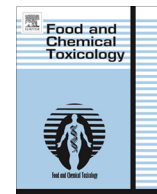




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Quantitative risk assessment of foods containing peanut advisory labeling

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ABSTRACT

Foods with advisory labeling (i.e. “may contain”) continue to be prevalent and the warning may be increasingly ignored by allergic consumers. We sought to determine the residual levels of peanut in various packaged foods bearing advisory labeling, compare similar data from 2005 and 2009, and determine any potential risk for peanut-allergic consumers. Of food products bearing advisory statements regarding peanut or products that had peanut listed as a minor ingredient, 8.6% and 37.5% contained detectable levels of peanut (>2.5 ppm whole peanut), respectively. Peanut-allergic individuals should be advised to avoid such products regardless of the wording of the advisory statement. Peanut was detected at similar rates and levels in products tested in both 2005 and 2009. Advisory labeled nutrition bars contained the highest levels of peanut and an additional market survey of 399 products was conducted. Probabilistic risk assessment showed the risk of a reaction to peanut-allergic consumers from advisory labeled nutrition bars was significant but brand-dependent. Peanut advisory labeling may be overused on some nutrition bars but prudently used on others. The probabilistic approach could provide the food industry with a quantitative method to assist with determining when advisory labeling is most appropriate.

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1. Introduction

Peanut is one of the most common allergenic foods with a worldwide prevalence of 0.6–2.9% (Osborne et al., 2011; Rona et al., 2007; Sicherer et al., 2010; Sicherer and Sampson, 2010). Peanut allergies are potentially life-threatening and the most common cause of food allergy-related fatalities in the United States (Bock et al., 2007; Keet and Wood, 2007; Rona et al., 2007). Peanut-allergic consumers must adhere to a strict avoidance diet and carefully examine ingredient labels (Hefle et al., 2007; Pieretti et al., 2009; Taylor et al., 1986; Yu et al., 2006). The presence of peanut in mislabeled or unlabeled packaged products has led to allergic reactions in consumers relying on clear and accurate ingredient statements (Kemp and Lockey, 1996; Yu et al., 2006).

In the US, the Food Allergen Labeling and Consumer Protection Act (FALCPA) that protects allergic individuals from unclear or

unlabeled products was passed in 2004 and became effective January 1, 2006 (FDA, 2006). Similar allergen labeling laws have been implemented in 18 other national regulatory frameworks to address the issue of improved labeling of allergens in food (Gendel, 2012). For public health authorities, the primary strategies have been to develop lists of priority allergenic foods and enact regulations to assure that any ingredients derived from these foods are declared on the labels of packaged foods (Gendel, 2012). FALCPA requires that companies must declare ingredients derived from the major allergenic foods including peanuts. Labeling of peanut is required by all 19 international regulatory frameworks that address allergen labeling (Gendel, 2012). However, advisory labeling for allergens is voluntarily used by the food industry and not directly regulated or addressed by FALCPA or most similar regulations elsewhere. The U.S. Food, Drug, and Cosmetics Act does require that label statements be “truthful and not misleading” (Chapter II, Sec. 201). Since advisory label statements are voluntary, a variety of advisory labels are used which can cause confusion and lead to weighted opinions of differing label statements. In a report by the U.S. Food and Drug Administration (FDA), both allergic and non-allergic consumers indicate that shorter “may contain” advisory labels are more likely to contain peanuts or other listed allergens. Additionally, both allergic and non-allergic consumers were more likely to serve a product with a longer “shared

Abbreviations: DBPCFC, Double-blind, placebo-controlled oral food challenge; FAAN, Food Allergy & Anaphylaxis Network; FALCPA, Food Allergen Labeling and Consumer Protection Act; FDA, U.S. Food and Drug Administration; LOAEL, Lowest Observed Adverse Effect Level; NHANES, National Health and Nutrition Examination Survey; NOAEL, No Observed Adverse Effect Level.

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facility” or “shared equipment” statement to an allergic individual than a product with a shorter “may contain” label (FDA, 2006). Allergic consumers are more likely to avoid products that state they “May contain” or were “Manufactured on the same/shared equipment” than products that state they were “Manufactured in a facility that also processes/uses” (Barnett et al., 2011; Hefle et al., 2007). However, peanut may be present in products that contain any form of advisory label for peanut (Hefle et al., 2007; Pele et al., 2007).

A US supermarket survey found 17% of products in 24 standard food industry categories contain an advisory label statement for food allergens (Pieretti et al., 2009). The wording of such statements was split evenly among products as 38% had “May contain”, 33% had “Same/shared equipment”, and 29% had “Shared facility” labels. Certain categories, such as chocolate candy, cookies, and baking mixes, had the highest prevalence of advisory statement usage with 40–54% of the products having an advisory label (Pieretti et al., 2009). While the use of advisory labeling is high, Hefle et al. (2007) found in a 2005 survey that only 7.3% of products with peanut advisory statements tested had detectable levels of peanut. Consumer avoidance of advisory labeled products has decreased and the prevalence of detectable peanut is low, but a risk of an allergic reaction still exists when consuming advisory labeled products (Hefle et al., 2007).

The current study surveyed packaged foods with an advisory label for peanut for the presence of peanut. Special attention was paid to the difference between foods with peanut advisory labeling and peanut labeled as a minor ingredient. Comparisons to a similar study conducted in 2005 by Hefle et al. (2007) were done. High levels of peanut in nutrition bars tested in 2005 and 2009 led to a second market survey focused on nutrition bars which sought to determine the levels of peanut in products with and without peanut advisory labeling. The potential risk to peanut-allergic consumers of nutrition bars was determined through the use of probabilistic risk assessment.

