

# Prolonged and Exclusive Breastfeeding Reduces the Risk of Infectious Diseases in Infancy

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## KEY WORDS

duration of breastfeeding, exclusive breastfeeding, gastrointestinal tract infections, infants, longitudinal study, upper and lower respiratory tract infections

## ABBREVIATIONS

aOR—adjusted odds ratio

CI—confidence interval

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**WHAT'S KNOWN ON THIS SUBJECT:** Exclusive breastfeeding seems to decrease the risk of infectious diseases in infancy. However, the World Health Organization has called for more research regarding the benefits for 6 months instead of 4 months of exclusive breastfeeding.



**WHAT THIS STUDY ADDS:** Exclusive breastfeeding to the age of 6 months tended to be more protective than exclusive breastfeeding until the age of 4 months and partially thereafter. Our findings support health-policy strategies that promote exclusive breastfeeding for 6 months in industrialized countries.

## abstract

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**OBJECTIVE:** To examine the associations of duration of exclusive breastfeeding with infections in the upper respiratory (URTI), lower respiratory (LRTI), and gastrointestinal tracts (GI) in infancy.

**METHODS:** This study was embedded in the Generation R Study, a population-based prospective cohort study from fetal life onward in the Netherlands. Rates of breastfeeding during the first 6 months (never; partial for <4 months, not thereafter; partial for 4–6 months; exclusive for 4 months, not thereafter; exclusive for 4 months, partial thereafter; and exclusive for 6 months) and doctor-attended infections in the URTI, LRTI, and GI until the age of 12 months were assessed by questionnaires and available for 4164 subjects.

**RESULTS:** Compared with never-breastfed infants, those who were breastfed exclusively until the age of 4 months and partially thereafter had lower risks of infections in the URTI, LRTI, and GI until the age of 6 months (adjusted odds ratio [aOR]: 0.65 [95% confidence interval (CI): 0.51–0.83]; aOR: 0.50 [CI: 0.32–0.79]; and aOR: 0.41 [CI: 0.26–0.64], respectively) and of LRTI infections between the ages of 7 and 12 months (aOR: 0.46 [CI: 0.31–0.69]). Similar tendencies were observed for infants who were exclusively breastfed for 6 months or longer. Partial breastfeeding, even for 6 months, did not result in significantly lower risks of these infections.

**CONCLUSIONS:** Exclusive breastfeeding until the age of 4 months and partially thereafter was associated with a significant reduction of respiratory and gastrointestinal morbidity in infants. Our findings support health-policy strategies to promote exclusive breastfeeding for at least 4 months, but preferably 6 months, in industrialized countries. *Pediatrics* 2010;126:e18–e25

Respiratory and gastrointestinal tract infections are the leading cause of morbidity in children.<sup>1,2</sup> Prospective cohort studies in industrialized countries revealed a prevalence of 3.4% to 32.1% for respiratory tract infectious diseases and 1.2% to 26.3% for gastrointestinal infectious diseases in infancy.<sup>3–8</sup> The risks of these infectious diseases are affected by several factors including birth weight, gestational age, socioeconomic status, ethnicity, number of siblings, day care attendance, and parental smoking.<sup>3,5,6,8–20</sup>

Breastfeeding has been suggested as a modifiable influencing factor. When given exclusively, breastfeeding reduces the risk of infectious diseases in infants in developing countries.<sup>21,22</sup> In industrialized countries, exclusive breastfeeding during the first 6 months seems to decrease the risk of gastrointestinal tract infections, compared with exclusive breastfeeding during only the first 3 to 4 months.<sup>23,24</sup> On the basis of these and other reports, the World Health Organization recommended in 2001 that all children be exclusively breastfed for 6 months instead of 4 months. However, the organization also called for more research regarding the benefits of 6 vs 4 months of exclusive breastfeeding.<sup>25</sup> Thus far, several studies in industrialized countries revealed that a shorter duration of breastfeeding increases the risk of common infectious diseases, such as respiratory and gastrointestinal tract infections.<sup>8,19,24,26–32</sup> However, in these studies, various definitions of the exclusiveness of breastfeeding were used<sup>24,27,28,30</sup> or the combination of duration and exclusiveness of breastfeeding was not taken into account.<sup>8,31</sup>

We used a population-based prospective cohort study in the city of Rotterdam, Netherlands, to examine the associations between duration of exclusive breastfeeding and upper and

lower respiratory and gastrointestinal tract infections during the first year of life.

