

Estimated risk reduction to packaged food reactions by epicutaneous immunotherapy (EPIT) for peanut allergy



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ABSTRACT

Background: Peanut allergy is a generally persistent, sometimes life-threatening food allergy. With no treatments demonstrating the ability to cure a food allergy, the focus of drugs in development has been on providing a level of protection against accidental exposure reactions. However, no study has estimated the relative risk reduction of a food-allergic population receiving a specific immunotherapeutic treatment for their allergies.

Objective: To estimate the relative risk reduction when consuming peanut-contaminated packaged food products in a double-blind, placebo-controlled Phase 3 study population of children treated with epicutaneous immunotherapy (EPIT) for 12 months with either a patch containing 250 μ g peanut protein (250- μ g patch) or a placebo patch.

Methods: The probability of an allergic reaction due to the unintended presence of peanut protein in packaged food products was modeled per study group and food category combination using Monte Carlo simulations. Risks per eating occasion of a contaminated packaged food product and the number of individuals per study population predicted to react on a yearly basis were investigated.

Results: The population treated with the 250- μ g patch demonstrated a significantly increased dose-response distribution after 12 months of treatment, which resulted in a relative risk reduction of 73.2% to 78.4% when consuming peanut-contaminated packaged food products. In contrast, no statistically significant change was observed for the placebo group at the 12-month point.

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Conclusion: Our study estimates a substantial relative risk reduction for allergic reactions among peanut-allergic children after 12 months of EPIT with the 250- μ g patch, supporting the potential real-world clinical relevance of this investigational immunotherapy and its possible role as a future therapy for peanut-allergic children. [ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT02636699) Identifier: NCT02636699

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Introduction

Peanut allergy is a generally persistent, sometimes life-threatening food allergy that is increasing in prevalence in Western countries.¹ No FDA-approved therapies exist for treatment of peanut allergy, and patients must strictly avoid peanut and be prepared to use rescue medication on symptoms caused by unintentional peanut ingestion.¹ However, complete avoidance of peanut is difficult, at least in part because of its widespread use as a food ingredient in packaged foods and in restaurant or catered meals. Unexpected allergic reactions to food including peanut are frequent, reportedly occurring in up to half of peanut-allergic patients on a yearly basis, with unpredictable symptoms that can be mild, moderate, and severe.^{2–6}

With no treatments demonstrating the ability to cure a food allergy, the focus of drugs in development has been on providing a level of protection against accidental exposure reactions by increasing the reaction threshold (ie, the amount at which an individual experiences an allergic reaction).⁷ Caregivers of peanut-allergic children have also expressed a desire for a “buffer” against reactions to accidental peanut exposures that will involve minimal risk.⁸ Thus, recent studies have aimed to quantitatively model the clinical benefits of increasing a hypothetical individual's threshold through immunotherapy in the American and European populations.^{9,10} A greater than 95% relative risk reduction was modeled for the risk of accidental allergic reactions attributable to peanut in packaged foods across food categories for the peanut-allergic individual who achieved an eliciting dose (ED) of 300 mg peanut protein or more after immunotherapy (from initial EDs of 1, 3, 10, 30 or 100 mg peanut protein), regardless of the immunotherapy method.^{9,10} However, no study has investigated the quantitative relative risk reduction of a food-allergic population receiving a specific immunotherapeutic treatment for their allergies.

Epicutaneous immunotherapy (EPIT) for peanut has previously been identified as a potential treatment approach that may provide some reassurance regarding reactions to accidental exposures (a minimal risk, fit-for-purpose treatment to provide a buffer against accidental exposures and a potential quality-of-life improvement for patients undergoing treatment).¹¹ In a recently published phase 3 study population, EPIT was shown to be superior to placebo with a high degree of adherence to therapy and a low rate of serious adverse events.¹² However, Fleischer et al¹² only evaluated the change in reaction threshold according to the predefined clinical trial protocols. An additional available option is to look at the impact on risk within the allergic population for an allergic reaction caused by accidental exposures to peanut.