Monte Carlo simulations have become popular in the quantitative assessment of microbial and chemical risks (EU, 2003; Kroes et al., 2000; Lammerding and Fazil, 2000; Larsen, 2006; Notermans et al., 1995) but their use with food allergens is a recent development. Probabilistic risk assessment of food allergens was introduced by TNO in the Netherlands and used to investigate the risk associated with undeclared hazelnut in chocolate spreads (Spanjersberg et al., 2007). Additional research conducted by the same group, and others in France, has shown the robust capabilities of the probabilistic models and expanded the concept to products with advisory labels for milk and peanut (Kruizinga et al., 2008; Rimbaud et al., 2010; Spanjersberg et al., 2010).

The current study uses a probabilistic risk assessment approach to estimate the risk of an allergic reaction to the peanut-allergic population. The risk assessment couples the Bayesian inference of input variables from the model and 2nd Monte Carlo simulations to separately propagate the variability and the uncertainty of these variables (adapted from Rimbaud et al. (2010)). Parametric distributions describe each input variable, i.e. the prevalence of peanut allergy, reflecting natural heterogeneity and diversity. In a Bayesian framework, model parameters are random variables with their own distributions and not fixed as in other standard statistical approaches. These distributions reflect uncertainty in each parameter due to measurement errors or model hypothesis and are incorporated as they reflect the state of knowledge available before data set analysis (Pouillot et al., 2003; Rimbaud et al., 2010). To date, probabilistic risk assessment of food allergens based on packaged products found in the US has not been done. This study aims to assess the risk to a peanut-allergic consumer who intentionally purchases nutrition bars with advisory labeling for peanut.

2. Methods and materials

2.1. Peanut advisory labeling studies

2.1.1. 2009 Packaged food samples

A total of 202 packaged food products bearing advisory statements regarding peanut (186) or products that had peanut listed as a minor ingredient (last three ingredients on statement; 16) were purchased in Lincoln, Nebraska, USA. Products were categorized as baked goods/mixes, baking ingredients, candy/confectionery, cereals/cereal bars, frozen desserts, instant meals, nutritional/meal bars, or snack foods. Two different lot numbers of each product were obtained leading to a total of 404 samples. Sampling was designed in an effort to replicate the 2005 study (Hefle et al., 2007) and 54 identical products were available to purchase again in 2009. If identical products (manufacturer/brand) were not available, similar products from the same manufacturers were targeted.

2.1.2. 2010 Nutrition bar market survey

Due to the level of peanut in nutrition bars with advisory labeling in the 2005 and 2009 surveys, an in depth survey of nutrition bars available in Lincoln, Nebraska, USA was conducted. Products were categorized by the nature of the declaration of peanut on the labeling including contains peanut, minor ingredient, advisory statement for peanut, unique advisory labeling (may contain nuts, contains + advisory statement, minor ingredient + advisory statement), declaration of peanut free, and no mention of peanut on the label. A total of 399 nutrition bars were recorded over all categories. Products stated to contain peanut before the last three ingredients on the statement were not tested (120). Subsequently, 279 were purchased for testing including 49 with minor ingredient declaration, 166 with advisory labeling statements, 15 declared peanut free, and 49 with no mention of peanut. In an effort to sample as many unique brand and flavor combinations as possible, a single lot number of each nutrition bar was tested in this study.

2.1.3. Peanut analysis

A representative sample from a single package was homogenized (1/2 of package) and then analyzed (5 g) for the presence of peanut using a commercial enzyme-linked immunosorbent assay (Peanut Veratox[®], Neogen) with a lower limit of quantification of 2.5 ppm (ppm, µg/g) whole peanut (0.63 ppm peanut protein). Samples were prepared and analyzed according to instructions provided with the kit. Identical analytical methods were used in the 2005 market survey.

2.2. Nutrition bar consumption

Consumption data for nutrition bars were extracted from the U.S. National Health and Nutrition Examination Survey (NHANES) using a combination of the 2003–2004, 2005–2006, and 2007–2008 surveys (CDC, 2004, 2006, 2008). Only individuals completing both of the 24 h dietary recall interviews were included in the dataset. Within the NHANES data, USDA food codes specific to high protein nutrition and meal replacement bars, PowerBar[™], and Snickers[™] Marathon bars (41435110, 53541200, 53544450, 91780010, and 91781010) were used to create the nutrition bar product category. Individuals were considered consumers if they ate nutrition bars during one of the two recall days. For individuals consuming multiple nutrition bars in a 24 h period, the intakes were summed to a daily consumption level. As there is no consumption database describing the dietary habits of allergic consumers, the assumption was made that allergic and non-allergic individuals consume nutrition bars at the same rate and quantities and their reasons for nonconsumption are the same.

2.3. Threshold doses

The distribution of individual threshold doses from DBPCFC of 450 peanut-allergic individuals based on objective symptoms was taken from Taylor et al. (2010). A Log-Normal probability distribution function was fitted to the No Observed Adverse Effect Levels (NOAELs) and Lowest Observed Adverse Effect Levels (LOAELs) from each individual to describe the population threshold dose expressed as mg whole peanut, as previously described (Taylor et al., 2009).

2.4. Quantitative approach to risk assessment

The probabilistic risk assessment model for food allergens was described by Spanjersberg et al. (2007) and Kruizinga et al. (2008). Briefly, data inputs for prevalence of food allergy, allergen thresholds, consumption patterns, and product test results can be fitted to statistical distributions for use in a Monte Carlo simulation. The current risk assessment incorporates a Bayesian framework into a 2nd order Monte Carlo simulation to estimation the risk of an allergic reaction from consumption of nutrition bars with advisory labeling for peanut (adapted from Rimbaud et al. (2010)). The simulation scheme can be seen in Fig. 3.1. The simulation will set and hold distribution parameter inputs for a single run and then resample to achieve a new set of parameter inputs for the next run. Each run consists of 100,000 iterations that randomly sample from each set distribution and match if the individual is allergic, a consumer of the type of product, and if the product

contains peanut to determine if there is a risk of an allergic reaction. An individual will have a predicted allergic reaction if the predicted consumed amount and concentration of peanut lead to a dose over the predicted allergen threshold for that individual. The process repeats until 50 runs have been completed.