## METHODS

### Design

This study was embedded in the Generation R Study, a population-based prospective cohort study from fetal life until young adulthood in the city of Rotterdam, Netherlands. The Generation R Study was designed to identify early environmental and genetic determinants of growth, development, and health and has been described previously in detail.<sup>33,34</sup> Mothers were enrolled early in their pregnancy (gestational age < 18 weeks) or until the birth of the child. All children were born between April 2002 and January 2006 and form a prenatally enrolled birth cohort that is currently being followed until young adulthood. The response rate for the Generation R Study is 61%. In total, 7893 parents gave informed consent for participation of their infants in the postnatal phase of the study.<sup>33</sup> The medical ethics committee of the Erasmus Medical Center (Rotterdam, Netherlands) approved the study. Written informed consent was obtained from all participants.

### Duration and Exclusiveness of Breastfeeding

Information about breastfeeding was obtained by postal questionnaires when infants were aged 6 and 12 months.<sup>33</sup> Mothers were asked whether they ever breastfed their infant (no or yes). The duration of breastfeeding was assessed by asking at what age (in months) the infant received breast milk for the last time. Three categories of breastfeeding were used for 3 groups of infants who received breastfeeding for less than 4 months, 4 to 6 months, or 6 months or longer. The duration of exclusive breastfeeding was defined by using in-

formation about at what age other types of milk and/or solids were introduced during the first 6 months of life. The information about duration and exclusiveness of breastfeeding was combined and grouped into the following 6 breastfeeding categories: (1) never; (2) partial for less than 4 months, not thereafter; (3) partial for 4 to 6 months; (4) exclusive for 4 months, not thereafter; (5) exclusive for 4 months, partial thereafter; and (6) exclusive for 6 months. “Never” indicates that the infant had never been breastfed, “partial” indicates that the infant was both breastfeeding and fed with formula or solids during this period, and “exclusive” indicates that the infant was breastfed and received no other milk, solids, or fluids. After the age of 6 months, all infants received other milk, fluids, and/or solids.

### Infectious Diseases

Information about infectious diseases was obtained with questionnaires given when the infants were aged 6 to 12 months. Parents were asked whether their infant had had a serious cold, ear or throat infection, pneumonia, bronchitis, bronchiolitis, or gastrointestinal tract infection (“no,” “yes, not visited a doctor,” or “yes, visited a doctor”). No information was available for the number of episodes of these infections. The respiratory tract infections were combined into doctor-attended and not doctor-attended upper (serious cold, ear infection, throat infection) and lower (pneumonia, bronchitis, and bronchiolitis) respiratory tract infections.

### Covariates

Information about the ethnicity and educational level of the mothers was obtained at the time of enrollment in the study. Ethnicity and educational level of the mothers were defined according to the classification of Statistics Netherlands.<sup>35,36</sup> Information on family his-

tory of asthma, house dust mite allergy, and hay fever was available from the questionnaires. Birth weight and date of birth were obtained from midwife and hospital registries. Gestational age was established by fetal ultrasound examination.<sup>37</sup> Information about siblings, day care attendance, and maternal smoking (no or yes) was obtained by questionnaire when the infants were 6 months old.

### Cohort for Analysis

Of the 7893 participants in the postnatal cohort, 7295 (92%) gave consent to receive questionnaires. Our analyses were restricted to singletons. Of 7116 infants, 60% and 69% of the participants responded to the questionnaires given when the infant was aged 6 and 12 months, respectively. Information about breastfeeding in infancy was available for 4618 infants (65%). Of those infants, information about at least 1 infectious disease at the ages of 6 and 12 months was available for 4164 and 3962 infants, respectively. We compared differences between subjects included and not included in the analyses. For the adjusted analyses, complete information about duration of exclusive breastfeeding, infectious diseases, and all confounders until the age of 6 months was available for 3504 (upper respiratory tract infections), 3489 (lower respiratory tract infections), and 3438 (gastrointestinal infections) infants. For the age period of 7 to 12 months, complete information on breastfeeding and infectious diseases was available for 2958 (upper respiratory tract infections), 3027 (lower respiratory tract infections), and 2938 (gastrointestinal infections) infants.

### Data Analysis

First, differences in subject characteristics between those included and not included in the analyses were compared by using  $\chi^2$  tests. Second, the

associations between duration of breastfeeding and upper and lower respiratory and gastrointestinal tract infections in infants aged 6 and 12 months were analyzed by using multiple logistic regression analysis. Third, to examine whether the effects of the duration of breastfeeding were a result of exclusive breastfeeding, the associations between duration of exclusive breastfeeding and upper and lower respiratory and gastrointestinal tract infections were examined. All models were adjusted for potential confounders, including maternal education, ethnicity, smoking, gestational age, birth weight, siblings, and day care attendance. Tests for trend were performed by including the breastfeeding categories as continuous variables in the regression models. The statistical analyses were performed by using SPSS 11.0 for Windows (SPSS Inc, Chicago, IL).