The current study quantifies the relative risk reduction in a double-blind, placebo-controlled phase 3 study population of children treated epicutaneously for 12 months with either a peanut patch (250 μ g peanut protein, referred to as 250- μ g patch) or a placebo patch.¹² Using pretreatment and post-treatment threshold data, the study population's relative risk reduction for the probability of an allergic reaction caused by the unintended presence of peanut protein in packaged food products was calculated.

Methods

Population-Based Quantitative Risk Assessment Inputs

Population-based quantitative risk assessments were conducted using Monte Carlo simulations with 3 primary inputs for the risk assessment: the study-population dose distributions at baseline and 12-month double-blind, placebo-controlled food challenges (DBPCFCs) (with 95% confidence intervals), the concentration of peanut protein in the consumed food product, and the amount of food consumed per eating occasion of selected packaged food products (eTable 1).

Dose Distributions

Study-population dose distributions were fitted to baseline and 12-month DBPCFC data from a recently described phase III clinical trial population ($n = 356$), including an ED at entry of 300 mg or less peanut protein.¹² The discrete ED was collected according to predefined stopping criteria at baseline DBPCFC and again after 12 months of daily application of a 250- μ g peanut patch ($n = 238$) or a placebo patch ($n = 118$).¹² An interval-censoring survival analysis approach was used because it has previously been described as the most appropriate method for determination of population-based dose distributions when using food challenge data.¹³ Interval-censoring survival analysis uses the interval between the discrete ED and the dose before the ED during DBPCFC. The exact dose that provokes a reaction in an individual is not known; however, the reactive dose is known to fall into the interval between the ED and the dose before the ED.

Peanut Protein Concentration

Peanut protein concentrations were selected from packaged food retail surveys from Europe and North America.^{9,14–25} From these 13 published studies, 281 positive samples ($\sim 10\%$ of tested products) were reported, with a range of 0.175 to 6500 ppm (mg/kg) peanut protein, and a log-normal distribution was fitted to the data (eFig 1), using `fitdistscens` within the `fitdistrplus` package in R (version 3.5.1) and RStudio (version 1.1.456). The simulated concentrations from the fitted log-normal distribution had a minimum of 0.175, median of 5.9, mean of 136, 99th percentile of 500, and 99.99th percentile of 7500 ppm (mg/kg) peanut protein, which were reflective of the reported concentration data in literature. No discernible difference in peanut concentrations was published for different food groups tested, and the same concentration distribution was used for all food groups in this study.

Consumption Data for Product Categories

Four commonly eaten packaged food groups previously indicated to have high risks for unintended allergen presence and a high rate of product recall (cookies, doughnuts, ice cream, salty snacks) were selected for use in the current study.⁹ Consumption data for the United States and Netherlands populations reporting consumption of the 4 product categories were used in this study (eTable 2). The consumption data for the United States were available for children 4 to 11 years of age as gleaned from the 2003–2010 National Health and Nutrition Examination Survey (NHANES) dietary surveys, and the food product categories for the current risk assessments were previously described in more detail by Baumert et al.⁹ Consumption data for the Netherlands were available for children from 7 to 11 years of age as gleaned from 2007–2010 Dutch

National Food Consumption Survey (DNFCS) of the National Institute of Public Health and the Environment, and the food product categories for the current risk assessments were previously described in detail by Remington et al.¹⁰

Absolute Risks for an Unexpected Allergic Reaction per Eating Occasion of a Contaminated Packaged Food Product

Population-based quantitative risk assessments were conducted using Monte Carlo simulations in R (version 3.5.1) and RStudio (version 1.1.456). Three primary inputs were used, including the baseline and 12-month DBPCFC study-population dose-distributions, the concentration of peanut protein in the consumed food product, and the amount of food consumed per eating occasion of selected packaged food products. Additionally, 100% of the products in the simulation were assumed to be contaminated. Risk assessments were conducted by simulating 100,000 eating occasions per study population and food category combination, obtaining a percentage predicted risk per eating occasion, and then repeating 50 times to get a distribution of the predicted risks. This created a total of 5,000,000 simulated eating occasions of a contaminated packaged food product per combination. Relative risk reductions for each study population were then calculated.

