


Estimating Cost-Effectiveness of Confirmatory Oral Food Challenges in the Diagnosis of Children With Food Allergy

Global Pediatric Health
Volume 6: 1–11
© The Author(s) 2019
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/2333794X19891298
journals.sagepub.com/home/gph


Abdullah Alsaggaf, MD¹, James Murphy, MD¹,
and Sydney Leibel, MD, MPH^{1,2} 

Abstract

Introduction. Food allergies affect 8% of the pediatric population in the United States with an estimated annual cost of US\$25 billion. The low specificity of some of the main food allergy tests used in diagnosis may generate false positives incurring unnecessary costs. We examined the cost-effectiveness of oral food challenges (OFC) as confirmatory tests in the diagnosis of food allergy. **Methods.** We constructed a decision tree with a Markov model comparing the long-term (15 years) cost and effectiveness—in the form of quality-adjusted life years (QALY)—of confirmatory OFCs compared with immediate allergenic food elimination (FE) after a skin prick test or blood immunoglobulin E (IgE) level in children with suspected food allergy. For costs, we included the costs of OFCs and the reported annual costs of having a food allergy, including direct medical costs and costs borne by families. **Results.** The cost of OFC strategy was \$8671 compared with \$18 012 for the FE strategy for the length of the model. Also, the OFC strategy had a total QALY of 21.942 compared with 21.740 for the FE strategy. In the OFC strategy, the total cost was \$9341 less than FE and the increase in QALY after OFCs led to a 0.202 higher effectiveness in the OFC strategy. **Conclusion.** In conclusion, our study shows that the confirmatory OFC strategy dominated the FE strategy and that a confirmatory OFC for children, within a year of diagnosis, is a cost-effective strategy that decreases costs and appears to improve quality of life.

Keywords

oral food challenge, food allergy, cost-effectiveness

Received August 29, 2019. Received revised October 31, 2019. Accepted for publication November 6, 2019.

Introduction

Food allergies (FAs) affect 8% of children in the United States with an estimated annual cost of US\$25 billion.^{1,2} The diagnosis of FA mainly relies on clinical history, skin prick test (SPT), and/or specific blood immunoglobulin E (IgE) levels.³ Despite the relatively high sensitivity of these tests, they have an estimated specificity of around 60%, potentially generating false positives and incurring unnecessary costs.⁴ The main treatment of FAs is to eliminate the allergenic food from the diet, with some allergists offering oral immunotherapy on an experimental and research level.³

Oral food challenge (OFC) tests provide the most definitive diagnosis of FA with a sensitivity and specificity approaching 100%.⁵ They take 2 to 4 hours to

perform and involve giving a small amount of the allergen incrementally to the presenting child while observing for any development of allergic reactions.⁵ A study by Couch et al, which reported that only 46% of OFC eligible candidates had their OFC within a year of being eligible, showed that delaying OFCs for patients was associated with significant costs.⁶ The authors found that allergist may decide to delay an OFC due to concerns of the process and management, lack of

¹University of California San Diego, La Jolla, CA, USA

²Rady Children's Hospital San Diego, San Diego, CA, USA

Corresponding Author:

Sydney Leibel, University of California San Diego, 9500 Gilman Drive, La Jolla, CA 92093-0021, USA.

Email: sleibel@ucsd.edu



comfort in performing an OFC, poor reimbursement, inadequate training, and lack of resources including space and staff to perform an OFC. Whether a physician was properly trained on how to conduct OFCs plays a major role on whether they will perform them.⁶ Caregivers may also delay an OFC because of concerns about passing a challenge or may not be interested in adding the food to the diet.⁶ Some parents find that the food may not provide nutritional benefit to their child's diet and thus delay or avoid the OFC. Moreover, regardless of the OFC result, multiple studies demonstrated a positive impact of OFCs on the health-related quality of life (HRQOL) of children with FA and their parents.^{7,8} Despite this improvement in QOL, OFCs are not performed regularly by many allergists and food elimination (FE) is practiced.⁹ In general, FE diets should be approached with caution as they can lead to overexclusion of food categories that were actually safe to be digested according to the results of an OFC.¹⁰

Considering the \$25 billion annual cost of FA, the relatively low specificity of the primary tests involved in diagnosis, and the effects of FA on HRQOL, we investigated the impact of the superior specificity of an OFC and its positive effect on HRQOL by conducting a cost-effectiveness analysis of an OFC as a confirmatory test to all or most children diagnosed with FA as compared with immediate FE based solely on SPT and/or IgE blood results.

Methods

We compared the cost-effectiveness of 2 approaches to diagnose a child with a suspected FA: (1) SPT/IgE followed by OFC confirmation (OFC strategy) and (2) SPT/IgE followed by food elimination (FE strategy). We built a decision tree with a Markov model looking at FE, reactions, retesting, and food introduction. This analysis focused on peanut allergy while examining values representing other allergies in sensitivity analyses. Our model was based on a societal perspective and extended for a time horizon of 15 one-year cycles assuming all children are diagnosed at age 2 and enter the model at the age of 3. The state-transition diagram demonstrates the flow of patients through 5 main states: FE, retesting, continued elimination, food introduction, and death. Finally, we applied half-cycle corrections and built the model using TreeAge Pro 2017 software (Figure 1).