## RESULTS

The median infant age at which parents filled in the 6- and 12-month questionnaire was 6.3 months (90% confidence interval [CI]: 5.7–8.8) and 11.9 months (90% CI: 11.6–13.6), respectively. Most of the mothers were highly educated (55%) and of Dutch ethnicity (61%) (Table 1). Median gestational age at birth was 40.1 weeks (90% CI: 37.1–42.1 weeks), and mean birth weight was 3456 g (SD: 547 g). Of all mothers, 88% initiated breastfeeding. Of all infants, 29% received breastfeeding for less than 4 months, 25% for 4 to 6 months, and 34% for 6 months or more. When the duration of partial and exclusive breastfeeding was taken into account, most mothers partially breastfed their infants for less than 4 months or for 4 to 6 months (29% and 29%) or breastfed their infants exclusively until the age of 4 months and partially thereafter (26%). Only 1.4% of all the infants were exclusively breastfed for 6 months. In the first 6 months

**TABLE 1** Maternal and Infant Characteristics of the Study Population

|   | Infants<br>(N = 4164) |
|---|-----------------------|
| <b>Mother</b>   |                       |
| Maternal age, mean (SD), y  | 31.1 (4.8)            |
| Education, % (n)  |                       |
| Low   | 6.2 (246)             |
| Intermediate  | 38.7 (1538)           |
| High  | 55.2 (2195)           |
| Non-Dutch ethnicity, % (n)  | 38.9 (1574)           |
| Smoking, % (n)  | 16.2 (647)            |
| <b>Infant</b>   |                       |
| Girl  | 50.6 (2107)           |
| Gestational age, median (95% range), wk                                 | 40.1 (37.1–42.1)      |
| Birth weight, mean (SD), g  | 3456 (547)            |
| Siblings, $\geq 1$ , % (n)  | 40.2 (1604)           |
| Day care attendance, % (n)  | 49.7 (1949)           |
| Family history of asthma, house dust mite allergy, and hay fever, % (n) | 59.0 (1839)           |
| Duration of breastfeeding, % (n)  |                       |
| Never   | 12.5 (519)            |
| <4 mo   | 29.1 (1203)           |
| 4–6 mo  | 24.5 (1012)           |
| $\geq 6$ mo   | 33.9 (1404)           |
| Duration of exclusive breastfeeding, % (n)                              |                       |
| Never   | 12.8 (519)            |
| Partial for <4 mo, not breastfed thereafter                             | 29.2 (1182)           |
| Partial for 4–6 mo  | 28.8 (1166)           |
| Exclusive for 4 mo, not breastfed thereafter                            | 2.0 (80)              |
| Exclusive for 4 mo, partially breastfed thereafter                      | 25.7 (1037)           |
| Exclusive for 6 mo  | 1.4 (58)              |
| Doctor-attended infectious diseases at $\leq 6$ mo, % (n)               |                       |
| URTI  | 39.5 (1644)           |
| LRTI  | 7.8 (323)             |
| GI  | 7.6 (309)             |
| Doctor-attended infectious diseases at 7–12 mo, % (n)                   |                       |
| URTI  | 26.6 (912)            |
| LRTI  | 10.2 (360)            |
| GI  | 8.7 (295)             |

Data were missing on education ( $n = 185$ ), ethnicity ( $n = 121$ ), smoking ( $n = 170$ ), birth weight ( $n = 3$ ), siblings ( $n = 171$ ), day care attendance ( $n = 240$ ), family history of asthma, house dust mite allergy, and hay fever ( $n = 1046$ ), duration of breastfeeding ( $n = 26$ ), and duration of exclusive breastfeeding ( $n = 122$ ). Data were missing for questionnaires at age 6 months for upper respiratory tract infections ( $n = 2$ ), lower respiratory tract infections ( $n = 36$ ), and gastrointestinal infections ( $n = 92$ ) and at age 12 months for upper respiratory tract infections ( $n = 737$ ), lower respiratory tract infections ( $n = 644$ ), and gastrointestinal infections ( $n = 772$ ). URTI indicates upper respiratory tract infection; LRTI, lower respiratory tract infection; GI, gastrointestinal infection.

of life, 40% of all the infants had an upper respiratory tract infection, 8% had a lower respiratory tract infection,

