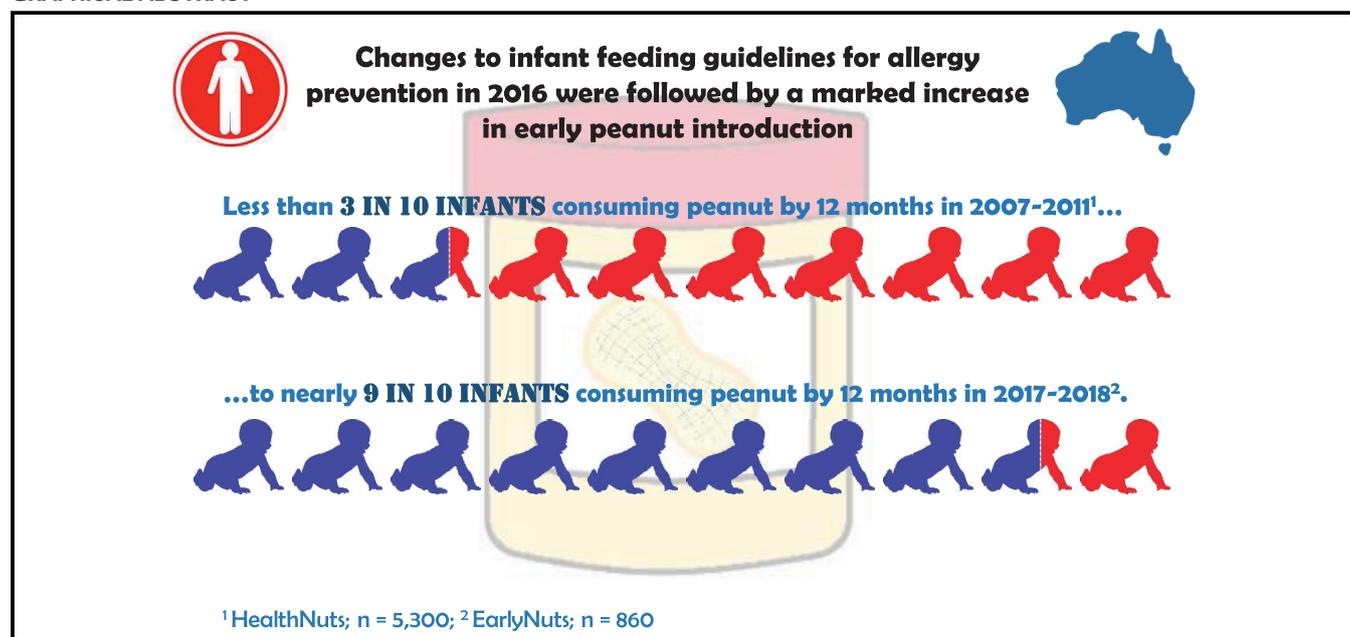


Earlier ingestion of peanut after changes to infant feeding guidelines: The EarlyNuts study



Victoria X. Soriano, BSc (Hons),^{a,b} Rachel L. Peters, MPH, PhD,^{a,b}
Anne-Louise Ponsonby, MBBS, FAFPHM, FRACP, PhD,^{d,f} Shyamali C. Dharmage, MBBS, MSc, MD, PhD,^d
Kirsten P. Perrett, MBBS (Hons), FRACP, PhD,^{a,c,d} Michael J. Field, BMBS, BCom/BA,^a
Andrew Knox, BA (Hons), MSc, GCEnv,^a Dean Tey, MBBS, FRACP,^{a,b,c,e} Sasha Odoi, BNS (Hons),^a
Grace Gell, BSc (Hons),^a Beatriz Camesella Perez, BNurs, MSc (PHDC), DLSHTM,^a
Katrina J. Allen, MBBS, BMedSc, FRACP, FAAAI, PhD,^{a,b,c*} Lyle C. Gurrin, PhD,^{a,d} and Jennifer J. Koplin, PhD^{a,d}
Parkville, Australia

GRAPHICAL ABSTRACT



Background: Randomized controlled trials demonstrate that timely introduction of peanut to infants reduces the risk of peanut allergy. However, much debate remains regarding how to best achieve earlier peanut introduction at the population level. Our previous study in 2007-2011 (HealthNuts, n = 5300) indicated that few infants were consuming peanut in the first year. Australian infant feeding guidelines were updated in 2016 to recommend introducing peanut before 12 months for all

infants. There were no data available on the subsequent effect on peanut introduction or peanut reactions. **Objective:** We sought to assess the consequences of a nonscreening approach to allergenic food introduction in a population-based sample of infants in their first year of life. **Methods:** EarlyNuts is a population-based, cross-sectional study of 12-month-old infants in Melbourne, Australia, recruited by

From ^aMurdoch Children's Research Institute, Parkville; ^bthe Department of Paediatrics and ^cthe School of Population and Global Health, University of Melbourne, Parkville; ^dthe Department of Allergy and Immunology and ^ethe Melbourne Allergy Centre and Children's Specialists (MACCS) Medical Group, Royal Children's Hospital, Parkville; and ^fthe Neuroepidemiology Research Group, Florey Institute for Neuroscience and Mental Health, Parkville.

*Former affiliations when this work was undertaken. No current affiliations.

This work was supported by funding from the National Health and Medical Research Council of Australia (NHMRC) and the Murdoch Children's Research Institute. Research at the Murdoch Children's Research Institute is supported by the Victorian Government's Operational Infrastructure Program. V.X.S. is supported by a PhD scholarship from the NHMRC-funded Centre for Food and Allergy Research (CFAR). Disclosure of potential conflict of interest: K. P. Perrett's institution, Murdoch Children's Research Institute, has received a research grant from DBV Technologies. K. J. Allen

was on the medical advisory board for Before Brands and Aravax. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication April 2, 2019; revised July 10, 2019; accepted for publication July 26, 2019.

Available online August 8, 2019.

Corresponding author: Jennifer J. Koplin, PhD, Murdoch Children's Research Institute, Royal Children's Hospital, Flemington Rd, Parkville, VIC 3052, Australia. E-mail: jennifer.koplin@mcri.edu.au.

The CrossMark symbol notifies online readers when updates have been made to the article such as errata or minor corrections

0091-6749/\$36.00

© 2019 American Academy of Allergy, Asthma & Immunology

<https://doi.org/10.1016/j.jaci.2019.07.032>

using an identical sampling frame and methods to HealthNuts (72% response rate vs 73% response rate in HealthNuts). We report here on the first 860 participants recruited between November 2016 and October 2018.

Results: Most infants (88.6%; 95% CI, 86.1% to 90.7%) had introduced peanut by 12 months (median age, 6 months), an increase from 28.4% (95% CI, 27.2% to 29.7%) in the HealthNuts study. By 12 months, the majority of these (76.4%) had consumed peanut more than 4 times, and 28% were eating peanut more than once per week. Preliminary results on parent-reported reactions show that 4.0% of those consuming peanut by 12 months had possible IgE-mediated reactions.

Conclusions: There has been a striking shift toward earlier peanut introduction, with a 3-fold increase in peanut introduction by age 1 year in 2018 compared with 2007-2011. (*J Allergy Clin Immunol* 2019;144:1327-35.)

Key words: *Infant feeding, early introduction, peanut, egg, food allergy, guidelines, timing of introduction, weaning, infants, observational*

IgE-mediated food allergy affects up to 10% of Australian infants.¹ Hospital admissions caused by IgE-mediated food allergy have increased significantly over the past decades in the United States, the United Kingdom, and Australia,²⁻⁴ creating an urgent need to identify, implement, and evaluate effective food allergy prevention strategies.