Model Probabilities

After entering the decision tree, branching ensued according to OFC and SPT sensitivities and specificities

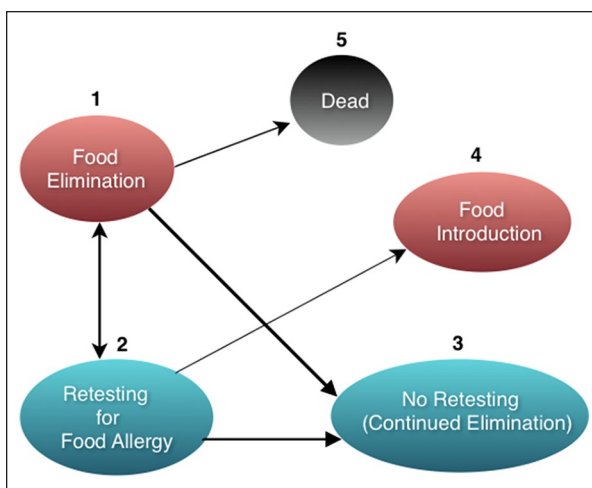


Figure 1. State-transition diagram showing 5 states: All children start at the (1) “food elimination state.” They transition into either (2) “retesting” or (3) “no retesting” (only a proportion of children will decide to retest every year and the rest will transition into no retesting and continue on food elimination) based on having a reaction (minor or major reaction) or not (a proportion of children not having a reaction will decide to retest). Children who retest and confirm resolution of allergy by an OFC will enter state (4), “food introduction.” Children who experience a fatal food allergic reaction will transition into state (5), “dead.”

into true positives, false negatives, false positives, and true negatives. Due to the nature of the OFC test and because not all children will be candidates for an OFC, we included only 70% of children in the OFC strategy—assuming 30% will not be candidates for an OFC—and compared it with the FE strategy representing presumed current practice. Also, we further examined that number in the sensitivity analysis. There are 3 types of OFCs: double-blinded placebo-controlled, single-blinded, and open nonblinded challenges.⁵ The majority performed in the United States are open nonblinded challenges.⁹ Therefore, we chose an OFC sensitivity and specificity of 98% while SPT/IgE values were obtained from a published meta-analysis.⁴ All true positives and false positives entered the Markov model in the FE state. True positives either had a major, minor, or fatal reaction, and those with a minor one entered retesting as well as a proportion of children without a reaction. The incidence of reactions was obtained from a prospective report of Canadian children, and the probability of reaction severity was calculated from the same report.¹¹ Unfortunately, no studies aimed at estimating the probability of children coming for annual FA retesting could be identified. Although Gupta et al reported the rate of visits per child, the nature of the visit was beyond the scope of their

Table 1. Model Validation^a.

	OFC Strategy	Food Elimination	Gupta et al
Cost in 2017 (US dollars)	\$3609	\$4323	\$4184

^aShows the predicted mean cost from a microsimulation (trials) of 100 000 random patients being sent through the model according to entered probabilities. Our model predicts the cost per individual in the United States to be \$4323, which is close to the reported value of \$4184.

Table 2. Costs Associated With Oral Food Challenge CPT Codes and Lost Productivity and Transportation.

CPT95076—Physician	\$383.85\$ (330.8-436.9)	Lost labor productivity (using mean national hourly labor wage ¹⁶ ; \$121.43) School absenteeism (\$63.76) Transportation (\$27.05)	
CPT95076—Facility	\$1302.53 (1076.47-1528.58)		
CPT95079—Physician	\$225.67 (205.46-245.9)		
CPT95079—Facility	\$648.68 (487.52-809.83)		
Total	\$2560.73	Total	\$212

Abbreviation: CPT, Current Procedural Terminology.

study, and we have chosen a value of 0.70, which we explored in sensitivity analyses.² Retested individuals either had outgrown their allergy or were still allergic. A time-dependent table, based on a prospective cohort, with probabilities that change every cycle, were used to represent the probability of outgrowing allergy annually.¹² Detecting those who outgrew their allergy is subject to the specificity of SPT/IgE. However, we assumed that the probability of outgrowing FA remains the same after age 12, as this is the length of follow-up in the prospective study that also reported little difference in the probability of outgrowing FA after 10 years of age.¹² Children who retested negative either proceeded with an OFC (no delay) and transitioned into food introduction, or they did not have an OFC (delayed) and entered the continued FE state along with those with major reactions and those retesting positive. This represented an area of uncertainty with only one study identified reporting that 46% of children did not delay their OFC.⁶ False positives entered the FE state; however, they were only subject to the probability of retesting (either retest or continue on FE without retesting), they did not develop a reaction (probability 0), and they were not subject to outgrowing allergy probabilities. Those who retested negative either underwent their OFC—proceeding to food introduction state—or they delayed it and entered the continued FE without retesting state. We assumed false negatives would experience a reaction and then retest correctly and proceed later on as true positives. True negatives never entered an elimination state and continued in a normal food introduction state. Finally, we assumed that no one develops new allergies, and due to low mortality in this age group and

for simplicity, we did not include death from other causes.¹³

We verified and validated our model by looking at the response of the model state probabilities when changing certain model values, and we also ran a microsimulation to compare how our model predicts cost compared with the study of Gupta et al² (Table 1).

Costs

Annual Cost of Food Allergy. An extensive cost analysis by Gupta et al estimated the annual cost of FAs to be \$4184 per child.² This number includes direct medical costs and costs borne by families (medical out-of-pocket costs, lost labor productivity, and opportunity costs), and we assumed that it also included annual SPT/IgE retesting costs. *OFC cost:* A survey by Pongracic et al shows that the majority of US OFCs are conducted in 3 hours, and this corresponds to Current Procedural Terminology (CPT) codes 95076 (first 2 hours) and 95079 (every extra hour).⁹ We searched the CPT code charges in the fairhealthconsumer.org website using 5 random zip codes in 5 different cities and 4 different states (New York/Los Angeles/Chicago/Houston/San Diego) and obtained averages and ranges using provided percentiles (Table 2).¹⁴ We also estimated the costs by utilizing Medicare physician fee schedule and device costs, and the amount (3 hours non-facility = \$626.89 and 3 hours facility = \$565.315) was close to the one obtained from fairhealthconsumer.org without including hospital outpatient fees (facility), which vary greatly.¹⁵ The total number we used may, however, overestimate the actual cost of OFCs. Also, we added the costs of lost labor

productivity for 5 hours, school absenteeism for 1 day, and transportation costs.^{2,16,17} Costs of an allergist visit were deducted when transiting through the no retesting state.² Finally, costs were adjusted to 2017 US dollars when possible using the consumer price index and 3% discounting per year was applied to costs and health utilities.