**TABLE 2** Maternal Characteristics and Breastfeeding Habits: Duration of Exclusive Breastfeeding

|  | Never<br>( <i>n</i> = 519),<br>% ( <i>n</i> ) | Partially for<br>< 4 mo, Not<br>Breastfed Thereafter<br>( <i>n</i> = 1182), % ( <i>n</i> ) | Partially for 4–6<br>mo ( <i>n</i> = 1166),<br>% ( <i>n</i> ) | Exclusive for<br>4 mo, Not<br>Breastfed Thereafter<br>( <i>n</i> = 80), % ( <i>n</i> ) | Exclusive for 4 mo,<br>Partially Breastfed<br>Thereafter<br>( <i>n</i> = 1037), % ( <i>n</i> ) | Exclusive for 6<br>mo ( <i>n</i> = 58),<br>% ( <i>n</i> ) | <i>P</i> |
|--|---|--|---|--|--|---|----------|
| Maternal age   |   |  |   |  |  |   |          |
| <26  | 12.8 (76)                                     | 44.4 (264)   | 25.4 (151)  | 1.0 (6)  | 16.0 (95)  | 0.5 (3)   |          |
| 26–30  | 14.9 (184)                                    | 29.8 (369)   | 29.1 (360)  | 1.7 (21)   | 23.1 (289)   | 1.4 (17)  |          |
| >30  | 11.6 (256)                                    | 24.9 (549)   | 29.7 (655)  | 2.4 (53)   | 29.7 (656)   | 1.7 (38)  | <.01     |
| Education  |   |  |   |  |  |   |          |
| Low  | 13.9 (32)                                     | 34.8 (80)  | 32.2 (74)   | 1.3 (3)  | 17.0 (39)  | 0.9 (2)   |          |
| Intermediate   | 18.2 (272)                                    | 37.2 (555)   | 24.5 (366)  | 1.9 (29)   | 17.6 (263)   | 0.5 (8)   |          |
| High   | 8.6 (183)                                     | 22.9 (490)   | 31.4 (672)  | 2.1 (45)   | 32.9 (704)   | 2.1 (46)  | <.01     |
| Ethnicity  |   |  |   |  |  |   |          |
| Dutch  | 14.1 (342)                                    | 27.6 (668)   | 26.8 (647)  | 2.1 (51)   | 27.6 (666)   | 1.8 (43)  |          |
| Non-Dutch  | 10.3 (155)                                    | 31.4 (474)   | 32.5 (490)  | 1.7 (26)   | 23.2 (350)   | 0.9 (13)  | <.01     |
| Smoking  |   |  |   |  |  |   |          |
| No   | 11.1 (360)                                    | 27.1 (882)   | 30.3 (985)  | 2.1 (68)   | 27.9 (906)   | 1.6 (52)  |          |
| Yes  | 20.4 (127)                                    | 39.9 (249)   | 22.4 (140)  | 1.4 (9)  | 15.2 (95)  | 0.6 (4)   | <.01     |
| Siblings   |   |  |   |  |  |   |          |
| No   | 12.0 (279)                                    | 31.8 (739)   | 30.0 (397)  | 1.9 (43)   | 23.2 (538)   | 1.1 (25)  |          |
| ≥1   | 13.4 (208)                                    | 25.1 (390)   | 27.3 (424)  | 2.3 (36)   | 30.0 (466)   | 1.9 (30)  | <.01     |
| Day care attendance  |   |  |   |  |  |   |          |
| No   | 14.3 (274)                                    | 29.8 (570)   | 28.0 (535)  | 1.6 (31)   | 24.9 (477)   | 1.4 (26)  |          |
| Yes  | 11.0 (209)                                    | 28.2 (537)   | 30.2 (576)  | 2.3 (44)   | 26.6 (507)   | 1.7 (32)  | <.05     |
| Family history of asthma, house dust mite allergy, and hay fever |   |  |   |  |  |   |          |
| No   | 11.5 (143)                                    | 29.4 (364)   | 30.6 (380)  | 1.9 (24)   | 25.7 (319)   | 0.8 (10)  |          |
| Yes  | 13.5 (242)                                    | 27.3 (489)   | 27.6 (494)  | 1.9 (34)   | 27.7 (496)   | 2.1 (37)  | <.05     |

Values are percentages (absolute numbers). Data were missing on education (*n* = 185), ethnicity (*n* = 121), smoking (*n* = 170), siblings (*n* = 171), day care attendance (*n* = 240), family history of asthma, house dust mite allergy, and hay fever (*n* = 1046), duration of breastfeeding (*n* = 26), and duration of exclusive breastfeeding (*n* = 122). Differences between groups were compared by using  $\chi^2$  tests.

and 8% had a gastrointestinal tract infection. Between the ages of 7 and 12 months, upper and lower respiratory and gastrointestinal tract infections were present in 27%, 10%, and 9% of the infants, respectively. Table 2 shows that mothers who were older than 30 years, more educated, and nonsmoking tended to breastfeed their infants longer and more exclusively. Compared with mothers who were included in the analyses, those who were not included because of missing data on breastfeeding were more frequently younger, less educated, and of non-Dutch origin (Table 3).