Estimation of Unexpected Allergic Reactions during the Course of 1 Year

The percentage of individuals in the study population predicted to experience an unexpected allergic reaction over a 1-year period for each study population (% of study population) was conservatively predicted per packaged food category and for all 4 food categories together by combining: a) the absolute risk per packaged food product category per eating occasion of a contaminated packaged food (%); b) the estimated contamination rate of packaged food product category (10%)^{9,14–25}; c) the consumption probability of packaged food product category over a 2-day period (% consumption days reported in US NHANES survey); and d) the number of 2-day consumption periods in 1 year (182.5). Additionally, because no discernible difference was found in frequency of peanut contamination or the concentration of peanut when detected in products with or without precautionary labeling,^{17,20–22,24} all products in the risk assessment were assumed to have the same frequency of contamination and same concentration pattern.

Study Population Relative Risk Reduction Calculations

The relative risk reduction of a predicted allergic reaction from eating packaged foods was calculated per study population and food category combination. The relative risk reduction per study population can be expressed as a percentage decrease in risk to further examine the benefits of immunotherapy for the allergic population. The percentage decrease in risk was calculated using the total percentage of predicted reactions per combination and using the following formula:

$$\left(1 - \frac{\text{Study population risk POST – immunotherapy}}{\text{Study population risk at baseline PRE – immunotherapy}}\right) \times 100\% = \text{Percentage decrease in risk (\%)}$$

Results

Dose Distributions

Population-based dose distributions and the amount of peanut protein predicted to cause an allergic reaction in a specified percentage of the study group were similar at baseline for the 250- μ g

patch and placebo groups (Fig 1A). A log-normal distribution (with 95% confidence intervals) was deemed to best fit the data, at both baseline and 12-month food challenges for the 250- μ g peanut patch and placebo patch populations, and used for further risk assessment simulations. No statistically significant change was observed for the dose distributions of the placebo group at baseline and at the 12-month timepoint (Fig 1B). In contrast to the placebo group, the 250- μ g patch population-based dose distributions demonstrate that the amount of peanut protein predicted to cause an allergic reaction in a specified percentage of that group was significantly increased from baseline after 12 months of treatment; this is indicated by the marked shift in the dose distribution with nonoverlapping 95% confidence intervals (Fig 1C). The dose distributions resulting from this study confirm the results reported by Fleischer et al,¹² which found a significant increase in the median and mean ED after 12 months of treatment with the 250- μ g patch.

Absolute Risks for an Unexpected Allergic Reaction per Eating Occasion of a Contaminated Packaged Food Product

Absolute risks for an unexpected allergic reaction per eating occasion of a contaminated packaged food product for the placebo population, dependent on the food category, were calculated between 1.30% (salty snacks) to 3.97% (ice cream) at baseline and between 1.35% (salty snacks) and 3.98% (ice cream) after 12 months (Table 1). These absolute risks equate to relative risk reductions between -0.3% and -3.9% per eating occasion of a contaminated packaged food product for the placebo population, indicating no change in risk or a slight increase in risk after 12 months (Table 2).

For the population undergoing treatment with the 250- μ g patch, absolute risks for an unexpected allergic reaction per eating occasion of a contaminated packaged food product were calculated between 0.99% (salty snacks) and 3.26% (ice cream) at baseline and between 0.21% (salty snacks) and 0.87% (ice cream) after 12 months of treatment, dependent on the food category (Table 1). These absolute risks equate to relative risk reductions between 73.2% and 78.4% per eating occasion of a contaminated packaged food product for the peanut-allergic population undergoing 12 months of treatment with the 250- μ g patch (Table 2).

Absolute risks for an unexpected allergic reaction per eating occasion of a contaminated packaged food product and relative risk reduction percentages were similar when determined using both US (Tables 1 and 2) and Dutch consumption data (eTable 3).