Outcome Measures

Quality-adjusted life years (QALY) is a measurement of a patient's health utility (HU) over time, while we used HU as a measure of a patient's HRQOL ranging from 1 (perfect health) to 0 (death). Many studies exist that investigate the effect of FA on the HRQOL of children and their parents.¹⁸ Unfortunately, the majority report values that cannot be used in a cost-effectiveness analysis (range 0 death to 1 perfect health). We excluded studies that report HU in Europe due to reports of differences between HU in the United States and Europe, and we finally extracted values from a national Canadian survey of 17 626 individuals that report HU as a Health Utility Index mark 3.^{19,20} Unfortunately, the youngest age surveyed was 12, which is higher than the minimum age of interest in our analysis. Also, many studies report a negative impact on the HRQOL of parents of children with FA, but none that provide values we can use in our analysis were identified.¹⁸ In a balance between the significance of the family burden and the lack of input values, we decided to include the HU of 1 parent in the analysis by deducting 0.04 from the reported US norms for median, upper quartile, and lower quartile value to generate a HU for a parent of a child with FA.²¹ This estimate of the magnitude of effect on parents (0.04) is similar to the difference between the HU of a child with FA (0.90) and a child with no chronic illness (0.94) in the Canadian survey.²⁰ OFCs improve HRQOL of patients with FA and their parents regardless of the result of the challenge.^{7,8} We chose a magnitude of 0.01 for this improvement as most reports provide values that cannot be utilized in a cost-effectiveness analysis. Also, we assumed no transition deduction of HU based on the type of reaction, and children with FA maintain a baseline HU of 0.90. Children in FE gain 0.02 HU if OFC was done after retesting with no gain occurring at the OFC side as they already started with the OFC HU benefit. Finally, we analyzed the model 3 times including the HU of the child only in the first time, and subsequently adding 1 parent's HU the second and third time assuming both parents would have the same HU.

Analysis

An incremental cost-effectiveness ratio (ICER)—a ratio of incremental cost per QALY gained—was used to compare both strategies. If the ratio fell below a willingness-to-pay (WTP) of 100 000/QALY, we considered the strategy cost-effective. This WTP threshold is commonly used in cost-effectiveness research; however, WTP varies according to country, region, and other factors.²² A strategy with less cost and more effectiveness gained is considered dominant, and a negative ICER will not be reported.

All inputs used for our base case analysis are presented in Table 3. We conducted deterministic sensitivity analyses for all inputs in the model, and we also examined the effect of annually retesting and not delaying OFCs on our final cost and HU. Also, to examine the values of allergies other than peanut allergy, we conducted a 2-way sensitivity analysis of the prevalence of allergy and the probability of outgrowing it. Finally, we conducted a probabilistic sensitivity analysis (PSA) using a Monte Carlo simulation of 100 000 iterations. We used β distributions (0-1 range) for all transition probabilities and health utilities, γ distributions (interval 0-infinity) for most costs, and we used a normal distribution for the deducted cost (−) when not retesting. The base case analysis results reports cost and effectiveness values generated from our best estimation of model inputs. Means, standard deviations, mostly 12.5% or 25% of mean, 95% confidence intervals, and distributions are presented in Table 2.

Ethical Approval and Informed Consent

Ethical approval and informed consent was not needed as no patients or their data were utilized in this study.

Results

Base Case Analysis

The OFC strategy had a total cost of \$8671 compared with \$18 012 for the FE strategy for the length of the model. Also, the OFC strategy had a total effectiveness (QALY) of 21.942 compared with 21.740 for the FE strategy. Despite the initial extra cost in the OFC strategy, the total cost was \$9341 less than FE and the increase in HU after OFCs led to a 0.202 higher effectiveness for the OFC strategy thus dominating the FE strategy.

Sensitivity Analyses

Our model is most sensitive to assumptions about the value of specificity of SPT/IgE tests (Figure 2). OFC

Table 3. Parameters For Cost-Effectiveness Model^a.

Parameter	Both		OFC		Food Elimination		Distribution for PSA	Standard Deviation (% × Mean)	First Author
	Value	95% CI	Value	95% CI	Value	95% CI			
Prevalence of peanut allergy	0.02	1.8 to 2.2			95%	89.75 to 98.1	β	25%	Gupta et al ¹
SPT and blood IgE sensitivity (peanut)							β	12.5%	Soares-Weiser et al ⁴
SPT and blood IgE specificity (peanut)					60%	46 to 72.8	β	25%	Soares-Weiser et al ⁴
OFC sensitivity			98%	0.72 to 1			β	12.5%	Nowak-Węgrzyn et al ⁵
OFC specificity	0.124	11.4 to 13.4	98%	0.72 to 1			β	12.5%	Nowak-Węgrzyn et al ⁵
Probability of having a food allergy reaction (peanut)	0.28	0.15 to 0.42					β	25%	Cherkaoui et al ¹¹
Probability of the reaction being a minor reaction	0.719	0.31 to 0.97					β	25%	
Probability of the reaction being a major reaction	6.13	3.25 to 11.56					β	25%	
Probability of having a fatal reaction (per million)	0.70	0.11 to 0.88					Triangular β	30%	Estimated
Probability of annual retesting	0.10	0.05 to 0.15						25%	Bégin et al ¹²
Probability of outgrowing allergy	0.18	0.10 to 0.27							
Age 4	0.22	0.14 to 0.39							
Age 6	0.26	0.15 to 0.41							
Age 8	0.27	0.15 to 0.41							
Age 10	46%	0.11 to 0.88					Triangular	43%	Couch et al ⁶
Age 12									
Probability of not delaying OFC									
Costs (\$)									
Annual cost per child with food allergy (2017; dollars)	\$4513	\$3748 to \$5350					γ	25%	Gupta et al ²
Ingestion challenge test (OFC)	-194.31	-242 to -146	\$2773	\$1582 to \$4248			γ	25%	Estimated (Table 2)
Cost deduction for not retesting							Normal	12.5%	Estimated
Health Utilities									
Child with food allergy	0.90	0.59 to 0.99					β	12.5%	Mittmann et al ²⁰
Child without allergy	0.94	0.57 to 0.99					β	12.5%	Mittmann et al ²⁰
Child after OFC			0.91	0.58 to 0.99			β	12.5%	Estimated
Parent of child with allergy	0.84	0.58 to 0.98					β	12.5%	Estimated
Parent of child after OFC	0.85	0.59 to 0.98					β	12.5%	Estimated
Parent with allergy-free children	0.88	0.58 to 0.99					β	12.5%	Fryback et al ²¹
Increment after OFC	0.02	0.01 to 0.03					β	25%	Estimated