### Duration of Breastfeeding

Infants who were breastfed for 4 months or 4 to 6 months did not have lower risks of upper and lower respiratory or gastrointestinal tract infections in the first 6 months compared with never-breastfed infants (all *P* >

.05) (Fig 1). Compared with never-breastfed infants, those who were breastfed for 6 months or longer had lower risks of upper respiratory tract

infections (adjusted odds ratio [aOR]: 0.62 [95% CI: 0.49–0.78]), lower respiratory tract infections (aOR: 0.61 [95% CI: 0.40–0.92]), and gastrointestinal

**TABLE 3** Differences in Maternal Characteristics Between Children With Missing and Nonmissing Data on Breastfeeding and Doctor-Attended Infectious Diseases at the Age of 6 Months: Eligible Cohort (*N* = 7116)

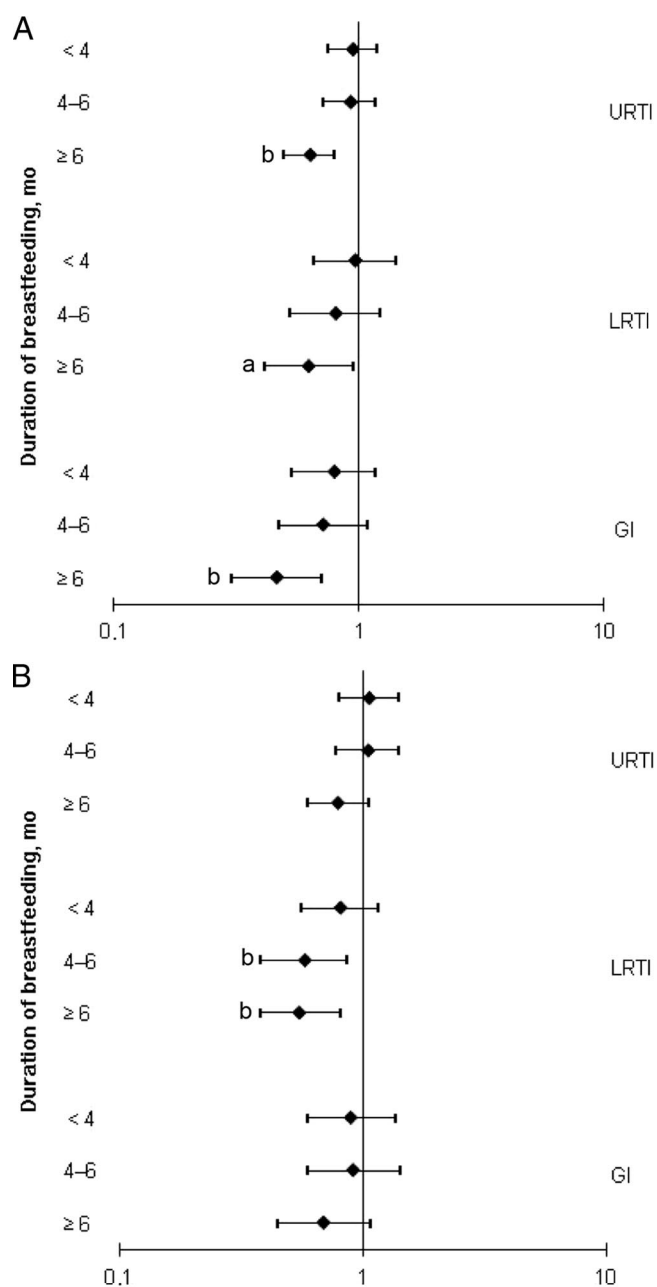
|              | Included in Analysis<br>( <i>n</i> = 4164), % ( <i>n</i> ) <sup>a</sup> | Not Included in Analysis  |  | <i>P</i> |
|--------------|---|---|--|----------|
|              |   | Missing Breastfeeding<br>Data ( <i>n</i> = 2498), % ( <i>n</i> ) <sup>b</sup> | Missing Infectious Diseases<br>Data ( <i>n</i> = 454), % ( <i>n</i> ) <sup>c</sup> |          |
| Maternal age |   |   |  |          |
| <26          | 15.0 (624)  | 28.9 (722)  | 14.1 (64)  |          |
| 26–30        | 30.5 (1270)   | 29.2 (729)  | 26.7 (121)   |          |
| >30          | 54.5 (2270)   | 41.9 (1047)   | 59.3 (269)   | <.01     |
| Education    |   |   |  |          |
| Low          | 6.2 (246)   | 14.1 (292)  | 9.9 (42)   |          |
| Intermediate | 38.7 (1538)   | 50.9 (1057)   | 32.3 (137)   |          |
| High         | 55.2 (2195)   | 35.0 (726)  | 57.8 (245)   | <.01     |
| Ethnicity    |   |   |  |          |
| Dutch        | 61.1 (2469)   | 44.6 (953)  | 58.0 (250)   |          |
| Non-Dutch    | 38.9 (1574)   | 55.4 (1184)   | 42.0 (181)   | <.01     |

