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RESEARCH LETTER

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Is yoghurt an acceptable alternative to raw milk for reducing eczema and allergy in infancy?

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To the editor

We have recently completed a randomized controlled trial of maternal supplementation of the probiotic *Lactobacillus rhamnosus* HN001 (HN001), exploring effects on maternal and infant health. The methodology[1] and the maternal outcomes, gestational diabetes and symptoms of postnatal depression and anxiety have recently been published.[2,3] Briefly, mothers were randomized at 14-16 weeks of gestation to receive HN001 (6×10^9 cfu) or placebo daily during pregnancy and for 6-month post-partum while breastfeeding. No study treatments were given directly to the infants. The mothers themselves or the biological fathers were required to have a history of treated asthma, hayfever or eczema.

Infant eczema was measured at 6 and 12 months using the UK Working Party's Diagnostic Criteria for atopic dermatitis,[4] modified for use in infants, and severity was assessed at the same time-points using SCORAD,[5] defined dichotomously as a score of ≥10. Skin prick tests were performed at 12 months of age using standardized protocols with positive control (histamine 10 mg/mL), negative control (phenolated glycerol-saline), *Dermatophagoides pteronyssinus*, cat fur, 5 grass mix, (Alyostal Stallergenes, Antony, France), egg white, peanut and cow's milk (ALK-ABELLO, Madrid, Spain). The positive control was measured at 10 minutes and allergens and the negative control at 15 minutes. A mean weal diameter of 3 mm or greater, after subtraction of any negative control response, was considered positive.

During the course of the study, we sought questionnaire information regarding maternal, infant and family health and about various aspects of the early childhood environment. For example, questions included the timing of introduction (0-6 and 6-12 months) and the frequency of consumption of yoghurt. All commercial yoghurt in New Zealand is required to contain live organisms and homemade yoghurt would invariably have been made from pre-seeded starter kits that generally use the same probiotics as commercial yoghurts.

Statistical analysis was performed using SAS version 9.3. Hazard ratios (HR) from a Cox's proportional hazards model were used to assess the effect of yoghurt consumption on the 12-month cumulative prevalence of eczema. The point prevalence of atopy at 12 months of age was compared using odds ratios and a chi-squared test. All analyses were adjusted for treatment group and other confounders, listed in the Table 1. In Table 1, the consumption of yoghurt during the first year of life was associated with significant reductions in reported eczema and atopic sensitization. For eczema, these were significant in both time periods (0-6, >6-12 months) and showed a dose–response effect between 6 and 12 months. For sensitization, the effects were significant between 6 and 12 months. Results were similar for observed eczema using SCORAD at 12 months for frequency, HR 0.86 (95% CI 0.80-0.95) per category increase (as described in the footnotes to Table 1), $P = .0003$.

Our study has some limitations. We cannot completely exclude reverse causation. For example, parents whose infants develop eczema in the first 6 months of life might preferentially exclude yoghurt from their infant's diet. However, for infants whose parents

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TABLE 1 Associations of yoghurt consumption with eczema and atopic sensitization, adjusted for study treatment, gender, preterm delivery (<37 wk), caesarean delivery, pets in home at birth, breastfeeding duration, number of previous pregnancies>20 wk of gestation and antibiotics during each yoghurt consumption period

Child yoghurt consumption	Eczema 77/400 (19.3%) Hazard ratios (95% CI)			Atopic sensitization 54/381 (14.2%) Odds ratios (95% CI)		
Any yoghurt <6 mo	44/390 (11.3%)	**0.25 (0.08-0.79)**	**0.02**	44/380 (11.6%)	0.41 (0.12-1.41)	0.15
Any yoghurt 6-12 mo	348/391 (89.0%)	**0.47 (0.26-0.86)**	**0.01**	338/380 (89.0%)	**0.36 (0.17-0.79)**	**0.01**
Frequency of consumption @6-12 months[a]		**0.76 (0.68-0.85)**	**<0.0001**	380	**0.73 (0.63-0.85)**	**<0.0001**
<once a month	84/391 (21.5%)	Ref		83/380 (21.8%)	Ref	
Once a month to once a week	77/391 (19.7%)	0.55 (0.29-1.03)	0.06	75/380 (19.7%)	0.67 (0.31-1.48)	0.32
2-6 times a week	138/391 (35.3%)	**0.29 (0.16-0.52)**	**<0.0001**	134/380 (35.3%)	**0.13 (0.05-0.33)**	**<.0001**
At least once a day	92/391 (23.5%)	**0.22 (0.11-0.47)**	**<0.0001**	88/380 (23.2%)	**0.27 (0.11-0.66)**	**0.004**
Any yoghurt <12 mo	347/390 (89.0%)	**0.47 (0.26-0.84)**	**0.01**	338/380 (89.0%)	**0.36 (0.17-0.79)**	**0.01**

