Proposal Title:
Effects of infant egg consumption on child health and cognition development

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1) Abstract

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Summary of Proposed Research

Early-life nutrition is critical in establishing lifelong health. As a highly digestible, low-calorie matrix of complete protein, essential fatty acids (e.g. DHA) and micronutrients (e.g. choline), hen eggs should be considered an influential whole food-based approach to promoting optimal child health and development. Despite their high nutritive value, many healthcare providers still recommend delaying or avoiding egg introduction to infants based on historical understanding and contradictory reports linking early egg consumption with food allergy. Further, while moderate egg consumption has been associated with no adverse cardio-metabolic outcomes in adults, very few studies have been conducted in children and adolescents. In addition, there is a substantial research gap on how infant egg consumption broadly influences multiple child health and developmental outcomes, as existing studies often narrowly focus on a single outcome. A comprehensive understanding of how infant egg consumption impacts a wide range of key child outcomes including physical growth, obesity, cardio-metabolic health, food allergy, and cognition could inform more precise evidence-based clinical guidelines on optimal infant nutrition that includes eggs.

We propose a 2-year study to examine how infant egg consumption (age of introduction and frequency of intake) influences physical growth, obesity, cardio-metabolic health, risk of food allergy, and cognition development in mid-childhood and adolescence. We will use existing data from two US longitudinal birth cohorts that tracked mother-child dyads from pregnancy to adolescence: 1) Project Viva (1999-present) that enrolled 2,341 pregnancies and followed children at delivery, 6 months (m), then yearly from 1 year (y) to 15 y of child age, and 2) the Infant Feeding Practices Study II (IFPS II, 2005-2007) that enrolled 3,033 pregnancies with surveys in late pregnancy, neonatal (1 m), then monthly from 2 m to 12 m of infant age, and at 6 y. For **Aim 1**, we will classify infants based on their age of egg introduction: never, <2 m, 2-3 m, 4-5 m, 6-8 m, 9-11 m, and ≥12 m. We will compare physical growth, obesity, cardio-metabolic health, food allergy, and cognition test scores in mid-childhood and adolescence. We will fit multivariable linear or logistic regression models with fractional polynomial functions of infant age of egg introduction. Both linear (e.g., earlier introduction, higher probability of the outcome) and non-linear (e.g., threshold effect) associations will be tested. For **Aim 2**, we will classify infants based on their frequency of egg intake: never, <once/week, once/week, 2–4 times/week, nearly daily or daily, and ≥2 times/day. We will use similar analytic methods mentioned above to compare their later outcomes. Finally, we will create an average probability of multiple child outcomes to balance across different aspects of child health and development. We will identify the lowest-risk infant egg consumption when the corresponding average predicted probability of the related adverse outcomes is the lowest.

Section 2: Detailed Research Plan

1) Background Information:

Early-life nutrition is highly influential in establishing lifelong health. During the first 1,000 days of life from conception to the end of the second year, nutrient exposure through both maternal and infant diet can significantly impact organ development and regulate gene expression through epigenetic events including DNA methylation and histone modification[1]. While early exposure to processed, energy dense foods can 'malprogram' developmental pathways toward disease risk, early-life consumption of whole foods (e.g. hen eggs) with superior nutrition can protect against chronic disease throughout the life course.

As an affordable, highly digestible, low-calorie matrix of complete protein, essential fatty acids (e.g. docoshexaenoic acid [DHA]) and micronutrients (e.g. choline, vitamins A and B12, and carotenoids), hen eggs contribute >50% of adequate intakes of critical nutrients during infancy[2,3]. Given their high nutritional value, it seems logical to include eggs as a dietary staple to promote optimal child development. However, past guidelines from health care professionals and federal agencies to limit exposure of infants to common allergenic foods such as peanuts and eggs have traditionally led to slow introduction or complete egg avoidance for infants in the first six months to one year of life[4,5].