Estimation of Unexpected Allergic Reactions during the Course of 1 Year

For the 118 individuals in the placebo population and the 238 individuals in the 250- μ g patch population of the phase 3 study at baseline, using the current model, up to 35 and 53 allergic reactions, respectively, would be predicted to occur after consumption of the 4 investigated packaged food products during the course of 1 year (US consumption data).

Placebo Patch Population

Predicted allergic reactions in the placebo baseline population (n = 118) varied per product category between 3 (doughnuts) and 17 (ice cream) allergic reactions. If all simulated reactions occurred in unique individuals who do not react to more than 1 food category, up to 29.7% of the placebo baseline population (35 of 118

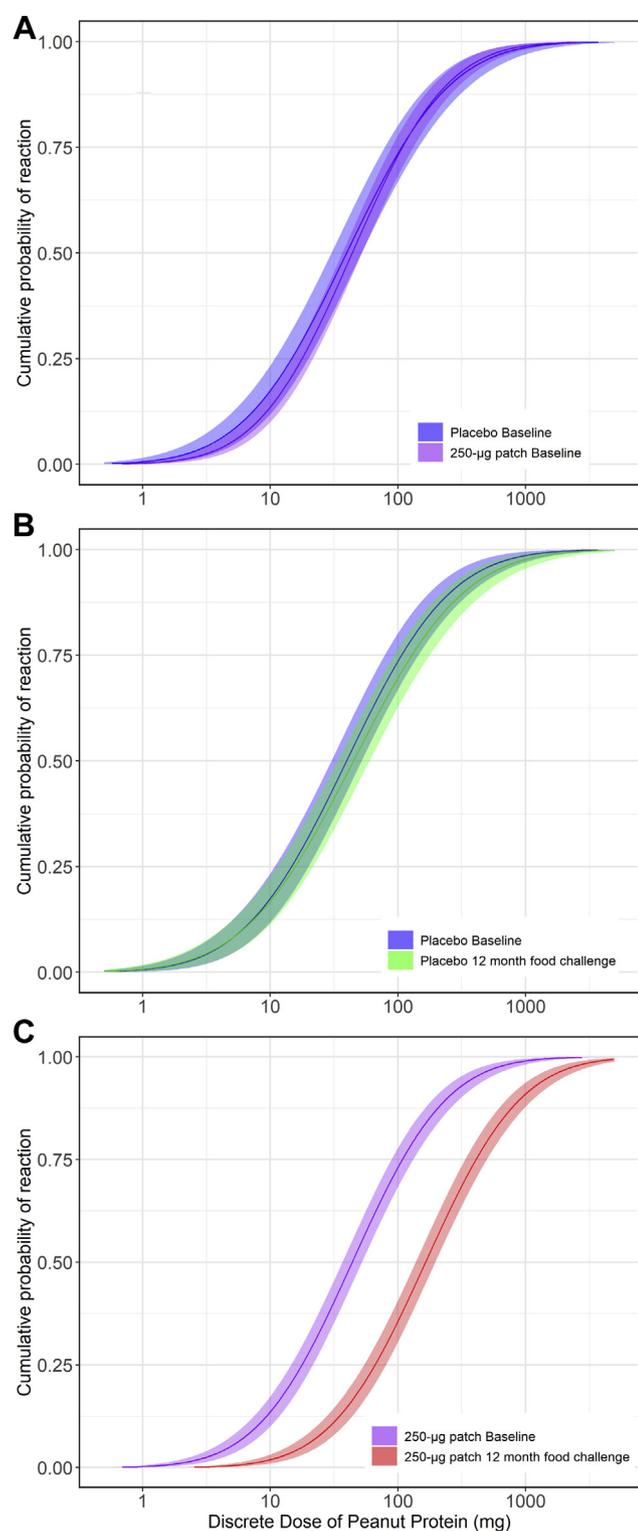


Figure 1. Comparison of discrete dose-response distributions for the peanut-allergic population undergoing EPIT with a 250- μ g patch or placebo patch as fit with interval-censoring survival analysis (ICSA), (A) baseline DBPCFC time point for placebo patch and 250- μ g patch populations, (B) baseline and 12-month DBPCFC timepoints for the placebo patch population, (C) baseline and 12-month DBPCFC timepoints for the 250- μ g patch population. The proportion of a peanut-allergic study population predicted to experience an allergic reaction according to the predefined clinical trial criteria (y-axis) in relation to each corresponding dose of peanut protein (x-axis) is presented.

