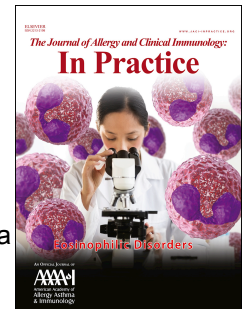


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An Approach to the Office-Based Practice of Food Oral Immunotherapy

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ABBREVIATIONS:

ED05: Eliciting dose of a food causing a reaction in 5% of allergic individuals

FA – food allergy

OFC – oral food challenge

OIT – oral immunotherapy

SDM - shared decision making

sIgE - specific IgE

SU – sustained unresponsiveness

88

89 **Abstract**

90 Oral immunotherapy (OIT) provides an active treatment option for patients with food allergies.

91 OIT may improve quality of life and raise the threshold at which a patient with food allergy may

92 react to an allergen, but it is a rigorous therapy that requires a high degree of commitment by

93 the clinician, patients, and families. Recent guidelines from the Canadian Society for Allergy and

94 Clinical Immunology (CSACI) have provided a framework for the ethical, evidence-based and

95 patient-oriented clinical practice of OIT, and the European Academy of Allergy Asthma and

96 Immunology (EAACI) guidelines have also recommended that OIT can be used as a potential

97 treatment. The recent FDA approval of an OIT pharmaceutical has accelerated the adoption of

98 OIT. This review provides a summary of the recent CSACI guidelines and a consensus of practical

99 experience of clinicians across the US and Canada related to patient selection, office and staff

100 preparation, the general OIT process, OIT-related reaction management, and treatment

101 outcomes.

102

Introduction

Food allergy (FA) is a common worldwide public health problem, with an increasing prevalence in the past 20 years.(1) FA may negatively impact quality of life and has historically been exclusively managed with dietary allergen avoidance.(2-6) However, in the past decade, the paradigm has shifted toward active management strategies for both prevention and treatment.(7-12) Oral immunotherapy (OIT) involves the regular ingestion of gradually increasing doses of one's allergen over time, to reduce reactivity and increase reaction threshold.(8) Experience with OIT dates back to the early 20th century.(2, 13-18) In 2020, the FDA approved Palforzia – a 12% light roast, defatted peanut flour OIT product (flour in capsule, capsule not ingested) for children ages 4-17 years.(19, 20) In addition, OIT studies, most using non-FDA approved 12% light roast flour, have identified key patient-centered outcomes such as quality of life (QoL) improvements(21, 22) and protection from accidental exposures.(23)

The burden of FA includes both the actual risk of a severe, and in rare cases, a fatal reaction(24, 25) from inadvertent exposure to a food allergen, as well as the psychological burden of living with a FA.(26) Anxieties about the potential risk of a severe or fatal reaction,(24) the need to effectively treat such reactions, social isolation and bullying(27, 28), dietary restriction, and challenges in trusting food handlers and caregivers all contribute to this burden.(4, 29) Food OIT provides patients an option capable of mitigating the risk from accidental allergen ingestion, with a relatively low risk of treatment-related life-threatening reactions in children through young adulthood.(8-10, 30)

OIT has the potential to decrease the burden of FA by increasing a patient's reaction threshold, thereby augmenting autonomy.(21) One unavoidable facet of OIT is that allergic

reactions, both immediate and delayed, may occur during all phases of OIT.(31, 32) However, reactions during OIT generally occur within a few hours of a scheduled dose when the patient (or parent) is expecting a possible reaction and is being observed, in contrast to the unexpected nature of accidental exposure.(8) Although some studies suggest that OIT may actually increase anaphylaxis risk and other complications compared to avoidance in the short term, the frequency of such reactions appears to decrease over a longer time horizon.(31-36) Such risks must be acknowledged by all parties during a shared decision-making (SDM) process before entering into OIT, and the patient/family must believe the trade-offs of OIT outweigh such risks.

Because OIT has the potential to raise the quantity of allergen necessary to trigger a reaction and may decrease reaction severity, many allergists have considered offering OIT to patients. Given an FDA-approved OIT product, multiple other published approaches using regular foodstuff in both research and clinical settings, and policy statements from the CSACI and EAACI supporting OIT as a therapy option, there is a useful framework to consider OIT.(8, 37) In particular, the CSACI guidelines highlight the importance of patient/family empowerment to partner with the clinician to choose (or not choose) a form of OIT as an available treatment option, driven “by a culture that promotes a sense of control vs one that promotes a sense of fear”.(8) Table 1 provides a summary of the CSACI context and recommendations. Operationalizing these recommendations in the clinical setting requires clinicians to have a clear understanding of necessary infrastructure, equipment requirements, the OIT process, patient selection, therapy risks and benefits, reaction management, and anticipated outcomes.

Orienting the Office to Provide OIT

Physical Space

Clinicians should allocate dedicated clinical space for OIT dose preparation, administration, and patient observation.(9) Tables E1 and E2 outline minimal equipment recommendations.(8) Dose preparation area(s) should have a counter, sink, and dedicated refrigeration space for OIT dose/food storage, a dedicated scale for measuring, and mixing tools. Supplies should include dishes, cutlery, snack options (e.g., individual applesauce or crackers), measuring spoons, syringes, and cleaning products for surfaces and equipment (Table E3)(38)

Daily OIT visit volume depends on clinician experience, office size, and staffing. Initial rapid up-dosing escalations require similar space to oral food challenges (OFC), and proceed similarly. Subsequent up-dosing visits are similar to a biologic drug administration, oral drug challenge, or subcutaneous immunotherapy visits.(39) Emergency preparedness for any OIT dose is identical to an OFC, and the clinical staff should be trained and comfortable with recognizing and treating anaphylaxis.(38, 40) Pre-specified written anaphylaxis protocols and a stocked/maintained emergency medication cart are necessary.(41) Injectable epinephrine and emesis basins should be readily available.(38)

Staffing

Clinical staff administering OIT require specific training to manage potential reactions and navigate both the physiological and psychological aspects of OIT.(8-10, 42) A point-person with primary responsibility for managing the OIT program is strongly recommended—either a

physician or advanced practice provider (nurse practitioner or physician assistant). Families may be anxious before starting and often have many questions about the process relating to home dose preparation, reaction management, and what to expect during the OIT course. (9, 10, 42)

All clinical staff involved in the OIT process must completely understand the protocols and be prepared to answer questions as they arise; and the prescribing clinician must clearly set and communicate treatment goals.(9, 10, 42) While there is a crucial patient education opportunity on the initial day of treatment, this process should start well in advance to best prepare families.(9, 42) Practices need to develop a routine for handling patient care responsibilities, establishing a procedural flow, and delegating key tasks such as patient assessment and dose measurement/administration during OIT initiation and up-dosing.(8, 42) Initial visits involving counseling and SDM may be best handled by the supervising clinician, while staff members with OFC preparation experience prepare and administer the OIT doses and observe for any signs/symptoms of reaction.(8, 10, 42) With increased demand, it may be more practical and cost-effective to train several staff members in dose preparation, or hire a dedicated person to handle such duties.(10) Well-trained and informed administrative staff may be needed to coordinate scheduling new patients, up-dosing visits, and OFC visits.(9, 43) A clinician must be present throughout the entire OIT dosing and monitoring.(9, 43) OIT is a procedure that requires skill in the diagnosis and management of food allergy, including performing oral food provocation challenges and treating severe allergic reactions.(9, 10) Traditionally, OIT is pursued under the care of an allergist. There are no published data studying non-allergy trained clinicians performing OIT, in particular in a primary care setting. The CSACI guidelines suggest that in areas with limited or no access to allergists, pediatricians and family physicians could

provide certain OIT services, after receiving adequate training and under close supervision by an allergist. While this suggestion advances equity and access to OIT, it should be highlighted that OIT in such circumstances should only be performed in partnership and under the supervision of an allergist experienced in providing OIT. The use of virtual care for certain visits, including OIT visits, may also be appropriate under certain extenuating contexts, but requires staff well-trained and experienced with the recognition and management of food allergy reactions as well as the use of approved virtual technology. Experience with virtual technology approaches is emerging and these approaches are not recommended for practices without robust OIT experience.(44)

Aversion to the OIT food is common, particularly during peanut OIT, and is a significant cause of discontinuing OIT.(45) Access to an experienced registered dietitian can be helpful in advising families about dosing options and food preparation that can improve adherence.(46) Both food aversion and anxiety related to eating a food after years of avoidance instruction are a burden for some OIT families. Referral to a psychologist familiar with food allergy and OIT can be very helpful.