With recent work highlighting that peanut introduction in early infancy can protect against peanut allergy development in childhood[6,7], there has been a shift in recommendations for complementary feeding practices. Contrary to traditional recommendations (ESPACI, 1999[8] and AAP, 2000[5]), recent national (AAP,2019)[9] and international (EAACI, 2014)[10] guidelines report that there is no evidence to suggest that withholding the introduction of allergenic foods to infants after 4-6 months is protective against allergy development. However, compared with peanuts, the ideal age for egg introduction into the infant diet is still debated (AAP, 2019)[9]. Egg allergy is often perceived as one of the most common food allergies in early childhood by health professionals and parents, contributing to a major consumer perception obstacle for the egg industry and a potential barrier to widespread egg infant consumption[10,11]. In support of current recommendations, more recent work has reported either no influence[12] or even a protective effect[13] of egg introduction at 4-6 months of age on allergy risk in infants older than 12 months. A recent systematic review and meta-analysis of 146 interventional and observational studies of timing of allergenic food introduction concluded that there was moderate-certainty evidence to support early egg introduction at 4-6 months to reduce egg allergy (risk ratio [RR], 0.56; 95% CI, 0.36-0.87; p=0.009)[14]. Five of the 6 studies reported a protective effect of early egg introduction on egg allergy (RR point estimate, 0.22-0.69). In the outlier study, Bellach et al. reported that infants randomized to egg white powder had a doubled risk of egg sensitization at 1 year of age versus those in the control rice powder group (5.6% versus 2.6%; RR 2.20; 95% CI, 0.68-7.14), however these results did not reach statistical significance (p=0.24)[15].

An optimal infant egg introduction strategy must consider multiple childhood and food-influencing factors, including both age of egg introduction, frequency (amount) of egg consumption, and egg fraction[14]. Tran et al.[16] recently investigated how early (0-6 months), usual (7-12 months), and delayed (avoidance during first year) timing of egg introduction influenced food sensitization. They reported that introduction of eggs at 0-6 months versus 7-12 months was associated with no increased risk of egg allergy at 1 year of age; further, total

avoidance of eggs in the first year of life increased the risk of egg sensitization. This data suggests the potential existence of an age threshold at which delayed egg introduction will increase egg allergy risk. This age threshold may be between 7-12 months (a relatively wide range for infants); however, additional research is required to narrow down to a more precise age. Other work suggests that not only the exposure window, but also the amount of egg consumed is an important consideration in infant egg introduction strategies. In 4-5-month-old infants, Natsume[17] reported that a small amount of heated egg powder (50 mg per day from 6-9 months of age and 250 mg per day thereafter until 12 months) was effective in preventing egg allergy in high-risk infants receiving optimal eczema treatment. We are unaware of any work that has specifically examined how the frequency of infant egg consumption affects allergy response or other health indices in infants. Treatment options for egg and other food allergies are limited[18]. Prevention strategies may be informed with a more precise understanding of the age and frequency of infant egg consumption that protects against allergic responses.

Importantly, complementary food exposure practices should balance allergy concerns with the nutritional benefits of eggs and other health interests of children[19]. Although allergic outcomes associated with any complementary infant feeding practice is critical, a full assessment of infant egg introduction approaches should include an evaluation of multiple childhood health outcomes, not just allergy alone, as untimely food introduction strategies can strongly influence whole-body health and development[4,20]. A recent meta-analysis from Eaton et al.[21] concluded that there was little quality evidence to assess the impact of animal source proteins (versus fortified grains or no intervention) on childhood growth and development. With eggs specifically, traditional guidelines that focused overwhelmingly on allergy have resulted in a scientific record that is inadequate to assess how early egg consumption influences a broader spectrum of childhood health indices including physical growth, obesity, cardio-metabolic health, and cognition. However, limited work does suggest that early egg introduction can positively influence diet quality, as recently demonstrated by Papanikolaou et al.[22] who reported that consumption of eggs in 6-9 month-old infants was associated with higher nutrient intakes including protein, choline, lutein + zeaxanthin, DHA, phosphorus, and VitB12. Supporting the work of others[23], their data also demonstrated that infant egg consumers had lower total and added sugar intake, highlighting eggs as a potentially important early-life disease risk reduction strategy as infant sugar consumption has been associated with childhood obesity[24]. However, as far as we are aware, no studies have directly tested the effects of early egg exposure on childhood obesity. These associations between early egg exposure and nutrient intake are further supported by clinical data linking infant egg consumption with improvements in childhood growth and development. In a 6-month randomized controlled study in 6-9 months old infants, Lanotti et al. (2017)[23] reported that consumption of 1 egg per day (versus no egg) increased length and weight-for-age *z* score and reduced the prevalence of stunting (by 47%) and underweight (by 74%). These improved growth responses could be attributed to enhanced infant blood levels of choline, betaine, methionine, as well as DHA[25].