Early introduction of allergenic foods is currently the most promising strategy for preventing food allergy. There is high-quality evidence from randomized controlled trials that earlier introduction of peanut and egg reduces the risk of allergy to these foods.^{5,6} As a result of these recent trials, Australian infant feeding guidelines were updated in 2016 to recommend introduction of allergenic foods, including peanut and egg, by age 12 months for all infants.⁷ This represents a major change to previous infant feeding advice and the second major change to this advice since the 1990s. Around 2008, infant feeding guidelines in Australia removed previous advice to delay introduction of allergenic foods, without stating when or how allergenic foods should be introduced.^{8,9} Previously, we documented a small shift toward earlier introduction of peanut and egg by age 1 year after this change. Overall, however, less than 10% of the sample changed their practices between 2007 and 2011, and most parents still delayed introduction past age 1 year.¹⁰

There is currently much debate regarding how to best achieve earlier peanut introduction at the population level.¹¹ Some countries, such as the United States, recommend prior screening for food sensitization in high-risk infants¹²; however, screening poses logistical challenges, as well as a risk of delaying peanut introduction because of screening delays.^{13,14} By contrast, Australian guidelines do not recommend screening before peanut introduction.^{7,15} There are no data on the subsequent effect of either of these approaches on peanut introduction or peanut reactions.

In light of recent international calls to assess the results of a nonscreening approach to allergenic food introduction,¹⁶ we present data from our new infant cohort, particularly on the introduction of allergenic foods in a population-based sample of infants in Melbourne, Australia, in their first year of life.

Abbreviations used

IQR: Interquartile range

MCHN: Maternal and child health nurse

METHODS

Design

The EarlyNuts study is a population-based, cross-sectional, observational study that aims to measure the prevalence of food allergy, document current practices around dietary introduction of allergenic foods, and evaluate whether changes to infant feeding practices at the population level have reduced the population prevalence of food allergy. We have used the same sampling frame structure and methods of recruitment and follow-up as the HealthNuts study in 2007-2011 to facilitate comparison between the 2 cohorts.¹⁷ One-year-old infants and their families were recruited from council-run immunization sessions in Melbourne, Australia. Recruitment commenced in November 2016 and is ongoing. Parents were unaware of the study until they attended the immunization session to minimize selection bias.

We compared the feeding practices of the first 860 EarlyNuts study participants (November 2016 to October 2018) with previously published data from the HealthNuts study.¹⁰ The HealthNuts study cohort was further divided into infants born before and after the September 2008 changes in the Australasian Society of Clinical Immunology and Allergy infant feeding guidelines and recruited at age 1 year between September 2007 to August 2009 (pre-2009) and September 2009 to August 2011 (post-2009).

Inclusion and exclusion criteria

All infants aged 11 to 15 months inclusive at council-run immunization sessions in Melbourne were eligible for recruitment regardless of past history of exposure or reaction to allergenic food. Participants were excluded only if the parent or guardian could not provide informed consent, complete the questionnaires in English, or both.

Interim analysis

We assessed the extent to which timing of allergenic food introduction of peanut and egg has changed after introduction of the new infant feeding guidelines in Australia in 2016. The sample size at the midpoint of recruitment is large enough to estimate the relevant prevalences with high relative precision (an assertion that we support with a formal power calculation in the next section). We also report preliminary results on parent-reported reactions to peanut, which were consistent with possible IgE-mediated reactions (skin [hives, rash, and/or swelling of lips, eyes, or face], gut [vomiting or diarrhea], and/or breathing [wheeze] problems within 1 hour of food consumption), and compare these with data from the HealthNuts cohort.¹⁸ Egg reactions were not reported because the proportion of infants consuming egg by 12 months changed little between the 2 studies, as shown below. Data on challenge-confirmed food allergy to egg and peanut will be available at the completion of the study.

Sample size and power

Sample size calculations for the EarlyNuts study were based on food allergy prevalence and infant feeding data from the HealthNuts study, a population-based cohort of 5300 twelve-month-old infants.¹⁷ The intended sample size of 2000 infants for the complete EarlyNuts study (2018-2019) provides 81% power to detect a 40% decrease (from 3.0% to 1.8%) in peanut allergy prevalence. Recruitment is ongoing. As of September 2018, we had data from the first 860 participants recruited, and the results below are based on these participants. A sample size of 800 infants in the current analysis provides greater than 99% power to detect a 10% change in early peanut

TABLE I. Baseline demographics for first participants of the EarlyNuts study population and comparison with the HealthNuts study population and with Victoria's Mothers, Babies and Children 2016 data

Characteristic	EarlyNuts study, 2017-2018	95% CI	HealthNuts study, 2007-2011	95% CI	VPDC, 2016
No.	860		5276		
Sex (% male)	51.8	48.4-55.1	50.8	49.5-52.2	51.3*
Mode of delivery (% vaginal)	65.0	61.7-68.2	66.8	65.5-68.1	66.0
Maternal age, mean (y)	33.4	SD, 0.2	33.0	SD, 4.8	31.1*
Mothers >34 y (%)	34.6	31.4-37.9	41.9	40.6-43.2	25.3
Preterm birth (<37 wk [%])	7.3	5.7-9.3	6.1	5.4-6.8	8.3
Maternal country of birth (% Australia)	59.4	56.1-62.7	71.8	70.5-73.0	61.5†
Family history of asthma (%)	31.3	28.2-34.6	30.7	29.4-31.9	NA
Family history of eczema (%)	30.0	27.0-33.3	30.5	29.3-31.8	NA
Family history of food allergy (%)	14.4	12.2-16.9	13.0	12.0-13.9	NA

NA, Not applicable; VPDC, Victorian Perinatal Data Collection by Consultative Council on Obstetric and Paediatric Mortality and Morbidity.

*Australian Institute of Health and Welfare.

†2005-2006 data were 75.2%.

introduction (eg, increase in peanut introduction before 12 months of age from 30% in the HealthNuts study to 40% in the current study).

Assessment of internal and external validity of the study

Parents who declined to participate were asked to complete a nonparticipation survey, which was used to assess selection bias.¹⁷ Demographic characteristics of the study participants were compared with publicly available 2016 data on Victorian mothers and births from the Consultative Council on Obstetric and Paediatric Mortality and Morbidity¹⁹ and the Australian Institute of Health and Welfare²⁰ to assess whether the EarlyNuts cohort was representative of the Victorian population.

Data collection

At recruitment, parents completed 1 researcher-administered and 1 parent-completed questionnaire. Trained researchers also conducted skin prick testing and an eczema assessment with infants within the advised 15- to 20-minute wait after immunization (data not reported here). The parent-completed questionnaire assessed demographic characteristics and known risk factors for food allergy, including family history of allergy, number of siblings, pet ownership, season of birth, and parents' country of birth,²¹⁻²³ as well as information on breast-feeding and use of infant formula. The researcher-administered questionnaire captured verbal parental reports of infant feeding practices, including age of introduction of allergenic foods (peanut products, hen's egg, tree nuts, and cow's milk), frequency and quantity of allergenic food consumption, and any reactions. We also collected data on parents' source content and compliance with infant feeding advice, including any reasons for not following this advice.

Outcome measure: Infant feeding practices relevant to food allergy

The primary outcome measure for this analysis was the age of introduction of peanut and egg. We categorized age of introduction of peanut and egg into completed months until 12 months of age. Introduction at less than 4 months was combined because of the low number of participants in both the peanut and egg groups (n = 7 and n = 6, respectively). Participants were categorized as greater than 12 months if they reported introduction at an age greater than 12 months or not introducing peanut or egg by recruitment (ie, at age 12 months). Peanut introduction was defined as introduction of any food containing peanut (eg, peanut butter, satay, or peanut-containing nut bars). Similarly, egg introduction was defined as introduction of any food containing egg product, including cooked egg (eg, scrambled, poached, boiled, fried, or omelet), baked egg (eg, cakes, biscuits, or pancakes), meringue, or other forms of egg (eg, custard or egg-based mayonnaise).

