SCOPING REVIEW EXAMINING THE EFFECTIVENESS OF PEANUT ORAL IMMUNOTHERAPY IN MANAGING PEANUT ALLERGIES IN PEDIATRIC POPULATIONS

MAIA BARBATI, TRACY CAI, PERSEPHONE MACKINLAY, LYLA MALIK
BACHELOR OF HEALTH SCIENCES (HONOURS), CLASS OF 2026, MCMASTER UNIVERSITY

ABSTRACT

Background: Peanut allergy is a prevalent food allergy amongst pediatric populations and a leading cause for food-related allergic reactions. Peanut oral immunotherapy is a promising, emerging therapeutic that can be used to initiate desensitization, remission, and tolerance.

Objective: To determine the effectiveness of peanut oral immunotherapy in managing peanut allergies in pediatric populations (defined as birth - 18 years).

Methods: PubMed was searched on December 22nd, 2024, for relevant studies on children published in the last five years. Studies were reviewed in duplicate by two independent reviewers.

Results: Five studies highlighted peanut oral immunotherapy's positive impact on the management of peanut allergy in children. Chu et al. (2022) found that P-OIT with or without antihistamines induced similar levels of desensitization. Jones et al.'s (2022) data suggest that following peanut oral immunotherapy, 71% of participants achieved desensitization and 21% of participants achieved remission. As per Loke et al. (2022), 46% of children in the PPOIT and 51% of children in the P-OIT group achieved the primary outcome of remission. Furthermore, Loke et al. (2024), found that when P-OIT induces remission, it also has long-term benefits including higher peanut ingestion rates, fewer and less severe reactions, as well as improved HRQL. Uhl et al. (2024) reported an 84% success rate in children for accomplishing peanut protein tolerance for a limit of over 750 mg.

Conclusion: Literature on P-OIT demonstrates effectiveness in desensitization, remission, and tolerance for pediatric PA management. Given the therapeutic novelty, further research is necessary to create a standardized treatment method and confirm the effectiveness of P-OIT in pediatric populations.

ABBREVIATIONS

DBPCFC - Double-blind placebo-controlled food challenge
HRQL - Health-related quality of life
OFC - Oral food challenge
OIT - Oral immunotherapy
PA - Peanut allergy
P-OIT - Peanut oral immunotherapy
PPOIT - Probiotic peanut oral immunotherapy
ps-IgE - Peanut-specific IgE skin prick test
SPT - Skin prick test

INTRODUCTION

1.1 Peanut Allergies

Peanut allergy (PA) is the leading cause of food-related allergic reactions and the most common cause of food anaphylaxis-related fatality, with 1-3% of children (birth to 18 years of age) in Western countries receiving a diagnosis for a peanut allergy (PA) [1,2]. PA typically manifests in childhood and often persists throughout one's life. In fact, 80% of children with an allergy diagnosis in infancy will have a PA persist into adulthood [2].

Currently, the only supported PA management is strict peanut avoidance and the use of rescue medication (for instance, epinephrine auto-injectors) following accidental

exposure [1]. Due to peanuts being present in many foods and possible contamination within the manufacturing process, accidents are common, and avoidance can be challenging [1]. Strict allergen avoidance and PA self-management can often cause anxiety for patients and caregivers as PAs are typically long term [3]. It may also lead to impairment in health-related quality of life (HRQL) and act as a significant burden on children and their families [1-4]. As reported by a United States cross-sectional study from 2021, with 637 participants, PA patients and caregivers of peanut-allergic children indicated worse HRQL than a sample of chronically ill patients, with adolescents with PA reporting total HRQL scores approximately 5 points lower than those of children with other chronic illnesses [5]. In fact, 24.8% of study participants indicated being somewhat dissatisfied with current approaches of PA reaction prevention [5].

1.2 Peanut Allergy and Oral Immunotherapy

Recently, peanut oral immunotherapy (P-OIT) has emerged as a novel, promising therapeutic for managing PA and was approved by the US Food and Drug Administration and European Medicines Agency in 2020 [6-8]. Oral immunotherapy (OIT) consists of daily low-dose ingestion of the allergen, starting at a dose below what would cause a reaction [9,10]. Gradually, the doses increase until a maintenance dose is reached [9,10]. This process can yield OIT effectiveness on PA [9].