Abbreviations: OFC, oral food challenge; CI, confidence interval; PSA, probabilistic sensitivity analysis; SPT, skin prick test; IgE, immunoglobulin E. ^aInterpolation was used for the probability of outgrowing allergy for the rest of the cycles. Blank cells at the author's column means it is the author's estimation (see Description in Methods).

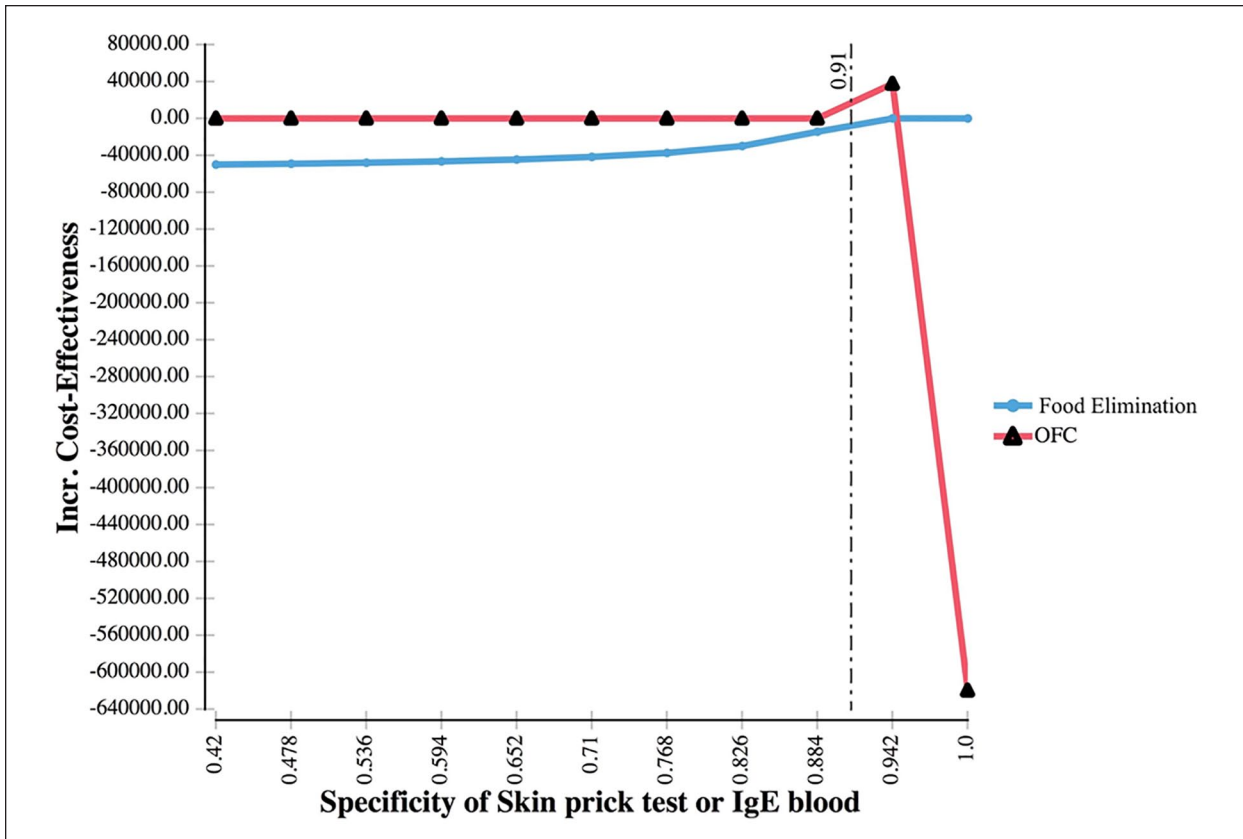


Figure 2. Sensitivity analysis: oral food challenge (OFC) ceases to dominate food elimination at a specificity threshold of 0.91.

ceases to dominate FE at an SPT/IgE test specificity of 0.91 or more. At 100% probability to retest and 100% not delaying OFCs, a 2-way sensitivity analysis revealed maintained dominance of OFC over FE. Despite OFC still being dominant, the costs of FE strategy (current practice) dropped from \$18 012 (base case) to \$12 744 at 100% no OFC delay and further dropped to \$6594 at both 100% of patients annually retesting and no delay in OFCs (Figure 3). Also, a 2-way sensitivity analysis of allergy prevalence and probability of outgrowing allergies did not change the orientation of dominance. Another sensitivity analysis was performed to evaluate the effect of reactions from subsequent positive challenges after the first diagnostic challenge and also found no change in the orientation of dominance. Finally, running the analysis 3 times including only the child's HU the first, 1 parent's HU the second, and 2 parents' HU the third still showed OFC dominant. Other HUs, costs, and probabilities did not have a significant effect on the model.

Probabilistic Sensitivity Analysis

All probabilities, costs, and health utilities were varied simultaneously in a PSA comparing OFC versus FE

over 100 000 iterations. OFC dominated FE in 65% of the iterations and was cost-effective in 72% of the iterations at a WTP threshold of \$100 000/QALY. The PSA results are presented as a scatterplot of incremental cost versus incremental effectiveness as well as a cost-effectiveness acceptability curve for different WTP thresholds (Figure 4; Appendix A).

