completely clear. Ondansetron acts on serotonin receptors both peripherally and centrally, and its benefit in chemotherapy-induced vomiting is thought to be through inhibition of serotonin receptors on vagal nerve afferents that initiate the vomiting reflex. Whether the effects of ondansetron are mediated centrally or peripherally, if the efficacy of ondansetron in FPIES reactions is confirmed, these findings may help shed light on the poorly understood pathophysiology of FPIES reactions. In addition, the apparent efficacy of ondansetron raises questions as to whether inflammation is truly the central mechanism underlying FPIES, as has been previously suggested, and whether corticosteroids truly have a role in the treatment of FPIES reactions. In this series, no patient was treated with corticosteroids, or even intravenous fluids once symptoms had resolved.

Further study is clearly warranted, but on the basis of the dramatic effects seen in this small case series, we would recommend that ondansetron be routinely used in the treatment of FPIES reactions, both in the food challenge setting and in the emergency room.

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Outcomes of the Childhood Asthma Prevention Study at 11.5 years

To the Editor:

During the 1990s, a number of birth cohorts were recruited to test the effect of allergen avoidance and other interventions for the primary prevention of asthma. Across studies and within studies, over time there has been variable success in achieving this outcome. The first study has recently reported outcomes at age 18 years.[1] The Isle of Wight study found that in children at high risk of developing asthma, implementation of a multifaceted intervention including modification of the mother's diet and allergen avoidance during the first year of life resulted in lower prevalence of asthma at age 18 years compared with standard care. Similarly, a study from Canada found that a multifaceted intervention was successful, compared with usual care, in reducing the prevalence of asthma at age 7 years.[2] The multifaceted intervention in that study included recommendations for allergen avoidance and promotion of breast-feeding during the first year of life. In contrast, a study from The Netherlands found that children who were randomized to a house dust mite (HDM) allergen avoidance intervention during early life did not have a lower prevalence of asthma at age 7 years compared with those randomized to usual care.[3] We have undertaken long-term follow-up on an Australian birth cohort that had participants in a 5-year randomized controlled trial of interventions for the primary prevention of asthma. Here we report findings on the effectiveness of the interventions for outcomes measured at age 11.5 years.

The Childhood Asthma Prevention Study was established as a randomized controlled trial designed to test the effectiveness of HDM avoidance and omega-3 fatty acid supplementation during the first 5 years of life as strategies for the primary prevention of asthma and allergy in high-risk children. We have measured outcomes in the children on 2 occasions since the completion of the 5-year trial; at age 8 and 11.5 years. Our last report, based on measurements of the children at age 8 years, showed no significant beneficial effect of these interventions on the prevalence of asthma, wheeze, or atopy at age 8 years, despite reduction in HDM allergen concentration in dust collected from beds and increased ratio of omega-3 to omega-6 fatty acids in plasma we observed at age 5 years.[4] In the current intention-to-treat analysis, we aimed to determine whether the interventions during the first 5 years of life reduced the prevalence of asthma, atopy, and/or related disorders at age 11.5 years. A secondary aim was to test whether the effect of the HDM avoidance intervention on asthma and related disorders was modified by the presence of atopy.

The study design has been described previously.[5] The study was a randomized, parallel-group controlled trial using a factorial design that separately tested 2 interventions from birth to 5 years: HDM avoidance and omega-3 fatty acid supplementation (see the Methods section in this article's Online Repository at www.jacionline.org for additional text). Results of assessments performed at ages 18 months, 3 years, 5 years, and 8 years have been reported previously.[4,6-8] The study was initially approved by the Human Research Ethics Committees of the University of Sydney, Children's Hospital at Westmead, and Sydney South West Area Health Services, and from 11 years, the approval was provided by Sydney South West Area Health Service (RPAH Zone) Human Ethics Committee.

Identical outcomes were measured at 11.5 years including parental reports of their child's symptoms and treatment by interviewer-administered questionnaire, lung function by spirometry, airway hyperresponsiveness by methacholine inhalation challenge test, allergic sensitization by skin prick test, airway inflammation by exhaled nitric oxide, and total IgE by blood test. Poor asthma control was defined as 1 or more of the following in the preceding 12 months: more than 12 attacks of wheezing, disturbed sleep due to wheezing at least once per week, wheezing limiting the child's speech to only 1 or 2 words at a time between breaths, use of a bronchodilator for night waking or early morning chest tightness more than 3 times per week, or hospital emergency department visit or admissions for asthma.

