



Peanut oral immunotherapy in very young children

See [Articles](#) page 359

Peanut oral immunotherapy is a disease-modifying treatment to raise the peanut quantity necessary to trigger an allergic reaction. Among children older than 4 years undergoing peanut oral immunotherapy, nearly 75–80% achieve desensitisation, although few gain lasting protection (eg, remission) after discontinuing oral immunotherapy.¹ Efficacy is balanced by an increased risk of treatment-associated anaphylaxis versus peanut avoidance, a preference-sensitive consideration manageable in partnership with a supervising allergist.^{2–4} Oral immunotherapy outcomes in very young children (eg, younger than 5 years) show similar safety and higher effectiveness than in older paediatric populations: in previous studies, up to 98% of children (aged 9–70 months) achieved desensitisation, with lower adverse event rates than in peanut oral immunotherapy trials with older children.^{5,6} However, many felt that a randomised, placebo-controlled oral immunotherapy trial in younger children was still needed.

In *The Lancet*, Stacie Jones and colleagues present findings from the IMPACT multicentre trial done in the USA, convincingly showing first-level evidence that peanut oral immunotherapy in very young children is safe and highly effective, similar to peanut oral immunotherapy in older children.⁷ The trial randomly assigned (2:1) 146 children aged 1–4 years (median age 39.3 months [IQR 30.8–44.7]; 99 [68%] were boys and 47 [32%] girls; and 95 [65%] were White, 18 [12%] were

Asian, six [4%] were Black, and 27 [18%] were mixed race) with baseline reactivity to 500 mg or less of peanut protein to receive peanut oral immunotherapy with 2 g of peanut daily maintenance dose (96 participants) or placebo (50 participants) for 134 weeks, followed by 26 weeks of avoidance. At week 134, 68 (71%, 95% CI 61–80) of 96 participants who received peanut oral immunotherapy versus one (2%, 0.05–11) of 50 who received placebo achieved desensitisation and tolerated a 5 g cumulative dose of peanut protein (risk difference 69%, 95% CI 59–79; $p < 0.0001$). Additionally, 20 (21%, 95% CI 13–30) of 96 participants receiving peanut oral immunotherapy tolerated a 5 g cumulative dose of peanut protein after discontinuing oral immunotherapy for 26 weeks. Adverse events rates were similar to other peanut oral immunotherapy studies, with 98% of participants receiving oral immunotherapy having an adverse event (mostly mild or moderate in severity), including 22% treated with epinephrine and one patient developing oral immunotherapy-related eosinophilic oesophagitis.^{1,2,7} More children received epinephrine than those who had anaphylaxis, showing that parents treated aggressively.

IMPACT has similar limitations to oral immunotherapy studies in older individuals, for whom oral immunotherapy is an accepted treatment option.^{1,2,4} Early childhood peanut oral immunotherapy is, in our view, ready for immediate real-world implementation, given evidence of higher efficacy and similar safety to oral immunotherapy for older individuals. Although additional trials might enhance the certainty of evidence for oral immunotherapy in these ages, further delay in implementing oral immunotherapy risks withholding proven benefit. Waiting for regulatory approval for commercial products for very young children for this treatment to be deemed ready does not benefit families. Commercial products represent an option to choose but are not a necessity when the flour used in IMPACT is cheap and widely available for purchase in stores and online.^{1,4,5}

Early childhood oral immunotherapy has good potential value, even better than peanut oral immunotherapy in older individuals. A 2021 cost-effectiveness analysis of real-world implementation of a Canadian early-life peanut oral immunotherapy



programme showed that oral immunotherapy dominated avoidance therapy (lower cost and higher quality of life).⁸ A cost-effectiveness analysis of peanut oral immunotherapy in older children using a commercial peanut product approved by the US Food and Drug Administration and European Medicines Agency versus peanut avoidance was low value by comparison.⁹ Early childhood oral immunotherapy could be integrated into clinical practice with minimal logistical and economic barriers, given that many allergists already offer older children oral immunotherapy.⁴

Remission outcomes remain elusive for most patients on oral immunotherapy and, in infants and toddlers, might be hard to differentiate from the up to about 30% who are expected to outgrow peanut allergy by age 6 years,¹⁰ raising the question of oral immunotherapy being worth the effort for only modest differences in this outcome. Parents might be seeking more modest goals (eg, bite proof protection)¹¹ and might prefer a tailored, lower (300 mg) maintenance dose that might be safer and equally effective as a higher (2 g) maintenance dose.^{5,6} Dose might matter less than timing of starting oral immunotherapy in very early childhood: Jones and colleagues noted that remission was associated with younger starting age for oral immunotherapy. Peanut allergy is a potentially severe and lifelong allergy developing in early childhood, associated with a substantial psychological and financial burden of illness.¹² Initiating oral immunotherapy in very early childhood can attenuate the developmental harm that might result through management by strict peanut avoidance, while protecting against reactions from accidental ingestion. For parents, such security might decrease the risk for developing maladaptive coping and anxiety about raising a child susceptible to anaphylaxis.

IMPACT data advance our understanding of peanut oral immunotherapy, showing that peanut oral immunotherapy can produce desensitisation in very young children with good safety. Although peanut oral immunotherapy at any age is not without some risk of an allergic reaction, this is a reasonable treatment consideration for very young children with peanut allergy, guided by an allergy specialist, in the context of shared decision making. Oral immunotherapy has the potential to help manage disease through treatment, not fear and avoidance.