Workflow

Measured patient flow and appropriate allergen choices are recommended for clinicians new to providing OIT, to help streamline workflow pathways, minimize errors, manage patient expectations, and enhance efficiency. Visits can be limited to specific days and/or times to better align workflow and supervision, and expanded as the practice gains comfort and experience.(9, 30)

Depending on the protocol and up-dosing (especially for day 1 rapid escalation), patients may be required to remain in clinic for up to six hours during the initial visit, and should be observed for at least one hour after their last dose.(9, 30) Scheduling should accommodate the possibility that staff could be heavily involved in each visit, accounting for difficulty or delay in dose administration, and the possibility of managing a dose-related adverse reaction.(30) Clear expectations must be set regarding patient conditions that permit up-dosing during follow-up visits (i.e., no infection, well-controlled atopic co-morbidities, absence of reactions) and communicated to the family early in the OIT course.(9)

Standardized documentation templates can help streamline the office visit, minimize errors, and facilitate outcome tracking.(9) Recommended elements for visit documentation are outlined in Table 2. There are US OIT coding recommendations,(47, 48) (see Table E4), although insurance coverage is variable, and not all payers may cover OIT.(49) Some practices offer OIT on a cash basis. The financially responsible party should be fully informed about OIT costs and options in advance. In Canada, some allergists bill the government using routine visit codes and others charge patients privately.(50)

Food Preparation

Dose preparation is a critical, detail-oriented step. A dedicated, clean and well-maintained preparation area is needed to eliminate cross-contamination risk. Precise measurement instruments are essential, as is a clearly written conversion chart specifying dry or liquid measurement food allergen protein content (Table 3 provides some approximations, but food weights and actual product labels should be used in this process). Dose orders should

be written (typed) and protein content re-verified by a second person. Small graduated vials, syringes, or measuring scoops can be used to prepare the initial smaller doses. Staff should be trained and practice preparing the various forms of foods to gain experience with measuring and transferring the food. Safeguards must be in place to ensure dosing accuracy and a quality control log should be maintained. Staff should also be trained to teach families how to measure and administer doses.(9) There are multiple options for preparing the initial low doses, including office- or pharmacy-prepared suspensions, capsules, soufflé cups or plastic dosing cups.(9, 30) Whichever is chosen, the process should ensure that the least amount of the dose is left in the vehicle.

Regarding commercial peanut OIT, Palforzia contains a 12% light roast defatted peanut flour from Golden Peanut, similar to the 12% light roasted defatted peanut flour in use in clinical OIT for years.(19) Many commercially available peanut flours are sourced from Golden Peanut and sold under a different brand, available in different roasts and defatted concentrations. As with all OIT foods, the clinician must be aware of the composition, which affects the protein content.

The OIT Process

Patient Selection:

OIT is a substantial commitment, requiring families who are highly motivated, with clear goals/preferences, and realistic expectations of the OIT process.(9, 43) Patients need to be truly allergic to the food or foods considered for treatment, and not just sensitized. Therefore, OFC may be necessary if the diagnosis is uncertain. The candidate's history should indicate very

clear IgE-mediated symptoms attributable to the allergen ingestion, with consistent sensitization to the allergen. An OFC is not required in such circumstances unless there is a desire to clarify diagnosis or establish baseline threshold pre-therapy. (9, 10, 45, 51) It is important to avoid unnecessary therapy in a non-allergic patient, therefore the diagnosis should be clearly established, ideally through OFC in ambiguous cases or cases where patients have been diagnosed solely by sensitization.(8) Nevertheless, an OFC may be deferred in the context of SDM with the patient and family, where risk to benefit ratio may not align.(9, 52-54)

Candidates and families must be fully informed regarding risks, benefits, alternative management options, and goals.(9, 10) SDM, discussed in the eSupplement, should be central to a decision to start therapy. Families should understand the time commitment required to reach maintenance, that maintenance may continue indefinitely, and the criteria by which OIT discontinuation may be recommended.(8, 9, 42) Discussion should include the risks of therapy-related adverse events including systemic reactions/anaphylaxis, and delayed gastrointestinal events (Eosinophilic Esophagitis-Like OIT-Related Syndrome, ELORS, and eosinophilic esophagitis), and how these events may be managed.(8, 9, 55-57) The SMD discussion, including enumerated risks should be documented with a signed consent.(58) Patient risk factors, including older starting age, high sIgE, and uncontrolled asthma, should be considered by the clinician.(10, 45, 59) Patients with a history of prior anaphylaxis to the food need not be automatically excluded from initiating OIT, though persons with severe episodes (e.g., hypotension requiring vasopressor support, respiratory symptoms requiring intubation, neurologic compromise, etc.) may fall outside the comfort range of many practices. Absolute contraindications to OIT are pregnancy and uncontrolled asthma, while relative

contraindications include active severe atopic dermatitis, pre-existing eosinophilic esophagitis (EoE), heart disease, or use of beta-blockers or angiotensin-converting enzyme inhibitors (Table 1).(8) A history of eosinophilic esophagitis is a listed contraindication of Palforzia, although at present robust data informing this contraindication are lacking.(19) For EoE, there may be some unique clinical scenarios where the benefit of OIT outweighs the risk of worsening EoE, such as when IgE-mediated food allergy develops after an elimination diet to treat EoE.(60) However, given that new onset EoE is a known risk of OIT, and that EoE has been an exclusion criterion in OIT studies, it is important for clinicians to appreciate that experience initiating OIT in patients with EoE is very limited.

Choosing the appropriate starting age to begin OIT is important and can be food dependent.(8, 9) Some evidence suggests OIT at younger ages may be associated with better outcomes(8, 20, 45, 61, 62) and fewer systemic reactions,(10, 11, 61) but this must be balanced against the natural history of the food allergy.(63-66) This is most relevant when considering milk or egg OIT, and therefore may warrant consideration of waiting or initiating ladders involving extensively heated milk or egg.(64-71) Still, evidence suggests incremental benefit of OIT compared to ingestion of baked egg, and families may opt to pursue OIT even in children tolerating foods with baked minor amounts of allergens.(72) OIT has been reported in children as young as nine months of age, and starting peanut OIT very soon after failed infant peanut introduction could result in improved outcomes.(61)

Goal setting is paramount to the SDM process, and realistic discussions regarding the probability of desensitization vs. being able to freely eat the allergenic food are crucial, so that realistic expectations are kept.(8-10, 20, 43, 45) Patient adherence is also crucial.(8, 53)

Families and patients must remain engaged from dose escalation through ongoing long-term maintenance dosing.(8, 9) Ultimately, the decision to pursue OIT should be the result of a careful SDM process with active engagement of clinicians with patients and families to choose what is right for them; there are no absolute “right” or “wrong” decisions when deciding whether to pursue OIT.(8, 43, 52)

Food Selection:

Foods used for OIT are administered based on their protein content. Therefore, the protein content of foods use for OIT should be clearly labeled. Clinicians must be mindful of the manufacturing processes, consistency and integrity of the protein and the risk of cross-contamination as well as the possibility that manufacturers may change their product formulations without public notice. There is an FDA approved product for peanut OIT but not for any other food.

