## Racial Differences in Timing of Food Allergen Introduction

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February 28, 2021

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Ph: 312-503-5581 Word Count: 1,200

Number of Tables and Figures: 3 Electronic Repository Materials: 6

### CONFLICTS OF INTEREST

Dr. Christopher Warren has served as an epidemiological consultant for Alladapt Immunotherapeutics and Before Brands

Dr. Hemant Sharma receives research grant support from Aimmune Therapeutics, DBV Technologies, Regeneron, Food Allergy Research & Education (FARE), and the National Institutes of Health (NIH).

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Dr. Tobin receives research grant support from The National Institutes of Health (NIH) and Stanford Sean N. Parker Center for Allergy Research.

Dr. Assa'ad receives grant support from Aimmune Therapeutics, DBV Technologies, Sanofi Aventis, Astellas, AstraZeneca, Regeneron and NIH.

Dr. Gupta receives research grant support from The National Institutes of Health (NIH), Food Research & Education (FARE), Stanford Sean N. Parker Center for Allergy Research, UnitedHealth Group, Thermo Fisher Scientific, Genentech, and the National Confectioners Association (NCA); and has served as a medical consultant/advisor for Aimmune Therapeutics, Genentech, Before Brands, Kaléo, DBV Technologies, ICER, DOTS Technology, and Food Allergy Research and Education (FARE).

The other authors do not have any conflicts of interest to disclose.

### FINANCIAL SUPPORT

This study was funded by the NIH (R01 AI130384).

### **KEYWORDS**

Food allergy, early introduction, racial differences, peanut, milk, egg

To the Editor:

Food allergy (FA) impacts 8% of children in the US, with the prevalence varying by race and highest rates among Black children. However, it is unclear what factors may underlie racial differences in prevalence. Differences in timing of food allergen introduction by race may influence FA development and disease manifestation. Following a reversal of the 2000 guidelines in 2008 advising not to delay the introduction of highly allergenic foods to infants, the NIAID released the Addendum Guidelines for the Prevention of Peanut Allergy in the United States in 2017 (PPA guidelines). The guidelines encourage peanut allergy risk assessment for infants and introduction of peanut products into an infant's diet around 4-6 months of age for those at high risk. <sup>3</sup>

In the Enquiring About Tolerance (EAT) study, non-White participants had higher rates of FA and were less likely to adhere to the early introduction feeding protocol.<sup>4</sup> Racial differences in the timing of food allergen introduction have yet to be extensively studied. Therefore, this study aims to identify potential racial differences in the timing of peanut, milk, and egg introduction among children with parent-reported allergies to these foods while also exploring predictors of earlier or later food allergen introduction during infancy.

Black and White children [?]12 years old with an allergist-diagnosed IgE-mediated FA were enrolled into the Food Allergy Outcomes Related to White and African American Racial Differences cohort (FORWARD), a multi-site, prospective cohort study. Study sites included: Ann & Robert H. Lurie Hospital of Chicago (Chicago, IL), Rush University Medical Center (Chicago, IL), Cincinnati Children's Hospital Medical Center (Cincinnati OH), and Children's National Hospital (Washington, D.C.). Parents/caregivers of study participants completed an intake survey that assessed demographics (child age, gender, race/ethnicity, parent/caregiver highest level of education, household income) and FA characteristics (current parent-reported FA(s), type of FA(s), if/when each reported food allergen was introduced, etc.). Among children whose parent/caregiver reported feeding specific allergenic foods, chi-squared tests assessed associations by race concerning the age ([?] 6 months, 6-11 months, [?]11 months) at which children with specific food allerges (i.e., milk, egg, and/or peanut) were first introduced to that specific food. Multiple logistic regression analyses assessed determinants of earlier or later allergen introduction, including race, age of introduction of allergens, household income, and parent/caregiver educational attainment. Analyses were stratified by child-birth year to examine correlations between PPA Guideline implementation and timing of reported allergen introduction.