individuals) would be predicted to have a reaction over a 12-month period (Table 1). However, that is an overly conservative assumption, because roughly half of consumers reported consumption of at

least 2 of the studied food categories, and based on available literature, likely some individuals would have multiple accidental reactions in a 1-year period.² Using a conservative estimate and assuming that all individuals predicted to react to ice cream are also the predicted reactors for the other 3 food groups, the overall percentage of the placebo baseline population predicted to have an unexpected reaction over a 1-year period was determined to be a more likely range of 14.4% to 29.7%. After 12 months of placebo patch application, the number of individuals predicted to experience unexpected allergic reactions in the placebo population after consuming 1 of the 4 tested packaged food categories remained stable at 14.4% to 29.7% over a 1-year period.

250 μ g Peanut Protein Patch Population

Predicted allergic reactions in the 250- μ g patch baseline population ($n = 238$) varied per product category between 4 (doughnuts) and 27 (ice cream) allergic reactions. If all simulated reactions occurred in unique individuals who do not react to more than 1 food category, up to 22.3% of the 250- μ g patch baseline population (53 of 238 individuals) would be predicted to have a reaction over a 12-month period, with a more likely range of 11.3% to 22.3% (Table 1). After 12 months of 250- μ g patch application, the number of unexpected allergic reactions estimated in the 250- μ g patch population for the year dropped significantly, with 3.4% to 5.9% predicted to experience a reaction after consuming 1 of the 4 tested packaged food categories.

Discussion

Recent publications suggest that EPIT for peanut was superior to placebo in a phase 3 study population, as demonstrated by an increased eliciting dose during a food challenge after 12 months of treatment.¹² Determination of the clinical significance of efficacy endpoints is needed. A recent review and meta-analysis of peanut oral immunotherapy studies questions the “utility of in-clinic oral food challenges as a primary (surrogate) measure of treatment efficacy” and describes the need for other measures focusing on “the risk and frequency of anaphylaxis and allergic reactions over time to real-world exposures rather than solely patient responses to provocation testing.”²⁶ In other forms of allergen immunotherapy (eg, respiratory allergens), prior international consensus expects that a measurable clinical benefit is recorded and that it is important to validate clinical trial results in terms of real-world patient-relevant outcomes, but exact methods for doing this are not specified or harmonized.²⁷ In food allergy, quantitative risk assessment modeling presents an additional way to evaluate the impact of potential food allergy immunotherapy treatments on clinically relevant real-world exposures. In previous allergic individual-based models, we and others have modeled a marked safety increase and relative risk reduction of more than 95% if an individual was able to reach a post-immunotherapy ED of 300 mg peanut protein from initial EDs of 1, 3, 10, 30, or 100 mg peanut protein, independent of the method of immunotherapy.^{9,10} Similar relative risk reduction results were seen for an individual moving from an ED of 300 mg peanut protein to 1000 mg peanut protein. However, these individual results are predicated on hypothetical individuals, assuming EDs from pre-immunotherapy and post-immunotherapy food challenges. Because food challenges are not widely used in clinical practice to establish ED thresholds, studying the predicted risks and relative risk reductions for the overall peanut-allergic study population being treated with any potential form of immunotherapy is important.