[a]Per category increase: less than once a month, 1-3 times a month, once a week, 2-4 times a week, 5-6 times a week, once a day, and 2 or more times a day. Significant results in bold

reported eczema in the first 6 months, 78% commenced yoghurt between 6 and 12 months. For infants with no reported eczema in the first 6 months, an identical proportion (78%) also commenced yoghurt between 6 and 12 months, suggesting that eczema was not influencing prospective parental decisions about yoghurt introduction. Our study was also amongst high-risk infants in that they had at least one parent with a history of a treated allergic condition, although we have previously shown that this now applies to 80% of the New Zealand population.[6] We do not have information on the type of yoghurt in terms of organisms involved or volume of yoghurt consumed.

We have previously shown in a series of randomized controlled trials that one probiotic (*Lactobacillus rhamnosus* HN001), given daily for 2 years to infants from birth, protects them from eczema to age 6 years and at 6 years shows a significant protection for atopic sensitization.[7]

A number of systematic reviews have confirmed these early protective effects for some probiotics but have emphasized caution in recommending their routine use because of heterogeneity of definitions and strain specificity.[8]

Recently, a prospective observational study in a rural population has shown inverse associations between yoghurt consumption in the first year of life and eczema in early childhood.[9] Another birth cohort study in an urban population (largely excluding other potential protective farm effects) has also recently confirmed these associations and has also shown a reduction in food sensitization with a dose–response effect for both outcomes.[10] In both of these studies, their prospective nature reduces the risk of reverse causation. The effect estimates in both these studies and ours are substantial, suggesting a 50%-80% reduction for eczema and sensitization. This is of similar magnitude to the studies of the protective benefits of farming exposures or raw milk consumption,[11] where both exposures in early life have been associated with substantial reductions in sensitization and allergic disease in later childhood.

These yoghurt associations raise a number of relevant issues both theoretical and practical. Firstly, they suggest that yoghurt consumption needs to be considered in studies of probiotics in this setting and the consumption of yoghurt should be recorded and included in analyses. Secondly, it could be considered that the strong inverse associations between yoghurt consumption and eczema and allergy support the concept that it is the microbial content of raw milk that is the important element conferring protection. Lastly, and perhaps most intriguingly, it might conceivably be the case that other more complex physiochemical aspects of yoghurt and the way that yoghurt "delivers" bacteria to the infant gut might be important for the protective effects. The corollary of this is that freeze-dried probiotics may be less efficacious when given alone than when given in the form of yoghurt. Raw milk has been shown to contain considerably higher concentrations of endotoxin than pasteurized and processed milk, but whether or not this is related to the protective effect is not clear.[12] We have not been able to find evidence of the endotoxin content of yoghurt but would have no reason to suppose that it was any higher than in pasteurized milk.

Early daily yoghurt consumption appears to reduce eczema and early atopic sensitization particularly to food antigens. In this regard, yoghurt is a safe alternative to raw milk (which has been

repeatedly associated with reduced allergy)[11] and is already available around the world. Indeed, unsweetened plain yoghurt is already encouraged as an infant food (from 6 to 7 months of age) by a number of expert groups including the World Health Organization, the National Health Service (UK) and in New Zealand by the Ministry of Health. Perhaps, while we await definitive evidence for the efficacy of specific strains, timing and dose of the probiotics that are protective or for clinical trials of yoghurt, we should encourage mothers, especially those at high risk of having allergic children, to consider introducing live unsweetened yoghurt regularly into their infant's diet, from 6 months of age, not only for its general nutritional value but also as a possible early protection against eczema and sensitization. Randomized trials of the early introduction of yoghurt appear warranted.

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