) and Scientific Citation Index databases.

Selection criteria: We selected observational and randomized studies, published in English, French, Portuguese and Spanish, assessing the effects of breastfeeding on blood pressure, obesity/overweight, total cholesterol, type-2 diabetes, and intellectual performance. Studies that restricted the measurement of outcomes to infancy were excluded from the meta-analyses. The type of comparison group used (e.g. never breastfed or breastfed for less than *x* months) did not constitute a selection criterion.

Data extraction and analysis: Two reviewers independently evaluated study quality, using a standardized protocol, and disagreement was resolved by consensus rating. Fixed and random-effects models were used to pool the effect estimates, and a random-effects regression was used to assess several potential sources of heterogeneity.

Effect on blood pressure: We included 30 and 25 estimates for systolic and diastolic blood pressure, respectively. In a random-effects model, systolic (mean difference: -1.21 mmHg; 95% confidence interval (CI): -1.72 to -0.70) and diastolic blood pressures (mean difference: -0.49 mm Hg; 95% CI: -0.87 to -0.11) were lower among breastfed subjects. Publication bias was evident, with smaller studies reporting a greater protective effect of breastfeeding. However, even among studies with $\geq$1000 participants a statistically significant effect of breastfeeding was observed (mean difference in systolic blood pressure: -0.59 mmHg; 95% CI: -1.00 to -0.19). Adjustment for confounding was also a source of heterogeneity between study results, but even among those studies controlling for several socioeconomic and demographic variables, systolic (mean difference: -1.19; 95% CI: -1.70 to -0.69) and diastolic (mean difference: -0.61; 95% CI: -1.12 to -0.10) blood pressures were lower among breastfed subjects. Publication bias and residual confounding may be responsible for part (but not all) of the observed effect of breastfeeding on blood pressure.

Effect on serum cholesterol: Breastfed subjects presented lower mean total cholesterol in adulthood (mean difference: -0.18; 95% CI: -0.30 to -0.06 mmol/L), whereas for children and adolescents the association was not statistically significant. Age at assessment of cholesterol explained about 60% of the heterogeneity between studies, whereas study size, control for confounding, year of birth and

categorization of breastfeeding duration did not play a significant role. The evidence suggests that breastfeeding is related to lower cholesterol levels and this association is not due to publication bias or residual confounding.

Effect on overweight and obesity: We obtained 39 estimates of the effect of breastfeeding on prevalence of overweight/obesity. In a random-effects model, breastfed individuals were less likely to be considered as overweight and/or obese, with a pooled odds ratio of 0.78 (95% CI: 0.72–0.84). Control for confounding, age at assessment, year of birth, and study design did not modify the effect of breastfeeding. Because a statistically significant protective effect was observed among those studies that controlled for socioeconomic status and parental anthropometry, as well as with $\geq$1500 participants, the effect of breastfeeding was not likely to be due to publication bias or confounding.

Effect on type-2 diabetes: We identified five papers that evaluated the relationship between breastfeeding duration and type-2 diabetes. Breastfed subjects were less likely to present type-2 diabetes (pooled odds ratio: 0.63; 95% CI: 0.45–0.89).

Effect on intelligence and schooling: For the assessment of performance in intelligence tests, we obtained data from eight studies that controlled for intellectual stimulation at home and collected information on infant feeding in infancy, in which the duration of breastfeeding was of at least one month among breastfed subjects. Performance in intelligence tests was higher among those subjects who had been breastfed (mean difference: 4.9; 95% CI: 2.97–6.92). Positive studies included a randomized trial. Regarding school performance in late adolescence or young adulthood, three studies showed a positive effect of breastfeeding.

Limitations: Because nearly all studies included in the analyses are observational, it is not possible to completely rule out the possibility that these results may be partly explained by self-selection of breastfeeding mothers or by residual confounding. Publication bias was assessed by examining the effect of study size on the estimates and was found not to be important for most outcomes. Very few studies were available from low/middle-income countries, where the effect of breastfeeding may be modified by social and cultural conditions.

Reviewers' conclusions: The available evidence suggests that breastfeeding may have long-term benefits. Subjects who were breastfed experienced lower mean blood pressure and total cholesterol, as well as higher performance in intelligence tests. Furthermore, the prevalence of overweight/obesity and type-2 diabetes was lower among breastfed subjects. All effects were statistically significant, but for some outcomes their magnitude was relatively modest.

I. Introduction

Breastfeeding brings clear short-term benefits for child health by reducing mortality and morbidity from infectious diseases. A collaborative reanalysis of studies conducted in middle/low-income countries reported a reduced risk of mortality from infectious diseases among breastfed infants, up to the second birthday (*1*). Kramer et al (*2*) reviewed the evidence on the effects on child health and growth of exclusive breastfeeding for 6 months. Infants who were exclusively breastfed for 6 months presented lower morbidity from gastrointestinal and allergic diseases, while showing similar growth rates to non-breastfed children.

Based on such evidence, WHO (*3*) and UNICEF (*4*) now recommend that every infant should be exclusively breastfed for the first six months of life, with continued breastfeeding for up to two years or longer. In this review we address the long-term consequences of breastfeeding on adult health and intellectual development.

Current interest in the long-term consequences of early life exposures has been fuelled by the original finding of Barker et al (*5*) that size at birth and in infancy was related to the development of adult diseases – including diabetes, hypertension and cardiovascular conditions. These findings led to the fetal origin hypothesis, which postulates that adverse intrauterine conditions would be responsible for fetal malnutrition and low birthweight, a process that would also increase the susceptibility to chronic natal exposures – such as infant growth and feeding patterns – that could also be related to the development of chronic diseases.

The notion that nutrition during early phases of human development can alter organ function, and thereby predispose – or programme – individuals to a later onset of adult disease, is an area of considerable interest to researchers and of great concern to public health. This idea originates from the more general concept in developmental biology which was defined by Lucas as "programming" (*11*). This is defined as the process whereby a stimulus or insult applied at a critical or sensitive period of development results in a long-term or permanent effect on the structure or function of the organism. This hypothesis is currently described as the "developmental origins of health and disease" (*12*).

Over 400 scientific publications are available on the association between breastfeeding and health outcomes beyond infancy. Some researchers claim that the benefits of breastfeeding include increased school achievement or performance in intelligence tests, reduced mean blood pressure, lower total cholesterol, and a lower prevalence of overweight and obesity. On the other hand, other studies have failed to detect such associations. The evidence on long-term effects of breastfeeding may be important for further promotion of this healthy practice throughout the world.

The Department of Child and Adolescent