Values are percentages (absolute numbers). Differences between included and nonincluded groups were compared by using  $\chi^2$  tests.

<sup>a</sup> Data were missing for education (*n* = 185) and ethnicity (*n* = 121).

<sup>b</sup> Data were missing for education (*n* = 423) and ethnicity (*n* = 361).

<sup>c</sup> Data were missing for education (*n* = 30) and ethnicity (*n* = 23).

**FIGURE 1**

Duration of breastfeeding and risk of infectious diseases in the first year of life. The reference group is never-breastfed infants. Values are ORs with 95% CIs (log scale), adjusted for maternal education, ethnicity, smoking, gestational age, birth weight, siblings, and day care attendance. A, Complete information about duration of exclusive breastfeeding, infectious diseases, and all confounders until the age of 6 months was available for 3504 infants (upper respiratory tract infections), 3489 infants (lower respiratory tract infections), and 3438 infants (gastrointestinal infections). B, For the age period of 7 to 12 months, complete information on breastfeeding and infectious diseases was available for 2958 infants (upper respiratory tract infections), 3027 infants (lower respiratory tract infections), and 2938 (gastrointestinal infections) infants. URTI indicates upper respiratory tract infection; LRTI, lower respiratory tract infection; GI, gastrointestinal tract infection. <sup>a</sup>  $P < .05$ ; <sup>b</sup>  $P < .01$ .

tract infections (aOR: 0.45 [95% CI: 0.30–0.69]). Between the ages of 7 and 12 months, infants who were breastfed for 4 to 6 months or 6 months or longer

had lower risks of lower respiratory tract infections (aOR: 0.56 [95% CI: 0.38–0.84] and aOR: 0.54 [95% CI: 0.37–0.79], respectively) than did infants

who were never breastfed. No associations were found with upper respiratory and gastrointestinal tract infections. The adjustment of confounders did not materially change the effect estimates of the crude analysis.

### Duration and Exclusiveness of Breastfeeding

Infants who were breastfed exclusively until the age of 4 months and partially thereafter had lower risks of upper and lower respiratory and gastrointestinal tract infections in the first 6 months after birth (aOR: 0.65 [95% CI: 0.51–0.83], aOR: 0.50 [95% CI: 0.32–0.79], and aOR: 0.41 [95% CI: 0.26–0.67], respectively) (Table 4). Infants who were breastfed exclusively for 6 months had lower risks of upper respiratory tract (aOR: 0.37 [95% CI: 0.18–0.74]) and lower respiratory tract and gastrointestinal tract (aOR: 0.33 [95% CI: 0.08–1.40] and aOR: 0.46 [95% CI: 0.14–1.59], respectively) infections, although the latter 2 were not statistically significant. Between the ages of 7 and 12 months, lower respiratory tract infections were less present in infants who were breastfed exclusively until 4 months and partially thereafter, compared with never-breastfed infants. No other associations of the various breastfeeding categories with upper and lower respiratory and gastrointestinal tract infections between the ages of 7 and 12 months were observed. All tests for trend for the associations between prolonged exclusive breastfeeding and upper and lower respiratory and gastrointestinal tract infections until the age of 6 months and lower respiratory tract infections between the ages of 7 and 12 months were significant ( $P < .01$ ).

