Health Impacts of Early Complementary Food Introduction Between Formula-fed and Breastfed Infants

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ABSTRACT

Background: Global health agencies agree that infants should not be fed complementary foods before 4 to 6 months of age. However, given the World Health Organization (WHO) definition of complementary food as ''anything other than breast milk,'' little is known about the relative risks of formula compared with other complementary foods on infant health. This article aims to fill this gap in the literature, by assessing how differences in the timing of the introduction of nonformula complementary food between breastfed and formula-fed infants impacts infant health.

Methods: Eight health outcomes by complementary food introduction, breast-feeding, formula feeding, and mixed feeding (breastfed and formula-fed) were predicted using logistic regression with generalized estimating equations on the newborn through 6-month waves of the Infant Feeding Practices Study II (IFPS-II).

Results: Complementary foods increased the likelihood for all health risks measured. Given greater prevalence of early complementary food introduction among formula-fed infants, most health differences between breast-feeding groups shift to nonsignificance in full models, with the exception of higher rates of hard stool and cough/wheeze among formula-fed and mixed-fed infants but lower rates of diarrhea (LO = −0.577; 95% confidence interval [CI] = −1.074 to 0.080) and runny nose or cold (LO = −3.19; 95% CI = −0.552 to −0.086) for mixed-fed than breastfed infants.

Conclusions: Our results confirm health benefits of exclusive breast-feeding and that the introduction of complementary foods before 4 to 6 months poses a greater risk to infant health than does formula. Greater attention to the early introduction of complementary foods is needed in research and clinical practice.

Key Words: generalized estimating equations, Infant Feeding Practices Study II, infant feeding

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What Is Known

- Infants exclusively breastfed for the first 6 months have lower rates of illness or other health problems than other infants.
- Complementary foods pose risks to infant health if given prematurely, that is, before 4 months of age.
- Formula-fed infants are more likely to be fed complementary foods prematurely.

What Is New

- This article more carefully measures what infants are fed to assess if the health benefits accrued to breastfed infants is because of their lower likelihood of being fed complementary foods before 6 months of age.
- We find support for complementary foods explaining much of the variance in most, but not all, health outcomes between breastfed and formula-fed infants.
- These results highlight the need for more research paying attention to the variety of foods infants are fed beyond breast milk.

In 2017, the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) Committee on Nutrition published their recommendations for complementary feeding for breastfed infants (1). They highlighted a significant gap in the literature regarding the relative impacts of formula compared with other complementary foods on infant health. Further, they find the World Health Organization (WHO) definition of complementary food as ''anything other than breast milk'' to be confusing for parents, health providers, and researchers (1), given that formula feeding from birth is commonly recommended for infants who cannot be breastfed but complementary foods other than formula are unsafe before 4 to 6 months of age. This confusion is

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compounded by the fact that research shows that formula-fed infants are significantly more likely to be given other complementary foods than are breastfed infants before 4 to 6 months of age (2–7). An analysis of data collected from 5 countries as part of the European Childhood Obesity Project, indicated that 37% of formula-fed, but only 17% of breastfed infants, were given solid foods prematurely (ie, before 4 months of age) (7). This article aims to fill this gap in the literature by assessing how early introduction (<4–6 months) of nonformula complementary foods impacts infant health and whether there are differences between breastfed and formula-fed infants.

METHODS

Data

For this research, we analysed the Infant Feeding Practices Study II (IFPS II), a widely used publicy acesssible, longitudinal sample of infants born in the United States (8–13). Data were collected by the US Food and Drug Administration (FDA) in collaboration with the Centers for Disease Control (CDC) between 2005 and 2007 from a nationally distributed consumer-opinion panel of over 500,000 households (7). Questionnaires were first mailed to mothers at the end of their pregnancies and then in the neonatal period when the infants were approximately 3 weeks old, then each month from month 2 through 12 (except months 8 and 11). We analyzed the data in long-form, meaning each infant had a health record for each month of the analysis.