We also examined the quantity and frequency of consumption. Quantity of peanut was defined as a bite/taste (eg, a lick or bite of peanut butter on toast), small portion (eg, <1 teaspoon of peanut butter), or large portion (eg, ≥1 teaspoon of peanut butter). Quantity of egg was defined as a bite/taste (eg, 1 teaspoon of cooked egg or a lick/bite of baked egg), small portion (eg, half a cooked egg or a few bites of baked egg), or large portion (eg, whole cooked egg or a whole baked product, such as a whole biscuit/muffin/pancake). Cooked and baked egg were analyzed separately. Frequency was initially defined as once, 2 to 4 times, or more than 4 times from first introduction by age 12 months. Frequency categories were updated in June 2018 to include 3 additional categories accounting for greater frequency of consumption: once per week, twice per week, and 3 or more times per week.

Statistical analysis

Prevalence estimates for demographic characteristics and other binary measures were calculated as the observed proportion with a 95% CI based on a binomial sampling distribution. Differences in 2-sample comparisons of categorical data, such as the demographics of the study participants and nonparticipants, were assessed by using the χ^2 test for contingency tables or the Fisher exact test when sample size was less than 5. Kaplan-Meier graphs were used to depict the timing of dietary introduction of peanut and egg, and comparisons of age of food introduction between the EarlyNuts (2018) and HealthNuts (2007-2011) cohorts were compared by using the log-rank test. All analyses were conducted with the Stata statistical software package (release 15; StataCorp, College Station, Tex).

Ethics

Ethical approval for the EarlyNuts study was obtained by the Royal Children's Hospital Human Research Ethics Committee (reference no. 36160A). Parents or guardians provided written informed consent before participation. The study was registered with the Australian New Zealand Clinical Trials Registry (registration #ACTRN12618001990213).

RESULTS

EarlyNuts sample characteristics

Baseline demographic characteristics of the participants are reported and compared with data from the HealthNuts study (2007-2011) and the population of live births in Victoria in 2016 (Table I). The proportion of EarlyNuts participants with a family history of asthma, eczema, and food allergy was similar to that observed in the HealthNuts study. Our sample had a lower proportion of mothers born in Australia compared with the HealthNuts study. This is consistent with changes that occurred in the population demographics of Victoria as the percentage of

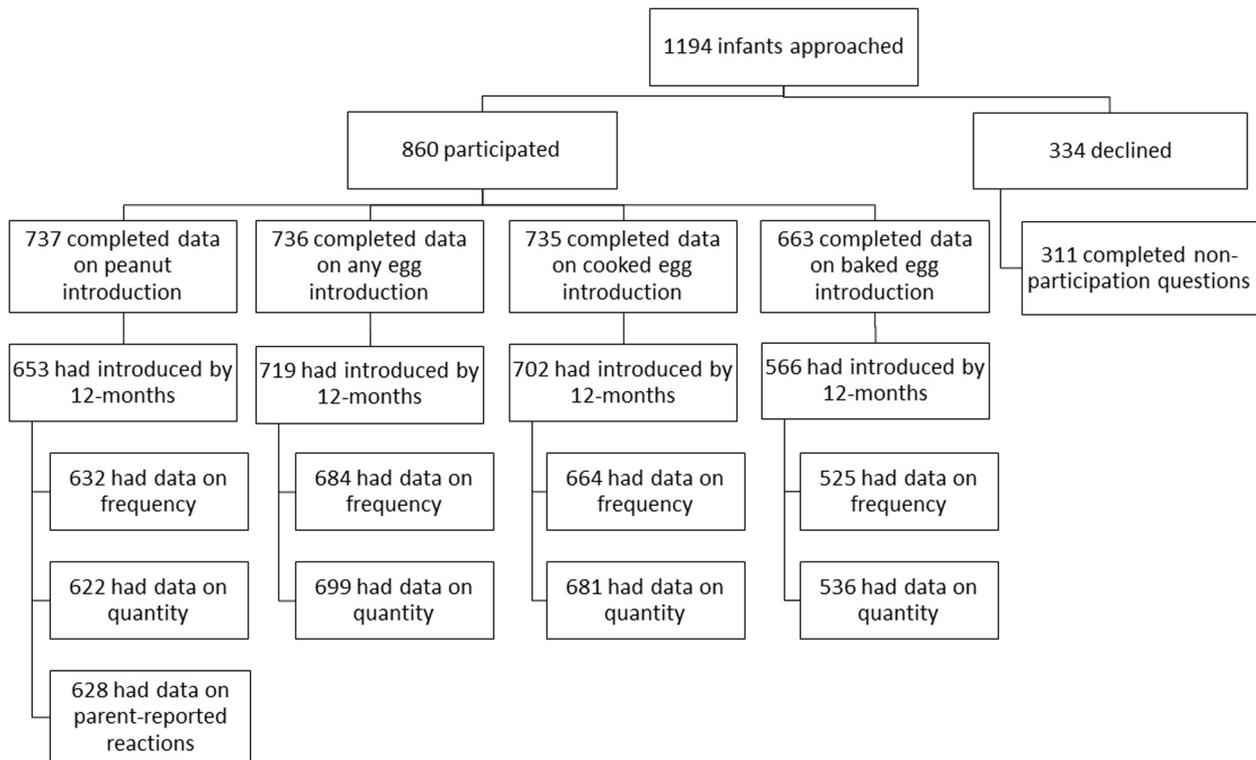


FIG 1. Data flow of study participation until October 1, 2018.

TABLE II. Comparison between study participants (n = 860) and those who chose not to participate but were willing to fill out a short questionnaire (n = 311)

Variable	Participants		Nonparticipants		χ^2 Test, P value
	Percentage	95% CI	Percentage	95% CI	
Child eating peanut	88.6	86.1-90.7	81.4	76.6 -85.3	.002
If eaten, child has reacted to peanut	4.0	2.7-5.8	3.6	1.9-6.8	.792
Child has food allergies	6.6	5.1-8.6	8.5	5.8-12.2	.316
Child has eczema	28.6	25.6-31.8	27.0	22.3-32.3	.585

Australian-born mothers decreased from 75.2% in 2005-2006 to 61.5% in 2016.¹⁹ The majority of population parameters for all births within Victoria fall within the 95% CI from our sample, with the exception of a greater mean maternal age and a greater percentage of mothers older than 34 years in our sample.

The results presented in the current article are from the first 860 participants recruited to the EarlyNuts study, with 72.0% (95% CI, 69.4% to 74.6%) of those approached participating in the study (Fig 1), which is similar to the 73.1% who participated in the HealthNuts study.¹⁷ The majority (93.1%; 95% CI, 89.8% to 95.6%) of parents approached at immunization sessions who did not participate in the study completed a nonparticipation questionnaire, which was similar to 94% in the HealthNuts study.²⁴ Participants and nonparticipants had a similar prevalence of parent-reported eczema and food allergy, although fewer nonparticipating children were eating peanut (81.4% vs 88.6%, $P = .002$, Table II). Among those who had consumed peanut, a similar proportion of participants and nonparticipants reported a possible IgE-mediated reaction to peanut. The most common reason given for not participating was that the child was already

eating all foods included in the study (31.4%, see Table E1 in this article's Online Repository at www.jacionline.org). Of those who did not participate, 17% were from a non-English-speaking background, and 3.6% reported that the child had a food allergy.

Current timing of infant introduction to allergenic foods

Among EarlyNuts participants, the median age of introduction for both peanut and egg was 6 months of age (peanut interquartile range [IQR], 6 to 8 months; egg IQR, 6 to 8 months; Fig 2). Of the different forms of egg, the median of cooked egg introduction was 6 months (IQR, 6 to 8 months) of age, with 35.7% (95% CI, 32.2% to 39.4%) introducing at 6 months and 95.5% (95% CI, 93.7% to 96.8%) of infants having had cooked egg by 12 months of age (Fig 2). The median age for baked egg introduction was 8 months (IQR, 6 to 11 months), with fewer infants eating it at 6 months (18.8%; 95% CI, 15.9% to 22.0%).