OIT may be offered to single or multiple allergens simultaneously.(9, 73, 74) Factors that may influence the choice to pursue multi-food over single-food OIT include younger age and milder reactions (historic or OFC).(45, 75, 76) Multi-food OIT may provide time and financial efficiency over sequential single allergen OIT courses, but is an individualized decision for families to consider with their clinician. Choosing multi-food OIT is not an irreversible decision; if repeated reactions occur during OIT, one or more food(s) can be held at a low dose or discontinued and then resumed at a later date.

Multi-food OIT can be particularly helpful with allergy to multiple tree nuts, but must be considered in the context of an understanding that tree nut cross-reactivity can be leveraged to decrease the number of nuts needed.(77-80) OIT to cashew will protect most patients against

pistachio reactions, and walnut may offer cross-immunotherapy for pecan, and to some degree for hazelnut and cashew as well.(81, 82) OFC's to potentially cross-reactive nuts before OIT for a more dominant tree nut, such as walnut or cashew, are not a requirement.(83, 84) Managing multi-food OIT is more complex for the staff and for the allergist. Practices should be experienced in single-food OIT before undertaking multi-food OIT.

Early doses are small and may be best administered as a liquid, e.g. diluted liquid or powdered egg white and nut flour/meal, but transitioned to whole foods promptly, which offer greater ease of dosing and more certainty in the consistency of the allergen.(8, 9) Families should be trained to weigh foods on appropriately accurate and precise small scales for home use (Table E3).(9, 85) It is recommended to use a single, consistent allergen source during the escalation phase of therapy (e.g. particular brand of milk, shelled peanut vs. peanut butter, etc.) to provide the most consistent protein content.(9) Clinicians must be mindful that there is product variability and manufacturers may change protein content without notification. Product variability is a particular issue with nuts and Bamba peanut sticks, and using actual food product weights can help mitigate concerns about food heterogeneity. If food sources are changed, the dose should be lowered and rebuilt, similar to aqueous immunotherapy when a new vial is mixed.(8, 9)

Patient Preparation:

OIT is a long-term commitment, requiring frequent office visits based on the stage of therapy.(8, 9) Careful SDM (eSupplement) should be undertaken before consenting a patient for therapy, which should be reinforced by continued education. SDM can help with patient

adherence, potentially reducing the risk of a systemic reaction from OIT.(86) Families should be made aware of the general visit schedule to best plan maximal adherence and to reach maintenance promptly.(8) For example, it may not be ideal to start OIT right before a child is expecting to be away from home for an extended period of time. Families have to plan and coordinate vacations so that dosing times can be safely scheduled and adequate dose supplies are available.

At each visit, patients and families should provide an interval history, including missed doses, timing of last dose, any recent illness, any interval dose-related symptoms, and current medication list (Table 2). A physical exam should document a lack of wheezing, eczema flares, allergic rhinitis, urticaria, significant oral lesions, or other active illnesses.(8, 9, 42) Pre-visit screening can help augment the on-site assessment before OIT dosing.(9) Asthma should be well controlled and peak flow measurements may be considered prior to or during the visit. Spirometry may be performed in the office as an additional marker of asthma control. Concomitant medications should be continued, although there should be strong consideration for stopping antihistamines taken for other indications, at least on the initial dose-escalation day. If the patient is responsible for supplying OIT food items, the dose should be prepared ahead of time and brought to the visit (with a written process in place to re-verify the dose before this is given to the patient). Patients may need to bring a snack to eat with the OIT dose to buffer absorption or mask the taste of the allergen if food aversion is an issue. Post-dosing observation times should be clearly communicated to patients for planning purposes, including monitoring times in the event of a reaction. Families should have access to self-injectable epinephrine at all times, including travel from the office back home. It may be helpful to

reiterate the potential need for a more extended observation before each visit, because families who have had multiple uneventful up-dosing visits may not fully be prepared for unexpectedly prolonged visits.

Protocol Considerations:

Practical skill with OIT continues to evolve and currently reflects a broad international clinical experience.(8, 10, 20, 45, 87, 88) In addition to an FDA approved prescribing information for Palforzia(19), protocols using non-pharmaceutical foodstuffs have been published elsewhere(10, 61, 73, 87, 88), including Appendix 6 of the recent CSACI guidance, and examples are included in Table E5 of the esupplement.(8) Protocols may use an initial dose escalation day or simply have a fixed dosing schedule. Starting OIT doses range from 0.01 to 0.1 mg protein (although lower initial doses have been used by some clinicians).(8, 9) Each of the example protocols listed (Table E5) pass the peanut ED05 during the day one escalation (the ED05 is the eliciting dose of a food causing a reaction in 5% of allergic subjects).(89, 90) The ability to individualize dosing is a strength of a patient-centered OIT approach. Initial day escalation has shifted to generally no more than a cumulative dose of 3-12mg of protein, and fewer dose-related reactions occur below this level.(8, 10, 45, 91) Downward adjustments for the initial day target protein dose may be considered for multi-food OIT (higher total allergenic load) and perceived high-risk patients.(9)

Buildup visits may occur a minimum of 1-2 weeks apart (with at least one week of dosing without adverse symptoms), with longer intervals for convenience, safety, or by protocol design.(8, 9) Dose titration may range from 20-100% increases but should be tailored to the

individual when necessary.(8, 9) Daily dosing at home should be administered with a meal or snack.(9) The many well recognized factors are associated with an increased risk of OIT dosing reaction are detailed in Table 4.(8, 9, 92) If a dose-related reaction is experienced, reducing or even withholding the dose for up to 72 hours will often allow safe continuation of OIT.(8, 9)

An individualized approach to maintenance dosing is appropriate in the context of family goals and SDM. Common maintenance doses vary by food and range from 300 mg to 2 grams of protein for many (but not all) foods.(8, 9) Some clinicians aim for lower maintenance doses. Palforzia is approved at 300 mg of peanut protein maintenance, and additionally, U.S., Canadian, European, German, and Japanese data suggest lower maintenance dosing may be reasonable.(11, 19, 20, 61, 62, 93-95) Lower target dosing may be chosen when the patient dislikes the food or has no interest in ever intentionally eating it, and can offer protection for exposures beyond the maintenance dose.(8, 9, 20, 61) Daily dosing generally continues for at least one year with ongoing Safe Dosing Rules (Table 5). Some clinicians then recommend a gradual reduction in dose frequency to foster long-term adherence, while others continue daily dosing indefinitely, though long-term studies defining the ideal maintenance regimen are lacking.(9)

Reaction Management

Minor, self-limited, transient reactions, such as mild oral itch or perioral hives, generally are not considered dose-limiting and do not need dose reduction/delay unless symptoms become persistent or escalate.(9, 20, 30, 45) Contact reactions (especially in young children) are common and typically not concerning.(11, 61) Education regarding mild symptoms as a

signal for desensitization can actually be beneficial for reducing anxiety.(96) Oral itch often resolves if the dose is followed by a food or beverage.(9, 10, 45) If recurrent antihistamine use is required, a dose reduction, delay in up-dosing, or consideration for discontinuation may be needed, since recurrent mild symptoms may indicate a lack of tolerance.(9) Avoidance of premedication during escalation and buildup may be preferred to avoid masking symptoms; however, experience with this approach has been varied (see e-supplement).