For the purposes of this review, effectiveness is defined in relation to desensitization, remission, and ideally, tolerance [9]. Desensitization is defined as temporary tolerance to the allergen when eaten regularly. In contrast, remission is the absence of clinical reactivity that persists after treatment has been discontinued for a period of time. Finally, tolerance is the complete ability to consume the allergen without an adverse reaction [9].

The objective of this scoping review is to determine the effectiveness of peanut oral immunotherapy in managing peanut allergies in pediatric populations (defined as birth - 18 years).

METHODS

2.1 Search Strategy and Eligibility Criteria

A scoping review was performed by searching PubMed on December 22nd, 2024, to gain a broad understanding of the effectiveness of P-OIT. Medical subject headings strung together by Boolean operators were used to produce the following search strategy: (treatment* OR therap*) AND (efficacy OR effectiveness) AND ("oral immunotherapy" OR OIT) AND (allerg* OR "allergic disease") AND (pediatric OR child* OR youth OR adolescen*). Filters were applied to include only individuals with peanut allergies and exclude papers published outside of the last five years, non-RCTs, non-English studies, preprints, and study populations that were not pediatric (defined as birth-18 years).

2.2 Data Collection

Four reviewers (MB, TC, LM, and PM) independently screened articles for titles, abstracts, and full texts in duplicate using Covidence. Conflicts were resolved by a third reviewer. The search produced 454 results. Seven duplicates were identified and automatically removed by Covidence. The included studies were then reduced to 5 through the exclusion of the papers that were not RCTs and those that did not include P-OIT as an intervention for PA during title and abstract screening and full-text review. Extracted data included study characteristics, methodology, intervention characteristics, outcomes, study strengths and limitations, and areas for future research.

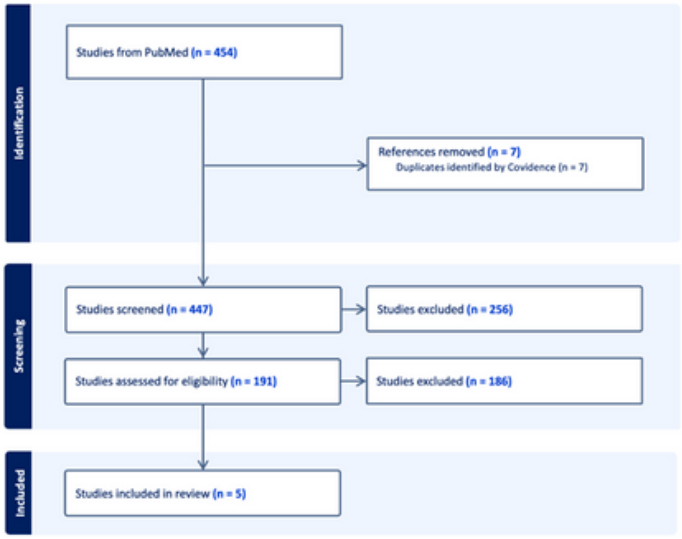

Figure 1. PRISMA Flow Diagram

RESULTS: EFFECTIVENESS OF P-OIT FOR PEDIATRIC PA

Research has demonstrated the effectiveness of P-OIT mainly by evaluating its success in inducing desensitization, remission, and tolerance. Below are five randomized controlled trials that are synthesized to highlight important findings on the effectiveness of P-OIT. The following articles were particularly chosen for their focus on P-OIT's effectiveness and their unique contribution to the ongoing discourse on P-OIT effectiveness in the scientific literature.

3.1 Peanut Oral Immunotherapy With or Without Antihistamine Premedication for Peanut Allergy

In 2022, Chu et al. conducted a placebo-controlled RCT at Hamilton Health Sciences' McMaster Children's Hospital in Canada to compare the effectiveness of P-OIT with or without concomitant use of desloratadine

and ranitidine, which are second-generation H1 antihistamines and H2 histamine blockers, respectively. Effectiveness was measured by the ability to induce desensitization. The primary outcome was the risk and incidence of adverse reactions.