Compared with the unadjusted analyses, the effect of duration of exclusive breastfeeding on the risks of upper and lower respiratory tract infections did not materially change in the adjusted analyses

**TABLE 4** Duration of Exclusive Breastfeeding and Risk of Infectious Diseases in the First Year of Life

| Duration of Breastfeeding                            | ≤6 mo, OR (95% CI)            |                               |                               | 7–12 mo, OR (95% CI) |                               |                  |
|--|-------------------------------|-------------------------------|-------------------------------|----------------------|-------------------------------|------------------|
|  | URTI                          | LRTI                          | GI                            | URTI                 | LRTI                          | GI               |
| Never breastfed                                      | 1.00                          | 1.00                          | 1.00                          | 1.00                 | 1.00                          | 1.00             |
| Partially for <4 mo, not breastfed thereafter        | 0.96 (0.76–1.21)              | 1.01 (0.68–1.50)              | 0.77 (0.52–1.15)              | 0.98 (0.75–1.27)     | 0.78 (0.55–1.09)              | 0.94 (0.68–1.28) |
| Partially for 4–6 mo                                 | 0.85 (0.67–1.07)              | 0.89 (0.60–1.34)              | 0.72 (0.48–1.09)              | 1.03 (0.76–1.39)     | 0.67 (0.47–1.02)              | 1.01 (0.71–1.44) |
| Exclusively for 4 mo, not breastfed thereafter       | 0.70 (0.41–1.20)              | 0.39 (0.12–1.31)              | 1.01 (0.44–2.38)              | 1.79 (0.99–3.14)     | 0.45 (0.17–1.19)              | 1.16 (0.59–2.27) |
| Exclusively for 4 mo, partially breastfed thereafter | 0.65 (0.51–0.83) <sup>a</sup> | 0.50 (0.32–0.79) <sup>a</sup> | 0.41 (0.26–0.64) <sup>a</sup> | 0.88 (0.66–1.16)     | 0.46 (0.31–0.69) <sup>a</sup> | 1.07 (0.77–1.49) |
| Exclusively breastfed for 6 mo                       | 0.37 (0.18–0.74) <sup>a</sup> | 0.33 (0.08–1.40)              | 0.46 (0.14–1.59)              | 0.63 (0.30–1.33)     | 0.54 (0.18–1.58)              | 0.93 (0.42–2.06) |
| <i>P</i>   | <.01                          | <.01                          | <.01                          | NS                   | <.01                          | NS               |

Reference group is never-breastfed infants. Values were adjusted for maternal education, ethnicity, smoking, gestational age, birth weight, siblings, and day care attendance. Complete information about duration of exclusive breastfeeding, infectious diseases, and all confounders until the age of 6 months was available for 3504 infants (upper respiratory tract infections), 3489 infants (lower respiratory tract infections), and 3438 infants (gastrointestinal infections). For ages 7 to 12 months, complete information on breastfeeding and infectious diseases was available for 2958 infants (upper respiratory tract infections), 3027 infants (lower respiratory tract infections), and 2938 infants (gastrointestinal infections). URTI indicates upper respiratory tract infection; LRTI, lower respiratory tract infection; GI, gastrointestinal infection; NS, not significant.

<sup>a</sup> *P* < .01.

(maximum decrease of the ORs: 6%). The effect estimates for gastrointestinal infections increased in the adjusted analyses (maximum: 13.4%).

Adjustment for family history of asthma, house dust mite allergy, and hay fever did not materially change the effect sizes for the duration of exclusive breastfeeding with upper and lower respiratory tract infections.

## DISCUSSION

The main findings of this population-based prospective cohort study were that breastfeeding for 6 months seems to have protective effects for development of respiratory and gastrointestinal tract infections during the first 6 months. Breastfeeding for 4 months or longer seems protective for lower respiratory tract infections between the ages of 7 and 12 months. When taking the exclusiveness of breastfeeding into account, infants who were breastfed exclusively until 4 months and partially thereafter had lower risks of respiratory and gastrointestinal tract infections until the age of 6 months and lower respiratory tract infections between the ages of 7 and 12 months. Several studies have revealed that a shorter period of breastfeeding increases the risks of physician visits

for illness, lower respiratory tract infections, and gastrointestinal symptoms.<sup>8,28,32</sup> Studies that were able to take the exclusiveness of breastfeeding into account revealed that exclusive breastfeeding, followed by partial breastfeeding, or predominant breastfeeding during 6 months or more was associated with a lower risk of gastrointestinal tract infection compared with breastfeeding for less than 3 months.<sup>24</sup> Infants who were breastfed for less than 4 months had a higher risk of hospitalization for infectious diseases (hazard ratio: 2.45 [95% CI: 1.28–4.66]) compared with those who were breastfed for more than 4 months. In addition, infants who were breastfed for 4 to 6 months showed higher risks of both pneumonia (OR: 4.27 [95% CI: 1.27–14.35]) and recurrent otitis media (OR: 1.95 [95% CI: 1.06–3.59]) compared with those who were breastfed 6 months or longer.<sup>29,30</sup> Authors of 1 study observed a protective effect of predominant breastfeeding for at least 6 months on doctor visits for 4 or more upper respiratory tract infections or 2 or more wheezing episodes compared with infants who were breastfed for less than 6 months.<sup>27</sup> Our results are difficult to compare with these studies, because different breastfeeding categories and various definitions of the breastfeeding