Gagging or immediate vomiting (without other symptoms) can be attributed to taste/texture aversion of the OIT food and may be treated by altering the food presentation, though these could indicate more persistent gastrointestinal OIT-related adverse effects.(9, 45) Dyspepsia, nausea, vomiting, abdominal pain or diarrhea within an hour of dosing are likely IgE-mediated reactions necessitating dose reductions.(9, 45, 97) Some clinicians and patients choose to continue dosing through mild, transient dyspepsia or abdominal pain, but without dose increases until there have been at least 7-14 reaction-free days.(9, 45) For more severe reactions, the dose should at least be reduced to the last tolerated, and held for one or more weeks before continuing escalation.(9) Gastrointestinal symptoms may indicate emerging eosinophilic gastrointestinal disease.

Significant GI symptoms occurring more than two hours after dosing are unlikely to be due to an IgE-mediated reaction and may indicate ELORS.(10, 56, 98) Substantial GI symptoms may require significant dose reduction (e.g., 25-50%), held for at least 1-3 months (or longer).(56, 99) Symptoms persisting with dose reduction may require endoscopic evaluation and may require OIT discontinuation, as biopsy-proven eosinophilic esophagitis is a potential outcome of OIT.(56)

Acute systemic reactions should be treated like any IgE-mediated food reaction.(38, 40)

When a serious reaction occurs, aforementioned co-factors should be sought.(8) Following a systemic reaction to an established dose, some clinicians skip the next dose and recommend a slow return to full dosing over several days. An alternative approach is to administer 25-50% of the current dose for one day, then 75% of the dose for one day, then return to the full dose. This is similar to the approach used in subcutaneous aeroallergen immunotherapy.(39)

Epinephrine-treated reactions during maintenance occur less frequently than during day one escalation or up-dosing(11, 97) and are most common during the first six months(11, 45) after reaching maintenance. These reactions can be associated with a failure to follow Safe Dosing Rules or to recognize co-factors.(11, 45)

Long Term Outcomes

The success of OIT can be defined by different, non-competing outcomes, including level of desensitization, level of sustained unresponsiveness (SU), continued consumption, and patient empowerment. Patient goals for OIT may range from protection against cross-contamination, to “bite proofing”, and “free eating” or unrestricted consumption.(8, 20, 61, 100, 101) “Bite proofing” may be a somewhat misleading term because it represents significant (though not necessarily complete) protection against inadvertent, single bite allergen exposures. Although it is impossible to quantify all cross-contamination exposures, most OIT approaches are sufficiently robust to protect against the majority of such cross-contamination exposures.(90) Most accidental peanut exposures involve 300 mg of peanut protein or less.(102, 103) For many patients such risk mitigation is the primary goal of OIT, though some patients may desire

unrestricted consumption (“free eating”).(10, 45, 61) Unrestricted consumption of a culprit food allergen can normalize life for many FA patients and families,(101, 104) particularly for staple foods like milk, eggs and wheat.(4) The maintenance dose necessary to permit unrestricted consumption is unknown and potentially variable.(45) In a preschool population, Vickery and colleagues suggested a maintenance dose of 300 mg of peanut protein may allow a patient to pass an OFC and continue consuming regular servings of peanut several times per week.(33, 61) Still, many OIT patients dislike their treatment food, and avoid eating the treatment food beyond OIT dosing because of taste aversion.(45)

There are no universally agreed upon criteria for the duration of maintenance, the duration of avoidance, or the change in biomarkers predicting successful SU challenge. Some clinicians offer an OFC (with or without OIT dose interruption) after 1-3 years of OIT to assess the extent of desensitization, following which switching to regular servings of the target food may be an option.(33) Eligibility for a follow-up OFC should be based on SDM between the patient (family) and allergist. The decision for when to offer an OFC may be influenced by significant decline in skin prick test and/or sIgE, as well as patient/parent motivation to learn about the extent of desensitization (Table E6). Because patients with food allergy (both those receiving and those not receiving OIT) have occasionally reacted after passing a food challenge, most clinicians recommend some ongoing exposure to the OIT food after tolerating a food challenge.(45) SU represents the ability to tolerate the allergenic food after a prolonged period of avoidance, which is distinct from free eating where the patient is permitted unrestricted addition of the OIT food to the diet while continuing regular maintenance dosing. The concept

of SU is complex, and SU development is uncertain. Determining SU requires a prolonged period of avoidance, and many patients may prefer not to interrupt OIT.(52, 105-107)

OIT discontinuations occur most commonly during initial day escalation or up-dosing due to systemic reactions, GI side-effects, or taste aversion, but this is less common once reaching maintenance.(45) There are very few long-term follow up reports, but long-term adherence to treatment is likely to vary by food, dose, individual patient, starting age, and context.(33, 108) Patients' objectives and preferences should be reassessed periodically to ensure active dosing remains the best option for them. Even in patients who discontinue OIT, their ability to self-manage without OIT can increase over time as a result of new experiential knowledge that breaks from the previous avoidance-fear cycle.

Conclusions

Providing patient and family-centered food allergy care is rapidly evolving. Recent CSACI guidance has provided helpful context for consideration of OIT in the clinic. This document, representing a consensus of the authors who are academic and private practice allergists in Canada and the US, builds upon these ethical principles to provide an additional practical perspective for translating evidence to practice. As clinicians begin to consider implementing OIT, a comprehensive understanding of the appropriate patient selection in the context of SDM, OIT space and staffing requirements, the OIT process itself, and the importance of a true partnership between the OIT team and the OIT family will help to create an environment in which patients can receive the safe and effective care that is right for them.

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Journal Pre-proof

803 **Table 1. CSACI guidelines for the ethical, evidence-based and patient-oriented clinical practice**
 804 **of oral immunotherapy in IgE-mediated food allergy.**

Dimension	Context	Recommendation
Sociopolitical dimension: promotion of the common good.	<i>Recommendations for a sociopolitical context for optimized food allergy management</i>	A large number of patients with food allergies are unable to access basic care for proper diagnosis and management, including avoidance or oral immunotherapy, leaving many with inadequate support from the healthcare system. Empowerment of patients and families should be promoted through shared responsibility with the healthcare system, in respect and support of patient choices
		A new culture should be fostered to transition from one that is fear-driven towards one that promotes a sense of control in food allergy through accurate information on the condition and the options available
		There is inadequate reliable communication between patients, families and healthcare professionals about oral immunotherapy, often accompanied by misinformation. This should be addressed through shared decision-making, and access to trustworthy, clear and transparent information
		Oral immunotherapy for food allergy should be developed and practiced in the spirit of personalized care, considering the heterogeneity and specificity of the condition and individual patient contexts
		Research should be encouraged to adequately inform clinical practice regarding OIT, through innovative study designs focusing on meaningful patient-centered and long-term outcomes, while appropriately reflecting the need for personalized care in real-world practice
Populational dimension: promotion of equity.	<i>Recommendations for the equitable provision of OIT</i>	The notion of severity is inadequate for determining eligibility for OIT, as the risk of a reaction and of it being severe are difficult to predict and does not necessarily correlate with the psychosocial impact on patients and families. The aim should thus be to make OIT available as an option for all patients wishing to receive it, provided there is no contraindication and a clear understanding of individual risks and benefits
		A lack of public investment has resulted in a situation of low capacity and disparities in access to care for the accurate diagnosis and proper management of food allergy. This applies to management choices that include both avoidance and OIT
Clinical dimension: promotion of health and	<i>Recommendations on eligible food allergens and types of clinical outcomes that can be achieved by OIT</i>	There is no convincing evidence of a clinically significant difference between food allergens in terms of safety and efficacy outcomes in OIT for the treatment of IgE-mediated food allergy