Eligible participants were between 5 to 10 years old and determined to be allergic to peanuts based on a positive ps-IgE, presenting clinical symptoms following ingestion of peanut, and a positive serum-specific IgE result. From 2012 to 2015, 43 participants underwent randomization with 10 randomized to placebo-OIT + placebo premedication, 16 to P-OIT with placebo H1 and H2 premedication, and 17 to P-OIT with H1 and H2 premedication.

Participants underwent a baseline OFC. Patients assigned H1 and H2 premedication were orally given desloratadine 2.5 mg in 5 mL once daily along with ranitidine 75 mg in 5 mL twice daily. A dosage of 500 mg of peanut protein was reached and maintained for 12 months. Chu et al. found that P-OIT with or without antihistamines induced similar levels of desensitization, with the highest dose prior to reaction being 3643 ± 1053 mg peanut protein in the P-OIT and placebo antihistamines group and 3683 ± 724 in the P-OIT with antihistamines group. This suggests that antihistamine premedication did not increase desensitization beyond the ability of P-OIT. However, patients randomized to P-OIT with antihistamines had fewer adverse events than those without.

A strength of this study is its randomized, double-blind, placebo-controlled design, which reduces bias and enhances its reliability. However, a major limitation to the generalizability of the findings is its small sample size. The study did not assess long-term tolerance which means no conclusions can be made about lasting benefits of P-OIT [11].

This study confirms the effectiveness of P-OIT in inducing desensitization and suggests that antihistamine premedication may enhance safety without altering overall effectiveness.

3.2 Efficacy and Safety of OIT in Children Aged 1-3 Years with PA

In a double-blind randomized placebo-controlled study conducted by Jones et al. in 2022, P-OIT effectiveness was assessed through desensitization and remission. Eligible participants were children aged 0-12 who were reactive to 500 mg or less of peanut protein during a double-blind placebo-controlled food challenge (DBPCFC). Participants were collected across five academic medical centers in the United States. They were randomly assigned to receive P-OIT or placebo for 134 weeks with 2000 mg peanut protein per day followed by a 26-week avoidance period. The final sample size contained 146 children with the primary outcome being desensitization at the end of week 134, and the secondary outcome being remission after avoidance at week 160.

At week 134, 71% of participants who received P-OIT compared with 2% of participants who received placebo met the primary outcome of desensitization. After avoidance, 21% of participants receiving P-OIT compared to 2% of participants who received placebo met the secondary outcome of remission. While this study demonstrates several strengths such as double-blinding, randomized assignment to treatment, and the presence of a control group, there are notable limitations. Specifically, although the study included children aged 0-12, only 12% of participants were younger than 4, limiting the generalizability to younger children. Additionally, there was a high dropout rate during the 26-week avoidance period. Further, 27% of participants who received P-OIT and 20% of those who received placebo did not reach the maximal maintenance dose of 2000 mg [12].

The findings of this study support the effectiveness of early-life P-OIT in achieving desensitization and remission, though adherence challenges and age distribution limit the generalizability of its effectiveness.

3.3 Probiotic Peanut Oral Immunotherapy Versus Oral Immunotherapy and Placebo in Children With Peanut Allergy

In 2022, Loke et al. conducted a randomized controlled trial to assess the outcome of sustained unresponsiveness, otherwise known as “remission,” to probiotic peanut oral immunotherapy (PPOIT). Eligible participants were children aged 1-10 years old, weighing more than 7 kg, with a PA confirmed by a DBPCFC and either a positive peanut skin prick test (≥3 mm) or the presence of peanut-specific IgE (≥0.35 kU/L). Participants were recruited from three tertiary hospitals in Australia. Random assignment was done in a 2:2:1 ratio and participants were randomly assigned to PPOIT, placebo probiotic and P-OIT, or placebo probiotic and placebo P-OIT.

Treatment involved dose escalation of peanut protein until a 2000 mg daily maintenance dose was reached, for a duration of 18 months, followed by an 8-week peanut avoidance period. The primary outcome was remission, defined as no allergic reaction to a cumulative 4950 mg dose of peanut protein during a DBPCFC at the end of the 18-month treatment period (T1), and after the 8-week avoidance period (T2).

The final sample size included 201 participants, and the researchers applied an intention-to-treat analysis to ensure results were unbiased and the randomization process was preserved. The results showed that 46% of children in the PPOIT and 51% of children in the placebo probiotic and P-OIT group achieved remission compared to only 5% of children in the placebo probiotic and placebo P-OIT group.