The threshold dose of an allergic individual can be estimated from the predictive posterior of the threshold variable, which is modeled by a Log-Normal dose-response distribution with normal prior distributions for the mean and standard deviation parameters. The normal prior distributions were created using the calculated estimate and standard error for the mean and standard deviation parameters from the LIFEREG procedure in SAS. The predictive posterior of the NHANES consumption amounts were modeled in a similar fashion. The predictive posterior for peanut concentration variable was modeled by a Log-Logistic distribution which utilized normal prior distributions for the intercept and scale parameters.

The number of allergic individuals in a population can be modeled by a binomial distribution of which the parameters are the prevalence of the allergy in the study population (p) and the size of the study population (n). Using the conjugate Beta(1, 1) prior distribution, the posterior distribution of the parameter p is the Beta(1 + x , 1 + n - x) with x representing the number of positive study responses. The beta distribution provides a new allergic prevalence probability estimate for the binomial distribution for every run in the simulation. In turn, the binomial distribution probability selects if an individual is allergic or not for every iteration in the simulation. The probabilities estimating allergic prevalence, peanut present in the nutrition bar, allergic shoppers purchasing advisory labeled products, and nutrition bar consumption are all modeled in a similar manner.

Six variables shape the allergen intake distribution: the probability of a nutrition bar containing advisory labeling for peanut, the probability of the allergic shopper purchasing advisory labeled products, the probability of eating nutrition bars, the probability of the nutrition bar to contain detectable levels of peanut, the concentration of peanut in the nutrition bar, and the amount of nutrition bar eaten. The 2010 nutrition bar survey determined the probability of nutrition bars containing advisory labeling for peanut. Surveys conducted at the Food Allergy & Anaphylaxis Network (FAAN) patient conferences were used to estimate how many allergic consumers buy products with advisory labeling on the package (Hefle et al., 2007). The probability of allergic shoppers purchasing advisory labeled products was conservatively estimated at 40% (258 of 645), the number of parents with food allergic individuals from the survey indicating that they would possibly purchase products with a "same facility" label. Nutrition bar products from all packaged food surveys conducted in 2005, 2009, and 2010 provided a total of 197 unique brand and flavor combinations with advisory labeling for peanut. As one lot number of each brand/ flavor combination was tested in 2010 and two lot numbers were testing in 2005 and 2009, each lot number was treated as an individual sample for a total of 270 tested products. For probabilistic risk assessment, those 270 products provided the raw data for distributions regarding the prevalence and the concentration of detectable peanut in advisory labeled nutrition bars. Distributions for the prevalence of nutrition bar consumption frequencies and the amount consumed were generated from the NHANES database.

Two simulations were run with differing inputs for consumption amounts based on empirical or parametric distributions. First, the simulation randomly selected a value from the empirical distribution of individual consumption amounts in NHANES to represent consumption. A second, repeated simulation fit the range of consumption levels to a parametric predictive posterior of the consumption variable modeled by Log-Normal distribution and simulated a value expressed as the consumed amount. Similar methods were used with the empirical and predictive posterior of the concentration variable modeled by Log-Logistic distributions for the concentration of peanut in advisory labeled nutrition bars.

2.5. Software and statistics

All statistical tests were done in SAS (version 9.2). The χ^2 test with a P value of less than 0.05 being significant was used to compare the frequency of positives from all 2005 and 2009 products, products purchased in both 2005 and 2009, and nutrition bars against all other products with minor ingredient labeling. Fisher's Exact Test with a P value of less than 0.05 being significant was used to compare the frequency of positives between advisory labeled products and products with no mention of peanut on the label in the 2010 nutrition bar survey due to an expected cell count of less than 5. For probabilistic modeling, the 2nd order Monte Carlo simulation is described in Section 2.4 and the stepwise method can be seen in Fig. 3.2.

3. Results

3.1. Peanut advisory labeling study

Peanut was detected in at least one lot in 8.6% (16/186) of products with peanut advisory statements and 37.5% (6/16) of products with peanut listed as a minor ingredient (Table 3.1). In the advisory labeled products, 6.5% (3/46) products with "may contain" statements, 13.8% (9/65) products with "shared equipment" statements, 2.9% (2/69) products with "shared facility" statements, and 33.3% (2/6) products with unique advisory labels had detectable levels of peanut in one or both lots. These results are similar to the 2005 survey conducted by Hefle et al. (2007) that found detectable peanut in 7.3% of advisory labeled products from the same categories ($P = 0.64$). Detectable peanut was found in the advisory labeled nutrition/meal bars (6/24), candy/confectionary (4/32), baking ingredients (2/16), cereal/cereal bars (2/20), snack foods (1/25), and baked goods/mixes (1/43) categories. No