well-being.		OIT is recommended as a treatment to achieve desensitization. A majority of patients will achieve a level desensitization to a daily dose of the allergen that will be sufficient to provide protection against trace exposure, while a sizable proportion of patients will be able to tolerate a full serving
		OIT can be recommended for long term management since a sizable proportion of patients will continue to regularly consume a sufficient amount of the food to maintain desensitization after reaching maintenance, without reverting to complete avoidance
		OIT may be recommended to achieve sustained unresponsiveness, but data is limited and variable
	Recommendations on who could benefit from OIT (indications)	An accurate diagnosis of IgE-mediated food allergy is essential before proceeding with OIT
		OIT is indicated for toddlers and preschoolers. <i>Important consideration:</i> While the likelihood of spontaneously outgrowing milk or egg allergy may be greater than for other foods, their impact on patients and families, if not outgrown, is high. Caregivers should be included in shared decision-making about, whether to initiate OIT early for these foods and based on individual prognosis, considering that OIT is well tolerated and has high efficacy in this age group
		OIT is indicated for school-age children and adolescents
		OIT may be indicated for adults
	Recommendations regarding contraindications	Previous history of anaphylaxis to the targeted food is not a contraindication for OIT
		Multiple food allergies are not a contraindication to OIT
		Uncontrolled asthma is an absolute contraindication to OIT. Asthma must be controlled before beginning OIT and pro-actively managed during OIT
		Pregnancy is an absolute contraindication for initiating OIT
		Conditions such as active severe atopic dermatitis, pre-existing eosinophilic esophagitis, heart disease, and those requiring the use of beta-blockers or ACE inhibitors are relative contraindications for OIT. A decision to pursue OIT in these patients should be based on clinical judgment, provider expertise and shared decision-making
		Patient- or caregiver-specific contexts that may jeopardize the safe administration of therapy must be assessed. These include but are not limited to unreliable adherence to protocol, reluctance to use epinephrine, language barrier, severe anxiety, psychiatric barriers, non-collaborative family dynamics, lack of schedule flexibility for proper dosing, and lack of commitment from patient or caregivers. If these cannot be satisfactorily addressed, they constitute contraindications for OIT

	<i>Recommendations for the safe provision of OIT</i>	OIT providers and patients should be prepared to recognize and treat allergic reactions, including anaphylaxis, during OIT. Food escalation should only be performed in a clinic with appropriate equipment and infrastructure available to treat anaphylaxis A personalized action plan should be provided to patients to guide management of reactions occurring at home Providers should only offer OIT in age groups in which they have training or experience in treating anaphylaxis Patients should be observed in clinic for 1 h following dose escalation. The observation period can be decreased as appropriate to a minimum of 30 min, based on various factors that include patients who are reliable, confident and comfortable with the management of allergic reactions Surveillance for the emergence of EoE or EGID should be based on monitoring for the emergence of clinical symptoms (e.g. dysphagia, esophageal spasms, vomiting, diarrhea). Endoscopy and biopsy should be used to confirm the diagnosis in suspected cases not responding to dose adjustments or medication
	<i>Recommendations on personalized OIT protocols</i>	OIT can be performed with many different food products The goals of OIT can be achieved with many different protocols. There is little evidence that specific dosing schedules are superior to others. Reference protocols can be useful to guide therapy but need to be selected and adapted based on the patient's specific situation The initial dose that will be ingested at home should be determined during an initial dose escalation in clinic (day 1). This consists of a graded introduction of the allergen to identify the highest tolerated dose at baseline. The planned starting and ending doses for the initial escalation in clinic should be below the expected reactivity threshold and determined through shared decision making with patients and families. The objective is not necessarily to identify the reactivity threshold and induce a reaction as this can become a barrier to treatment. An alternative to multi-step escalation is to start treatment directly with a single dose assumed to be below the patient's reactivity After initiating daily home ingestion of the tolerated dose, up-dosing increments should be adapted to patient evolution throughout therapy. Transient mild local reactions are to be expected in the first days following a dose increase. In the absence of any signs of reaction, the protocol could be accelerated. In the event of persistently recurring, moderate to severe or systemic reactions, dose progression must be decreased. The up-dosing intervals can be prolonged for medical or logistical reasons, or for personal preferences

		The final target dose for the therapy should be guided by the patient's individual clinical response and personal goals, which can range from protection against accidental exposures to small amounts to unrestricted inclusion of the allergen into the diet. There is a lack of evidence that high maintenance doses will increase the likelihood of sustained unresponsiveness
		During follow-up, persistence of desensitization is monitored by documenting a patient's continued consumption of the food allergen. A decision to test for other outcomes should be guided by a patient's personal objectives. Complete desensitization can be assessed by performing a high threshold challenge to the food. The risk of dosing reactions associated with cofactors can be assessed by performing a food challenge in the presence of cofactors (e.g. alcohol and non-steroidal anti-inflammatory drugs, exercise). Sustained unresponsiveness can be assessed by the progressive increase in dosing intervals
		When performing OIT in patients with multiple food allergies, the preferred approach is to treat multiple foods simultaneously
		Short-term concomitant use of omalizumab can be considered in challenging cases
	<i>Recommendations for patient-centered care</i>	The ultimate goal of food allergy care should be the empowerment of patients and their caregivers to manage the risk of food allergy reactions, reduce food-related anxiety and achieve a sense of control over their condition. This can be achieved in different ways for different patients. Tactful and empathic shared decision making with patients, their caregivers and the OIT provider, is necessary before making a decision to proceed with OIT
		Informed consent must be obtained before initiating OIT. This should include clear discussion of potential outcomes, risks and benefits, as well as of patients' and their caregivers' concerns, expectations and goals. Patients should be informed on how to recognize and manage reactions during therapy. Throughout treatment, patients' goals and perceived benefits should be reassessed periodically to ensure that clinical decisions continue to reflect their personal objectives. When appropriate, expected mild reactions should be framed in a positive manner that reduces perceived burden of therapy and promotes a sense of control
Organizational dimension: promotion optimized organization of care	<i>Recommendations for the promotion of optimized organization of care</i>	To optimize human resources and ensure optimal delivery of quality care in food allergy, a multidisciplinary approach adapted to patient needs should be promoted, and should include nurses, registered dietitians, psychologists and peer supporters, when possible
		In areas with limited or no access to allergists, pediatricians and family physicians could provide certain

		OIT services, after receiving adequate training and under close supervision by an allergist
Economic dimension: promotion of sustainability	Recommendations for sustainable provision of OIT	In the development of OIT, extreme care should be taken to avoid creating unnecessary financial barriers that could limit access to treatment based on ability to pay
		Investment by the healthcare system in food allergy treatment should be guided by patients' best interests and system sustainability. As such, investments should be encouraged toward measures that contribute to building the capacity for OIT within the system (e.g. multidisciplinary teams, preparation of personalized food products, treatment monitoring) in order to achieve meaningful and cost-effective impacts on patient outcomes

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807 **Table 2. Documentation elements of patient visit**