Strengths of this study include the use of randomization, the presence of multiple control groups, and the application of an intention-to-treat analysis applied—offering pragmatic results. However, some limitations include the lack of available data on participant demographics, differences in group sizes, and the absence of a clear rationale for choice of probiotic [4].

While probiotics did not enhance outcomes, this study reinforces the effectiveness of P-OIT alone in achieving remission in children with PA.

3.4 Two-Year Post-Treatment Outcomes Following P-OIT

In 2024, Loke et al. conducted a long-term follow up study to the previous 2022 randomized controlled trial, to assess the long-term outcomes of PPOIT and P-OIT.

Methods of the 2022 study have been thoroughly reported above. Based on the results of the previous study, participants were classified into the following groups: remission (passed both T1 and T2), DWR (desensitized at T1 but no remission at T2), or allergic (failed T1). Following these classifications, participants with remission were instructed to consume peanuts without restriction, DWR participants to ingest one to two peanuts daily, and allergic participants to continue strict avoidance.

Peanut ingestion, reactions, and HRQL measures were monitored prospectively over two years post-treatment. At two years, peanut ingestion rates were both substantially higher for PPOIT (86.7%) and P-OIT (78.7%), than for placebo (10.3%). Reactions decreased across all groups over time. At two years, remission and allergic groups had comparable reaction rates, but DWR participants experienced significantly more reactions than remission and allergic groups. Adrenaline injector use was 0% for remission participants compared to 5.3% for DWR and 2.3% for allergic participants. Remission participants also showed significantly greater HRQL improvements than DWR and allergic participants.

Strengths of this study include a high retention rate of participants continuing in the long-term follow up study, blinding, and treatment adherence. Despite these strengths, there are some limitations such as potential bias from clinical outcome awareness, a potent concentration of highly motivated participants due to their desire to follow-up, conservative classification of allergic participants, heterogeneity within groups, and the reliance on caregiver-reported quality of life measures [13].

This follow-up study demonstrates the long-term effectiveness of P-OIT and PPOIT in maintaining peanut ingestion rates and improving quality of life in children with prior remission.

3.5 High Degree of Desensitization After 1 Year of Early-Life P-OIT

In 2024, Uhl et al. conducted an interim analysis on the Small Children Oral Immunotherapy (SmaChO) study, an open-label randomized controlled trial at Sachs' Children and Youth Hospital in Sweden, to assess the effectiveness and safety of P-OIT. The primary outcome of this interim analysis was tolerance to a minimum of 750 mg of peanut protein following 1 year of P-OIT or avoidance.

Eligible participants were children aged 1 to 3 years living in Stockholm with IgE-antibodies to peanut protein. To be included, participants had to react to a baseline OFC of 250 mg peanut protein. 75 randomly selected participants underwent block randomization 2:1 to P-OIT or avoidance, forming groups of 50 and 25, respectively. In the P-OIT group, up-dosing of peanut protein occurred every 4 to 6 weeks until the maintenance dose of 285 mg was reached. P-OIT continued with a daily maintenance dose and clinical visits every 3 months for 1 year with 63 participants.

43 participants in the P-OIT group and 20 in avoidance received the 1-year OFC. 7 participants in the P-OIT group withdrew. At the 1-year OFC, 36 of 43 participants in the P-OIT group (84%) and 1 of 20 participants in the avoidance group (5%) tolerated a minimum cumulative dose of 750 mg of peanut protein. The P-OIT group had a median cumulative tolerated dose of 3,500 mg of peanut protein, compared with 2.8 mg in the avoidance group.

The study has a well-powered study size and relatively low dropout rates. However, it is limited by its open study design. These findings indicate that P-OIT with slow up-dosing and a low maintenance dose may be a safe and effective method of developing tolerance to peanuts in children aged 1 to 3 years [9].

The results of this study support the effectiveness of low-dose, early life P-OIT in safely achieving substantial desensitization among young children with PA.

