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Role of early egg ingestion in induction of tolerance: an unanswered question. Reply
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Reply to Qurat-ul Ain Kamili

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Kamili et al\(^1\) have raised some important questions that we are pleased to address regarding our recent randomised control trial (RCT) on the effects of early regular egg exposure in infants with eczema\(^2\). First, to address the process of subject recruitment, the RCT participant flow profile is shown in Figure 1. Initial recruitment for our RCT was undertaken by placing newspaper advertisements and flyers at baby health clinics. 243 potential participants were initially screened, of whom 109 infants were ineligible (46 due to infant age >4 months, 37 did not have moderate to severe eczema), 32 did not consent (16 due to parents not wanting to introduce solid foods at 4 months of age) and 16 were lost to follow up after initial contact.

Second, it is important to note that in Australia breastfeeding rates are higher than those reported by Kamili et al for the United States in their letter to the Editor. In Australia, the initiation of breastfeeding occurs in 95.9% of infants and 60.1% are breastfed at six months of age\(^3\). At the commencement of the study at 4 months of age, >80% of the participating infants in both groups were breastfed as described in our paper. We agree that small doses of egg protein (3.2ng/mL after the consumption of one whole cooked egg\(^4\)) can be transmitted to the infant via breast milk and maternal dietary egg intake data was collected during this study. For the entire duration of the intervention period (from 4 to 8 months of age), 27/42 (64%) of the egg group infants were breastfed with 15/27 (56%) of their breastfeeding mothers consuming >2 eggs per week in their maternal diet compared to 26/35 (74%) of the control group infants being breastfed but with only 8/26 (31%) of their mothers were consuming >2 eggs per week.
In our RCT\textsuperscript{2}, the egg-specific IgG4 levels were significantly ($P<0.001$) higher in the egg group at both 8 and 12 months of age. Allergen-specific IgG4 has been reported to be a useful marker of the development of immune tolerance in oral immunotherapy studies. The favourable changes in these immunological measures are not the same as clinical tolerance, but provide reassurance of the early regular egg allergen exposure approach. We are in complete agreement with Kamili et al regarding the limitations of our trial imposed by the unforeseen logistic issues that resulted in insufficient power to show statistically significant definitive clinical results. Even so, the trend for lower incidence of egg allergy in the egg group (33\%) compared to the control group (51\%) reduces previous concerns that early introduction of this allergenic food would be associated with increased egg allergy risk. We also agree that the question of whether early egg exposure can reduce egg allergy development requires further investigation before evidence based clinical recommendations can be made and eagerly await the results from current RCTs also investigating this question.

**Figure Legends:**

Figure 1: Participant flow profile.

**References:**