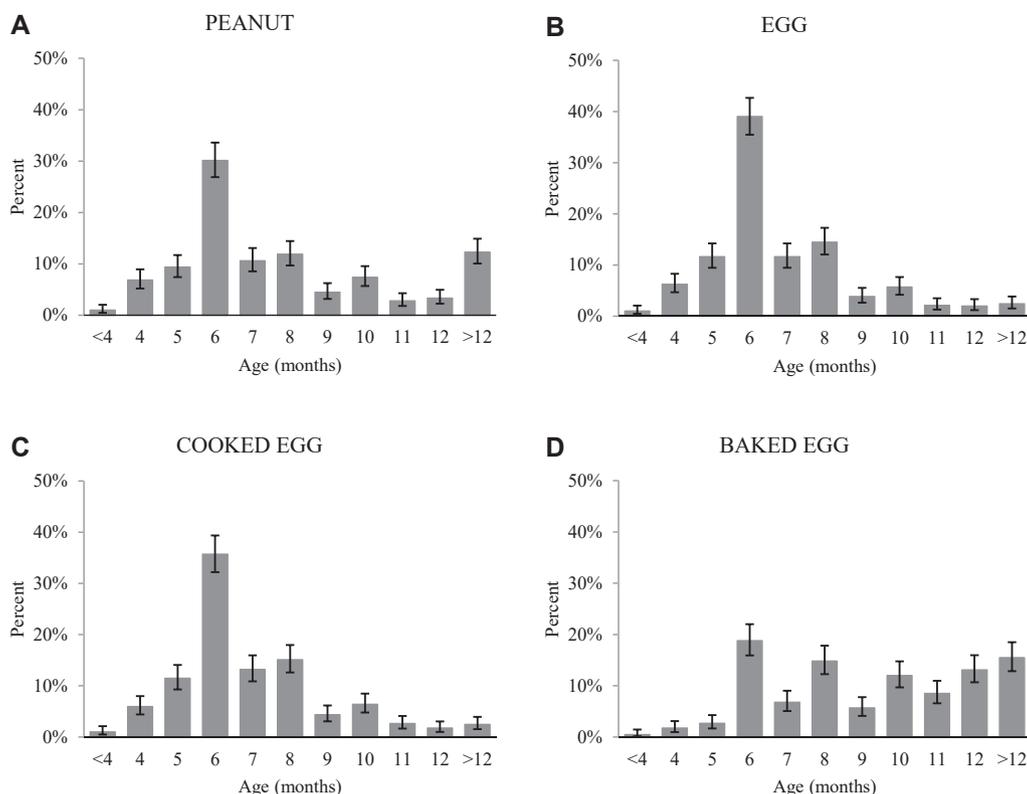


FIG 2. Infant's first exposure to allergenic food by month of introduction. **A**, Age of first peanut introduction (n = 717). **B**, Age of first form of hen's egg introduction (n = 705). **C**, Age of first cooked hen's egg introduction (n = 689). **D**, Age of first baked hen's egg introduction (n = 634). *Age greater than 12 months indicates infants who had not been introduced to the food by 12 months of age. Error bars indicate 95% CIs.

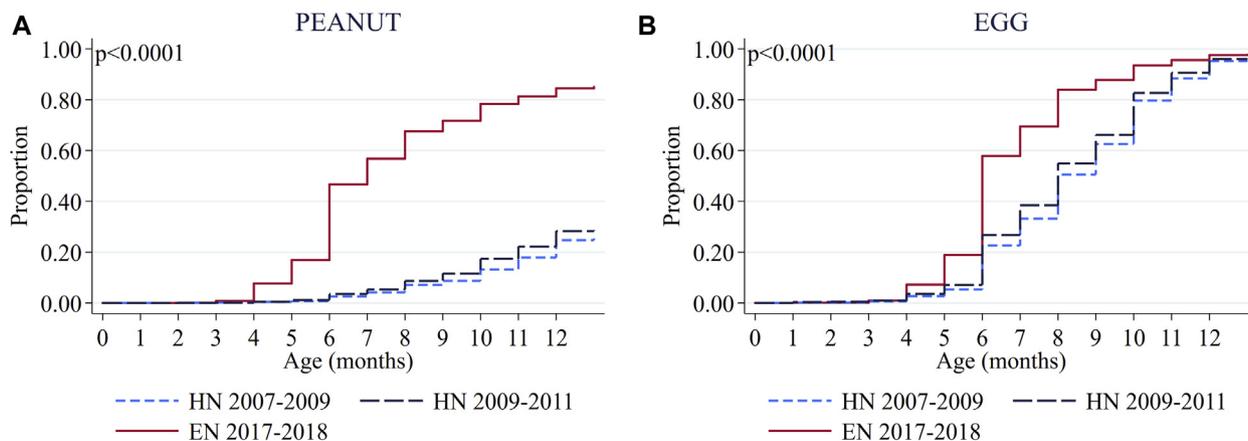


FIG 3. Comparison of age of first introduction of infants to allergenic foods in 2017-2018 in the EarlyNuts (EN) cohort to the HealthNuts (HN) cohort before (2007-2009) and after (2009-2011) guideline changes. **A**, Kaplan-Meier graph for peanut butter introduction by study cohort. **B**, Kaplan-Meier graph for egg introduction by study cohort. P values in graphs are derived by using the log rank test.

Changes in timing of introduction of allergenic foods over the last 10 years

Infants were introduced to both peanut and egg earlier in the EarlyNuts study (2017-2018) compared with the HealthNuts study (2007-2011) (log rank test: peanut, $P < .0001$; egg, $P < .0001$; Fig 3). In the EarlyNuts study the majority of parents had introduced peanut by 12 months of age (88.6%, 95% CI, 86.1% to 90.7%) compared with only 28.4% (95% CI, 27.2% to

29.7%) in the HealthNuts study. The change was less marked for egg, with 97.6% (95% CI, 96.2% to 98.6%) of infants consuming egg by 12 months of age in the EarlyNuts study compared with 95.7% (95% CI, 95.1% to 96.3%) in the HealthNuts study; however, introduction has shifted toward introduction by 6 months (57.9% vs 25.0%).

We performed a sensitivity analysis restricted to Australian-born mothers in both cohorts to examine the potential

TABLE III. Source of advice family received on introduction of solid and allergenic foods

Source	Percentage*	95% CI
MCHN	68.1	64.9-71.2
Lactation consultant	0.6	0.2-1.4
General practitioner	4.1	2.9-5.6
Pediatrician	5.2	3.9-6.9
Allergist	1.6	1.0-2.7
Friend	4.7	3.4-6.3
Family member	9.4	7.6-11.6
Previous child	8.4	6.7-10.4
Online	9.1	7.3-11.2
Other	2.1	1.3-3.3
Missing	0.8	0.4-1.7

*These are not mutually exclusive. The questionnaire permitted multiple answers, with the exception of the "other" source, which was excluded if families answered any alternative option.

contribution of the previously mentioned differences in the population demographics of Victoria between the 2 studies to our findings. Among Australian-born mothers, 93.1% (95% CI, 90.4% to 95.1%) were introducing peanut by 12 months compared with 81.5% (95% CI, 76.6% to 85.6%) of non-Australian-born mothers. Introduction of egg by 12 months was similar in Australian-born and non-Australian-born mothers (98.7% vs 96.2%). Accordingly, the overall increases in early egg and peanut introduction in the EarlyNuts study compared with the HealthNuts study reported above was even more marked when restricting to Australian-born mothers (see Fig E1 in this article's Online Repository at www.jacionline.org). Peanut and egg introduction was high across the sample, irrespective of socioeconomic status (see Table E2 in this article's Online Repository at www.jacionline.org).

When families were asked where they received information on infant feeding, 68.1% (95% CI, 64.9% to 71.2%) reported maternal and child health nurses (MCHNs) as their primary source of information (Table III). Of these, 10.9% received advice from medical doctors (general practitioners, pediatricians, or allergists), but almost 10% were receiving advice from family members or online, although it is important to note that these categories are not exclusive, and each participant could check multiple options.