DISCUSSION

4.1 Challenges and Risks

Despite the many benefits, P-OIT faces various challenges, specifically when implementing conclusions from controlled trials into real-world situations. Safety is still paramount according to studies led by the University Children's Hospital of Zurich and Basel, specifically during up-dosing, which carries an enhanced risk of anaphylaxis, especially in doses above 300 mg of peanut protein [14]. This indicates that adverse reactions are typically mild to moderate, with gastrointestinal symptoms being the most common in clinical studies evaluating the safety of P-OIT [15]. The time taken to achieve the maintenance phase was longer in patients

with other allergies or asthma, though comorbid conditions did not significantly impact the reaction's severity [14]. Another concern is the variability in patient response, with factors including non-adherence and avoidance of peanut doses commonly reported [11]. The presence of cofactors, such as exercise, have been associated with increasing the risk of allergic reactions and, therefore, may complicate the application of P-OIT in real-life situations [15].

Furthermore, real-world data illustrates that the amount of peanut protein in food products varies and thus might affect treatment effectiveness outside clinical trials [16]. These findings suggest that, while P-OIT is generally well-tolerated with mild to moderate adverse events, including rare cases of eosinophilic esophagitis (EoE), more research is needed to refine treatment protocols and accurately predict patient responses [11,15]. Despite the limitations of trial eligibility criteria and the strict guidelines often present in P-OIT clinical studies, real-world applications may involve a broader patient population, further emphasizing the need for individualized management [15]. Significant knowledge gaps create challenges when applying P-OIT in the real world.

4.2 Research Gaps

Many vital gaps remain in P-OIT research, especially regarding the long-term effects and sustainability of the treatment. A key issue concerns the duration of desensitization post-therapy—after treatment has stopped, it is unclear if protection may or may not be retained [11,15,16]. Moreover, there is a lack of reliable biomarkers that can predict the patient response to P-OIT, which makes the personalization of treatments complex and limits the understanding of how factors such as IgE levels influence the outcomes [14]. The absence of standardized dosing protocols further complicates treatment since different doses may lead to inconsistent results across studies and clinical practices [14,15]. More studies have also been conducted in controlled environments, thus lacking real-life analysis concerning variables such as changing peanut content and poor adherence on the part of patients. Finally, research regarding the psychosocial and immune mechanisms associated with the P-OIT reaction might help develop methods for improving tolerance during treatment or foreseeing specific responses in certain individuals [11]. Addressing these research gaps is crucial for optimizing P-OIT treatment.

4.3 Future Directions

The future of P-OIT is poised for significant advancements through continued research and innovation. One key area of focus is the long-term effects of P-OIT, particularly after the maintenance phase, to understand its sustained impact on patients' lives [16]. Research should be directed to patient goals and challenges so as to improve treatment adherence and success, particularly in diverse real-world settings. More extensive studies are needed to confirm safety data, evaluate the feasibility of higher doses, such as 1000 mg, and test various treatment protocols for optimal protection and the ability to safely introduce peanuts into the diet [14,16]. Moreover, specific IgE levels impact treatment outcomes, highlighting the need for standardized dosing and maintenance protocols in P-OIT to improve both safety and effectiveness [14]. Newer forms of delivering current P-OIT, such as powders, may decrease the burden of therapy. On the other hand, biologics such as anti-IgE therapy-omalizumab hold promise in minimizing adverse reactions while optimizing treatments [11,15]. As well, shared decision-making between allergists and families will be critical in determining the timing for early introduction and P-OIT treatment [17]. With these advancements, the future of P-OIT management looks more promising, focusing on personalized care, patient safety, and improved treatment outcomes.

4.4 Strengths and Limitations

A strength of our scoping review is our reliable data collection methods. Using Covidence and our data extraction table, we were able to identify which articles could be included and analyze their individual information. This plays into our second strength: the replicability of our study. With a clearly defined methodology, search strategy, and inclusion/exclusion criteria, other researchers can replicate our study to test its findings.

Limitations include the solo use of PubMed, which narrows the range of results. Furthermore, the absence of standard P-OIT dosages employed in studies makes comparisons difficult. Standardized protocols would enhance the consistency and applicability of research. Few studies are Canadian-specific, making it challenging to determine the effectiveness of P-OIT in the context of the local health care system. While the studies included within our review are geographically diverse, spanning Canada, the U.S., Europe, and Australia, this broad scope limits the applicability of our findings to the Canadian context, as regional differences in healthcare access and regulations are not standardized. Additionally, since the trials are conducted in varied healthcare systems, drawing accurate cross-context comparisons presents a challenge. Moreover, P-OIT is a novel treatment with unknown long-term consequences. Limited follow-up in studies also influences the data on long-term desensitization and remission. A more precise review could be carried out by research professionals in the field of OIT. The exclusion of grey literature and unpublished research could lead to publication bias, and a majority of the studies involved were conducted in controlled environments, which might not represent real-world situations. These flaws call for additional research efforts to standardize treatment, optimize P-OIT protocols, and determine its long-term effectiveness in pediatric populations.

