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Fish oil supplementation in pregnancy and childhood allergies: reply

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1 **Reply to Qun Ui Lee**

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22 Health and Medical Research Council (ID 399389) and a grant from the Australian Egg
23 Corporation Limited. The treatment and placebo capsules were donated by Efamol, UK.

24

25 **Key words**

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

27

28 Lee¹ has raised some questions that we are pleased to address regarding our randomised
29 controlled trial (RCT) on the effect of n-3 long-chain polyunsaturated fatty acids (LCPUFA)
30 supplementation, predominantly as docosahexaenoic acid (DHA), in pregnancy on the
31 cumulative incidence of IgE-mediated allergic disease in the first 3 years of life². As
32 reported in our paper published in the British Medical Journal (BMJ)³, which focussed on
33 eczema and food allergy outcomes over the first year of life, compliance with the trial
34 products were good, with less than 2% of mothers in each group choosing not to take any
35 capsules. At 28 weeks' gestation, 284/368 (77.2%) of mothers in the n-3 LCPUFA group and
36 280/338 (79.9%) of mothers in the control group reported that they had missed 0 to 3
37 capsules per week from a total of 21 capsules³. The cord blood concentrations of total n-3
38 LCPUFA, DHA and eicosapentaenoic acid in the plasma phospholipids from women in the n-
39 3 LCPUFA group were higher (median 8.8%, 7.5% and 0.54%) compared to the control
40 group (median 7.2%, 6.2% and 0.27%, $P < 0.0001$ for all comparisons)³. Hence we do not
41 consider that lack of compliance contributed to our finding that overall n-3 LCPUFA
42 supplementation during pregnancy did not significantly reduce IgE-associated allergic
43 disease in the first three years of life.

44

45 We specifically chose the panel of allergens to be tested at 3 years of age to reflect those
46 found to be most commonly associated with allergen sensitisation in Australian children.

47 Another study found that the most common allergens to which children are sensitised at 4
48 years of age are house dust mite (11.9%), grass pollen (7.8%) and cat (5.8%)⁴. Dog

49 sensitisation was only reported in 2.5% of children in this study and was not associated with
50 the presence of a dog in the household⁴. In our trial, 62.9% of families in the n-3 LCPUFA
51 group had a dog as a pet in the first 3 years of life compared to 65.7% of families in the
52 control group ($P=0.44$), hence dog ownership was unlikely to have influenced our trial
53 outcomes.

54

55 More infants (96.1%) in the n-3 LCPUFA group were initially breastfed than in the control
56 group (91.0%)³. As breastfeeding was a post-randomisation variable we did not adjust for this
57 in statistical analyses, however in exploratory analyses we found no relationship between the
58 initiation of breastfeeding and atopic eczema or egg sensitisation³. Although the cow's milk
59 allergen extract became unavailable from the supplier for an extended period during the 3
60 year assessments, cow's milk skin prick testing was performed on 666/706 (94.3%) of infants
61 at 1 year of age, by which age 99% infants had been introduced to cow's milk³. We did not
62 find a difference between the groups for cow's milk sensitisation at 1 year of age, with 1.7%
63 infants in the n-3 LCPUFA group having a positive skin prick test compared with 1.0%
64 infants in the control group ($P=0.51$)³. This was despite more infants in the control group
65 (79.8%) consuming cow's milk protein formula in the first six months of life than the n-3
66 LCPUFA group (72.0%)³. Collectively these data suggest that the small imbalance between
67 breastfeeding and formula feeding in the first 6 months of life did not influence the outcomes
68 of the trial.

69

70 In summary, we thank Lee¹ for raising their questions, however we do not believe that any of
71 the issues raised influenced the allergy outcomes of the children in the trial.

72

73 Debra J Palmer, Thomas Sullivan and Maria Makrides

74

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