According to the lipid hypothesis, high blood cholesterol is a causative agent and primary prevention target of cardiovascular disease (CVD)[26]. A consequence of this hypothesis was the recommendation to limit intake of high cholesterol foods, including eggs. Eggs are a

rich source of dietary cholesterol (~200 mg) and have been estimated to contribute about a quarter of the daily cholesterol intake in U.S. adults and children[27,28]. However, recent research suggests that the low-density lipoprotein cholesterol (LDL-C) raising effects of dietary eggs in adult populations is largely negligible and highly variable depending on individual genetic and metabolic factors[29]. Further, increased cholesterol intake from eggs has been associated with an improved lipoprotein profile and high-density lipoprotein (HDL) functionality in adults[27]. Our understanding of how infant egg consumption influences surrogate lipid markers of CVD risk (LDL-C, HDL-C, and triglycerides) in childhood is insufficient. However, a previous study reported that egg consumption in children aged 8-12 years old had no effect on serum lipid concentrations and even resulted in a less atherogenic lipoprotein distribution pattern in a subset of children with small LDL particles[30]. Considering that metabolic disease risk factors in early life can be predictive of future disease risk patterns in adulthood[31], more research is required to understand how infant exposure to eggs, a significant source of dietary cholesterol and other important bioactive nutrients, impacts childhood health.

DHA (22:5n-3), an essential long-chain fatty acid found in conventional and omega-3 enriched eggs, is critical for early fetal growth and the development of neurological function[32]. Pregnant and nursing women are advised to consume at least 200 mg of DHA daily; however, dietary intake is below recommendations in the majority of US women during pregnancy[33]. Previous work has reported that children from mothers supplemented with DHA from delivery until 4 months have better sustained attention at 5 months of age[32] and improved psychomotor development measured at 2.5 years of age[34]. Further, maternal supplementation of choline, another egg-rich nutrient has been associated with protection against cognitive impairment due to prenatal alcohol exposure[35]. However, although a recent prospective cohort study reported that egg consumption was associated with enhanced cognitive performance in adults[36], the impact of infant egg consumption on cognitive performance during childhood is not known.

Summary of Current Knowledge and Research Priorities:

- **Allergy concerns have traditionally led to slow introduction practices or complete avoidance of eggs during the first year of life, despite the high nutrient value of eggs.**
- **Although recent research supports early infant egg exposure to reduce childhood egg allergy, optimal egg introduction strategies (age, frequency/amount, fraction) are still debated among parents and healthcare professions, creating a barrier for widespread infant egg consumption.**
- **Optimal infant egg consumption guidelines must balance allergy concerns with broader assessments of child health and development, including physical growth, obesity, cardio-metabolic health, and cognitive development.**
- **Currently, there is insufficient knowledge of how the age of infant egg introduction and frequency of egg intake influence whole-body child health and development.**

2) Research Project Objectives and Hypotheses:

Objectives: To examine the longitudinal associations of infant age of egg introduction (**Aim 1**) and frequency of infant egg intake (**Aim 2**) with physical growth, obesity, cardio-metabolic health, risk of food allergy, and cognition development in mid-childhood and adolescence.

Hypotheses: The effects of infant age of egg introduction and frequency of egg intake will vary by the child outcome of interest (**Hypothesis 1**). We predict a non-linear association between age of egg introduction and the average probability of multiple child outcomes (i.e., stunting, underweight, obesity, high risk of metabolic syndrome, food allergy, and cognitive delay), with the optimal age being a time point that falls between 6-12 months (**Hypothesis 2**). We also predict a non-linear association between frequency of infant egg intake and the average probability of multiple child outcomes, with the optimal frequency being 2-4 times per week (**Hypothesis 3**).

3) Project Design:

Sample/Data. We propose a 2-year study to examine the extent to which two important aspects of infant egg consumption (i.e., age of introduction and frequency of intake) influence physical growth, obesity, cardio-metabolic health, risk of food allergy, and cognition development in mid-childhood and adolescence. Guided by a life course framework (**Figure 1**), we will use existing secondary data from two US longitudinal birth cohorts that tracked mother-child dyads from pregnancy to adolescence: 1) **Project Viva** (1999-present, N=2,128 newborns) that followed children at delivery, 6 months (m), 1 year (y), 2 y, 3 y, 4 y, 5 y, 6 y, 7 y, 8 y, 9 y, 10 y, 11 y, 12-13 y, 14 y, and 15 y of child age,[37] and 2) **Infant Feeding Practices Study II** (IFPS II, 2005-2012, N=3,033 newborns) that followed children at neonatal (1 m), 2 m, 3 m, 4 m, 5 m, 6 m, 7 m, 9 m, 10 m, 12 m, and 6 y of child age.[38,39] The PI has access to both datasets, and has 3 publications on infant nutrition, early childhood diet, growth, and obesity using Project Viva[40,41] and IFPS II[42] data since 2014. These two studies have a similar study design and complementary measures of child outcomes, which provide a unique opportunity for comprehensive analysis on the health effects of infant egg consumption and also external replication of findings.