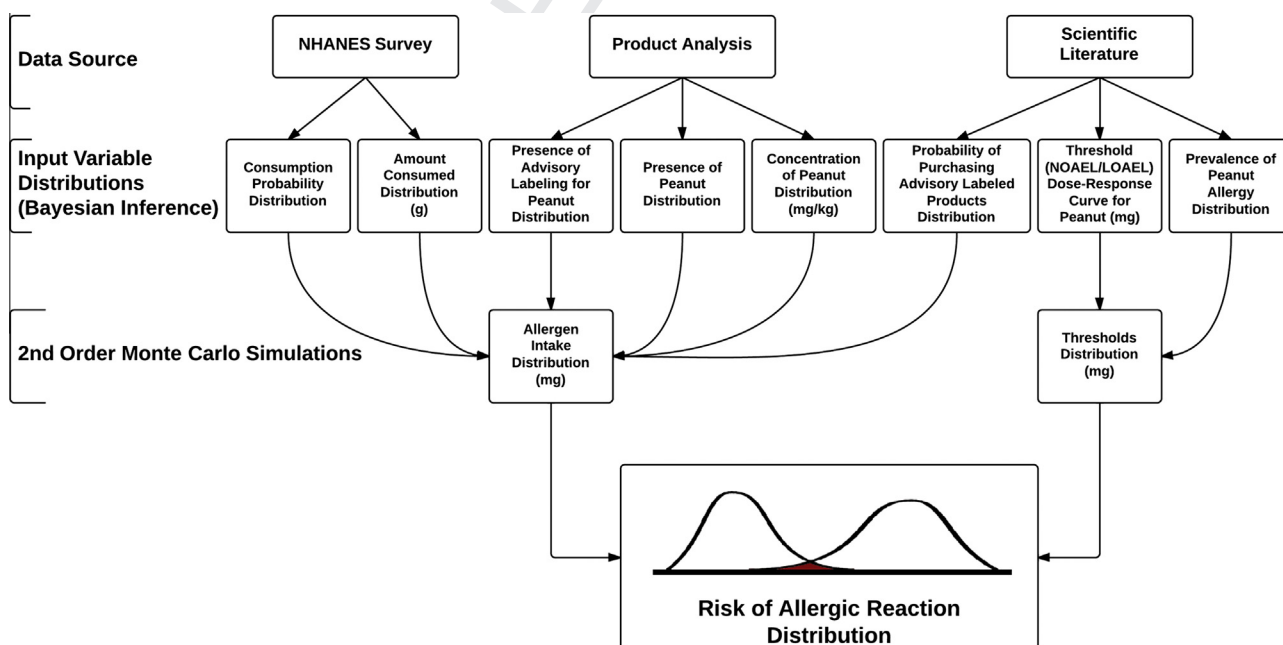


Fig. 3.1. Probabilistic risk assessment model for food allergens in advisory labeled products in the US. The general framework of the simulation is a 2nd order Monte Carlo simulation. Distributions of input variables were estimated with a Bayesian inference. Secondary simulations were run using empirical distributions for the amount consumed and/or the concentration of peanut.

detectable peanut was found in the advisory labeled frozen desserts products (0/9) or the instant meals (0/17).

The 16 advisory labeled products with detectable levels of peanut had levels ranging from 3 to 510 ppm. Inconsistencies were seen as only 43.8% (7/16) of products had both lots test positive for detectable peanut. Detectable peanut in the 6 products with minor ingredient labeling ranged from 5 to 69,000 ppm. Both lots tested positive for peanut in 83.3% (5/6) of cases.

Of 54 products tested in both the 2005 and 2009 advisory labeling surveys, peanut was detected in 13.0% (7/54) and 16.7% (9/54) of similar products in 2005 and 2009, respectively. These percentages were not significantly different even though FALCPA was implemented in 2006 ($P = 0.59$).

3.2. Nutrition bar market survey

Of 399 different nutrition bars, peanut is listed on 84% of labels, 42.4% (169/399) contain peanut in the ingredient statement and 41.6% (166/399) have an advisory label for peanut. A small number of nutrition bars, 3.8% (15/399), claim to be peanut free and 12.2% (49/399) have no declaration of peanut on the label. Detailed category breakdowns and ppm ranges can be found in Table 3.2. Among nutrition bars with minor ingredient labeling, 34 of 44 tested positive for peanut. Products contained up to 44,000 ppm whole peanut with 9 products over 1100 ppm, 9 between 50–650 ppm and 16 between 3.5–11 ppm. Five nutrition bars had peanut listed both as a minor ingredient and had an advisory statement indicating they were processed in the same facility with peanut; all tested positive at a range of 17–49,000 ppm. Of 159 nutrition bars with advisory labeling, 12 contained peanut with one 26,000 ppm sample, 4 samples between 70–150 ppm and 7 samples between 3–40 ppm. Seven nutrition bars were labeled “may contain nuts” and 2 of 7 samples tested positive for peanut at 2.8 and 16.2 ppm. No detectable peanut was found in 15 products with various peanut-free statements including “peanut free facility”, “nut free facility, peanut free”, or “nut free”. Two of 49 nutrition bars with no mention of peanut on the label tested positive at 13 and 1260 ppm. No significant difference was found in the

frequency of detectable peanut in products with advisory labeling for peanut (12/159) and products that had no mention of peanut on the label (2/49) ($P = 0.20$).

3.3. Quantitative risk assessment

The simulation input parameters and results are listed in Table 3.4. From the combined labeling surveys, 11.1% of nutrition bars with advisory labels for peanut were found to contain detectable levels of peanut residues at concentrations ranging from 2.5 to 26,000 ppm whole peanut. Two of the 30 positive samples (6.7%) contained peanut at 26,000 and 4000 ppm whole peanut. Five samples (16.7%) had 131–510 ppm whole peanut present. Four samples (13.3%) were between 70–87 ppm whole peanut and 4 more samples (13.3%) were within 27–39 ppm whole peanut. The remaining 15 samples (50%) contained between 2.5 and 18 ppm whole peanut. From the NHANES survey, the probability of consuming nutrition bars was estimated to be 0.82% (201 of 24,621), including 35 individuals consuming nutrition bars both days. The average consumption of nutrition bars was 64 g per day, close to a common serving size for a single nutrition bar (Table 3.3). The 90th percentile intake was 130 g (2 nutrition bars). The 99th percentile intake was 204 g (3 nutrition bars) and the maximum amount consumed was 272 g (4 nutrition bars) in 1 day.