We limited our analysis to only the first 6 months of records, as this is the WHO and American Academy of Pediatrics (AAP) recommended minimum duration for exclusive breast-feeding and the age at which there is general agreement that introducing complementary foods is safe (6). There is controversy in the literature as to whether ‘‘premature’’ introduction of complementary foods should be defined relative to a 4 or 6-month cut-off (14). Although most health agencies recommend no complementary foods before 6 months, there is consistent evidence only that introducing foods before 4 months is unsafe but mixed evidence for delaying complementary food introduction beyond 4 months (6). Given the general agreement that feeding complementary foods is safe at 6 months, we attempt to address this controversy by using a 6 months cut-off per health organization recommendations, while reporting final results by month to address those who suggest 6 months is later than necessary (14).

We employed list-wise deletion to remove any cases that were missing at all waves of the data. As the research method allows for uneven survey response, some infants had data for all waves, and others only some of the waves. As such, the sample sizes differed by month and by variable. Through this process, 262 cases that were missing data at all waves were removed, primarily because of nonresponse across surveys on the item hard stool (see Appendix A, Supplemental Digital Content, *http://links.lww.com/MPG/B753*, for details). Our final analytic sample was 2794 infants, which included 11,675 infant-month observations.

Measures

We analyzed 8 health outcomes based on parental assessments, from the months 2 through 6 questionnaires: diarrhea; fever; cough or wheeze; runny nose or cold; received antibiotics; received other prescriptions; hard stool; and hospitalized. The first 4 items came from a survey question asking parents to mark an ‘‘X’’ in a box to indicate that their baby had one of a list of health problems during the past 2 weeks. All of the included items were coded 1 if the item was checked, 0 if not. Diarrhea, cough/wheeze, and fever are particularly important measures of infant health as pneumonia (which involves cough and fever as symptoms) and diarrhea are the most common childhood illnesses and the illnesses most likely to lead to hospitalization (15). Parental reports of whether the baby received antibiotics or other prescription medicines in the past 2 weeks were asked as individual items in the survey. These were included to offer a proxy for an assessment of health by a medical provider and were coded as 1 for yes, 0 for no. Hard stool was based on a survey question where parents were asked to describe their baby’s stool in the past 7 days as hard, formed, soft, semi-watery, or watery by indicating with an X all that applied. We used this to measure hard stool by coding any reported hard stool as 1 and no mention of hard stool as 0. Finally, hospitalization was measured with an item that asked parents if their baby had been hospitalized for any reason or had been taken to a hospital for any outpatient procedure or surgery in the past 4 weeks (coded as 1 for yes, 0 for no).

The main independent variables were related to what the infant was fed. First, complementary food introduction was assessed by combining a series of individual food items into monthly dichotomous measures of any food. The neonatal questionnaire asked how frequently the newborn was fed 7 items and the remaining monthly questionnaires contained 17 food and drink items (baby cereal, 100% fruit/vegetable juice, fruit, vegetables, meat/chicken/combo dinners, other cereals/starches, dairy foods, other foods, sweet drinks, cow’s milk, eggs, sweet foods, french fries, other milk [ie, not formula or cow], other soy foods, peanuts or nuts, or fish/shellfish). Infants who were given any of the foods or liquids were coded as 1 for ‘‘fed food’’ and those who received none of the above were coded as zero. As shown in Appendix B (Supplemental Digital Content, *http://links.lww.com/MPG/B753*), the majority of infants who were fed anything other than breast milk or formula were given baby or other cereal or fruits or vegetables (as food or juice) at months 1–2 (and water and sugar water at month 1, the only month these items were assessed). As babies aged, a greater variety of foods were introduced.

Secondly, breast-feeding status was assessed in terms of whether the baby was breastfed, formula-, or mixed-fed, based on parental reports of how many times per day the babies were breastfed or fed formula. At each time point, those who reported a frequency of zero for formula, but greater than zero for breast-feeding were coded as breastfed, those who reported a frequency of zero for breast-feeding and greater than zero for formula were coded as formula-fed and those who recorded a frequency greater than zero for both breast-feeding and formula were coded as mixed fed. As the dependent variables regarding health began at month 2, all feeds from birth through the 2-month interview were collapsed into a measure of feeding type up until 2 months old.