PRIOR TO VISIT
Reminder email/phone call
Suitability to dose determined by patient (i.e., healthy, asthma controlled, infrequent reactions, no anticipated challenges) and concerns communicated to clinic
IF PATIENT DEEMED BY FAMILY POTENTIALLY SUITABLE FOR UPDOSE
Patient or parent should confirm the treatment food to prevent error
Current Dose
Last Visit
Number of missed doses
History of illnesses necessitating skipping doses
Interval reaction history and treatment required
Delayed or immediate GI symptoms
Asthma control, if applicable (many clinics will use Asthma Control Questionnaire)
Current medications
Change in Health
Other patient concerns
IF PATIENT IS DEEMED BY CLINICIAN SUITABLE TO DOSE
Alignment of anticipated dose with prepared product with check by at least 2 different staff
Vital signs (including temperature, heart rate, respiratory rate, blood pressure)
Spirometry or PEF may be considered for select patients
Physical examination including HEENT, lung and skin exam
Dosing time
Signs or symptoms of reaction and treatment required
Medication prescription
Referrals necessary (specialist, asthma educator, dietitian, counsellor etc)
Future appointment date
Discharge time

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Allergen		Amount of protein
Chicken's egg	1 mg of powdered-egg whites	0.8 mg (80% weight)
	1 whole egg	~ 5000 mg
	1 ml liquid egg white	111 mg
	1 ml raw egg* mixed	100 mg
	Note: Raw egg is not recommended for children under 1 year old unless pasteurized due to risk of bacterial contamination	
Peanut	1 gm peanut (~ 1 peanut)	~ 250 mg (~25% weight)
	2.4 mg of powdered peanut butter (PB2®)	1 mg
	2 mg of defatted peanut flour	1 mg
	Peanut flour 12%	50% of weight
	Peanut flour 28%	41% of weight
	1 peanut stick snack (Bamba®)	~ 80 mg (~18% weight)
Cow's milk	1 ml milk (any percent of fat)	33.3 mg
	2.8 mg of powdered milk	1 mg
	1 cm of string cheese stick (6g protein for 12cm stick)	~ 500 mg
Almond	1.25 gm almond (~1 almond)	~ 250 mg (~20% weight)
	4.6 mg of almond flour	~ 1 mg (~21% weight)
	2.6 mg of powdered almond butter (PB2®)	1 mg
	1 ounce Elmhurst unsweetened almond milk	625 mg
Hazelnut	1.25 gm hazelnut (~1 hazelnut)	~ 220mg (~ 18% weight)
	4.8 mg of hazelnut flour	~ 1 mg (~ 21% weight)
	1 ounce Elmhurst unsweetened hazelnut milk	250 mg
Cashew	1.4 gm cashew (~1 cashew)	~ 250 mg (~18% weight)
	5.6 mg of cashew flour	~ 1 mg (~18% weight)
	1 ounce Elmhurst cashew milk	500 mg
Pecan	3 gm pecan (~1 pecan)	~ 300 mg (~10% weight)
	10 mg of pecan meal	~ 1 mg (~10% weight)
Pistachio	0.7 gm pistachio (~1 pistachio)	~140 mg (~20% weight)
	4.6 mg of pistachio flour	~1 mg (~21% weight)
Walnut	4 gm walnut (~1 walnut)	~ 664 mg (~17% weight)
	6 mg of walnut meal	~ 1 mg (~17% weight)
	1 ounce Elmhurst walnut milk	375 mg
Sesame	1 ml tahini	~167 mg (variable by brand)
	2.5 mg defatted sesame flour (40% protein)	1 mg
	Sesame seeds	~18-22% of weight
	Some clinicians suggest against using whole sesame seeds unless crushed to allow release of the allergen contained in the seed.	
Soy	1 ml soy milk (7g/250 ml)	28 mg
Oat	7.5 mg of oat flour	1 mg
Barley	9.3 mg of barley baby cereal	1 mg
Rye	7.5 mg of rye flour	1 mg (13.3% weight)
Buckwheat	7 mg of buckwheat flour (14.3% protein)	1 mg
Wheat	1 slice of whole wheat bread (32g)	4380 mg
	Vital wheat gluten	70% weight

	10 mg of white all-purpose flour	1 mg
	White flour may not contain all relevant wheat proteins in wheat. Consider instead vital wheat gluten.	

* Exact allergen protein content may vary according to brand and food product size (i.e., kernel size for nut or stick size for bamba or cheese). Recommend weighing total food weight and calculating actual protein content for non-standard food products (such as nuts). It is much more reliable to use nut weight rather than individual nuts. Food escalations in clinic should be performed with the same product that will be used at home. Protein content is based on the USDA database (<https://fdc.nal.usda.gov/fdc-app.html#/food-details/532086/nutrients>) and Nuts.com.

**Adapted with permission from: Begin P, Chan ES, Kim H, Wagner M, Cellier MS, Favron-Godbout C, 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.

Table 4. Reaction Risk Factors

- Exercise immediately prior (within 30-60 minutes) of dosing
- Exercise within two hours after dosing (longer for some patients)
- Hot tub/hot shower/bath
- Empty stomach
- Fever
- Infection (respiratory tract)
- Gastroenteritis
- Non-steroidal anti-inflammatory drugs
- Dental extraction or procedure
- Surgery (e.g., Tonsillectomy)
- Menstruation
- Sleep deprivation
- Increased total allergenic exposure (e.g., pollen season or animal exposure)
- Unstable allergic disease (asthma, allergic rhinitis, or eczema)

Table 5. Sample Safe Dosing Rules for Patients*

- Make sure your epinephrine auto-injector is out and in clear view when you take your daily dose.
- Do not exercise vigorously for two hours after taking your dose or within 30-60 minutes before a dose.
- Try to avoid taking your dose immediately before bedtime (or after 8 pm). Stay awake for at least 1 hour after taking your dose.
- If you are ill, having worsening nasal allergy symptoms, an asthma flare, or have recently had dental work, contact the clinic for instructions, as you may need to reduce your dose.
- Consider reducing your dose (e.g. by $\frac{1}{4}$ to $\frac{1}{2}$ of your regular dose) while you are away from home (e.g. on vacation). Other changes in your daily routine may also require a dose reduction.
- If it has been more than 48 hours since your last dose, call the clinic for instructions before taking your next dose.
- If you are using a liquid solution dose, shake the solution to mix it well immediately before drawing it up into a syringe.
- If you are experiencing new continuing stomach problems that occur randomly throughout the day, contact the clinic.
- Take your dose with a meal or snack. Suggested snacks include a banana, applesauce, crackers, pretzels, or dry cereal (if not allergic to these foods).
- Contact the clinic early if you expect to need a refill of your OIT preparation, so that you do not miss any doses.
- If you experience a reaction after taking one of your doses, treat your symptoms according to your food allergy and anaphylaxis action plan. Contact the clinic if you experience a severe reaction or if you are frequently experiencing mild reactions after your doses. For a few hives, a mildly itchy mouth and throat, or if you vomit once, treatment is optional. If hives increase, take a fast-acting non-drowsy antihistamine (cetirizine [Zyrtec, Reactine], fexofenadine [Allegra], or rupatadine [Rupall] – preferred over loratadine [Claritin] which has a slower onset of action or diphenhydramine [Benadryl] which may be sedating). For repeated vomiting or other symptoms such as lightheadedness or sleepiness, shortness of breath, wheezing, or repeated coughing use your epinephrine auto-injector and follow your food allergy and anaphylaxis action plan.
- Return visits to the clinic for dose increases should be no sooner than seven days.

*This handout is provided as an example. OIT practitioners should provide safe dosing rules for their patients based on the regimens and procedures used in their practice.