In the current study, a relative risk reduction of 73.2% to 78.4% was predicted across the study population undergoing EPIT with the 250- μ g patch, with no improvement in the placebo patch group. These percentages are derived from the absolute risks for an

Table 1
Predicted Absolute Risk for an Unexpected Allergic Reaction for the Peanut-Allergic Study Population at Baseline or after 12 Months of Treatment with a 250- μ g Patch or Placebo Patch^a

1. Risk per eating occasion of a contaminated packaged food product (%)					
	Cookies	Doughnuts	Ice cream	Salty snacks	
Placebo patch population					
Baseline risk	1.43%	2.40%	3.97%	1.30%	
12-Month time point	1.47%	2.45%	3.98%	1.35%	
250- μ g Patch population					
Baseline risk	1.09%	1.90%	3.26%	0.99%	
12-Month time point	0.24%	0.45%	0.87%	0.21%	
2. Yearly risk (% study population predicted to have a reaction)					
	Cookies	Doughnuts	Ice cream	Salty snacks	Sum of yearly risk across foods
Placebo patch population					
Baseline risk	7.6%	2.5%	14.4%	5.1%	29.7%
12-Month time point	7.6%	2.5%	14.4%	5.1%	29.7%
250- μ g Patch population					
Baseline risk	5.5%	1.7%	11.3%	3.8%	22.3%
12-Month time point	1.3%	0.4%	3.4%	0.8%	5.9%

^aAbsolute risks were calculated using United States consumption patterns and are presented as 1) risk per eating occasion of a contaminated food product; and 2) yearly risk (including frequency of consumption and frequency of contamination).

unexpected allergic reaction per eating occasion of contaminated packaged food products. Previously, 11.3% to 55% of peanut-allergic individuals were reported to have had an unexpected allergic reaction during a 1-year period,^{2–5} with 22.9% of peanut-allergic individuals reporting a food allergy-related emergency department visit in the past year.⁶ Of note, packaged foods were found to be the most reported cause of unexpected allergic reactions, causing nearly half of the unexpected reactions.² For the population of the phase 3 study at baseline, using the current model, one could conservatively predict that between 11.3% and 29.7% of the population would have an unexpected allergic reaction to 1 of these 4 packaged foods during the course of 1 year, in line with what is reported in the literature, supporting the relevance of our simulation assumptions. Therefore, 1 potential impact of EPIT treatment for peanut allergy may eventually be a substantial reduction of peanut allergic reactions in the community, even if one only focuses on reactions to packaged foods. Although the ability and potential benefit of EPIT to reduce accidental reactions had previously been anticipated,¹¹ our study is the first to quantify the potential reduction of risk in packaged foods.

In addition to the predicted risk of reaction and associated risk reduction (Tables 1 and 2), similar population-based quantitative risk assessments were done using a different allergen contamination concentration pattern previously used by Baumert et al⁹ and Remington et al.¹⁰ The change in contamination pattern resulted in higher predicted absolute risks, but similar relative risk reduction results were found compared with the results presented in Table 2 (eTables 4 and 5). These results indicate that the relative risk reduction results of our study hold even under more conservative

conditions. Similar relative risk reduction results were also found in simulations using the cumulative reactive doses and cumulative dose before the cumulative reactive doses in place of the ED and dose before the ED to generate the dose distributions (data not shown). Additionally, absolute risks for an unexpected allergic reaction per eating occasion of a contaminated packaged food product and relative risk reduction percentages were similar when determined using both US and Dutch consumption data; with the Dutch consumption data being representative for other countries in Europe,¹⁰ the results presented are predicted to apply to the larger American and European populations.

A limitation of our study is that exposure scenarios exist beyond the scope of our packaged food risk assessment, as meals prepared in restaurants, catered meals, meals prepared at home, and other larger unpackaged foods, for example, which are known to possibly contain high levels of allergen exposures.¹⁷ However, recent data from the newly updated Victoria State Government Anaphylaxis Notification System indicates that prepacked foods, unpackaged foods from food premises, and other food consumptions were all responsible for high numbers of anaphylaxis notifications ($n = 214, 270, 248$ respectively) over the first 6 months of reporting, indicating that severe reactions occur in all eating scenarios.²⁸ Within our study, modeled accidental exposure levels exceeded several grams of peanut protein, or the equivalent of multiple peanut kernels. The results of our study do not suggest that the peanut-allergic study population being treated with EPIT became less diligent with their peanut avoidance diet or begin consuming peanut-containing products.