A total of 632 children (234 Black and 398 White; mean [SD] age=6.0[3.7]) were included in the analyses

(Table 1). Only 5.3% of peanut-allergic Black children [?] 6 months of age and 58.9% at [?]11 months were introduced to peanut, compared to peanut-allergic White children (13.8% and 31.8%) respectively, (Black vs. White p< 0.001) (Table 2). Peanut products were never introduced to 29.8% of peanut-allergic Black children compared to 35.2% of peanut-allergic White children. Milk products were introduced to 24.5% of milk-allergic Black children [?] 6 months of age and 45.3% at [?]11 months, compared to milk-allergic White children (42.3% and 17.5%) respectively, (Black vs. White p<0.001). However, 20.8% of milk-allergic Black children were never introduced to milk products compared to 16.5% of their White peers. Egg introduction was delayed among egg-allergic Black children (5.8% [?] 6 months and 42.3% at [?]11 months), compared to egg-allergic White children (19.2% and 31.2%) respectively, p<0.001. Egg was never introduced before 12 months of age in 36.5% of egg-allergic Black children compared to 21.9% of egg-allergic White children.

After adjusting for participant demographics and FAs characteristics, White children with peanut allergy were more likely introduced to peanuts (Odds Ratio (OR) 3.6, 95% Confidence Interval (CI) 1.5-9.8), milk (OR 2.9, CI 1.2-7.2), and egg (OR 3.1, CI 1.3-9.0) at [?] 6 months, compared to Black children (**Table 3**). Delay of introduction (11 months of age) was less likely among White children for peanuts (OR 0.2, CI 0.1-0.4), egg (OR 0.4, CI 0.2-0.8), and milk (OR 0.2, CI 0.1-0.4) compared to Black children. Examining early introduction by birth year, there was no significant difference by race in introduction of peanut products at [?] 6 months of age between 2008-2014 (Appendix eFigure 1a). White children born 2017-2019 were less likely to delay (> 11 months of age) introducing peanuts compared to their Black peers (Race and Birth year Interaction P<.05) (Appendix eFigure 2a).

This study is the first to explore racial differences in food allergen feeding practices during infancy. The observed differences in introduction timing of peanut, milk and egg in this study relate to what is known about the growing burden of and increased prevalence of FAs among Black children.<sup>1,5,6</sup> Nearly 89% of Black children with peanut allergy were not introduced to peanuts early or never introduced peanuts compared to 67% of White children with peanut allergy. It is unclear if decisions to withhold or delay peanut feeding were due to varying clinician recommendations, parental fears of introducing allergens, or high allergic sensitization to peanut, but it is possible that differences in knowledge regarding the safety and effectiveness of early allergen introduction for prevention varies. A recent study surveying parents/caregivers of children with FA found that while caregiver knowledge about pediatric food allergies is generally suboptimal, misperceptions were more frequently reported among racial/ethnic minority respondents and those reporting lower household income.<sup>7</sup>

White children with peanut allergy in our study were more often introduced to peanut products at recommended ages compared to Black children with peanut allergy born between 2017-2019 during which time PPA Guideline implementation occurred. Our study reports similar findings to a study conducted among a predominantly White population describing challenges with parent/caregiver adherence to the PPA Guidelines and delayed peanut product introduction (>11 months of age).<sup>8</sup> However, our findings suggest possible racial disparities where the most vulnerable may have received inadequate support to adhere to PPA Guideline-recommended practices.

This study has several limitations. Recall bias is possible, as parents/caregivers were asked to report feeding practices that occurred at various time points in the past. Selection bias is also possible, however the completion rate among eligible respondents in the study was very high, >95%. Finally, the case definitions applied for peanut, milk and egg allergy relied fully on caregiver-report, which may result in false positive cases.

Our study demonstrates that Black children were less likely introduced to food allergens early compared to White children. This underscores the need to better characterize racial differences, by examining if barriers and facilitators exist to "early" introduction of allergen foods to infants, which may inform culturally specific strategies to educate families on the benefits of early introduction of common food allergens. Additionally, it is necessary to explore how physician recommendations for early introduction of food allergens influence parents' decision to introduce foods. Finally, the fact that many parents/caregivers in this cohort of FA patients nevertheless report introducing allergenic proteins "early" –including peanut—suggests that further

work is needed to better characterize the dietary exposures of diverse samples of allergic and non-allergic patients. Such work has the potential to inform ongoing intervention studies that seek to determine not only the ideal timing of allergenic protein introduction during early childhood, but also support targeted interventions to reduce FAs in diverse pediatric populations, as well as optimize dosing, frequency, preparation, and dietary patterns for FA prevention.