TABLE I. Effect of the interventions on clinical outcomes assessed at age 11.5 years

	HDM intervention			Omega-3 supplement intervention		
Outcome	Active	Control	Absolute risk reduction* (95% CI)	Active	Control	Absolute risk reduction* (95% CI)
Atopy (%)	57.2	53.8	−3.5 (−14.9 to 8.0)	49.7	62.0	12.4 (1.0 to 23.7)
HDM allergy (%)	45.5	44.8	−0.7 (−12.1 to 10.8)	43.8	46.7	2.9 (−8.6 to 14.4)
Wheeze (%)	27.5	22.7	−4.8 (−13.7 to 4.0)	25.7	24.6	−1.1 (−9.9 to 7.8)
AHR (%)	9.5	14.3	4.8 (−3.0 to 12.5)	10.6	13.3	2.7 (−5.0 to 10.5)
Asthma (%)	23.8	20.4	−3.4 (−11.8 to 5.1)	21.9	22.4	0.5 (−8.0 to 8.9)
Poor asthma control (%)	10.6	9.9	−0.6 (−6.8 to 5.6)	11.8	8.7	−3.0 (−9.2 to 3.2)
Eczema (%)	20.7	13.5	−7.2 (−15.7 to 1.4)	15.8	18.6	2.8 (−5.9 to 11.3)
Rhinitis (%)	41.3	34.3	−7.0 (−16.9 to 2.8)	34.2	41.5	7.3 (−2.6 to 17.2)
FENO (ppb)† (geo mean)	2.64	2.66	1.01 (0.95 to 1.07)	2.64	2.66	1.01 (0.95 to 1.07)
IgE (IU)† (geo mean)	162.39	154.47	0.95 (0.65 to 1.40)	138.38	179.47	1.28 (0.88 to 1.90)
DRR† (geo mean)	4.22	4.66	1.10 (0.93 to 1.31)	4.30	4.57	1.06 (0.90 to 1.26)
FEV_1 (L), mean (SD)	2.27 (0.36)	2.28 (0.41)	0.017 (−0.07 to 0.11)	2.31 (0.37)	2.23 (0.39)	−0.08 (−0.17 to 0.01)
FEV_1/FVC (L), mean (SD)	0.87 (0.07)	0.86 (0.07)	−0.006 (−0.02 to 0.01)	0.87 (0.07)	0.86 (0.07)	−0.006 (−0.02 to 0.0)

AHR, Airway hyperresponsiveness; *DRR*, dose response ratio; *FVC*, forced vital capacity.
*Absolute risk reduction = control-active.
†Geometric ratio and 95% CI.

Outcome data were available for 370 (60%) of the original randomized 616 participant children. Between the 8-year and the 11.5-year assessments, 29 children withdrew from the study and another 93 children were not available for testing at the 11.5-year assessment. Comparison of baseline characteristics between responders (n = 370) and nonresponders (n = 246) at the 11.5-year assessment showed that fewer respondent mothers smoked during pregnancy and that respondent mothers were older and more highly educated than nonrespondent mothers and more respondent mothers than nonrespondent mothers were in full-time employment. Respondent fathers were also older and more highly educated than nonrespondent fathers, and more respondent fathers were in full-time employment than nonrespondent fathers. Baseline characteristics did not differ between the intervention and control groups, except for maternal country of birth (79.1% vs 67.8% born in Australia for the intervention group and the control group, respectively). In addition, we assessed whether there was selective loss to follow-up by intervention groups. The only significant finding was that compared with those lost to follow-up, those who participated at age 11.5 years included a higher proportion of fathers in full-time employment in the HDM active intervention group than in the HDM control group. It is unlikely that this selection bias has any effect on these results.

The prevalence of clinical outcomes assessed at 11.5 years did not differ between active and control groups of the HDM avoidance or the omega-3 supplementation interventions (Table I), except that there was a lower prevalence of atopy among children in the active omega-3 supplementation group than in those in the supplement control group. There were no significant interactions between the 2 interventions ($P > .30$ for all outcomes except poor asthma control, which was $P > .07$).

In our previous report, we found that among children who were atopic at age 8 years, the active HDM avoidance intervention was associated with an absolute risk reduction of 10.6% (95% CI, 0.1-21.0) in the prevalence of poor asthma control compared with those in the control group at this age. This beneficial effect of the HDM avoidance intervention on poor asthma control in atopic children was not evident at 11.5 years with an absolute risk reduction of 4.8% (95% CI −6.8 to 16.3).

Finding that the prevalence of atopy at 11.5 years was lower among children randomized to the omega-3 supplementation was not expected but may be useful for generating future hypotheses. Because of the imbalance in withdrawals, we reanalyzed atopy by including children who had withdrawn and assigning them the atopic status they had at the 8-year assessment. In this analysis, the prevalence of atopy was not statistically different between active and control diet intervention groups. So, although there were nonsignificant beneficial effects for allergy-related outcomes such as rhinitis and, to a lesser extent, eczema (Table I), it is possible that this protection against atopy is a spurious finding.

This long-term follow-up of children enrolled in a primary prevention study shows that in children with a family history of asthma neither HDM avoidance nor omega-3 fatty acid supplementation, as implemented in this study from birth to age 5 years, reduced the prevalence of asthma, atopy, or other atopic disorders at age 11.5 years. Identifying effective interventions to prevent asthma remains an elusive challenge. Understanding why some studies have succeeded, while others have not, whether because of components of their interventions or because of local environmental characteristics, may be important to solving this mystery and making progress in the prevention of asthma.

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