Exposure measures (infant egg consumption). We will focus on age of introduction and frequency of intake as the key exposure measures of infant egg consumption, because evidence supports their potential influences on child health and development[43]. We recognize that other aspects of infant egg consumption such as different egg fractions (i.e., white vs yolk[44]) may also influence child outcomes but they were not collected in Project Viva or IFPS II.

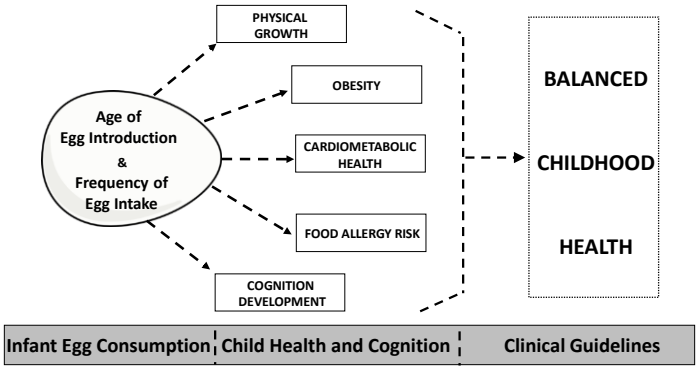

Figure 1. Conceptual framework on effects of infant egg consumption

Age of egg introduction. At Project Viva visits, the age of infant egg introduction was asked at 6-m and 12-m using the same question - "*How old was your baby when you first fed him/her eggs*". In the IFPS II, mothers reported their infant's intake of 18 types of foods in the past 7 days through monthly surveys from 2-12 m of infant ages. The question used for infant food intake was - "*In the past 7 days, how often was your baby fed each food listed below? Include feedings by everyone who feeds the baby and include snacks and night-time feedings.*" "Eggs" were one of the 18 types of foods. Accordingly, we will derive the infant age of egg introduction from IFPS II mothers' monthly responses to infant egg consumption. Our previous analysis on infant dietary patterns showed that 1.7% and 63.0% of IFPS II infants had been introduced eggs by 6 m and 12 m of age, respectively[42].

Frequency of egg intake. At the 2-y survey in Project Viva, the frequency of infant egg intake in the past month was obtained from the mothers' response to the question -"*Please check the box that best represents how often your child eats each of the foods listed, on average, in the past month*". One of the food items for this question was "Whole eggs". Response options for the frequency of consuming "Whole eggs" included "never", "<once/week", "once/week", "2–4 times/week", "nearly daily or daily", and "≥2 times/day".

The same question was asked again at surveys at 3 y and 7 y. As mentioned above, mothers in the IFPS II reported their infant's intake of eggs in the past 7 days through the monthly surveys from 2-12 m of infant ages. Infant egg intake was reported as the number of feedings per day or per week. Our analysis on infant dietary patterns showed the mean egg intake among IFPS II infants was 0.01 (SD, 0.10) and 0.27 (SD, 0.37) serving/week at 6 m and 12 m, respectively[42].

Child outcome measures. We will focus on child physical growth, obesity, cardio-metabolic health, risk of food allergy, and cognition development (**Figure 1**). These child outcomes were chosen because they 1) may be influenced by infant egg consumption (see '**Background**'), 2) are clinically important, and 3) were measured in Project Viva and/or IFPS II.

Physical growth. In Project Viva, birth weight was obtained from birth certificates. Research staff measured children's length/height, weight, and waist circumference at 6 m (infancy), 3 y (early childhood), 7 y (mid-childhood), 12-13 y (early teen), and 14-15 (mid-teen)[37,45]. Additional data on child weight and length/height were obtained from medical records at well-child visits. In IFPS II, mothers reported infant birth weight and length in neonatal survey; weight, length, and age at their most recent doctor's visit in 3-m, 5-m, and 7-m, 12-m, and 6-y surveys[38,42]. Body mass index (BMI) was calculated as, weight in kg/(height in meters)^2. We will define stunting as height-for-age z score < -2, and underweight as sex- and age-specific BMI < 5th percentile according to Word Health Organization (WHO) Growth Standards[46,47].