Timing of peanut introduction in high-risk infants

The overall proportion of infants who had been introduced to peanut before 12 months in the EarlyNuts study was similar in the subgroup of high-risk infants (infants with eczema diagnosed by age 6 months and requiring use of topical steroids, $n = 97/637$). The majority of these high-risk infants (83.5%; 95% CI, 74.6% to 89.7%) had introduced peanut before 12 months, which was similar to the low-risk population (89.6%, $n = 540$).

Reported reactions to peanut under early introduction guidelines

Of the infants introduced to peanuts, parents reported reactions within 1 hour of consumption in the EarlyNuts study more often than in the HealthNuts study (4.0% vs 2.4%, $P = .054$; Table IV), likely because of the increase in peanut introduction by 12 months of age in high-risk infants in the EarlyNuts study compared with

the HealthNuts study. Most reactions in both studies only involved skin symptoms; however, there were 2 cases of wheezing combined with skin reactions in the EarlyNuts study, with no evidence of a difference in the proportion of reactions with reported wheeze in the EarlyNuts study compared with the HealthNuts study. Of the 25 infants with reported reactions in the EarlyNuts study, 12 participants tried peanut on a subsequent occasion, and 5 of these reported tolerating peanut on further ingestion, whereas 7 reported repeated reactions. Of the 13 who did not eat peanut again, 8 parents reported the reaction was on first taste of peanut before 9 months of age.

Frequency and quantity of peanut and egg consumption

In the EarlyNuts study most participants had eaten both peanut and egg more than 4 times (peanut, 76.3% [95% CI, 72.8% to 79.4%]; egg, 89.6% [95% CI, 87.1% to 91.7%]) by 12 months of age from the first introduction and were eating large portion sizes (peanut, 53.7% [95% CI, 49.8% to 57.6%]; egg, 70.8% [95% CI, 67.3% to 74.1%]), with a greater percentage of infants eating egg more frequently and in larger portions than peanut (Table V). Preliminary results, including additional frequency categories, indicate almost 30% of infants were eating peanut 2 or more times a week, and almost 45% were consuming egg that often (see Fig E2 in this article's Online Repository at www.jacionline.org). Cooked egg was consumed more frequently and in larger portions than baked egg (Table V). The majority of infants who had eaten peanut or egg once had only a bite or taste, and most infants who had eaten peanut or egg more than 4 times had large portions (see Fig E3 in this article's Online Repository at www.jacionline.org).

DISCUSSION

This is the first evaluation of infant feeding practices after the adoption of changes in feeding guidelines internationally in 2016 recommending early introduction of a range of allergenic foods.^{7,12} We report that there has been a dramatic shift toward earlier introduction of peanut and egg in 2018 after guideline changes compared with a similar sample in 2007-2011. In 2018, the vast majority of parents had introduced peanut and egg in the first year of life, with both foods most commonly introduced by 6 months of age. This is in contrast to data from the same population in 2007-2011 that showed most parents (71.6%) had avoided peanut introduction until after 12 months of age, and those that did introduce peanut usually did so after 10 months of age.¹⁰ Although the proportion of infants eating egg by 12 months of age was similar between the cohorts, we also observed a shift toward earlier egg introduction in 2018, with a peak at 6 months of age. The majority of parents gave their children cooked egg rather than baked egg in accordance with guideline recommendations to introduce in the cooked form and to minimize sugar consumption in the infant's diet.^{25,26} Although infants were likely to eat large portions of peanut and egg on multiple occasions by 12 months, most were still consuming peanut and egg less than the twice a week recommended in Australasian Society of Clinical Immunology and Allergy guidelines.²⁶ Tey et al¹⁰ previously reported a gradual small shift toward earlier introduction of allergenic foods by 2009-2011 after removal of advice to delay their introduction from infant feeding guidelines in 2008 (eg, peanut introduction

TABLE IV. Parent-reported reactions to peanut within 1 hour of consuming food (possibly IgE-mediated) in high- and low-risk infants who had consumed peanut by 12 months of age

Reaction in 1 h	EarlyNuts study			HealthNuts study			P value
	No.	Percentage	95% CI	No.	Percentage	95% CI	
Any reaction	25	4.0	2.7-5.8	32	2.4	1.7-3.4	.054
Skin/gut*	23	3.7	2.5-5.5	31	2.3	1.6-3.3	.093
Wheeze†	2	0.3	0.1-1.3	1	0.2	0.0-0.5	.239

P values were measured by using a χ^2 test and the Fisher exact test (when $n < 5$).

*Skin reactions include hives, rash, and/or swelling of the lips, eyes, or face. Gut reactions include vomiting, diarrhea, or both. Two of 23 and 2 of 31 infants reported both skin and gut reactions in the EarlyNuts and HealthNuts studies, respectively. Two infants reporting skin-only reactions in the EarlyNuts study, but missing a reaction time, were included. An additional 2 infants in the EarlyNuts study had a reported skin-only reaction 1 to 4 hours after ingestion.

†Cases of wheeze ($n = 2$) also involved skin reactions and occurred at 6 and 8 months on first introduction. There was 1 case of suspected food protein-induced enterocolitis syndrome in the EarlyNuts study caused by reactions, including vomiting and becoming pale and floppy to peanut, oats, rice, coconut, and cow's milk.

TABLE V. Frequency and quantity of peanut and egg consumption in infants introduced to peanut and egg by 12 months of age

	Frequency at 12 mo				Maximum quantity*			
	No.	Once	2-4 Times	>4 Times	No.	Bite/taste	Small	Large
Peanut	632	5.5%	18.2%	76.3%	622	12.7%	33.6%	53.7%
Egg	684	1.9%	8.5%	89.6%	699	7.3%	21.9%	70.8%
Cooked egg	664	2.1%	11.6%	86.3%	681	12.0%	22.0%	65.2%
Baked egg	525	9.9%	23.2%	66.9%	536	17.5%	47.9%	34.5%

*Quantity of peanut was defined as a bite/taste (eg, a lick or bite of peanut butter on toast), small portion (eg, <1 teaspoon of peanut butter), or large portion (eg, ≥ 1 teaspoon of peanut butter). Quantity of egg was defined as a bite/taste (eg, 1 teaspoon cooked egg or a lick/bite of baked egg), small portion (eg, half a cooked egg or a few bites of baked egg), or large portion (eg, whole cooked egg or a whole baked product, including biscuit, muffin, or pancake).

after 12 months decreased from 73.9% to 69.8%), suggesting a small change in community behavior that was not due to changes in population demographics.

Following the Learning Early About Peanut (LEAP) study,⁵ a consensus communication by leading international allergy, immunology, and pediatric bodies in 2015 recommended that peanut-containing products should be introduced between 4 and 11 months of age and that high-risk infants might benefit from a clinical evaluation before peanut introduction.²⁷ This was followed by multiple international feeding guidelines in 2016-2017 recommending early introduction of a range of allergenic foods, although some countries, including the United States, recommend screening high-risk infants before introducing peanut.^{7,12,15,28} Challenges have emerged for screening implementation, including delays in screening and concerns about low compliance to early introduction among parents.^{13,14} There has also been confusion as to the definition of "high-risk infants," as well as what is categorized as a positive test result if screened.²⁹ Health economic analyses of screening high-risk infants for peanut and egg allergy indicate that screening before introduction of peanut could cost US\$654,115,322 or even more if egg screening is included, and recommend a no-screening approach.^{30,31}

Our results show that parents in Australia are undertaking early introduction of peanut without prior screening for peanut allergy. Even among high-risk infants, early introduction was common; the majority had introduced peanut before 12 months of age, a much greater proportion than seen in the HealthNuts study, in which almost 80% of those with eczema were avoiding peanut.¹⁸ We observed a greater proportion of parent-reported reactions among those who had introduced peanut compared with the HealthNuts study but no increase in severe reactions with wheeze as a symptom. This is likely to be due to the increase in the proportion of high-risk infants introducing peanut by 12 months in the EarlyNuts study compared with the HealthNuts study.¹⁸

Further analysis of different high-risk subgroups is planned at the conclusion of the study, when we have additional statistical power, because we are currently underpowered for less common outcomes.