Another limitation to our current study is that it only follows individuals to 12 months of EPIT treatment. Possibly the 250- μ g patch

Table 2
Relative Risk Reductions (RRR) at the 12-Month Time Point DBPCFC for the 250- μ g Patch and Placebo Patch Populations, for All Food Product Categories with Consumption Patterns Simulated from American Consumers^a

Study population relative risk reduction (RRR%) at 12-month time point	Cookies	Doughnuts	Ice cream	Salty snacks	Across foods
Placebo patch population					
1. RRR per eating occasion of a contaminated packaged food product	-3.0%	-2.2%	-0.3%	-3.9%	
2. Yearly RRR	0%	0%	0%	0%	0%
250- μ g patch population					
1. RRR per eating occasion of a contaminated packaged food product	77.7%	76.3%	73.2%	78.4%	
2. Yearly RRR	76.9%	75.0%	70.4%	77.8%	73.6%

^aRelative risk reductions are presented 1) per eating occasion of a contaminated food product and 2) per year (including frequency of consumption and frequency of contamination).

population would increase their threshold even further with continued treatment and thus experience an even greater risk reduction over time, as previously demonstrated by a phase 2b clinical trial using the 250- μ g patch.²⁹ Additional open-label follow-up studies with the 250- μ g patch are ongoing (PEOPLE, [ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT03013517) Identifier: NCT03013517), and relative risk reduction calculations for the open-label extension populations remain to be determined.

In conclusion, our study estimates a substantial 73.2% to 78.4% relative risk reduction for allergic reactions among peanut-allergic children when consuming peanut-contaminated packaged food products after 12 months of EPIT with the 250- μ g patch (approximately 1/1000 one peanut), supporting the potential real-world clinical relevance of this investigational immunotherapy and its possible role as a future therapy for peanut-allergic children.

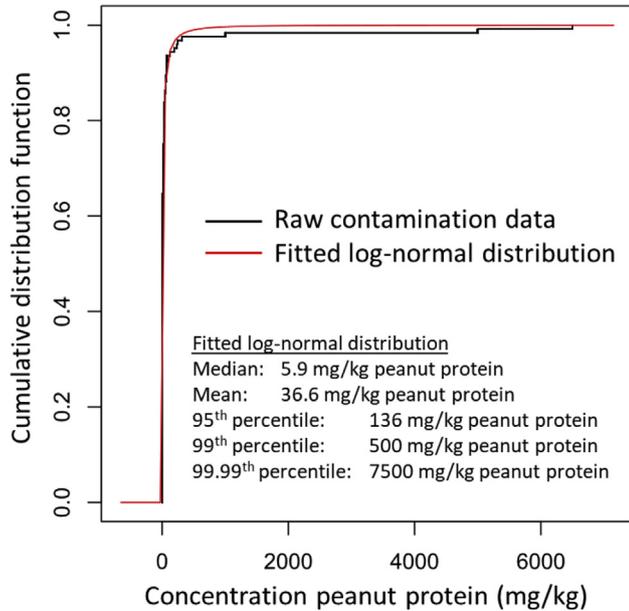
Supplementary Data

Supplementary data related to this article can be found online at <https://doi.org/10.1016/j.anai.2019.08.007>.

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Supplementary Data



eFigure 1. The cumulative distribution function for the peer-reviewed reported concentrations of peanut protein in the consumed food products, along with the fitted log-normal distribution.

eTable 1

Population-Based Quantitative Risk Assessment Inputs

Risk assessment source input variables	Distribution shape
Study population dose–response curve	
Placebo study population	
Baseline timepoint	Log-normal (μ, σ)
12-month timepoint	Log-normal (μ, σ)
250 μ g-patch study population	
Baseline timepoint	Log-normal (μ, σ)
12-month timepoint	Log-normal (μ, σ)
Consumption estimate per food category	
United States NHANES	Empirical (raw data)
Netherlands DNFCs	Empirical (raw data)
Contamination estimate	Log-normal (μ, σ)

eTable 2

Consumption Summary Statistics for Children in the United States 2003–2010 NHANES Dietary Survey (4–11 years) and for Children in the 2007–2010 Netherlands DNFCs (7–11 years)^a