A variable for the month was included along with 3 interactions between month and food, formula feeding, and mixed feeding, to take into account the importance of the timing of complementary food introduction and based on model fit. Additional confounding variables were included to control for geographic region; if the child spent up to 3 days in the NICU versus not at all (children with longer NICU stays were not sampled); household size; birth weight (plus a quadratic for birth weight based on model fit and to account for the nonlinear relationship between birthweight and health); mother’s age; and household income recoded to the midpoint of the ranges provided in the codebook (the top value was multiplied by 1.5).

Statistical Analysis

Descriptive statistics split by complementary food introduction were calculated in Stata along with confidence intervals in Excel. For the feeding and health outcome, significance between infants who were and were not fed complementary foods were carried out using bivariate logistic regressions with generalized estimating equations. For the time-invariant or nearly time-invariant confounding variables, such as health status at birth and household demographics, statistical significance was tested with basic bivariate *t*-tests at month 2 only. Descriptive statistics were then carried out to assess raw differences between breastfed, mixed fed, and formula-fed infants at each time point on complementary food introduction and each of the health items.

Multivariate logistic regressions with generalized estimating equations (GEE) (17–19) were then calculated in STATA to assess the impact of complementary food introduction and breast-feeding status, controlling for each other and the confounding variables on the measures of infant health for each month. GEEs are the most appropriate method to use with repeated measures and dichotomous-dependent variables. The best fitting correlation structure was assessed using the QIC statistic (16). For ease of interpretation, we also calculated predicted margins based on the results of the regression models split by breast-feeding and complementary feeding status by month, with all confounders set to their mean.

Ethics

As this study was a retrospective study, formal ethical approval was not obtained per the Canadian Tri-Council Policy on the Ethical Conduct for Research Involving Humans. Nonetheless, the data were treated in accordance with said policy.

RESULTS

The sample split nearly evenly between those who were introduced to complementary foods before 6 months (52%) and those who were not (48%). As shown in Table 1, babies fed complementary foods were more likely to be given no breast milk than were babies not given complementary foods. In terms of health outcomes, infants fed complementary foods have higher rates of ill health, except hospitalization, which does not significantly differ between feeding groups across all waves at the aggregate level. Infants fed complementary foods are no more likely than those not fed complementary foods to have stayed in the NICU, but they do have statistically significantly lower birthweights and household incomes, come from larger families, and have younger mothers on average.

As shown in Appendix C (Supplemental Digital Content, *http://links.lww.com/MPG/B753*), with no controls for confounders, formula-fed infants are more likely to be fed complementary food across all time points. Specifically, at 2 months old, 46% of formula-fed, 30% of mixed fed and only 1% of breastfed infants are fed complementary foods. Across all time points, differences

TABLE 1. Descriptive statistics by complementary food introduction (Infant Feeding Practices Study II 2008)