Discussion

Although seemingly without cost, FE in a food allergic child proved to be very costly with an annual estimated cost of US\$25 billion.² A retrospective report showed that over 50% of food-allergic children delayed their OFC for a mean time of 35.5 months and that delay was associated with significant costs.^{2,6} In other words, a correct diagnosis with a gold standard OFC could potentially reduce the annual costs of FA by compensating for the relatively low specificity of SPT/IgE.² In addition, despite OFCs being costly and bearing a risk, they increase the QOL of children and their parents regardless of the result.^{7,8} As one may expect, HRQOL improves in those that pass the OFC as they can now consume foods that were previously restricted. Interestingly, those that

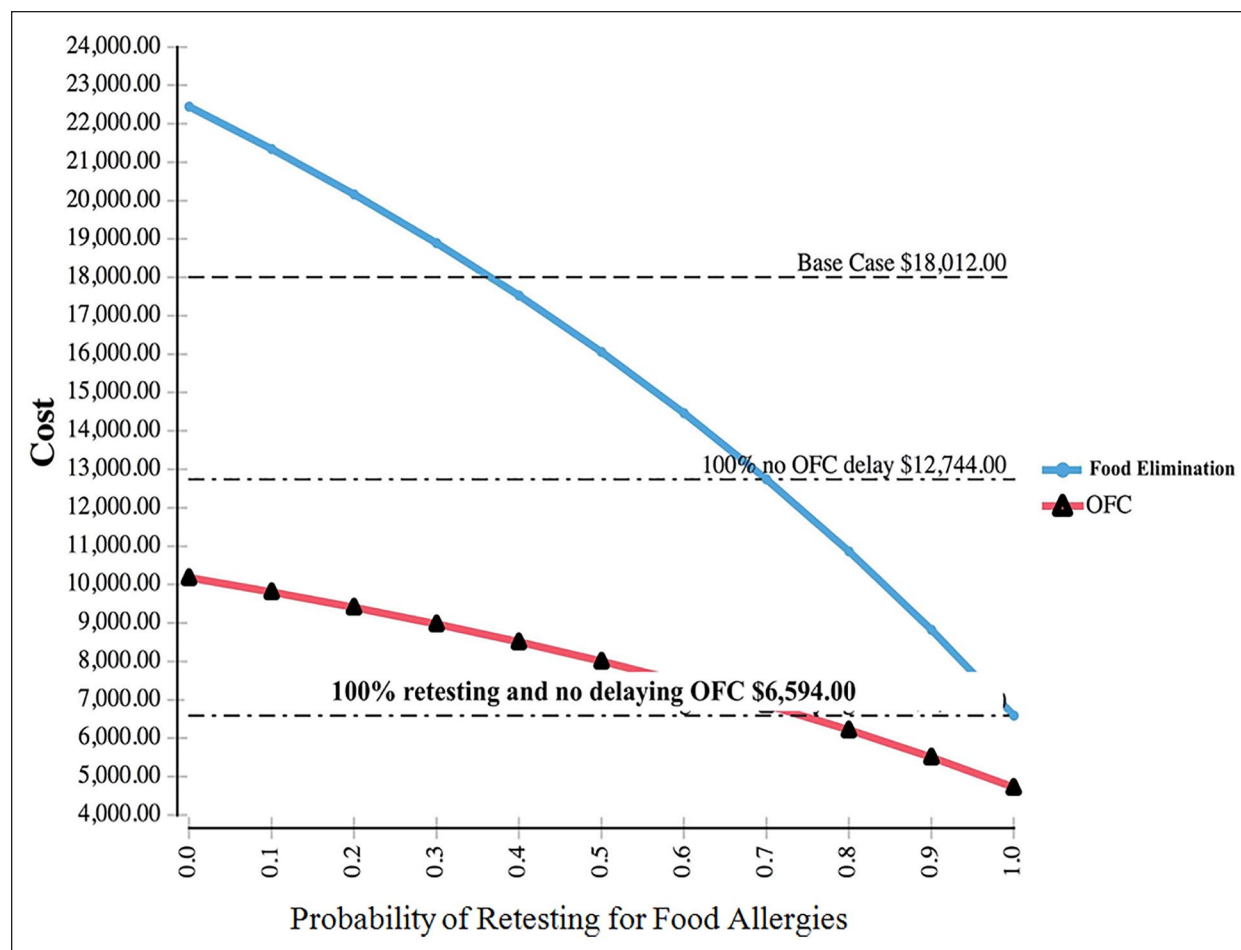


Figure 3. Sensitivity analysis: shows the sensitivity and effect of 2 probabilities on the cost of the food elimination (FE) strategy (presumed current practice). Top dashed line shows the total cost of the FE strategy with base case values (base case analysis = \$18 012). The middle dashed line shows the cost when there is no oral food challenge (OFC) delay (\$12 744 = 29% reduction from base case). The bottom dashed line shows the total cost of FE strategy with no delay in OFCs and 100% of children retesting annually (\$6594 = 63% reduction from base case).

fail an OFC also have demonstrated an improvement in HRQOL related to a better sense of control of the condition and reduced anxiety. Cited reasons include a better understanding of their symptoms and knowledge of how to treat a reaction for both child and parent.^{7,8}

With this effect on cost and a positive impact on QOL, we attempted to answer the question, “Are OFCs cost-effective?”