CONCLUSION

Through our scoping review, we were able to identify the literature surrounding P-OIT and its effectiveness for achieving desensitization, remission, and allergen tolerance in pediatric populations in the last five years, following its approval in 2020. In this study we found a lack of standardization between P-OIT treatment in doses and timelines. Implementing a standardized P-OIT treatment may improve P-OIT utilization and improve patient outcomes. Based on our findings, P-OIT is a promising therapeutic as assessed through effectiveness. However, given the novelty of the treatment, future studies are necessary to standardize P-OIT methods and confirm its effectiveness in pediatric populations.

1. Grzeskowiak LE, Tao B, Knight E, Cohen-Woods S, Chataway T. Adverse events associated with peanut oral immunotherapy in children–a systematic review and meta-analysis. *Scientific reports*. 2020;10(1):659. https://doi.org/10.1038/s41598-019-56961-3
2. Lloyd M, Loke P, Ashley S, Lozinsky AC, Orsini F, O'Sullivan M, et al. Interaction between baseline participant factors and treatment effects following peanut oral immunotherapy. *The Journal of Allergy and Clinical Immunology: In Practice*. 2024;12(4):1019-28. https://doi.org/10.1016/j.jaip.2023.12.028
3. Fernandez-Rivas M, Vereda A, Vickery BP, Sharma V, Nilsson C, Muraro A. Open-label follow-on study evaluating the efficacy, safety, and quality of life with extended daily oral immunotherapy in children with peanut allergy. *Allergy*. 2021;77(3):991-1003. https://doi.org/10.1111/all.15027
4. Loke P, Orsini F, Lozinsky AC, Gold M, D O'Sullivan M, Quinn P, et al. Probiotic peanut oral immunotherapy versus oral immunotherapy and placebo in children with peanut allergy in Australia (PPOIT-003): a multicentre, randomised, phase 2b trial. *The Lancet Child & Adolescent Health*. 2022;6(3):171-84. https://doi.org/10.1016/S2352-4642(22)00006-2
5. Nowak-Wegrzyn A, Hass SL, Donelson SM, Robison D, Cameron A, Etschmaier M, Duhig A, McCann WA. The peanut allergy burden study: impact on the quality of life of patients and caregivers. *World Allergy Organization Journal*. 2021;14(2):100512. https://doi.org/10.1016/j.waojou.2021.100512
6. Breiding M, Soomann M, Roth M, Trück J, Bellutti Enders F. Safety of oral immunotherapy for cashew nut and peanut allergy in children-a retrospective single-centre study. *Schweizerische Medizinische Wochenschrift*. 2024;154(11):3691. https://doi.org/10.57187/s.3691
7. Dantzer JA, Kim EH. New approaches to food allergy immunotherapy. *The Journal of Allergy and Clinical Immunology: In Practice*. 2024;12(3):546-52. https://doi.org/10.1016/j.jaip.2023.10.018
8. Kidon MI, Shavit R, Levy Y, Haj Yahia S, Machnes-Maayan D, Frizinsky S, et al. Peanut oral immunotherapy using an extensively heated and baked novel composition of peanuts. *Pediatric Allergy and Immunology*. 2024;35(5):14146. https://doi.org/10.1111/pai.14146
9. Uhl C, Klevebro S, Sverremark-Ekström E, Tedner SG, Brandström J, Papageorgiou C et al. High degree of desensitization after 1 year of early-life peanut oral immunotherapy: Small Children Oral Immunotherapy (SmaChO) randomized controlled trial. *The Journal of Allergy and Clinical Immunology: In Practice*. 2024;12(5):1297-305. https://doi.org/10.1016/j.jaip.2024.02.030
10. Cronin C, Ramesh Y, De Pieri C, Velasco R, Trujillo J. 'Early Introduction' of Cow's Milk for Children with IgE-Mediated Cow's Milk Protein Allergy: A review of current and emerging approaches for CMPA management. *Nutrients*. 2023;15(6):1397. https://doi.org/10.3390/nu15061397
11. Chu DK, Freitag T, Marrin A, Walker TD, Avilla E, Freitag A, et al. Peanut oral immunotherapy with or without H1 and H2 antihistamine premedication for peanut allergy (PISCES): A placebo-controlled randomized clinical trial. *Journal of Allergy and Clinical Immunology: In Practice*. 2022;10(9):2386-2394. https://doi.org/10.1016/j.jaip.2022.05.015.
12. Jones SM, Kim EH, Nadeau KC, Nowak-Wegrzyn A, Wood RA, Sampson HA, 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. *The Lancet*. 2022;399(10322):359-71. https://doi.org/10.1016/S0140-6736(21)02390-4
13. Loke P, Wang X, Lloyd M, Ashley SE, Lozinsky AC, Gold M, et al. Two-year post-treatment outcomes following peanut oral immunotherapy in the Probiotic and Peanut Oral Immunotherapy-003 Long-Term (PPOIT-003LT) study. *Allergy*. 2024;79(10):2759-74. https://doi.org/10.1111/all.16262
14. Breiding M, Soomann M, Roth M, Trück J, Bellutti Enders F. Safety of oral immunotherapy for cashew nut and peanut allergy in children – a retrospective single-centre study. *Swiss Medical Weekly*. 2024;154:3691. https://doi.org/10.57187/s.3691.
15. Ciaccio C, Goldsobel AB, Anagnostou A, Beyer K, Casale TB, Deschildre A, et al. Participant characteristics and safety outcomes of peanut oral immunotherapy in the RAMSES and ARC011 trials. *Annals of Allergy, Asthma & Immunology*. 2022;129(6):758-768.e4. oi.org/10.1016/j.anai.2022.07.0331016/j.anai.2022.07.033.
16. Blackman AC, Staggers KA, Kronisch L, Davis CM, Anagnostou A. Quality of life improves significantly after real-world oral immunotherapy for children with peanut allergy. *Annals of Allergy, Asthma & Immunology*. 2020;125(2):196-201.e1. https://doi.org/10.1016/j.anai.2020.03.028.
17. Chua GT, Greenhawt M, Shaker M, Soller L, Abrams EM, Cameron SB, et al. The case for prompt salvage infant peanut oral immunotherapy following failed primary prevention. *Journal of Allergy and Clinical Immunology: In Practice*. 2022;10(10):2561-2569. https://doi.org/10.1016/j.jaip.2022.05.040.