Obesity. In both Project Viva and IFPS II, we will define child obesity as sex- and age-specific BMI ≥ 95th percentile according to WHO Growth Standards[46,47]. In Project Viva, skinfold thickness was measured at 3 y, 7 y, 12-13 y, and 14-15 y. In addition, fat, lean and trunk fat mass were measured through whole-body dual X-ray absorptiometry (DXA) scans performed at 7 y, 12-13 y, and 14-15 y. Accordingly, we will calculate fat mass index (FMI, kg/m^2), lean mass index (LMI, kg/m^2), and trunk fat mass index (TFMI, kg/m^2).

Cardio-metabolic health. At the 7-y and 12-13-y visits in Project Viva, the child's systolic (SBP) and diastolic blood pressure (DBP) were measured with automated oscillometric monitors. In addition, the child's fasting blood was used to measure plasma glucose, insulin, adiponectin, and C-reactive protein (CRP), serum total cholesterol (TC), triglycerides (TG), and HDL[48]. We will calculate LDL as, total cholesterol – HDL − (triglycerides/5). We will estimate insulin resistance through the homeostatic model assessment of insulin resistance (HOMA-IR = [glucose mg/dL × insulin μIU/mL]/405). A metabolic syndrome z score was derived by calculating the mean of five age- and sex-specific internal z scores for waist circumference, SBP, inverted HDL, natural log-transformed TG, and natural log-transformed HOMA-IR[48].

Risk of food allergy. In Project Viva, mothers reported the child's food allergy annually from 2 y to 11 y, at 12-13-y and 14-15-y of child age through the questions, - "In the past month, has your child avoided any foods because of a food allergy, intolerance, or sensitivity?", and "If yes, please specify". More details on food allergy were reported at the 7-y and 12-13-y visits using the question, - "Has your child ever had an allergic reaction to fish, shellfish, sesame seeds, peanuts or tree nuts?". In addition, at the 7-y and 12-13-y visits, food allergen sensitization of the child was defined as any serum specific IgE level of 0.35 IU/mL or greater to one of the food allergens listed, i.e., egg white, milk, wheat, peanut, and soybean[49]. In the IFPS II, mothers reported whether their infant had food allergy in the past 2 weeks at 2-12 m of infant ages. Additional information on infant food allergy was collected at 4, 9, and 12 m:

whether food allergy (e.g., allergic reaction, sensitivity, or intolerance) happened at the first time of eating, exposure pathway, initial age, allergic symptoms, doctor visit, methods for testing food allergy, diagnosis, treatments, and food allergens including eggs. At the 6-y follow-up, mothers reported the child's status and history of food allergy, initial age, symptoms, testing methods, diagnosis, treatments, outgrowing food allergy, and food avoidance.

Cognition development. In Project Viva, the child's cognition development, including intelligence, visual-motor, and memory-learning, was measured at 3 y and 7 y of age[50]. For the intelligence domain, trained research staff administered the Peabody Picture Vocabulary Test-3rd edition (PPVT-III, a test of receptive language) at 3 y of age, and the Kaufman Brief Intelligence Test-2nd edition (KBIT-II, verbal and non-verbal intelligence) at 7 y of age. For the visual-motor domain, research staff administered the Wide Range Assessment of Visual Motor Abilities (WRAVMA) at the 3-y visit. WRAVMA includes the fine motor (pegboard), visual spatial (matching), and visual motor (drawing) subtests. Subtest scores were combined to yield the total WRAVMA score. At the 7-y visit, staff administered the WRAVMA visual motor (drawing) subtest only. For the memory-learning domain, staff administered the design memory and picture memory subsets of Wide Range Assessment of Memory and Learning (WRAML) at the 7-y visit. These two subset scores were combined to yield the total WRAML score.

Effect modifier. We are interested in effect modification by child sex (Boys vs Girls).

Confounders. Potential confounders include family income; health history of family members; parental education attainment, employment, and preconception BMI; and maternal intelligence, age, race/ethnicity, marital status, parity, pregnancy complications, prenatal vitamins, smoking, and delivery method; early mode of infant feeding including breastfeeding duration and exclusivity. We will also adjust for child actual age at assessments.

Data analysis. All our analyses will be first conducted among boys and girls separately to examine the potential sex differences (if significant, sex-stratified results will be reported).