	Complementary food introduced	95% Confidence interval	No complementary food introduced	95% Confidence interval
Over all months†:				
Formula-fed (no breast milk)	52.63%***	52.61–52.65	21.47%	21.46–21.49
Breast fed (no formula)	22.47%***	22.45 22.48	46.48%	46.45–46.50
Mixed-fed (both formula and breast milk)	24.90%***	24.89–24.92	32.05%	32.03–32.07
Baby's stool was hard	4.09%***	4.09–4.10	0.66%	0.66–0.67
Diarrhea	7.63%***	7.62–7.64	4.51%	4.50–4.51
Fever	11.24%***	11.23–11.25	7.84%	7.84–7.85
Cough or wheeze	17.92%***	17.91–17.93	13.50%	13.49–13.51
Runny nose or cold	31.72%***	31.70–31.74	27.52%	27.50–27.53
Baby received antibiotics	8.34%***	8.33–8.34	5.33%	5.33–5.34
Baby received other prescription meds	11.73%**	11.72–11.74	9.83%	9.82–9.84
Baby hospitalized	2.70%	2.70–2.70	2.83%	2.82–2.83
At month 2 survey:				
Baby stayed in NICU for 3 days or less versus not at all	2.79%	2.79–2.79	2.06	2.06–2.06
Birthweight in pounds	7.44***	7.36–7.52	7.68	7.63–7.72
Household income, recoded to midpoint	$41,189.23***	38,817.04–43,561.42	$55,444.85	53,785.88–57,103.82
Household size	3.41*	3.30–3.51	3.27	3.22–3.33
Mother's age	27.41***	26.96–27.86	29.54	29.30–29.77
Geographic region of the United States				
New England	3.86%	3.85–3.87	4.08%	4.07–4.08
Pacific	6.91%***	6.89–6.93	12.82%	12.82–12.83
Middle Atlantic	14.95%	14.91–14.99	13.34%	13.33–13.34
East North Central	22.03%	21.97–22.08	21.18%	21.16–21.18
West North Central	5.79%**	5.77–5.80	9.58%	9.57–9.58
South Atlantic	16.88%	16.85–16.93	14.77%	14.76–14.77
East South Central	9.97%***	9.94–10.00	4.45%	4.44–4.45
West South Central	12.06%	12.02–12.09	10.22	10.21–20.22
Mountain	7.56%*	7.53–7.58	10.27	10.26–20.27

*$P \leq 0.05$.
**$P \leq 0.01$.
***$P \leq 0.001$.
†Models covering multiple months have standard errors adjusted for clustering on ID and employ an independent correlation structure. Due to the nature of the longitudinal data, the sample size shifts with each variable.

TABLE 2. Generalized estimating equation logistic regression results (log odds) predicting infant health (Infant Feeding Practices Study II 2008)

	Baby's stool was hard, past 7 days[§]	Diarrhea, past 2 weeks[§]	Fever, past 2 weeks[§]	Cough or wheeze, past 2 weeks[§]	Runny nose or cold, past 2 weeks[§]	Baby hospitalized[§]	Antibiotics, past 2 weeks[§]	Other prescriptions, past 2 weeks[§]
Complementary Food given	1.289** (0.429)	0.883*** (0.223)	0.406* (0.180)	0.628*** (0.141)	0.562*** (0.116)	0.598* (0.281)	0.567** (0.214)	0.407** (0.159)
Formula-fed[†]	6.318*** (1.564)	−0.056 (0.273)	0.322 (0.220)	0.509** (0.177)	−0.140 (0.137)	−0.069 (0.390)	−0.038 (0.266)	0.063 (0.202)
Mixed-fed[†]	5.659*** (1.567)	−0.577* (0.254)	0.113 (0.197)	0.423** (0.158)	−0.319** (0.119)	0.330 (0.327)	−0.011 (0.235)	0.135 (0.174)
Month[‡]	1.263*** (0.335)	−0.098 (0.075)	0.149** (0.056)	0.175*** (0.046)	0.109*** (0.034)	−0.158 (0.107)	0.151* (0.066)	0.091+ (0.050)
Complementary food* month	−0.099 (0.151)	−0.167* (0.076)	−0.075 (0.059)	−0.164*** (0.047)	−0.159*** (0.0374	−0.163 (0.105)	−0.129+ (0.069)	−0.156** (0.051)
Mixed-fed* month	−1.088*** (0.335)	0.233** (0.083)	−0.001 (0.060)	−0.063 (0.050)	0.114** (0.038)	−0.059 (0.125)	−0.013 (0.074)	0.016 (0.057)
Formula-fed* month	−1.097*** (0.328)	0.179* (0.081)	−0.066 (0.061)	−0.065 (0.050)	0.036 (0.039)	0.116 (0.122)	0.051 (0.072)	0.076 (0.057)
y-intercept	−9.441*** (2.031)	−1.042 (0.980)	−3.532** (1.379)	−1.982*** (0.728)	−1.700** (0.633)	−3.933 (2.866)	−2.645* (1.160)	−2.815* (1.336)
No. infant-months	11,307	11,270	11,270	11,270	11,270	11,246	11,135	11,137
No. infants	2794	2794	2794	2794	2794	2794	2794	2794
correlation Structure	Exchangeable	Unstructured	Independent	independent	independent	Unstructured	Unstructured	Unstructured
QIC	2331.459	5116.509	7075.463	9745.950	13,648.906	2823.501	5529.826	7549.648