Simulation risk results are presented in three ways including the allergic user risk, the risk to the peanut-allergic population, and the risk to the overall population. These three risk values represent the same number of predicted reactions expressed three different ways. The allergic user risk, or probability of a reaction in peanut-allergic users of the product, assumes every individual is allergic to peanut and consumes advisory labeled nutrition bars. The predicted number of reactions varied between 5.5 ± 2.0 per 1000 peanut-allergic user consumptions (empirical consumption distribution/parametric peanut concentration distribution) and 8.1 ± 1.7 per 1000 peanut-allergic user consumptions (parametric consumption distribution/empirical peanut concentration distribution). To estimate the risk for the peanut-allergic population, all individuals are allergic to peanut, 0.82% consume nutrition bars

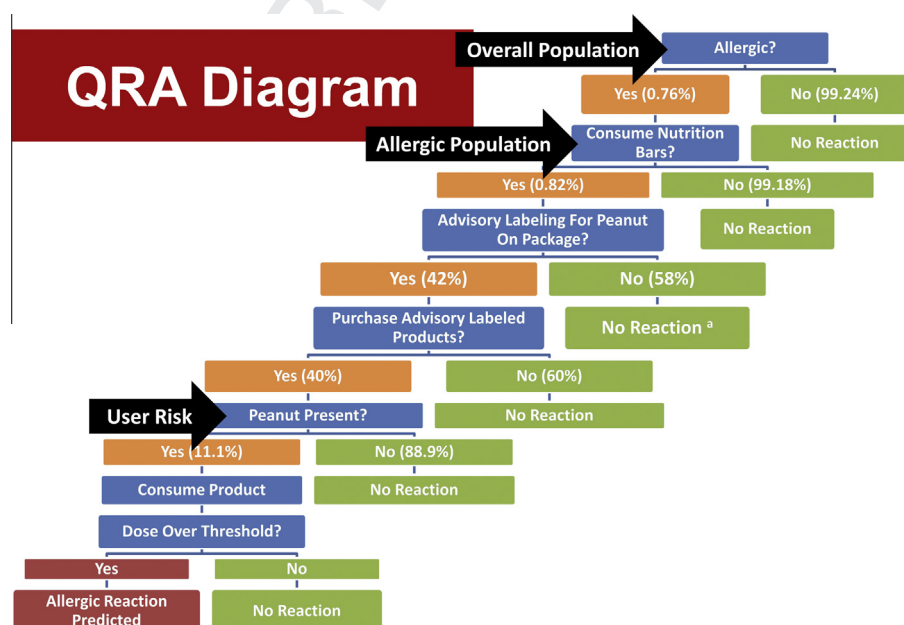


Fig. 3.2. Stepwise progression of the Monte Carlo Simulation. ^a Consumers that follow advisory labeling warnings and avoid nutrition bars with advisory labeling for peanut are still at risk for an allergic reaction, as nutrition bars without peanut on the label have been shown to contain detectable levels of peanut.

Table 3.1
Concentration and serving-size doses of peanut in packaged foods bearing allergy advisory statements for peanut (2009 survey).

Product category	“May contain” labeling			“Shared equipment” labeling			“Shared facility” labeling			Other unique labeling			Total	Minor ingredient labeling		
	No. ^a	Conc. ^b	Dose ^c	No.	Conc.	Dose	No.	Conc.	Dose	No.	Conc.	Dose	No.	No.	Conc.	Dose
Baked goods/mixes	14 (0)	–	–	14 (1)	8 ppm, BLQ	0.2 mg, <0.08 mg	15 (0)	–	–	–	–	–	43 (1)	–	–	–
Baking ingredients	4 (1)	3 ppm, BLQ	0.1 mg, <0.07 mg	6 (1)	9 ppm, 11 ppm	0.3 mg, 0.3 mg	6 (0)	–	–	–	–	–	16 (2)	–	–	–
Candy/confectionary	8 (1)	15 ppm, BLQ	0.8 mg, <0.1 mg	13 (3)	24 ppm, BLQ	0.8 mg, <0.1 mg	10 (0)	–	–	1 (0)	–	–	32 (4)	2 (1)	93 ppm, BLQ	1.7 mg, <0.05 mg
	–	–	–	–	3 ppm, BLQ	0.1 mg, <0.1 mg	–	–	–	–	–	–	–	–	–	–
	–	–	–	–	5 ppm, BLQ	0.2 mg, <0.1 mg	–	–	–	–	–	–	–	–	–	–
Cereal/cereal bars	5 (0)	–	–	8 (0)	–	–	5 (0)	–	–	2 (2)	97 ppm, 19 ppm, 20 ppm, 19 ppm	3.4 mg, 0.7 mg, 0.6 mg, 0.5 mg	20 (2)	8 (2)	11 ppm, 27 ppm, 32 ppm, 32 ppm	0.3 mg, 0.6 mg, 1.1 mg, 1.1 mg
	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Frozen desserts	5 (0)	–	–	2 (0)	–	–	2 (0)	–	–	–	–	–	9 (0)	–	–	–
Instant meals	–	–	–	2 (0)	–	–	15 (0)	–	–	–	–	–	17 (0)	–	–	–
Nutrition/meal bars	7 (1)	4 ppm, BLQ	0.2 mg, <0.1 mg	7 (3)	17 ppm, 32 ppm	0.7 mg, 1.3 mg	9 (2)	4 ppm, BLQ	0.2 mg, <0.1 mg	1 (0)	–	–	24 (6)	3 (3)	86 ppm, 121 ppm	6.7 mg, 9.4 mg
	–	–	–	–	510 ppm, 11 ppm	20.4 mg, 0.4 mg	–	4 ppm, 29 ppm	0.2 mg, 1.2 mg	–	–	–	–	–	5 ppm, 5 ppm	0.3 mg, 0.3 mg
	–	–	–	–	3 ppm, 131 ppm	0.1 mg, 5.2 mg	–	–	–	–	–	–	–	–	69,000 ppm, 56,000 ppm	3795 mg, 3080 mg
Snack foods	3 (0)	–	–	13 (1)	3 ppm, BLQ	0.1 mg, <0.1 mg	7 (0)	–	–	2 (0)	–	–	25 (1)	3 (0)	–	–
Total	46 (3)	–	–	65 (9)	–	–	69 (2)	–	–	6 (2)	–	–	186 (16)	16 (6)	–	–

BLQ, below the lower limit of quantitation: 2.5 ppm whole peanut.