Table E1. Minimal Safety Medications, Equipment and Supplies

Category	
Vital sign assessment	- Stethoscope - Sphygmomanometer and blood pressure cuffs - Oxygen saturation monitor - Personal protective equipment (gloves, mask, eye shield) - Watch or clock
Medications	- Intramuscular epinephrine (3 doses) - Albuterol (with MDI and spacer or nebulizer) - Second generation antihistamine
Airway	- Oropharyngeal airway (adult and pediatric)
Breathing	- Self inflating bag-valve-mask (adult and pediatric) - Disposable face masks (adult and pediatric) - Oxygen tank - Oxygen extension tubing - Oxygen nasal cannula - Non-rebreather mask (adult and pediatric)
Circulation	- Tourniquet - Tape - Alcohol swabs - Drip chamber - Syringe with needles - T-connector - Extension tubing - Intravenous 0.9 normal saline (two 1 liter bags) A method to establish parenteral access which could include any of: - Intravenous butterfly needles - Indwelling catheters - Intraosseous devices
Other	- Written anaphylaxis management protocol - Flow chart for recording times and events - 911 script for office staff to use

*Reproduced from Begin P, Chan ES, Kim H, Wagner M, Cellier MS, Favron-Godbout C, 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.

Table E2: Additional equipment and medications to consider, depending on provider experience, skill and location

Category	
Vital sign assessment	- Automated BP cuff, HR, and O2 saturation monitor - 5-minute timer
Airway	- Portable suction - Nasal airway - Laryngeal airway masks (LMA) with lubrication - Laryngoscope with blades, ET tubes, stylet and CO2 detector, tape and suction, and Magill forceps - Alternative airway devices (e.g.: King Airway)
Breathing	- Nebulizer mask
Circulation	- Pediatric Armboard - Set up for 3-way stopcock for pediatric fluid bolus - Intraosseous devices - AED
Medications for treatment of allergic conditions	- Ipratropium bromide (spacer with MDI or nebulizer) - Diphenhydramine IV - Corticosteroid for injection - Racemic epinephrine
Medications for treatment of non-allergic conditions	- Nitroglycerine spray - ASA - Naloxone - Lorazepam or diazepam - Glucose gel - Glucagon or vasopressin for adults on beta blocker

*Adapted from Begin P, Chan ES, Kim H, Wagner M, Cellier MS, Favron-Godbout C, 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.

Table E3. Non-Food OIT Supplies:

General
Precision scales
Examples:
• H&C Veritas S303 (310 gm capacity, 1 mg readability) • HOMGEEK High-Precision Digital Mg Pocket Scale 50g / 0.001g Reloading, Jewelry Scale • American Weigh Scales GEMINI-20 Portable Milligram Scale • Weigh Gram Scale Digital Pocket Scale • Others
Lab spoons
Weighing scoops
Refrigerator with temperature monitor
Large twist cap containers for bulk food
Sink
Dishwashing supplies
Hair net
Lab coat
Cleaning supplies
Mortar and pestle
Distilled Water
Snack Size sealable plastic bags
Aluminum wrappers, plastic medicine cups
Disposable 4 oz paper cups
Plastic spoons, forks, knives
Paper plates and bowls to mix dose with vehicle food
For pre-weighted powder doses
Small (1oz and 2oz) cups and caps for individual doses
Paper bags to dispense doses
For suspensions
Measuring cups
Suspension media – water, Kool Aid, juice
Electric mixer
Twist cap 100mL graded containers
Glass bottles (e.g., www.sks-bottle.com)
4 OZ Flint Glass Boston Round with White Metal Foil Lined Cap 22/400 24/CS Stock # 4000-30
8 OZ Flint Glass Boston Round with White Metal Foil Lined Cap 24/400 12/CS Stock # 4000-31
20MM Natural LDPE Orifice Reducer, 0.192 Orifice 144/BAG, Stock # 2620-30
Plastic Caps, White Polypro Ribbed PE F217 Lined Caps (144 bag) Stock # 2100-25

(4oz bottles) Plastic Caps, White Polypro Ribbed PE F217 Lines Caps (144 bag) Stock # 2100-76 (8oz bottles)
Plastic Bottles- (e.g., www.sks-bottle.com) 4 oz Amber PET Boston Round, 20/410, 690/CS, Stock# 003300-40.01S 8 oz Amber PET Boston Round, 24/410, 400/CS, Stock# 003300-80.01S Plastic Caps, Black Smooth Closure w/F-217 Liner 144/bag, Stock#2250-139 (4oz bottles) Plastic Caps, Black Smooth Closure w/F-217 Liner 144/Bag Stock#2250-72 (8oz bottles) 20MM Natural LDPE Orifice Reducer, 0.192 Orifice 144/Bag Stock# 2620-30(4oz bottles) 24MM Natural LDPE Orifice Reducer, 0.192 Orifice 144/Bag Stock# 2620-31(8 oz bottles)
Syringes 1 cc Baxter Syringes non-LS oral with cap 100/pk, item code - 1218698 3 cc BD oral dispensing syringe clear with tip cap, item code - 9870265 5 cc BD oral dispensing syringe clear with tip cap, item code - 9875700 10 cc Baxter Syringe f/Oral Medic Clear, item code- 9910823
For capsules
Gelatin capsules and (if compounding)
Capsule machine
Office supply
Binders for logs and reference manuals
Calculator
Computer and printer
Identification stickers
Fine point felt-tipped pen

Table E4. Approaches to OIT Coding in 2020

Visit Type	Code	Alternatives	Comments
Day 1	CPT® 95076: Ingestion challenge test (sequential and incremental ingestion of test items e.g. food, drug or other substance); initial 120 minutes of testing; and CPT® 95079: each additional 60 minutes of testing (List separately in addition to code for primary procedure).	CPT® 95119: unlisted allergy/clinical immunology procedure	CPT® 95180: as written, is not intended for oral administration. Some payers specifically prohibit its use for OIT. CPT® 95119: because it is non-specific reimbursement will be unpredictable
Up-dosing visits	CPT® Established Patient E/M Code (select appropriate E/M level) CPT® 99354: Prolonged evaluation and management service(s); first hour (List separately in addition to code for Evaluation and Management) CPT® 99355: each additional 30 minutes (List separately in addition to code for prolonged service).	CPT® 95119: unlisted allergy/clinical immunology procedure	CPT® 95075: may not be appropriate as it specifies at least two doses for the ingestion challenge CPT® 95180: is interpreted to require at least two doses and is not intended for oral administration CPT® 95119: because it is non-specific reimbursement will be unpredictable CPT® 99354 and CPT® 99355: required direct face-to-face visit contact

<https://www.aaaai.org/practice-resources/running-your-practice/practice-management-resources/coding/oit-code>
<https://college.aaaai.org/advocacy/advocacy-insider/food-oit-here-how-do-i-get-paid>