This analysis showed that offering an OFC as a confirmatory test to most diagnosed children within a year of diagnosis results in lower costs and better QOL than immediate FE despite the initial high estimated cost of OFC (\$2773). The decrease in overall cost despite a high cost of OFC is most likely due to a drop in the number of false positives incurring unnecessary costs. With the understanding that OFCs consume time, effort, include a risk, and that not every child is a candidate for

an OFC, we compared confirmatory OFC testing of only 70% of SPT/IgE diagnosed children to the FE strategy (presumed current practice), and the OFC strategy was still the better option. The analysis also revealed that annual retesting and not delaying OFCs for those who test negative may lead to markedly decreased overall cost and better QOL despite OFC still dominating FE (29% estimated drop in FE cost at 100% not delaying OFCs and 63% estimated drop in cost at 100% not delaying OFC and 100% annually retesting). This maintained dominance is due to retesting being also subject to the specificity of SPT/IgE and because retesting also had a positive effect on the proposed OFC strategy. FE strategy is also not dominated at a SPT/IgE specificity of 0.91, which is a value that exceeds the range reported in the meta-analysis.⁴ SPT/IgE did not dominate OFC until a specificity of nearly 99%, and this is probably

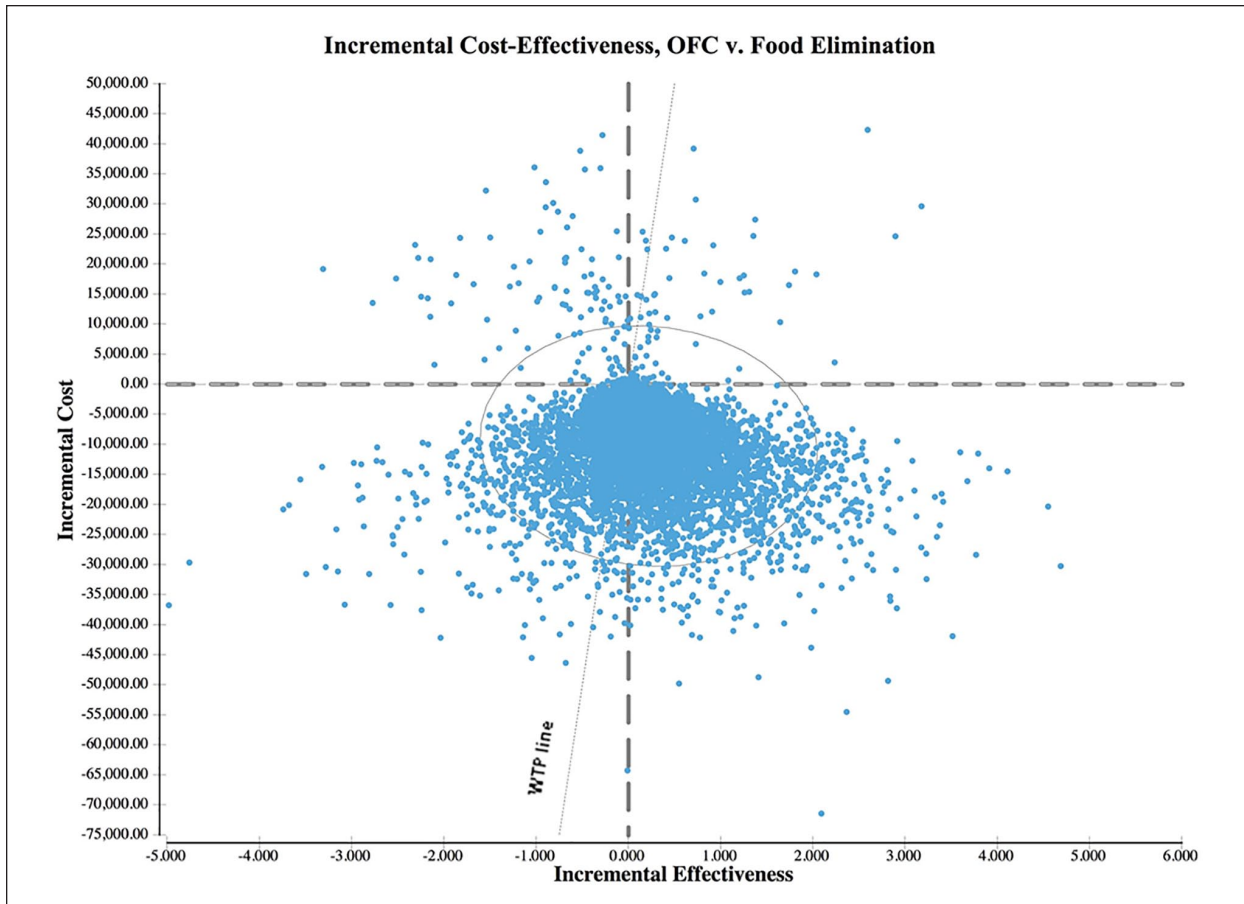


Figure 4. Probabilistic sensitivity analysis scatterplot. This plot compares the cost-effectiveness of OFC strategy versus food elimination (FE) strategy by showing distributions of incremental cost and incremental effectiveness for each iteration (dots) of the probabilistic sensitivity analysis. Dots below the willingness-to-pay (WTP) line represent iterations where oral food challenge (OFC) strategy was cost-effective compared with FE strategy.

due to OFC having a positive effect on HU. However, hypothetically if SPT/IgE specificity reached high values, we would expect it to have a positive effect on HU.