MG is a paid consultant for Aquestive, related to epinephrine drug development; has received personal fees for medical advisory board work related to food allergy, eczema, and eosinophilic oesophagitis management and treatment strategies from DBV Technologies, Sanofi/Regeneron, Genentech, Nutricia, Novartis, Acquestive, Allergy Therapeutics, Pfizer, US World Meds, Allergenics, ALK-Abello, AstraZeneca, Aravax, and Protax; is the senior associate editor for the *Annals of Allergy, Asthma, and Immunology*, for which he receives a stipend; has received one-time honorarium for continuing medical education lectures from ImSci, MedLearningGroup, and multiple state and local allergy societies; is an unpaid member of the scientific advisory council for the National Peanut Board related to peanut allergy education, the Brighton Collaboration Criteria Vaccine Anaphylaxis 2.0 working group for adverse reactions to vaccines, and the Joint Taskforce on Allergy Practice Parameters, which creates conjoint practice guidelines for the American Academy of Allergy, Asthma and Immunology and the American College of Allergy, Asthma and Immunology. EMA is a part-time employee of the Public Health Agency of Canada (PHAC), but the views expressed are her own and not those of PHAC. MS is an associate editor for the *Annals of Allergy, Asthma, and Immunology*, for which he receives a stipend; is an unpaid member and co-chair of the Joint Taskforce on Allergy Practice Parameters, which creates conjoint practice guidelines for the American Academy of Allergy, Asthma and Immunology and the American College of Allergy, Asthma and Immunology; serves on the editorial boards of the *Journal of Allergy and Clinical Immunology In Practice* and the *Journal of Food Allergy*; and has a family member who is chief executive officer of Altrix Medical (not involved in allergy treatments or related products).

***Matthew Greenhawt, Marcus Shaker, Elissa M Abrams**
matthew.greenhawt@childrenscolorado.org

Section of Allergy and Clinical Immunology, Children's Hospital Colorado, University of Colorado School of Medicine, Aurora, CO 80045, USA (MG); Dartmouth-Hitchcock Medical Center, Section of Allergy and Immunology, Lebanon, NH, USA (MS); Dartmouth Geisel School of Medicine, Hanover, NH, USA (EMA)

- 1 Begin P, Chan ES, Kim H, et al. CSACI guidelines for the ethical, evidence-based and patient-oriented clinical practice of oral immunotherapy in IgE-mediated food allergy. *Allergy Asthma Clin Immunol* 2020; **16**: 20.
- 2 Chu DK, Wood RA, French S, et al. Oral immunotherapy for peanut allergy (PACE): a systematic review and meta-analysis of efficacy and safety. *Lancet* 2019; **393**: 2222–32.
- 3 Greenhawt M. Shared decision-making in the care of a patient with food allergy. *Ann Allergy Asthma Immunol* 2020; **125**: 262–67.
- 4 Wasserman RL, Factor J, Windom HH, et al. An approach to the office-based practice of food oral immunotherapy. *J Allergy Clin Immunol Pract* 2021; **9**: 1826–38.
- 5 Soller L, Abrams EM, Carr S, et al. First real-world effectiveness analysis of preschool peanut oral immunotherapy. *J Allergy Clin Immunol Pract* 2021; **9**: 1349–56.
- 6 Vickery BP, Berglund JP, Burk CM, et al. Early oral immunotherapy in peanut-allergic preschool children is safe and highly effective. *J Allergy Clin Immunol* 2017; **139**: 173–81.
- 7 Jones S, Kim EH, Nadeu KC, et al. Efficacy and safety of oral immunotherapy in children aged 1–3 years with peanut allergy (the Immune Tolerance Network IMPACT trial): a randomised placebo-controlled study. *Lancet* 2022; **399**: 359–71.
- 8 Shaker M, Chan ES, Protudjer JLP, Soller L, Abrams EM, Greenhawt M. The cost-effectiveness of preschool peanut oral immunotherapy in the real-world setting. *J Allergy Clin Immunol Pract* 2021; **9**: 2876–84.
- 9 Shaker M, Greenhawt M. Estimation of health and economic benefits of commercial peanut immunotherapy products: a cost-effectiveness analysis. *JAMA Netw Open* 2019; **2**: e193242.
- 10 Peters R, Koplin J, Ponsonby A, Perret K, Dharmage SC, Allen K. The natural history of peanut and egg allergy and predictors of persistence: the Healthnuts Longitudinal study, 6-year-old follow-up. *J Allergy Clin Immunol* 2019; **143**: AB421.
- 11 Greenhawt M, Marsh R, Gilbert H, Sicherer S, DunnGalvin A, Matlock D. Understanding caregiver goals, benefits, and acceptable risks of peanut allergy therapies. *Ann Allergy Asthma Immunol* 2018; **121**: 575–79.
- 12 Shaker M, Chalil JM, Tran O, et al. Commercial claims costs related to healthcare resource use associated with a diagnosis of peanut allergy. *Ann Allergy Asthma Immunol* 2020; **124**: 357–65.

Reproduced with permission of copyright owner. Further reproduction prohibited without permission.