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### **ACKNOWLEDGEMENTS**

This study was funded by the NIH (R01AI130384). We would like to thank additional FORWARD team members for their work contributing to the study design/enrolling participants. Team members include: Ann & Robert H. Lurie Children's Hospital of Chicago: Lucy Bilaver, Johnathan Choi, Ososese Enaholo, Jamie Fierstein, Isabel Galic, Gwen Holtzman, Haley Hultquist, Khalid Ibrahim, Ashwin Kulkarni, Pamela Newmark, Sai Nimmagada, Jacqueline Pongracic, Eileen Vincent, Mark Wlodarski; Rush University Medical Center: Aame B Andy-Nweye, Susan Fox, Mahboobeh Mahdavinia; Cincinnati Children's Hospital Medical Center: Annika Chura; Children's National Hospital: Amaziah Coleman, Izeris Ortiz-Rodriguez.

### IMPACT STATEMENT

Food allergy burden varies by race and ethnicity. It is possible that differences in timing of food allergen introduction may contribute to the racial difference in food allergy prevalence.

### **AUTHOR CONTRIBUTION**

Audrey Brewer: Conceptualization (equal), methodology (equal), writing – original draft preparation (lead), writing – review and editing (equal). Jialing Jiang: Conceptualization (equal), investigation (equal), methodology (equal), project administration (equal), writing – original draft (supporting); writing – review and editing (equal). Christopher Warren: Conceptualization (equal), formal analysis (lead), software (lead), methodology (equal), writing – review and editing (equal). Hemant Sharma: Conceptualization (equal), funding acquisition (equal), writing – review and editing (equal). Mary C. Tobin:Conceptualization (equal), funding acquisition (equal), methodology (equal), supervision (equal), writing – review and editing (equal). Amal Assa'ad: Conceptualization (equal), funding acquisition (equal), methodology (equal). Ruchi Gupta: Conceptualization (equal), funding acquisition (equal), supervision (equal), supervision (equal), writing – review and editing (equal).

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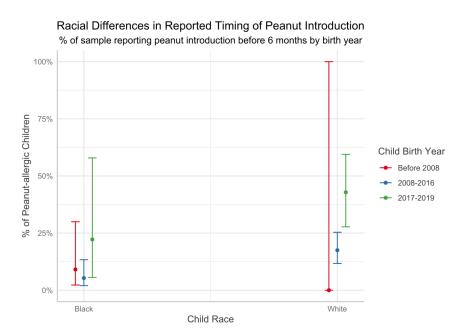
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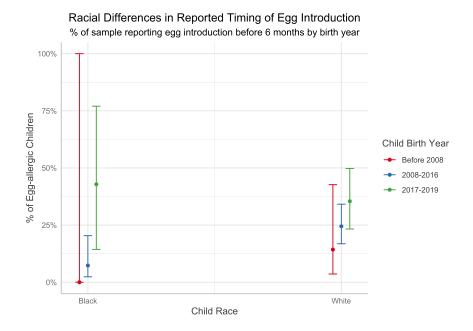
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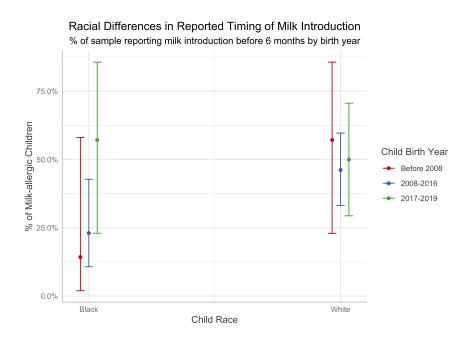
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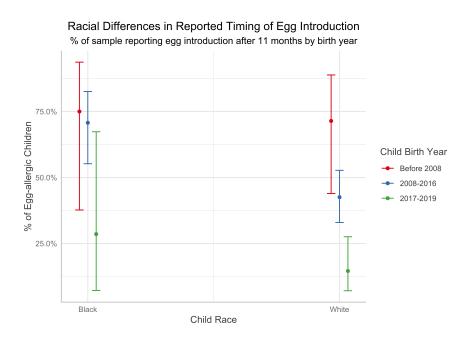
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# Racial Differences in Reported Timing of Peanut Introduction % of sample reporting peanut introduction after 11 months by birth year 75% Child Birth Year Before 2008 2008-2016 2017-2019 Child Race



# Racial Differences in Reported Timing of Milk Introduction % of sample reporting milk introduction after 11 months by birth year 75.0% Child Birth Year Before 2008 2008-2016 2017-2019 Child Race