QIC = quasi-likelihood under the independence model criterion.
*$P \leq 0.05$.
**$P \leq 0.01$.
***$P \leq 0.001$ (standard error in parenthesis).
[†]Omitted category is only breastfed, never given formula.
[‡]Month is categorized as 1 = 2 months, 2 = 3 months, 3 = 4 months, 4 = 5 months, and 5 = 6 months old.
[§]All models included the confounding variables. See Appendix E (*http://links.lww.com/MPG/B753*) for full results.

between rates of complementary food introduction among breastfed, mixed-fed, and formula-fed infants are statistically significant at the P less than 0.05 level. Similarly, there are statistically and substantially meaningful differences across breast-feeding and formula-feeding groups' incidence of hard stool, with zero breastfed babies experiencing hard stool before month 4, compared with 2% to 6% of formula-fed babies reported to have hard stool between 2 and 6 months old. Diarrhea rates also tend to be higher for infants fed only formula than those fed only breast milk. At 2 months of age, twice as many formula-fed (11%) as breastfed (5%) infants report diarrhea, which is a statistically significant difference at the $P < 0.05$ level. However, at this age, there are no differences in diarrhea rates between the breastfed and mixed-fed infants. In fact, at 3 months of age, mixed fed infants have the lowest rates of diarrhea, although they are not statistically significantly different from breastfed infants.

There are few significant differences between feeding groups on rates of fever, hospitalization, or antibiotic usage. There are statistically and substantively large differences in cough or wheeze among 2 and 3 months old infants by feeding groups. At 2 months old, twice as many formula-fed infants (18%) than breastfed infants (9%) experience cough or wheeze. However, the breastfed-formula-fed gap diminishes at 3 months and moves to nonsignificance at 4 months old, widens at 5 months, then returns to nonsignificance again at 6 months. Runny nose or cold also have few differences aside from a finding of higher rates for breastfed (35%) than formula-fed (30%) infants at 4 months old. Prescriptions other than antibiotics were more likely to be given to formula-fed than breastfed infants across all months. (Not reported here but available in Appendix D, Supplemental Digital Content, *http://links.lww.com/MPG/B753*, are descriptive statistics by complementary food introduction, by infant age.)

The GEE logistic regression results indicate that the negative relationship between premature complementary food introduction and health remained for all measures when controlling for feeding type and the other confounding variables (see Table 2). Including all confounders, complementary foods increase the likelihood of a baby developing hard stool ($P = 0.003$), diarrhea ($P < 0.001$), fever ($P = 0.024$), cough or wheeze ($P < 0.001$), a runny nose or cold ($P < 0.001$), being hospitalized ($P = 0.033$), or given prescribed antibiotics ($P = 0.008$) or other medication ($P = 0.010$). Formula-fed and mixed-fed infants are more likely to have a hard stool ($P < 0.001$ for both) or a cough or wheeze ($P = 0.004$ and $P = 0.008$, respectively) than fully breastfed infants, controlling for complementary food and the other confounding variables. Mixed-fed infants are *less* likely to have diarrhea ($P = 0.023$) or a runny nose or cold ($P = 0.007$) than fully breastfed infants, including confounders.

To increase the interpretability of the logistic regression results, predicted margins were calculated for breastfed, mixed-fed, and formula-fed infants by complementary food introduction each month, with confounding variables set to their means (see Table 3). These calculations provide the predicted probability that an average baby would experience each health item, given their feeding status. Overall, across all health indicators, infants fed complementary foods have a higher predicted chance of the markers used as indicators of ill health than do infants not fed complementary foods. Within the complementary foods given and not given groups, breastfed infants generally had lower chances of experiencing the health outcome than did mixed-fed or formula-fed infants, with a few exceptions. Formula appears to have a clearly constipating effect, as hard stool is exceedingly unlikely among breastfed infants and highly likely among formula- or mixed-fed infants, regardless of complementary food introduction. The average breastfed infant is predicted to have a chance of experiencing hard stool of close to zero until 6 months when the probability is just under 2%. Comparatively, the average formula-fed infant fed complementary foods is predicted to have a 63.5% probability of experiencing hard stool.