Cookies	Number of individuals	Average (g)	P90 (g)	P95 (g)	Max (g)
United States	2110	35.9	65	88	320
Netherlands	591	36.8	59	72	135
Doughnuts					
United States	405	60.2	108	130	276
Netherlands	35	50.9	70	91.4	140
Ice cream					
United States	1589	105.1	194	241	777
Netherlands	273	71.5	105	120.8	183
Salty snacks					
United States	1656	32.6	60	70	208
Netherlands	90	29.4	53.3	59	100

^aIn the instance that multiple consumptions of a product category were reported, only the maximum consumption reported per individual was used for further risk assessment.

eTable 3
Risk Simulations Using the Netherlands (NL) Consumption Data^a

Absolute risks per eating occasion of a contaminated food product (%)	Cookies (NL)	Doughnuts (NL)	Ice Cream (NL)	Salty Snacks (NL)
Placebo patch population				
Baseline risk	1.48%	2.06%	2.87%	1.17%
12-Month time point	1.58%	2.17%	2.98%	1.26%
250- μ g Patch population				
Baseline risk	1.15%	1.64%	2.32%	0.90%
12-Month time point	0.24%	0.36%	0.55%	0.18%
Study population relative risk reduction (RRR%) at 12-month time point	Cookies (NL)	Doughnuts (NL)	Ice cream (NL)	Salty snacks (NL)
Placebo patch Population RRR	-6.8%	-5.4%	-3.8%	-7.6%
250- μ g Patch Population RRR	79.1%	77.8%	76.1%	79.9%

^aResults presented as 1) predicted absolute risks per eating occasion of a contaminated food product and 2) relative risk reductions (RRR) at the 12-month time point food challenges for the 250- μ g patch and placebo patch populations.

eTable 4
Predicted Absolute Risk for an Unexpected Allergic Reaction per Eating Occasion of a Contaminated Packaged Food Products Assumed to Have an Equal Chance to Be Contaminated with 1, 3, 10, 30, 100, 300, or 1000 ppm (mg/kg) of Peanut Protein^a

	Cookies	Doughnuts	Ice cream	Salty snacks
Placebo patch population				
US consumption				
Baseline risk	9.1%	13.4%	18.5%	8.7%
12 Month time point	9.0%	13.2%	18.0%	8.7%
NL consumption				
Baseline risk	9.6%	12.4%	15.5%	8.1%
12-Month time point	9.5%	12.2%	15.2%	8.0%
250- μ g Patch population				
US consumption				
Baseline risk	8.0%	12.3%	17.4%	7.7%
12-Month time point	2.2%	3.9%	6.7%	1.9%
NL consumption				
Baseline risk	8.5%	11.3%	14.4%	7.1%
12-Month time point	2.3%	3.3%	4.8%	1.7%

^aAbsolute risks were calculated for the peanut-allergic study population at baseline or after 12 months of treatment with a 250- μ g patch or placebo patch.

eTable 5
Relative Risk Reductions for at the 12-Month Time Point Food Challenges for the 250- μ g Patch and Placebo Patch Populations, for Food Products Assumed to Have an Equal Chance to Be Contaminated with 1, 3, 10, 30, 100, 300, or 1000 ppm (mg/kg) of Peanut Protein

Study population Relative risk Reduction (%) at 12 month time point	Cookies	Doughnuts	Ice cream	Salty snacks
Placebo patch population				
US consumption	0.9%	1.8%	2.3%	0.5%
NL consumption	1.0%	1.5%	2.1%	0.5%
250- μ g Patch population				
US consumption	73.0%	68.0%	61.5%	74.6%
NL consumption	73.6%	70.6%	66.7%	75.4%