categories (predominant or exclusive) and the outcomes (self-reported or doctor-diagnosed infections) were used. We observed protective effects of breastfeeding on infectious diseases mainly in the first 6 months of life. Most studies have revealed protective effects of breastfeeding on common infections in the first 8 to 12 months of life.<sup>8,27,29,30</sup> One study, which distinguished between infectious diseases until and from the age of 6 months, revealed results similar to those from our study.<sup>24</sup> Although the authors used exclusive breastfeeding for 3 months as the reference group, exclusive breastfeeding for 6 months reduced the risk of gastrointestinal tract infections between the ages of 3 and 6 months but not between the ages of 6 and 12 months.<sup>24</sup> We cannot explain why breastfeeding duration was only associated with lower risks of lower respiratory tract infection from 7 to 12 months. Additional studies are needed to assess the associations of breastfeeding duration with the risks of infectious diseases beyond the age of 6 months. Breastfeeding might have a prolonged protective effect by influencing the severity, including hospital admission and frequency, of common infectious diseases.<sup>8,38</sup> However, immunologic evidence of a prolonged protective effect

of increased dose and duration of breastfeeding has not been well established. Short-term protective effects are caused by several factors in human breast milk. Epidermal growth factor helps to induce maturation of the intestinal epithelium, immunoglobulin A and oligosaccharides prevent attachment of pathogens, and lactoferrin has broad antimicrobial properties including disruption of the bacterial outer membrane.<sup>39,40</sup>

The strength of this study is its prospective population-based cohort design with a large number of subjects and the possibility to adjust for all major confounders. In addition, we were able to categorize the various breastfeeding habits in combination with the duration of breastfeeding. Some methodologic considerations need to be considered. Of all postnatal eligible participants of the Generation R Study, questionnaires with breastfeeding data were available for 65%. Compared with mothers who were included in the analyses, those who were not included because of missing data on breastfeeding were more frequently younger, less educated, and of non-Dutch origin. Our results revealed that these characteristics were associated with a shorter period of exclusively breastfeeding. Also, infectious diseases until the age of 6 months were more present in infants for whom there was no information about breastfeeding (50%) than for those for whom there was information (44%). These differences may have led to an underestimation of our effect estimates of infectious diseases. There were no differences in the prevalence of infectious diseases from the age of 7

through 12 months between those with (35%) and without (36%) breastfeeding data. Of all participants with breastfeeding data, 10% and 14% had missing data on infectious diseases at the ages of 6 and 12 months, respectively. Among those infants for whom there were no data on infectious diseases, on average 28% were exclusively breastfed for 4 months, and 1.7% were exclusively breastfed for 6 months. Because these frequencies did not differ from the frequencies in our cohort for analysis (27% and 1.4%, respectively), biased estimates caused by selective loss to follow-up seem unlikely.

Information about breastfeeding was prospectively collected by questionnaires without direct reference to upper and lower respiratory and gastrointestinal tract infections. Although assessment of breastfeeding by questionnaire seems to be a valid method, misclassification may occur. A recent review of studies performed between 1966 and 2003 showed that maternal report of breastfeeding is reliable through the age of 3 years.<sup>41</sup> The main outcomes in our study were self-reported upper and lower respiratory and gastrointestinal tract infections. This method is widely accepted in epidemiologic studies and reliably reflects the true incidence of those infections.<sup>27,42</sup>

## CONCLUSIONS

Exclusive breastfeeding until the age of 4 months followed by partial breastfeeding was associated with a significant reduction of respiratory and gastrointestinal infectious diseases in

infants. Exclusive breastfeeding until the age of 6 months tended to be more protective than exclusive breastfeeding until the age of 4 months and partially thereafter (*P* for trend significant for risks of upper and lower respiratory and gastrointestinal tract infections at  $\leq 6$  months and lower respiratory tract infections between 7 and 12 months). However, because of the small numbers, the association between exclusive breastfeeding until the age of 6 months and the risks of infectious diseases was not statistically significant when compared separately with the group of never-breastfed infants. We consider that our results are in line with the World Health Organization recommendation of exclusive breastfeeding until infants are 6 months old instead of 4 months, and our results support current health-policy strategies that promote exclusive breastfeeding for 6 months in industrialized countries.

Biological, cultural, and social constraints related to breastfeeding habits need to be studied more extensively. The effects of prolonged and exclusive breastfeeding on infectious diseases at older ages in industrialized countries remain to be studied.

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