The Centers for Disease Control and Prevention reported an 18% increase in FA prevalence from 1999 to 2007, and a rise in costs will naturally follow, so approaches that consider cost as well as effectiveness in the management of FA are necessary.²³ The OFC approach could prove useful in controlling the rising cost of FA until better diagnostic tools emerge. Barriers to performing OFCs include the time and space needed, which can lead to relative poor remuneration in some offices. Also, providers may not be trained and/or comfortable in performing OFCs or feel they are adequately prepared to manage significant reactions.⁶ Caregivers may also decline OFCs given they may not want to introduce the food and concerns about the risks of a reaction during an OFC. However, practice workshops and training sessions through professional membership

organizations, that is, American Academy of Allergy, Asthma and Immunology (AAAAI) and American College of Allergy, Asthma and Immunology (ACAAI), are available to improve comfort level and efficiency in performing OFCs. Furthermore, discussing with caregivers that OFCs improve both parent and child QOL may help decrease concerns about their child undertaking them. Although symptoms are usually mild, in OFCs that are not passed, caregivers and children have reported reduced anxiety in managing future reactions after they have been treated for symptoms during a challenge.^{7,8}

There are several limitations to this study. A major limitation involves the quality of the model inputs extracted from the literature. While we modeled annual repeat OFCs, evidence on QOL after repeat OFCs is absent. However, the likelihood of a reaction on repeat OFC to peanut and tree nut has been reported at 61%.²⁴ It is possible that some of the improvement in QOL for those that fail a challenge would decrease over time. The effect of

repeat OFCs on QOL would be an interesting area of future research. Although the probabilities of retesting and delaying OFCs hold a large proportion of uncertainty, they did not seem to change the outcomes even at extreme values in the sensitivity analysis. Despite many reports on the burden and effect of FA on parents, none provide a value that can be used in a cost-effectiveness analysis, and most of our HU parent values were based on our best estimation. However, we conducted the analysis excluding the parents HU, and it yielded the same result. Having further applicable input measures would strengthen the model. Furthermore, our model does not account for the possibility of having multiple kids with FA in the same family, multiple FA per child, and it assumes food introduction will be successful after a negative challenge and also that the effects on health outcomes are maintained. Fortunately, the rate of recurrence after passing a challenge is low, 8% with peanut allergy, specifically.²⁵ Finally, this model does not account for the group of patients that might be receiving oral immunotherapy, nor does it take into consideration potential experimental preventive approaches.

Ultimately, whether to proceed with an OFC or continue to avoid a food is a shared decision between a clinician and family. Clearly, a child who presents with sensitization to a food but has never consumed it is different than a child who has had anaphylaxis from a management standpoint. Cost-effectiveness is only one aspect of whether a clinician would perform an OFC. Even though the OFC is the “gold standard” in the diagnosis of FA, the clinician will need to take many factors into consideration on a case by case basis including aspects of the presenting history, family dynamics, and laboratory/skin testing results in deciding whether to proceed. Hence, this model, based on the available literature, suggests that performing an OFC is preferable to continued food avoidance from a cost-effectiveness perspective and may help clinicians and families in deciding among many factors whether to proceed with an OFC.

In conclusion, our study shows that confirmatory OFCs for children, within a year of diagnosis, is a cost-effective strategy that decreases costs and seems to improve QOL.

Appendix A

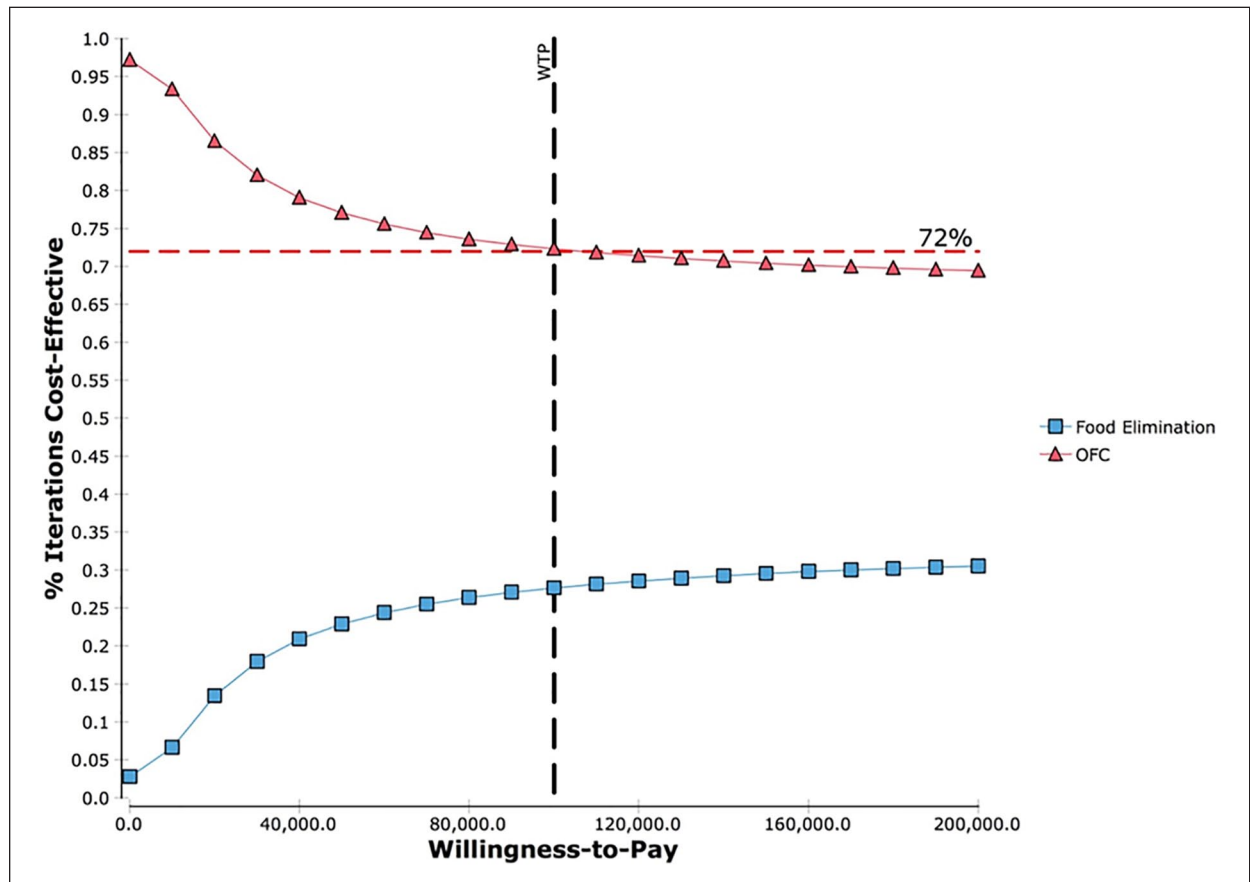


Figure A1. Cost-effectiveness acceptability curve comparing the cost-effectiveness of confirmatory oral food challenges to immediate food elimination after skin or blood testing.