^a Number of samples tested (number of samples with detectable peanut in one or more lots).

^b Concentration in parts per million (micrograms whole peanut per gram of the respective food product).

^c Dose in milligrams per suggested serving.

Table 3.2

Concentration of peanut in packaged nutrition bars in 2010 market survey.

Nutrition bars	No.	No. tested	No. positive	PPM range	Mean PPM	Median PPM
Contains peanut	104	0	–	–	–	–
Minor ingredient	44	44	34	3.6–44,000	1963	87.5
Advisory label	159	159	12	3.1–26,000	2207	28.4
May contain	50	50	1	3.1	–	–
Shared equipment	34	34	4	87–26,000	6576	115
Shared facility	75	75	7	5.6–70	24.3	15.4
Unique label	28	13	7	2.8–49,000	7065	23
Contains peanut + advisory statement ^a	16	0	–	–	–	–
Minor ingredient + advisory statement	5	5	5	17.8–49,000	9887	25
May Contain Nuts ^b	7	7	2	2.8–16.2	–	–
Peanut free label	15	15	0	–	–	–
No mention of peanut	49	49	2	13–1260	–	–
Total	399	279	55			

^a Not tested because they contain peanut and have an advisory label.^b “May Contain Nuts” or nut advisory label statements not specifically mentioning peanut.**Table 3.3**

Consumption of nutrition bars using NHANES 2003–2008 foodcodes.

Age Group	Sex	Percent of population consuming nutrition bars	Avg. daily consumption (g)	Std. deviation	90th Percentile consumption	Maximum consumption	No. of consumers	No. of people in age group
Total Population		0.82	64.7	38.9	130	272	201	24,621
Infants		0.04	8.5		8.5	8.5	1	2751
Children		0.22	59.0	12.9	85.1	85.1	9	4077
Teenagers	Female	0.61	52.1	12.3	75	100	15	2479
	Male	0.69	59.5	11.4	68	130	17	2449
Adults	Female	1.48	62.2	39.9	130	204	100	6752
	Male	0.97	71.0	46.9	136	272	59	6113

Table 3.4

Inputs and results of the probabilistic modeling approach to risk assessment of nutrition bars with advisory labeling for peanut. All nutrition bars in the simulation are assumed to contain advisory labeling for peanut.

Parameter inputs	Average value (%)	Distribution shape	Source of data
Prevalence of peanut allergy	0.76	Beta	Sicherer et al. (2010)
Allergic peanut threshold		Log-Normal	Taylor et al. (2010)
Probability of purchasing advisory labeled products	40	Beta	Hefle et al. (2007)
Consumption probability	0.82	Beta	NHANES database
Amount eaten		Log-Normal	NHANES database
Presence of peanut probability	11.1	Beta	Labeling surveys
Level of peanut present		Log-Logistic	Labeling surveys
Presence of advisory labeling for peanut	41.6	Beta	Labeling surveys
Simulation results		Mean	Std. dev.
Reaction probability in allergic user population		5.5–8.1 per 1000	1.5–2.0
Reaction probability in peanut-allergic population		0.8–1.1 per 100,000	0.2–0.3
Reaction probability in overall population		5.8–8.5 per 100,000,000	2.0–2.3

on a daily basis, 40% are assumed purchase advisory labeled nutrition bars, and 42% of nutrition bars contain advisory labeling for peanut. The predicted number of reactions per day varied between 0.8 ± 0.3 per 100,000 peanut-allergic individuals (empirical consumption distribution/parametric peanut concentration distribution) and 1.1 ± 0.3 per 100,000 peanut-allergic individuals (parametric consumption distribution/empirical peanut concentration distribution). To estimate the risk to the overall population, the inputs include that 0.76% of people are allergic to peanut, 0.82% consume nutrition bars on a daily basis, 40% are assumed to purchase advisory labeled nutrition bars, and 42% of nutrition bars bear advisory labeling for peanut. The predicted number of reactions per day due to nutrition bars with advisory labeling for peanut varied between 5.8 ± 2.3 per 100,000,000 people in the US

(empirical consumption distribution/parametric peanut concentration distribution) and 8.5 ± 2.0 per 100,000,000 people in the US (empirical consumption distribution/empirical peanut concentration distribution). No differences were noted between using simulation inputs to generate the predictive posteriors of the consumption and concentration variables versus using a random selection of actual consumption levels and concentrations taken from the empirical distributions.

The number of allergic reactions in peanut-allergic consumers can be predicted on a per day basis by utilizing the number of predicted peanut advisory labeled nutrition bars consumed in the US per day, the prevalence of peanut allergy, and the allergic user risk. The number of peanut advisory labeled nutrition bars consumed can be calculated with the equation below:

Consumed overall per day = U.S. population × Nutrition bar consumption probability × Probability of nutrition bar with advisory labeling for peanut
1.03 million nutrition bars = 300 million × 0.0082 × 0.42

The number of nutrition bars with advisory labeling for peanut consumed is used to estimate the number of allergic individuals purchasing nutrition bars with advisory labeling for peanut on a daily basis as shown in the equation below:

Consumed by allergic individuals = Consumed overall × Prevalence of peanut allergy × Probability of purchasing advisory labeled products
3131 advisory labeled nutrition bars consumed by peanut-allergic per day = 1.03 million × 0.0076 × 0.40

The number of expected allergic reactions per day can then be calculated by multiplying the number of peanut advisory labeled nutrition bars consumed by allergic individuals by the risk to the allergic user population in the equation below:

Of reactions = # Consumed by allergic individuals × Allergic user risk
18–26 predicted reactions per day = 3131 × 0.0055–0.0081

The predicted reactions were heavily influenced by the two samples with the highest concentration of peanut (26,000 ppm and 4000 ppm). These samples each account for 3.3% of the positive samples but are respectively responsible for ~35% and ~22% of predicted reactions. Still, nutrition bars with lower concentrations also pose a risk as products with levels of less than 100 ppm whole peanut led to 15–25% of the predicted reactions. Roughly 50% of the predicted reactions occurred at consumption amounts of 65 g or less, a common nutrition bar serving size. Approximately 10% of the reactions involved predicted consumption values over 130 g or 2 or more nutrition bars and ~1% involved predicted consumption values were over 204 g. The simulation predicts that 70–80% of the reactions involve a dose above 10 mg whole peanut, ~85% of the reactions involve a dose above 5 mg whole peanut, and ~99.5% of the reactions involve a dose above the most sensitive recorded individual threshold of 0.4 mg whole peanut as observed in Taylor et al. (2010). These results indicate that consuming nutrition bars with advisory labels for peanut would present a significant health risk to the peanut-allergic community (Fig. 3.3A). When the 26,000 ppm and 4000 ppm samples are removed from the simulation, the number of predicted reactions was reduced by 50%, but 23% of the predicted reactions occurred at a dose of more than 20 mg whole peanut (Fig. 3.3B). The lower concentrations of peanut in advisory labeled nutrition bars would still present a significant health risk to the peanut-allergic community.

When using the predictive posteriors of variables modeled by Log-Normal and Log-Logistic curves, the simulation can predict unrealistic values for the consumption and ppm values at the extreme high and low ends of the curve. For instance, consumption values up to 563 g or 8–10 nutrition bars were predicted to cause a reaction in one simulation. Additionally, concentration values as low as 0.0000007 ppm peanut and higher than one million parts per million peanut (clearly impossible) were predicted by the predictive posterior of the concentration variable modeled by Log-Logistic curve. However, these extreme values are statistically expected when repeating the simulation with a large number of iterations. A simulation was run using the predictive posterior of the concentration variable modeled by a Log-Logistic curve with the lower and upper extremes of the concentration values capped

at 2.5–26,000 ppm respectively. No significant changes in the results were seen when comparing the unbounded simulations to the simulations with concentration values capped at 2.5–26,000 ppm whole peanut. Thus it is not necessary for practical

purposes to introduce such limits.

4. Discussion

Detectable levels of peanut were found in 8.6% (16/186) of packaged products during the 2009 advisory labeling survey.

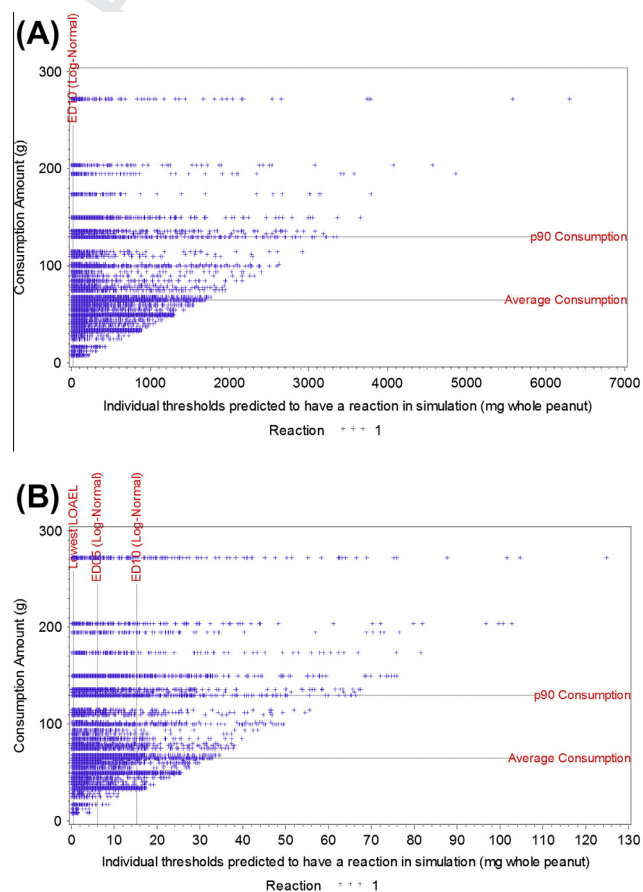


Fig. 3.3. Thresholds of predicted reactions expressed as mg whole peanut with the predicted consumption for each reaction: (A) All nutrition bars with advisory labeling for peanut included in simulation and (B) two samples containing high concentrations of detectable peanut (26,000 and 4000 ppm whole peanut) were removed from the simulation. The ED05 and ED10, or doses predicted to provoke a reaction in 5% and 10% of the peanut-allergic population, are 5.2 mg and 12.3 mg whole peanut respectively (Taylor et al., 2010) and labeled where possible. Additionally, the most sensitive individual threshold in the peanut dataset is labeled.