For **Aim 1 (infant age of egg introduction)**, we will first classify the infants based on their age of egg introduction: never, <2 m, 2-3 m, 4-5 m, 6-8 m, 9-11 m, and 12 m. Then we will compare their physical growth, obesity, cardio-metabolic risk profile, risk of food allergy, and cognition test scores in mid-childhood and adolescence using Chi-square tests (categorical outcomes) or ANOVA tests (continuous outcomes). We will fit multivariable linear (continuous outcomes) or logistic (binary outcomes) regression models with fractional polynomial functions of infant age of egg introduction, adjusted for significant confounders. Both linear (e.g., earlier introduction, high probability of the outcome) and non-linear (e.g., threshold effect) associations will be tested. The non-linear trend will be examined through visualization of scatter plots and statistical tests of polynomial term of infant age of egg introduction in the regression models. If the polynomial terms of age are not significant, we will drop it and consider the association to be linear.

Then, we will fit a mixed effect model (SAS PROC MIXED) for continuous outcomes (height z-score and BMI z-score) and a generalized linear mixed effect model (SAS PROC GLIMMIX) for binary outcomes (obesity and diagnosis of food allergy) that were measured repeatedly across multiple age points. The mixed effect model will include random intercepts, random slopes for age effects, and autoregressive variance-covariance matrix across different time points. Independent variables in the model will include infant age of egg introduction, outcome age point (mid-childhood and adolescence), the 2-way interaction term (infant age of

egg introduction × outcome age point), and significant covariates. The 2-way interaction term quantifies the extent to which infant age of egg introduction can affect the specific outcome. The PI has experience with using mixed effect models for examine child growth measures and multiple publications in this area.[51,52]

For **Aim 2 (frequency of infant egg intake**), we will first classify the infants based on their frequency of egg intake: never, <once/week, once/week, 2–4 times/week, nearly daily or daily, and ≥2 times/day. Then, we will use similar analytic methods mentioned above for Aim 1 to compare their health and developmental outcomes.

In addition, we will create an **average probability of multiple child outcomes** to balance across different aspects of child health and development using the methods published by Oken et al.[53] for identifying the lowest-risk exposure level when multiple outcomes are considered. Specifically, we will focus on 6 binary child outcomes including stunting, underweight, obesity, high risk of metabolic syndrome (e.g., z score ≥ 95th percentile), food allergy, and cognitive delay (e.g., standardized cognition score < 85 points). We will use estimates from aforementioned logistic models to generate predicted probabilities of each of the 6 adverse outcomes when the independent variable of infant egg consumption (i.e., age of egg introduction or frequency of egg intake) varies across the observed range within our study sample. We will calculate the average probability of the 6 outcomes, assuming these outcomes are equally important. We will identify the lowest-risk infant egg consumption when the corresponding average probability of the 6 adverse outcomes is the lowest.

We will handle missing data with Multiple Imputation.[54] Specifically, we will first generate 20 replicates of datasets (PROC MI in SAS) with imputed values for missing data on infant egg consumption, child outcomes, and significant covariates, based on a bayesian approach. The 2nd stage is to use standard statistical methods (e.g., Linear Regression) to fit the model of interest to examine the association between infant egg consumption and the specific outcome within each of the 20 imputed datasets. The 3rd stage is to pool the analytic results from all 20 imputed datasets to get the average estimates of the association (PROC MIANALYZE). The PI has experience with Multiple Imputation for large datasets.[55]

All our analyses will be first conducted among boys and girls separately to examine the potential sex differences. A formal interaction test will be conducted by including the interaction term of egg consumption and sex into the regression models. If the interaction term is significant, sex-stratified results will be reported. Otherwise, sex-pooled analytic results will be reported.

Statistical Power. We expect sufficient statistical power for our hypothesis-driven data analyses for both Aims, because 1) the 2 cohorts had relatively large sample sizes (N=2,128 for Project Viva and N=3,033 for IFPS II), which are sufficient to detect a small odds ratio (1.46 for Project Viva, 1.38 for IFPS II with type 1 error being 0.05 and power being 0.8) of binary child outcomes (e.g., food allergy) between infants with different egg consumption (e.g., egg introduced at ≥12 m vs 6-8 m) or a small effect (effect size=0.054 for Project Viva, 0.051 for IFPS II) of infant egg consumption on continuous outcomes (e.g., intelligence score); 2) most child outcomes were measured repeatedly; 3) infant egg consumption varied largely within cohorts.