The majority of parents reported receiving information on infant feeding from MCHNs. MCHNs are part of the services offered by the Australian Department of Education, and they provide support and information to all families with children less than 6 years of age free of charge.^{32,33} In the state of Victoria, the MCHNs see new parents 10 times in the first 3½ years, 5 of which are before 4 months of life, and total up to 5 hours of time per family.^{34,35} State-wide participation rates at the 4-month consultation, at which food introduction is discussed, was 93.8% (nonaboriginal and Torres Strait islander population) in 2016-2017.³⁶ During these visits, nurses provide information on a range of topics, from breast-feeding and weaning to sleeping and development.

The demographics of our sample were similar to those in Victoria, providing the EarlyNuts study with external validity in its representation of the general population. Mothers in our study were older than the average population in Victoria; however, we saw similar demographics in the HealthNuts study, with older mothers more likely to participate.³⁷ The percentage of Australian-born mothers decreased from 2007-2011 to 2017-2018, which is consistent with changes in Victorian demographics over the last decade¹⁹; however, we showed in a sensitivity analysis that this did not explain the increase in early introduction of peanut and egg. Participation rates in the EarlyNuts and HealthNuts studies were similar (72% and 73%), as were nonparticipation questionnaire completion rates (93% vs 94%). In the EarlyNuts study nonparticipating children had a similar prevalence of parent-reported food allergy and eczema as participants. Lower rates of peanut consumption in nonparticipants (89% vs 81%) could be attributed to these families being less aware of

the risks of food allergy and the importance of early introduction, which would have also contributed to their nonparticipation.

The strengths of the EarlyNuts study include that it shares an identical sampling frame and protocol as the HealthNuts study, allowing a comparison of the same population over 2 time points by using the same methodology. We are gathering information on the natural history of infant feeding practices in the general population, with relatively high participation rates caused by low participant burden, which is essential to minimize bias in prevalence estimates, and a nonparticipation questionnaire, which allows us to assess potential selection bias. By collecting cross-sectional data at 12 months of age rather than longitudinal data, we avoid possible bias because of changes in participant feeding behavior caused by the awareness of being studied³⁸; however, we increase the chance of potential recall error or recall bias.

The rapid change in infant feeding practices that we observed only a year after publication of the new infant feeding guidelines in Australia is perhaps surprising. There is often a significant lag in changes to culture/clinical practice after new clinical guidelines are published, particularly if they introduce opposing recommendations from prior held beliefs. One contributing factor to this rapid uptake might be the ongoing relationship and communication between food allergy researchers in Melbourne and MCHNs, who provided most of the infant feeding advice to parents. Several of the authors of this article have presented regularly about food allergy research at MCHN meetings and conferences since the HealthNuts study started in 2007, as well as hosting the National Summit on Food Allergy Introduction in 2016, where experts in the field of infant feeding and food allergy, state and federal health care agencies, expert specialist bodies, consumer groups, and patient advocacy and support groups reached consensus to update the guidelines.³⁹ Because of observational evidence, there was already talk of the possible benefits of introducing allergenic foods early, even before the LEAP results and guideline changes. This might have helped to “set the scene” to contribute to the receptiveness of MCHNs and others to the new guidelines when these were released in 2016. In addition, there has been substantial media coverage on food allergy in Melbourne, likely because of our high food allergy prevalence rates and community awareness of and interest in food allergy. This means that new research findings and guideline changes in food allergy are rapidly communicated to the community through the media.

In conclusion, we report that the recent implementation of new Australian infant feeding guidelines in 2016, which do not recommend screening before peanut introduction, were followed by a striking shift toward earlier peanut introduction in the population. Most parents are now introducing their infants to peanut and egg by 12 months of age, which is much earlier than a decade ago. We will be able to assess the important question of the effect of earlier introduction of allergenic foods on challenge-improved food allergy prevalence in the population at completion of the current EarlyNuts study.

We thank the children and parents who participated in the EarlyNuts study, as well as the staff of Melbourne’s Local Government Areas, for access to the community immunization clinics. We thank the additional EarlyNuts team members Anita Hubbard, Claire Buchanan, Deborah Anderson, Natalie Schreurs, Carrie Service, Kirsty Bowes, Helen Czech, and Hannah Elborough.

Clinical implications: Revised infant feeding guidelines in Australia released in 2016 have been associated with a substantial increase in peanut introduction by age 1 year at a population level.

REFERENCES

- Peters RL, Koplin JJ, Gurrin LC, Dharmage SC, Wake M, Ponsonby A-L, et al. The prevalence of food allergy and other allergic diseases in early childhood in a population-based study: HealthNuts age 4-year follow-up. *J Allergy Clin Immunol* 2017;140:145-53.e8.
- Gupta R, Sheikh A, Strachan DP, Anderson HR. Time trends in allergic disorders in the UK. *Thorax* 2007;62:91-6.
- Rudders SA, Arias SA, Camargo CA Jr. Trends in hospitalizations for food-induced anaphylaxis in US children, 2000-2009. *J Allergy Clin Immunol* 2014;134:960-2.e3.
- Mullins RJ, Dear KBG, Tang MLK. Time trends in Australian hospital anaphylaxis admissions in 1998-1999 to 2011-2012. *J Allergy Clin Immunol* 2015;136:367-75.
- Du Toit G, Roberts G, Sayre PH, Bahnon HT, Radulovic S, Santos AF, et al. Randomized trial of peanut consumption in infants at risk for peanut allergy. *N Engl J Med* 2015;372:803-13.
- Ierodiakonou D, Garcia-Larsen V, Logan A, Groome A, Cunha S, Chivinge J, et al. Timing of allergenic food introduction to the infant diet and risk of allergic or autoimmune disease: a systematic review and meta-analysis. *JAMA* 2016;316:1181-92.
- Australasian Society of Clinical Immunology and Allergy (ASCI). ASCIA guidelines: infant feeding and allergy prevention. 2016. Available at: <https://www.allergy.org.au/patients/allergy-prevention/ascia-guidelines-for-infant-feeding-and-allergy-prevention>. Accessed November 27, 2018.
- Koplin JJ, Allen KJ. Optimal timing for solids introduction—why are the guidelines always changing? *Clin Exp Allergy* 2013;43:826-34.
- Netting MJ, Allen KJ. Advice about infant feeding for allergy prevention: a confusing picture for Australian consumers? *J Paediatr Child Health* 2017;53:870-5.
- Tey D, Allen KJ, Peters RL, Koplin JJ, Tang ML, Gurrin LC, et al. Population response to change in infant feeding guidelines for allergy prevention. *J Allergy Clin Immunol* 2014;133:476-84.
- Tang MLK, Koplin JJ, Sampson HA. Is skin testing or sIgE testing necessary before early introduction of peanut for prevention of peanut allergy? *J Allergy Clin Immunol Pract* 2018;6:408-13.
- Togias A, Cooper SF, Acebal ML, Assa’ad A, Baker JR Jr, Beck LA, et al. Addendum guidelines for the prevention of peanut allergy in the United States: report of the National Institute of Allergy and Infectious Diseases-sponsored expert panel. *World Allergy Organ J* 2017;10:1.
- Pratt AL, Hemler JA. Implementation of the NIAID peanut allergy guidelines: outcomes and experience. *Ann Allergy Asthma Immunol* 2019;122:207-8.e1.
- McKean M, Caughey AB, Leong RE, Wong A, Cabana MD. The timing of infant food introduction in families with a history of atopy. *Clin Pediatr* 2015;54:745-51.
- National Health and Medical Research Council (NHMRC). Infant feeding guidelines: information for health workers (amendments added 2015). 2012. Available at: <https://nhmrc.gov.au/about-us/publications/infant-feeding-guidelines-information-health-workers>. Accessed November 28, 2018.
- Fisher HR, Keet CA, Lack G, du Toit G. Preventing peanut allergy: where are we now? *J Allergy Clin Immunol Pract* 2019;7:367-73.
- Osborne NJ, Koplin JJ, Martin PE, Gurrin LC, Lowe AJ, Matheson MC, et al. Prevalence of challenge-proven IgE-mediated food allergy using population-based sampling and predetermined challenge criteria in infants. *J Allergy Clin Immunol* 2011;127:668-76, e1-2.
- Koplin JJ, Peters RL, Dharmage SC, Gurrin L, Tang MLK, Ponsonby A-L, et al. Understanding the feasibility and implications of implementing early peanut introduction for prevention of peanut allergy. *J Allergy Clin Immunol* 2016;138:1131-41.e2.
- Department of Health & Human Services. Victoria’s mothers, babies and children 2016. Melbourne: Victorian Government; 2016. Available at: <https://www2.health.vic.gov.au/hospitals-and-health-services/quality-safety-service/consultative-councils/council-obstetric-paediatric-mortality/mothers-babies-children-report>. Accessed August 27, 2019.
- Australian Institute of Health and Welfare 2018 (AIHW). Australia’s mothers, babies and children 2016: in brief. Canberra: AIHW; 2016. Available at: <https://www.aihw.gov.au/>. Accessed January 16, 2019.
- Koplin JJ, Peters RL, Ponsonby AL, Gurrin LC, Hill D, Tang ML, et al. Increased risk of peanut allergy in infants of Asian-born parents compared to those of Australian-born parents. *Allergy* 2014;69:1639-47.