Author Contributions

AA: Contributed to conception and design; contributed to acquisition; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

JM: Contributed to conception and design; contributed to acquisition, analysis, and interpretation; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

SL: Contributed to conception and design; contributed to acquisition, analysis, and interpretation; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iD

Sydney Leibel  <https://orcid.org/0000-0001-9857-7657>

References

- Gupta R, Springston EE, Warriar MR, et al. The prevalence, severity, and distribution of childhood food allergy in the United States. *Pediatrics*. 2011;128:e9-17.
- Gupta R, Holdford D, Bilaver L, Dyer A, Holl JL, Meltzer D. The economic impact of childhood food allergy in the United States. *JAMA Pediatr*. 2013;167:1026-1031.
- Sicherer SH, Sampson HA. Food allergy: epidemiology, pathogenesis, diagnosis, and treatment. *J Allergy Clin Immunol*. 2014;133:291-307.
- Soares-Weiser K, Takwoingi Y, Panesar SS, et al; EAACI Food Allergy and Anaphylaxis Guidelines Group. The diagnosis of food allergy: a systematic review and meta-analysis. *Allergy*. 2014;69:76-86.
- Nowak-Wegrzyn A, Assa'ad AH, Bahna SL, Bock SA, Sicherer SH, Teuber SS; Adverse Reactions to Food Committee of American Academy of Allergy, Asthma & Immunology. Work Group report: oral food challenge testing. *J Allergy Clin Immunol*. 2009;123(6 suppl):S365-S383.
- Couch C, Franxman T, Greenhawt M. The economic effect and outcome of delaying oral food challenges. *Ann Allergy Asthma Immunol*. 2016;116:420-424.
- Van der Velde JL, Flokstra-de Blok BM, de Groot H, et al. Food allergy-related quality of life after double-blind, placebo-controlled food challenges in adults, adolescents, and children. *J Allergy Clin Immunol*. 2012;130:1136-1143.e2.
- Soller L, Hourihane J, DunnGalvin A. The impact of oral food challenge tests on food allergy health-related quality of life. *Allergy*. 2014;69:1255-1257.
- Pongracic JA, Bock SA, Sicherer SH. Oral food challenge practices among allergists in the United States. *J Allergy Clin Immunol*. 2012;129:564-566.
- Fleischer DM, Bock SA, Spears GC, et al. Oral food challenges in children with a diagnosis of food allergy. *J Pediatr*. 2011;158:578-583.e1.
- Cherkaoui S, Ben-Shoshan M, Alizadehfar R, et al. Accidental exposures to peanut in a large cohort of Canadian children with peanut allergy. *Clin Transl Allergy*. 2015;5:16.
- Bégin P, Paradis L, Paradis J, Picard M, Des Roches A. Natural resolution of peanut allergy: a 12-year longitudinal follow-up study. *J Allergy Clin Immunol Pract*. 2013;1:528-530.e1-e4.
- Centers for Disease Control and Prevention. GMWK23R: death rates by 10-year age groups: United States and each state, 1999-2007. <https://www.cdc.gov/nchs/nvss/mortality/gmwk23r.htm>. Accessed November 18, 2019.
- FairHealth Consumer Cost Lookup. <https://www.fairhealth-consumer.org/>. Accessed November 18, 2019.
- Centers for Medicare & Medicaid Services. Overview. <https://www.cms.gov/Research-Statistics-Data-and-Systems/Computer-Data-and-Systems/ESMD/index.html>. Accessed November 18, 2019.
- US Bureau of Labor Statistics. May 2016 national occupational employment and wage estimates. https://www.bls.gov/oes/2016/may/oes_nat.htm. Accessed November 18, 2019.
- Educational Finance Branch. Public Education Finances: 2014. <https://www2.census.gov/govs/school/14f33pub.pdf>. Published June 2016. Accessed November 18, 2019.
- Morou Z, Tatsioni A, Dimoliatis IDK, Papadopoulos NG. Health-related quality of life in children with food allergy and their parents: a systematic review of the literature. *J Investig Allergol Clin Immunol*. 2014;24:382-397.
- DunnGalvin A, Koman E, Raver E, et al. An examination of the Food Allergy Quality of Life Questionnaire performance in a countrywide American sample of children: cross cultural differences in age and impact in the US and Europe. *J Allergy Clin Immunol Pract*. 2017;5:363-368.e2.
- Mittmann N, Trakas K, Risebrough N, Liu BA. Utility scores for chronic conditions in a community-dwelling population. *Pharmacoeconomics*. 1999;15:369-376.
- Fryback DG, Dunham NC, Palta M, et al. US norms for six generic health-related quality-of-life indexes from the National Health Measurement Study. *Med Care*. 2007;45:1162-1170.
- Olsen JA, Smith RD. Theory versus practice: a review of "willingness-to-pay" in health and health care. *Health Econ*. 2001;10:39-52.

23. Branum AM, Lukacs SL. Food allergy among US children: trends in prevalence and hospitalizations. *NCHS Data Brief*. 2008;(10):1-8.
24. Wainstein BK, Saad RA. Repeat oral food challenges in peanut and tree nut allergic children with a history of mild/moderate reactions. *Asia Pac Allergy*. 2015;5: 170-176.
25. Fleischer DM, Conover-Walker MK, Christie L, Burks AW, Wood RA. Peanut allergy: recurrence and its management. *J Allergy Clin Immunol*. 2004;114:1195-1201.
26. Umasunthar T, Leonardi-Bee J, Hodes M, et al. Incidence of fatal food anaphylaxis in people with food allergy: a systematic review and meta-analysis. *Clin Exp Allergy*. 2013;43:1333-1341.