The average breastfed and formula-fed infant is predicted to have a similar probability of contracting diarrhea, which is higher than that predicted for their mixed-fed peers, regardless of complementary food introduction. For example, at 2 months, breastfed and formula-fed infants fed other complementary foods are predicted to have a 12% chance of contracting diarrhea compared with just a 7% probability for mixed-fed infants fed complementary foods. The predicted probabilities are lower among those not fed complementary foods but follow a similar pattern in terms of breast-feeding status.

As was shown in the regression results, breast-feeding has a clear positive impact on cough/wheeze regardless of feeding type, although feeding complementary foods has a greater negative

TABLE 3. Predicted margins for health outcomes by feeding behavior by month (Infant Feeding Practices Study II 2008)

	Fed complementary foods			Not fed complementary foods		
	Breastfed	Mixed-fed	Formula-fed	Breastfed	Mixed-fed	Formula-fed
Hard stool						
2 Months old	0.01%	2.84%	5.17%	0.00%	0.82%	1.56%
3 Months old	0.04%	8.64%	14.28%	0.01%	2.77%	5.05%
4 Months old	0.13%	21.18%	30.08%	0.04%	8.46%	14.01%
5 Months old	0.46%	38.73%	47.90%	0.13%	20.84%	29.70%
6 Months old	1.59%	55.73%	63.53%	0.45%	38.34%	47.54%
Diarrhea						
2 Months old	12.28%	7.34%	11.70%	5.53%	3.19%	5.25%
3 Months old	11.28%	6.71%	10.74%	5.04%	2.91%	4.78%
4 Months old	10.35%	6.13%	9.84%	4.60%	2.64%	4.36%
5 Months old	9.48%	5.59%	9.02%	4.19%	2.40%	3.97%
6 Months old	8.69%	5.10%	8.26%	3.81%	2.18%	3.61%
Fever						
2 Months old	7.67%	8.50%	10.26%	5.25%	5.84%	7.10%
3 Months old	8.78%	9.72%	11.70%	6.04%	6.71%	8.14%
4 Months old	10.04%	11.10%	13.31%	6.94%	7.70%	9.32%
5 Months old	11.46%	12.64%	15.11%	7.96%	8.82%	10.64%
6 Months old	13.05%	14.37%	17.10%	9.12%	10.09%	12.13%
Cough or wheeze						
2 Months old	12.14%	17.28%	18.51%	6.92%	10.15%	10.95%
3 Months old	14.09%	19.86%	21.22%	8.12%	11.83%	12.73%
4 Months old	16.28%	22.69%	24.19%	9.51%	13.74%	14.76%
5 Months old	18.74%	25.80%	27.42%	11.10%	15.89%	17.04%
6 Months old	21.47%	29.15%	30.89%	12.91%	18.30%	19.59%
Runny nose or cold						
2 Months old	34.26%	27.62%	31.25%	23.13%	18.03%	20.77%
3 Months old	36.70%	29.81%	33.59%	25.09%	19.67%	22.59%
4 Months old	39.21%	32.10%	36.01%	27.16%	21.43%	24.53%
5 Months old	41.78%	34.47%	38.50%	29.33%	23.29%	26.56%
6 Months old	44.39%	36.92%	41.05%	31.59%	25.27%	28.71%
Baby hospitalized						
2 Months old	4.46%	6.09%	4.18%	2.51%	3.46%	2.35%
3 Months old	3.84%	5.25%	3.59%	2.16%	2.97%	2.01%
4 Months old	3.30%	4.53%	3.09%	1.85%	2.55%	1.73%
5 Months old	2.83%	3.90%	2.65%	1.58%	2.19%	1.48%
6 Months old	2.43%	3.35%	2.27%	1.36%	1.87%	1.27%
Baby received antibiotics						
2 Months old	6.81%	6.74%	6.58%	3.99%	3.95%	3.85%
3 Months old	7.83%	7.75%	7.56%	4.61%	4.56%	4.45%
4 months old	8.98%	8.88%	8.68%	5.32%	5.26%	5.13%
5 Months old	10.28%	10.17%	9.94%	6.13%	6.06%	5.92%
6 Months old	11.74%	11.62%	11.36%	7.05%	6.97%	6.81%
Baby received other prescription medication						
2 Months old	10.44%	11.75%	11.03%	7.23%	8.18%	7.66%
3 Months old	11.31%	12.71%	11.94%	7.86%	8.88%	8.32%
4 Months old	12.24%	13.74%	12.91%	8.54%	9.64%	9.03%
5 Months old	13.23%	14.83%	13.95%	9.26%	10.45%	9.80%
6 Months old	14.29%	15.99%	15.06%	10.05%	11.32%	10.62%