22. Koplin JJ, Allen KJ, Gurrin LC, Peters RL, Lowe AJ, Tang MLK, et al. The impact of family history of allergy on risk of food allergy: a population-based study of infants. *Int J Environ Res Public Health* 2013;10:5364-77.
23. Koplin JJ, Dharmage SC, Ponsonby AL, Tang ML, Lowe AJ, Gurrin LC, et al. Environmental and demographic risk factors for egg allergy in a population-based study of infants. *Allergy* 2012;67:1415-22.
24. Koplin JJ, Wake M, Dharmage SC, Matheson M, Tang ML, Gurrin LC, et al. Cohort profile: the HealthNuts study: population prevalence and environmental/genetic predictors of food allergy. *Int J Epidemiol* 2015;44:1161-71.
25. World Health Organization. Guideline: sugars intake for adults and children. 2015. Available at: https://www.who.int/nutrition/publications/guidelines/sugars_intake/en/. Accessed March 27, 2019.
26. Australasian Society of Clinical Immunology and Allergy (ASCIA). ASCIA PCC: how to introduce solid foods FAQ 2018. 2018. Available at: <https://www.allergy.org.au/patients/allergy-prevention/ascia-how-to-introduce-solid-foods-to-babies>. Accessed November 27, 2018.
27. Fleischer DM, Sicherer S, Greenhawt M, Campbell D, Chan E, Muraro A, et al. Consensus communication on early peanut introduction and prevention of peanut allergy in high-risk infants. *Pediatr Dermatol* 2016;33:103-6.
28. Fewtrell M, Bronsky J, Campoy C, Domellof M, Embleton N, Fidler Mis N, et al. Complementary feeding: a position paper by the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) Committee on Nutrition. *J Pediatr Gastroenterol Nutr* 2017;64:119-32.
29. Greenhawt MJ, Fleischer DM, Atkins D, Chan ES. The complexities of early peanut introduction for the practicing allergist. *J Allergy Clin Immunol Pract* 2016;4:221-5.
30. Shaker M, Stukus D, Chan ES, Fleischer DM, Spergel JM, Greenhawt M. "To screen or not to screen": comparing the health and economic benefits of early peanut introduction strategies in five countries. *Allergy* 2018;73:1707-14.
31. Shaker M, Verma K, Greenhawt M. The health and economic outcomes of early egg introduction strategies. *Allergy* 2018;73:2214-23.
32. Grant J, Mitchell C, Cuthbertson L. National standards of practice for maternal, child & family health nurses in Australia. Adelaide: Child and Family Health Nursing Practice in Australia; 2017.
33. Maternal, Child & Family Health Nurses Australia (MCAFHNA). 2019. Available at: <https://www.mcafhna.org.au/Home.aspx>. Accessed June 13, 2019.
34. State Government of Victoria. Maternal and Child Health Service: key ages and stages framework. Melbourne: State Government of Victoria; 2018. Available at: <https://www.education.vic.gov.au/Documents/childhood/professionals/health/mchkasframework.pdf>. Accessed August 27, 2019.
35. For parents: Maternal and Child Health Service. Melbourne: State Government of Victoria; 2019. Available at: <https://www.education.vic.gov.au/parents/services-for-parents/Pages/mch.aspx>. Accessed June 13, 2019.
36. State Government of Victoria. Maternal & Child Health Services annual report 2016-2017. Melbourne: State Government of Victoria; 2018. Available at: <https://www.education.vic.gov.au/Documents/childhood/professionals/health/201617statewidereportmch.pdf>. Accessed August 27, 2019.
37. Osborne NJ, Koplin JJ, Martin PE, Gurrin LC, Thiele L, Tang ML, et al. The HealthNuts population-based study of paediatric food allergy: validity, safety and acceptability. *Clin Exp Allergy* 2010;40:1516-22.
38. Landsberger HA. Hawthorne revisited: Management and the worker: its critics, and developments in human relations in industry. Ithaca (NY): Cornell University; 1958:119.
39. Netting MJ, Campbell DE, Koplin JJ, Beck KM, McWilliam V, Dharmage SC, et al. An Australian consensus on infant feeding guidelines to prevent food allergy: outcomes from the Australian Infant Feeding Summit. *J Allergy Clin Immunol Pract* 2017;5:1617-24.