APPENDIX

Study ID	Location	Study Design	Study Objective	Sample Size	Age of Participants	Outcomes
Chu et al., 2022	Canada	Randomized controlled trial	To determine whether premedication with desloratadine and ranitidine results in fewer side effects during peanut OIT/desensitization.	43	Median = 7.6 years	Risk and incidence rate of adverse reactions over time, HRQL
Jones et al., 2022	United States	Randomized controlled trial	To assess whether peanut oral immunotherapy can induce desensitisation or remission in children aged 1-3 years.	146	1-4 years (median = 3.3 years)	Adverse events, desensitization
Loke et al., 2022	Australia	Randomized controlled trial	To investigate whether addition of a probiotic adjuvant improved the efficacy or safety of peanut oral immunotherapy.	201	1-5 years = 104 (52%), 6-10 years = 97 (48%)	SU, ps-IgE and SPT results
Loke et al., 2024	Australia	Randomized controlled trial	To follow-up on outcomes at 1-year and 2-years post-treatment in participants completing the probiotic and peanut oral immunotherapy (PPOIT) -003 randomized trial	151	Mean age = 5.9 years	HRQL, number and severity of reactions, desensitization
Uhl et al., 2024	Sweden	Randomized controlled trial	To determine the safety and effectiveness of peanut OIT with a slow up-dosing strategy and low maintenance dose in children aged 1 to 3 years who were allergic to peanuts, through a 1-year interim analysis.	75	1-3 years (median = 30.5 moths)	Tolerance, adverse events

Table 1. Extracted Information from Included Studies