Results calculated based on the results from the generalized estimating equation logistic regression models detailed in Table 2 with all control variables set to their means.

impact on cough-wheeze. Thus, for example, at 2 months of age among complementary fed infants, 19% of those fed formula are predicted to contract cough or wheeze compared with 12% of breastfed infants. At the same age, all infants not fed complementary foods have a lower probability of cough or wheeze regardless of breast-feeding status, though exclusively breastfed babies have the lowest predicted probability (7%) of contracting a cough or wheeze of all infants. In terms of fever, hospitalization, and antibiotic and other prescriptions there were few meaningful differences between breastfed, mixed fed, and formula-fed infants, but larger differences between those fed and not fed complementary foods. Overall, for every health item except hard stool, formula-fed infants not fed complementary foods have a lower predicted probability than breastfed infants fed complementary foods.

DISCUSSION

These results indicate that the premature introduction of complementary foods is a relatively common practice, but has numerous negative impacts on infant health. Otherwise healthy infants fed complementary foods before 6 months of age are statistically significantly more likely to have hard stool, diarrhea, fever, cough or wheeze, a runny nose or cold, and to receive medication or be hospitalized than infants not fed complementary foods, controlling for breast-feeding status, birthweight, time spent in the NICU, household income and size, mother's age, and geographic region of the US. Further, we see that formula significantly increases the chance of hard stool and cough/wheeze, but lowers the incidence of the common cold, controlling for complementary food introduction and the other confounders.

These results are in line with the only study we found that controlled specifically for whether the infants were fed additional solid foods, which examined differences in upper respiratory infection, lower respiratory infection, acute otitis media, diarrhea and/or vomiting, dermatitis, hypochromic anemia, and others, based on blood tests and clinician assessments, in a small sample of 25 breastfed and 25 ''bottle fed'' upper middle class infants (19). The authors of that publication found ''no statistically significant differences in morbidity between the 2 groups except for a borderline greater frequency of upper respiratory infections in the bottle-fed group'' (p. 492).

There are some limitations of our study, such as that the data are based on parental reports, rather than doctor reports, of infant health. Additionally, given that these data are more than a decade old and that infant formula has changed in the interval, differences between breastfed and formula-fed infants may be even smaller with more recent data. For example, substances, such as prebiotics have been added to formulas, which have been reported to change the stool patterns of formula and mixed-fed infants by making them looser (20). Though this is speculative, further research with more recent data is warranted.

Further, although the composition of human milk is different from formula, our results raise questions as to whether these differences have a direct impact on infant health or are correlated with other feeding and environmental confounding factors. Considering the relative cost of formula compared with complementary foods and our finding that formula-fed infants are far more likely than breastfed infants to be fed complementary foods before 4 months of age, learning if young formula-fed infants are being given complementary foods as a means to stretch family food budgets is important (21). More important than drawing any definitive conclusions, these results should be viewed as a call for clearer measures of ''not breastfed'' within infant health and nutrition research.

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