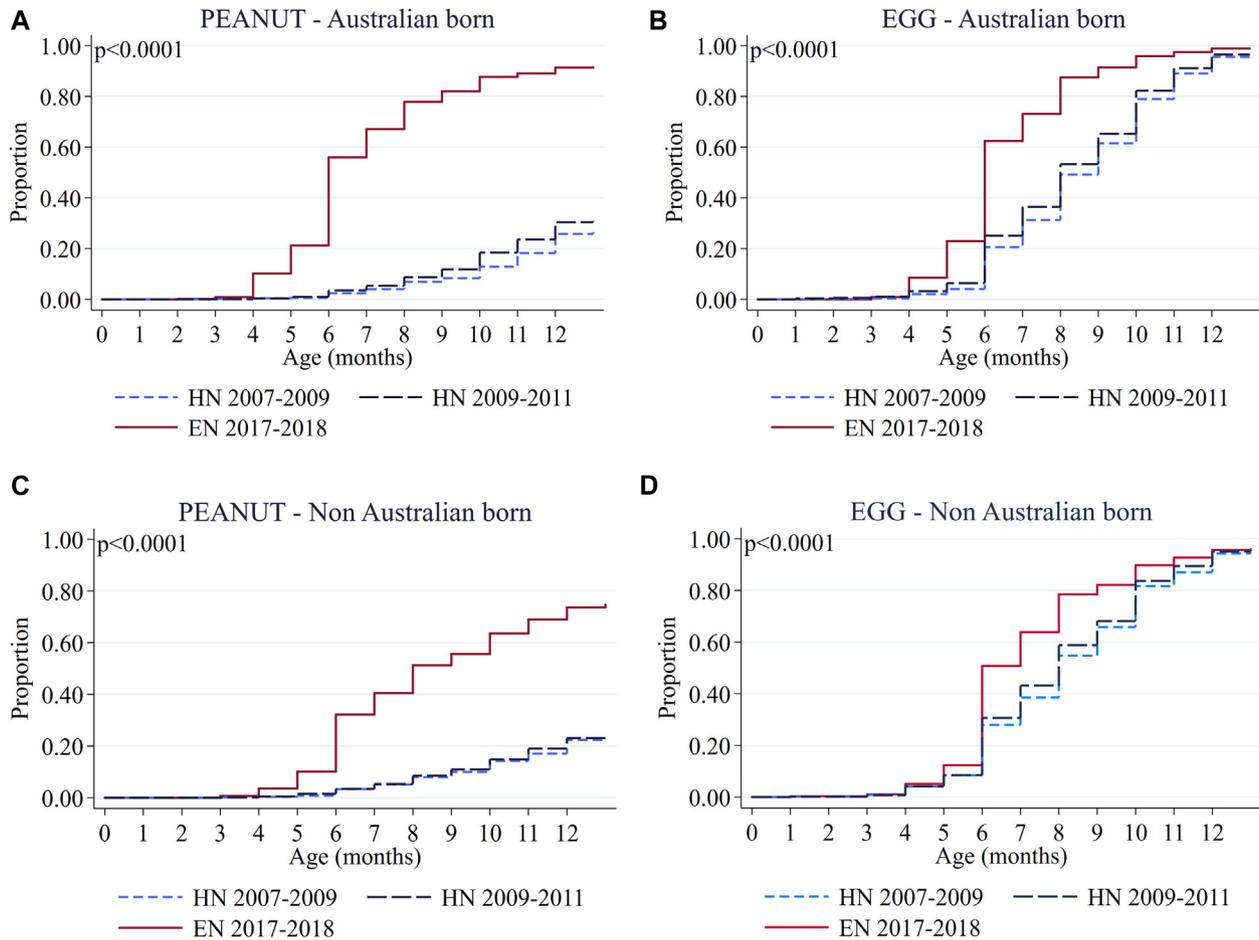


FIG E1. Comparison of age of first introduction of infants to allergenic foods between Australian- and non-Australian-born mothers in 2017-2018 in the EarlyNuts (*EN*) cohort and the HealthNuts (*HN*) cohort before (2007-2009) and after (2009-2011) guideline changes. **A**, Kaplan-Meier graph for peanut butter introduction by Australian-born mothers by study cohort. **B**, Kaplan-Meier graph for egg introduction by Australian-born mothers by study cohort. **C**, Kaplan-Meier graph for peanut introduction by non-Australian-born mothers by study cohort. **D**, Kaplan-Meier graph for egg introduction by non-Australian-born mothers by study cohort. *P* values in graphs are derived by using the log rank test.

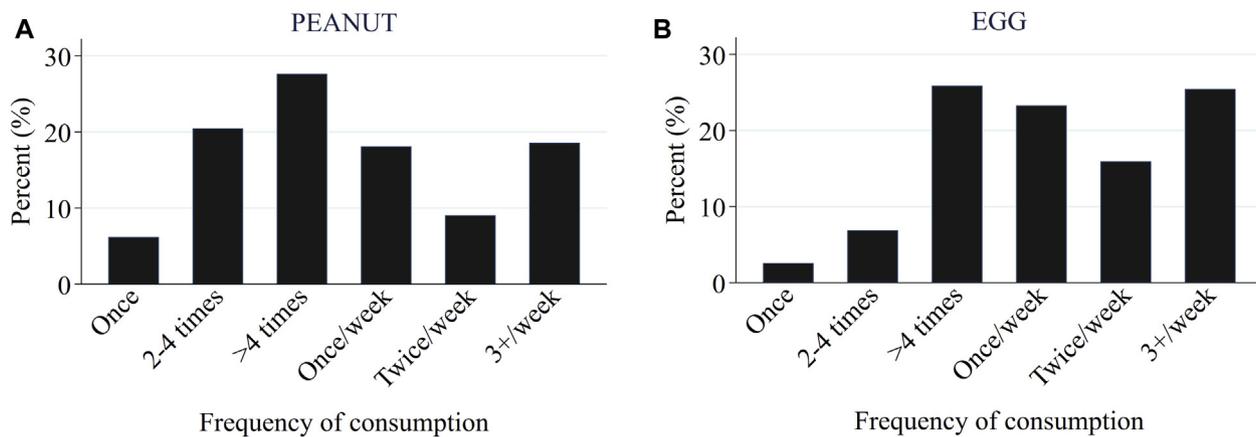


FIG E2. Percentage of infants consuming allergenic foods at different frequencies, including additional frequency categories added to the questionnaire (June 2018). **A**, Peanut consumption by frequency (n = 210). **B**, Any hen's egg consumption by frequency (n = 232).

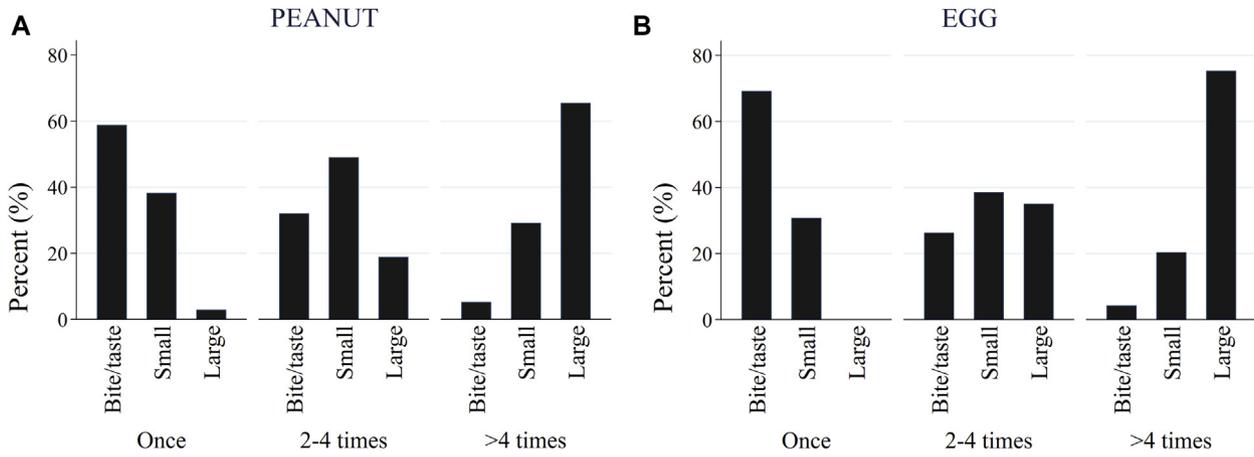


FIG E3. Percentage of infants consuming differently sized portions of allergenic food by frequency of consumption. **A**, How often and how many infants are consuming peanut? **B**, How often and how many infants are consuming egg?

TABLE E1. Nonparticipants' reasons for not participating

Reason*	No.	Percentage
Non-English-speaking background	57	17.1
Child has food allergy	12	3.6
Child eating all foods being tested	105	31.4
Family too busy/not interested	104	31.1
Child upset after immunization	37	11.1
Other†	19	5.7
Total	334	100

*Categories are mutually exclusive and were ranked by importance in the order seen in the table.

†Other reasons include mother or father not being present to provide consent for the child, family not waiting after immunization, and child being asleep/breast-feeding.

TABLE E2. Peanut and egg introduction by 12 months of age by socioeconomic status, divided into quintiles within the study population

SES quintile*	Not introduced		Introduced		P value
	No.	Percentage	No.	Percentage	
Peanut					
Quintile 1	16	11.8	120	88.2	.886
Quintile 2	13	9.0	132	91.0	
Quintile 3	16	10.8	132	89.2	
Quintile 4	18	11.9	133	88.1	
Quintile 5	18	12.6	125	87.4	
Egg					
Quintile 1	4	2.9	132	97.1	.598
Quintile 2	5	3.5	138	96.5	
Quintile 3	3	2.0	145	98.0	
Quintile 4	2	1.3	149	98.7	
Quintile 5	2	1.4	141	98.6	

*Socioeconomic status (SES) was assigned on the basis of home postcode by using Socio-Economic Indexes for Areas measures derived from the 2016 Australian census, which assessed relative socioeconomic advantage/disadvantage, economic resources (income, assets, and expenditure), and educational and occupational characteristics. Quintiles 1 to 5 indicate least advantaged to most advantaged, respectively.