D. J. Palmer, T. Sullivan, and M. Makrides
Fish oil supplementation in pregnancy and childhood allergies: reply
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Reply to Qun Ui Lee

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Key words

Allergy prevention; eczema; fatty acids; pregnancy; randomised controlled trial.

Lee[1] has raised some questions that we are pleased to address regarding our randomised controlled trial (RCT) on the effect of n-3 long-chain polyunsaturated fatty acids (LCPUFA) supplementation, predominantly as docosahexaenoic acid **(**DHA), in pregnancy on the cumulative incidence of IgE-mediated allergic disease in the first 3 years of life[2]. As reported in our paper published in the British Medical Journal (BMJ)[3], which focussed on eczema and food allergy outcomes over the first year of life, compliance with the trial products were good, with less than 2% of mothers in each group choosing not to take any capsules. At 28 weeks' gestation, 284/368 (77.2%) of mothers in the n-3 LCPUFA group and 280/338 (79.9%) of mothers in the control group reported that they had missed 0 to 3 capsules per week from a total of 21 capsules[3]. The cord blood concentrations of total n-3 LCPUFA, DHA and eicosapentaenoic acid in the plasma phospholipids from women in the n-3 LCPUFA group were higher (median 8.8%, 7.5% and 0.54%) compared to the control group (median 7.2%, 6.2% and 0.27%, $P<0.0001$ for all comparisons)[3]. Hence we do not consider that lack of compliance contributed to our finding that overall n-3 LCPUFA supplementation during pregnancy did not significantly reduce IgE-associated allergic disease in the first three years of life.

We specifically chose the panel of allergens to be tested at 3 years of age to reflect those found to be most commonly associated with allergen sensitisation in Australian children. Another study found that the most common allergens to which children are sensitised at 4 years of age are house dust mite (11.9%), grass pollen (7.8%) and cat (5.8%)[4]. Dog sensitisation was only reported in 2.5% of children in this study and was not associated with the presence of a dog in the household[4]. In our trial, 62.9% of families in the n-3 LCPUFA group had a dog as a pet in the first 3 years of life compared to 65.7%% of families in the control group (P=0.44), hence dog ownership was unlikely to have influenced our trial outcomes.

More infants (96.1%) in the n-3 LCPUFA group were initially breastfed than in the control group (91.0%)[3]. As breastfeeding was a post-randomisation variable we did not adjust for this in statistical analyses, however in exploratory analyses we found no relationship between the initiation of breastfeeding and atopic eczema or egg sensitisation[3]. Although the cow's milk allergen extract became unavailable from the supplier for an extended period during the 3 year assessments, cow's milk skin prick testing was performed on 666/706 (94.3%) of infants at 1 year of age, by which age 99% infants had been introduced to cow's milk[3]. We did not find a difference between the groups for cow's milk sensitisation at 1 year of age, with 1.7% infants in the n-3 LCPUFA group having a positive skin prick test compared with 1.0% infants in the control group (P=0.51)[3]. This was despite more infants in the control group (79.8%) consuming cow's milk protein formula in the first six months of life than the n-3 LCPUFA group (72.0%)[3]. Collectively these data suggest that the small imbalance between breastfeeding and formula feeding in the first 6 months of life did not influence the outcomes of the trial.

In summary, we thank Lee[1] for raising their questions, however we do not believe that any of the issues raised influenced the allergy outcomes of the children in the trial.

Debra J Palmer, Thomas Sullivan and Maria Makrides

References:

1. Lee QU. Fish oil supplementation in pregnancy and childhood allergies. *Allergy* 2014; **XX**(X): XXX-X.
2. Palmer DJ, Sullivan T, Gold MS, Prescott SL, Heddle R, Gibson RA, Makrides M. Randomised controlled trial of fish oil supplementation in pregnancy on childhood allergies. *Allergy* 2013;**68**(11):1370-6.
3. Palmer DJ, Sullivan T, Gold MS, Prescott SL, Heddle R, Gibson RA, Makrides M. Effect of n-3 long chain polyunsaturated fatty acids (LCPUFA) supplementation in pregnancy on infant allergies in the first year of life: a randomised controlled trial. *BMJ* 2012;**344**:e184.
4. Arshad SH, Tariq SM, Matthews S and Hakim E. Sensitization to common allergens and its association with allergic disorders at age 4 years: a whole population birth cohort study. *Pediatrics* 2001; **108**(2): e33.