Detectable peanut residues were found in most, but not all product categories. However, it should not be presumed that certain product categories never contain detectable levels of peanut. Only 2 distinct lots of each product were tested and this was not an exhaustive market survey of all US products with peanut advisory statements. Detectable levels of peanut might be found if more lots were tested. Results were not significantly different from a similar study conducted in 2005 before FALCPA fully went into effect. As found in the 2005 study, nutrition/meal bars and candy/confectionary products tested in 2009 were most likely to contain peanut among products with advisory labels. Our results indicate that 25% (6/24) of advisory labeled nutrition bars contained peanut in 2009, as compared to 14% (4/28) in 2005. However, the expanded 2010 market survey for nutrition bars found peanut in only 7.5% (12/159) of advisory labeled nutrition bars. While all nutrition bars available in the Nebraska market were tested, a lower prevalence of peanut in the 2010 survey may be attributed to testing of only one lot number compared to two in previous surveys. The lack of positive samples does not necessarily mean the labels are misleading since only one or two lot numbers and a single sample from each were tested. However, the criteria used for advisory labeling within the food industry vary and the probability of detectable peanut can range from high to nearly nonexistent. Advisory labeling leads to consumer frustration and confusion and may lead to a false sense of security because a failure to react after consumption of a product with an advisory label for peanut might cause a peanut-allergic consumer to conclude that all such products are safe. Allergic consumers are most likely to avoid products that state "May contain" an allergen on the label by comparison to products with labels stating "Manufactured on shared equipment" or "Manufactured in a facility that also uses/processes" allergens, but similar levels of peanut were associated with products bearing all three types of advisory labels. In 2009, products with "shared equipment" labels had the highest levels of detectable peanut, but such products had the lowest levels in 2005. The products with "shared facility" labels had the highest levels in 2005 but had the lowest prevalence of positive tests in 2009. Based on such inconsistencies and the presence of detectable peanut in 8.6% of advisory labeled products, peanut-allergic individuals should be advised always to avoid such products regardless of the wording of the advisory statement.

In some instances, minor ingredient declarations for peanut have been used by food companies as a stronger deterrent than advisory labeling. In 2005, 33% (7/21) products with minor ingredient statements had detectable levels of peanut. No change was found in 2009 with 37.5% (6/16) containing detectable peanut. Nutrition bars with minor ingredient labeling had a significantly higher rate of detectable peanut with 79.7% (47/59) positive during the combined 2005, 2009, and 2010 surveys compared to a combination of all other products with minor ingredient labeling where 20.3% (13/64) tested positive ($P < 0.0001$). While, these surveys comprise a small sample of all products with minor ingredient statements for peanut, such products demonstrate a significant risk to peanut-allergic consumers. It is strongly recommended that peanut-allergic consumers avoid products with peanut listed as a minor ingredient.

It is clear that many products with advisory labeling for peanut contain over 0.4 mg whole peanut, the individual threshold for an objective allergic reaction of the most sensitive peanut-allergic patients (Taylor et al., 2010), but how large a health risk do they present? The ED05 and ED10, or doses predicted to provoke a reaction in 5% and 10% of the peanut-allergic population, were 5.2 mg and 12.3 mg whole peanut respectively (Taylor et al., 2010). Of predicted reactions in the simulation, 70–80% involve a dose above 10 mg whole peanut and ~85% have a dose over 5 mg whole pea-

nut. Probabilistic risk assessment indicates that nutrition bars with advisory labels for peanut constitute a serious risk for many peanut-allergic individuals. This risk assessment predicts that 18–26 allergic reactions should be occurring in the US each day from ingestion of nutrition bars. Removal of samples with 26,000 or 4000 ppm from the risk assessment results in 13 predicted allergic reactions per day. No evidence exists to suggest that the prevalence of allergic reactions to nutrition bars with advisory labeling is so high. The simulation seems to greatly overestimate the number of reactions per day in the US due to a number of conservative input estimates, including the number of peanut-allergic consumers purchasing nutrition bars and more specifically advisory labeled nutrition bars. The current simulation does not account for consumer preference for products without advisory labeling. However unlikely, it is assumed that 40% of allergic individuals will purchase an advisory labeled nutrition bar at the same rate as a product without advisory labeling. Additionally, consumption estimates are conservatively based on daily consumption, not individual eating occurrences and 28 individuals (13.9% of nutrition bar consumers) reported more than one eating occasion per day. However, utilizing individual eating occurrences instead of summed daily consumption did not significantly alter the simulation results (data not shown), due in part to the concentration of peanut detected in advisory labeled nutrition bars and in part to the nature of reported consumptions in the NHANES database. We chose summed daily consumptions to provide a more conservative risk assessment. Furthermore, mild reactions to these products may go unnoticed or unreported by peanut-allergic individuals. Still, our results indicate that advisory labeling for peanut is justified on many nutrition bars. The overlap of predicted exposure doses with confirmed DBPCFC peanut thresholds is sufficient to create a probable risk.

Conversely, the choice to consume products with no mention of peanut on the label will not remove all risk of an allergic reaction in peanut-allergic individuals. Two nutrition bars from the 2010 survey that contained detectable levels of peanut (12.6 and 1260 ppm respectively) did not list peanut on the label. While two data points are not enough to run a probabilistic simulation, the large serving size of nutrition bars demonstrates that a risk does exist for peanut-allergic consumers of these 2 products. Nutrition bars labeled as peanut free or produced in a peanut free facility did not contain detectable peanut. While only 15 peanut free samples were tested, these results are encouraging for peanut-allergic individuals and suggest a safer choice for peanut-allergic individuals who want to consume nutrition bars.

The only strategy to avoid an allergic reaction is avoidance of the food. Current food allergen regulations allow for ambiguous advisory statements to be placed on a label and more consumers are beginning to ignore these labels (Hefle et al., 2007). This study demonstrates that a risk is present to peanut-allergic consumers of nutrition bars with and without advisory labeling for peanut. Quantitative risk assessment gives risk assessors a flexible tool to help inform decisions on labeling, product release, and product recalls. A full quantitative risk assessment was not necessary to see the risk in nutrition bars with advisory labeling for peanut, but it provides justification for an advisory label beyond that provided by a simple deterministic approach. In cases with lower concentrations of peanut, such as the baking ingredient category in Table 3.1, quantitative risk assessment could detail the low risk of a product in realistic consumption scenarios and support the removal of advisory labeling from the product. The use of quantitative risk assessments by the food industry to make decisions about advisory labeling would help clarify the current situation, expand choices for allergic consumers, and reduce the potential for allergic reactions caused by packaged foods by making advisory labels more meaningful.

Conflict of Interest

The authors declare that there are no conflicts of interest.

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