Table E5. Example Protocols from the US and Canada

A. Wasserman Peanut Oral Immunotherapy Protocol

Dose #	Schedule	Frequency of dosing	Peanut protein (mg)	Concentration	Volume of solution (ml)	Type of food	Peanut flour (mg)*	Peanut Weight (g)	TruNut (tsp)	TruNut (g)	Peanut Butter & Co/Skippy flavored		
											peanut butter (tsp)	Peanut M&Ms	Bamba (g)
1	Day 1	q20 mins	0.1	250mcg/ml	1	Peanut flour suspension	0.25						
2	Day 1	q20 mins	0.2	250mcg/ml	2	Peanut flour suspension	0.5						
3	Day 1	q20 mins	0.4	250mcg/ml	4	Peanut flour suspension	1						
4	Day 1	q20 mins	1	2.5mg/ml	1	Peanut flour suspension	2.5						
		x1 Day 1 then											
5	Day 1	QD	2	2.5mg/ml	2	Peanut flour suspension	5						
6	Escalation	QD	4	2.5mg/ml	4	Peanut flour suspension	10						
7	Escalation	QD	6	2.5mg/ml	6	Peanut flour suspension	15						
8	Escalation	QD	8	2.5mg/ml	8	Peanut flour suspension	20						
9	Escalation	QD	10	25mg/ml	1	Peanut flour suspension	25						
10	Escalation	QD	15	25mg/ml	1.5	Peanut flour suspension	37.5						
11	Escalation	QD	20	25mg/ml	2	Peanut flour suspension	50						
12	Escalation	QD	26			Peanut fragments	64	0.1					0.2
13	Escalation	QD	53			Peanut fragments	128	0.2		0.1			0.4
14	Escalation	QD	79			Peanut fragments	192	0.3		0.2			0.7
15	Escalation	QD	105			Peanut fragments	257	0.4		0.3			0.9
16	Escalation	QD	158			Peanut fragments	385	0.6		0.4			1.3
						1 Peanut (cross contamination)							
17	Escalation	QD	250				609	0.95	1/4	0.6	1/4	2	2.1
18	Escalation	QD	500			2 Peanuts	1219	1.9	1/2	1.2	1/2	3	4.2
19	Escalation	QD	750			3 Peanuts	1828	2.85	3/4	1.8	3/4	5	6.2
						4 Peanuts (accidental ingestion)							
20	Escalation	QD	1000				2 tsp	3.8	1	2.4	1	6	8.3
21	Escalation	QD	1500			6 Peanuts	3 tsp	5.7	1 1/2	3.6	1 1/2	10	12.5
22	Escalation	QD	2000			8 Peanuts	4 tsp	7.6	2 1/2	4.8	2	14	17
23	Escalation	QD	2500			10 Peanuts	5 tsp	9.5	3	6.0	2 1/2	17	21
24	Escalation	QD	3000			12 Peanuts	6 tsp	11.4	4	7.2	3	20	25
	Final dose		6000			24 Peanuts	12 tsp (4 T)	22.8	8	14.4	6	40	50
	Maintenance												
	QD		2000			8 Peanuts		7.6	2 1/2	4.8	2	14	17

*28% fat peanut light flour (Byrd Mill Co)

B. Canadian Preschool Peanut Oral Immunotherapy Protocol

Week #	Hybrid (PB2* then Bamba**)	PB2*-Only	Bamba**-Only
0	28.8 mg PB2 (12 mg PP)	First day escalation (every 15-30 minutes) 0.24 mg PB2 (0.1 mg PP) 0.48 mg PB2 (0.2 mg PP) 0.96 mg PB2 (0.4 mg PP) 1.92 mg PB2 (0.8 mg PP) 3.6 mg PB2 (1.5 mg PP) 7.2 mg PB2 (3 mg PP) 14.4 mg PB2 (6 mg PP)	1/8 Bamba stick (~10 mg PP)
2	60 mg PB2 (25 mg PP)	28.8 mg PB2 (12 mg PP)	¼ Bamba stick (~20 mg PP)
4	120 mg PB2 (50 mg PP)	60 mg PB2 (25 mg PP)	½ Bamba stick (~40 mg PP)
6	1 Bamba stick (~80 mg PP)	120 mg PB2 (50 mg PP)	1 Bamba stick (~80 mg PP)
8	1.5 Bamba sticks (~120 mg PP)	180 mg PB2 (75 mg PP)	1.5 Bamba sticks (~120 mg PP)
10	2 Bamba sticks (~160 mg PP)	240 mg PB2 (100 mg PP)	2 Bamba sticks (~160 mg PP)
12	3 Bamba sticks (~240 mg PP)	300 mg PB2 (125 mg PP)	3 Bamba sticks (~240 mg PP)
14	4 Bamba sticks (~320 mg PP=Maintenance Dosing)	374.4 mg PB2 (156 mg PP)	4 Bamba sticks (~320 mg PP=Maintenance Dosing)
16	Maintenance dosing	468 mg PB2 (195 mg PP)	Maintenance dosing
18	Maintenance dosing	588 mg PB2 (245 mg PP)	Maintenance dosing
20	Maintenance dosing	720 mg PB2 (300 mg PP=Maintenance Dosing)	Maintenance dosing

PB2: Powdered Peanut Butter

PP: peanut protein

*Allergists who chose to use Peanut flour instead of PB2 adjusted for protein content.

**Note: there are different types of Bamba packages and similar products from other manufacturers with different protein content. The calculations in this table for the number of Bamba sticks are based on the package with 5g protein/28g Bamba.

Reproduced from Soller L, Abrams E, Carr S, et al. First Real-World Safety Analysis of Preschool Peanut Oral Immunotherapy. Journal of Allergy Clin Immunol Pract 2019; 7: 2759-67.

C. New England Food Allergy Treatment Center Peanut Oral Immunotherapy Protocol

Visit	DOSE (protein)	VOLUME IN SYRINGE	CONCENTRATION (protein)
Day 1 - Dose 1	0.1 mg	Volume in syringe 0.1 ml	1 mg/ml concentration
Day 1 - Dose 2	0.2 mg	Volume in syringe 0.2 ml	1 mg/ml concentration
Day 1 - Dose 3	0.4mg	Volume in syringe 0.4 ml	1 mg/ml concentration
Day 1 - Dose 4	0.8 mg	Volume in syringe 0.8 ml	1 mg/ml concentration

Day 1 - Dose 5		1.5 mg		Volume in syringe 1.5ml	1 mg/ml concentration	
Day 1 - Dose 6		3 mg		Volume in syringe 3 ml	1 mg/ml concentration	
2		3 mg		Volume in syringe 3ml	1 mg/ml concentration	
3		4.5mg		Volume in syringe 4.5ml	1 mg/ml concentration	
4		6 mg**		**switch concentration** Volume in syringe 0.6ml	**switch concentration** 10 mg/ml concentration	
5		9 mg		Volume in syringe 0.9ml	10 mg/ml concentration	
6		12 mg		Volume in syringe 1.2ml	10 mg/ml concentration	
7		18 mg		Volume in syringe 1.8ml	10 mg/ml concentration	
8		25 mg		Volume in syringe 2.5ml	10 mg/ml concentration	
9		35mg		Volume in syringe 3.5ml	10 mg/ml concentration	
10		50 mg		Volume in syringe 5ml	10 mg/ml concentration	
11		75 mg**		**switch** peanut flour in cup		
12		100 mg		peanut flour in cup		
13		125 mg		peanut flour in cup		
14		165 mg		peanut flour in cup		
15		225 mg		peanut flour in cup		
16		300 mg		peanut flour in cup		
17		400 mg		peanut flour in cup		
18	2 ½ peanuts	3 peanut M&M's	4 PN butter M&M's	Don't use at this dose	Don't use at this dose	Don't use at this dose
19	3 peanuts	4 peanut M&M's	5 PN butter M&M's	PB2 (5gm/2TBSP) 3/4 tsp (-3 peanuts) PB2 (6gm/2 TBSP) 1/2 tsp (-2.5 peanuts)	1 miniature Reese's peanut butter cup (-3 peanuts)	½ tsp Peanut butter (-3 peanuts)

Adapted from Afinogenova Y, Rubin T, Patel S, Powel R, et al. Community Private Practice Experience with Peanut Oral Immunotherapy. Journal of Allergy Clin Immunol Pract 2020; 8(8):2727-2735.

Table E6. Consideration for Oral Challenges After an Extended Period of OIT

- Eligibility for a follow-up OFC should be based on shared decision-making between the patient, family, and allergist. Some considerations to help guide this decision include:

- One to three years of daily maintenance dosing.
- Significant decrease in skin prick test size or sIgE

Challenge dose:

- Age appropriate serving

Duration of avoidance if assessing sustained unresponsiveness:

- 4 weeks

Post-challenge dose/frequency:

- The maintenance dose given daily or age appropriate servings at least once a week but ideally several times per week(33)

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