Original Article

# Skin Prick Test Predictive Values for the Outcome of Cashew Challenges in Children

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***What is already known about this topic?*** Skin prick test (SPT) cut-offs with 95% positive predictive value (PPV) for food allergy are used commonly in clinical practice, but to date are limited to only a few food allergens.

***What does this article add to our knowledge?*** This article is the first to report the SPT wheal size that correlates to 95% PPV for a positive food challenge for cashew in both a population and a clinic-based cohort of children, at 10mm and 14mm respectively.

***How does this study impact current management guidelines?*** It is known that 95% PPVs can vary depending on the population they are generated from and this study has highlighted considerable variation between clinic and population based cohorts for the 95% PPV for cashew SPT and the generic SPT cut-off of 8mm used commonly in clinical practice may be too conservative for cashew.

**BACKGROUND: Cashew is a common cause of tree nut allergy in children. To date there have been few studies of diagnostic tests for cashew allergy, and positive predictive values (PPVs) for cashew as well as other tree nuts are largely extrapolated from studies of peanut allergy. How relevant these cutoffs are for cashew has not been formally explored.**

**OBJECTIVE: We aimed to establish skin prick test (SPT) wheal sizes that correlated to 95% PPV for a positive food challenge for cashew.**

**METHODS: We included all cashew oral food challenges (OFCs) conducted as part of the HealthNuts (n = 108; age, 4-6 years) and SchoolNuts (n = 37; age, 10-14 years) studies, both recruited from the community (population cohort). A second cohort of all cashew OFCs conducted at the Royal Children's Hospital (RCH) allergy center (n = 343) (2011-2016) and a private allergy clinic based at RCH (n = 43) was included via electronic medical record review (clinic cohort). The 95% PPV for cashew SPT was calculated for both cohorts.**

**RESULTS: Among the population cohort (n = 145), 62% of cashew OFCs were positive compared with 20% of the clinic cohort (n = 386). The SPT cutoff for 95% PPV derived from the population cohort was 10 mm (95% confidence interval [CI],**

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Conflicts of interest: V. McWilliam reports personal fees from speaker honorariums for Aspen Global, Abbott Australasia, and Nestle Health Sciences and personal fees from an Advisory Panel Consultancy for Nestle and Nutricia outside the submitted work. K. J. Allen was previously on the medical advisory board of Before Brands. M. L. K. Tang is on the Nestle Medical Advisory Board Oceania; is a past member of the Danone Nutricia Global Scientific Advisory Board and Medical Advisory Board ANZ; has received lecture fees from Danone Nutricia, Abbott Australasia, and Nestle; is employed by and holds stock options for Prota Therapeutics; had performed consultancy services for Deerfield Consultancy, GLC Consultancy, and Bayer; and has a patent through MCRI. The rest of the authors declare that they have no relevant conflicts of interest.

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*Abbreviations used*
*AUC- Area under the curve*
*CI- Confidence interval*
*IQR- Interquartile range*
*LR- Likelihood ratio*
*MACCS- Melbourne Allergy and Children's Centre*
*NPV- Negative predictive value*
*OFC- Oral food challenge*
*PPV- Positive predictive value*
*RCH- Royal Children's Hospital*
*sIgE- Serum IgE*
*SPT- Skin prick test*

**7.5-12.0). For the clinic cohort, the 95% PPV was 14 mm (95% CI, 9.5-unknown). An SPT wheal size of 8 mm had a PPV of 89% (95% CI, 79-95) in the population cohort and 62% (95% CI, 45-78) in the clinic cohort.**
**CONCLUSION: A higher SPT wheal size may be more appropriate than the commonly used 8 mm cutoff to guide clinical decisions around when to perform OFC for cashew.** **© 2019 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2019;■:■-■)**

***Key words:*** *Food allergy; Tree nut allergy; Cashew allergy; Population; Predictive value of tests; Skin prick test*

Tree nut allergies, such as peanut allergy, are thought to be increasing in prevalence, affecting up to 3% of Australian children.[1] Cashew has been reported as the most common tree nut allergen and the most common cause of adverse food reactions and anaphylaxis.[1-3] It has also been reported that reactions to cashew can be more severe than those to peanut.[4-7] Despite these reports, cashew allergy remains understudied.

Diagnosis of IgE-mediated food allergy is reliant on a detailed medical history and physical examination, in conjunction with diagnostic testing of IgE levels either via serum specific IgE measurements (sIgE) or skin prick testing (SPT).[8] Diagnosis of cashew allergy, like other tree nuts, can be problematic with allergy screening tests often performed for tree nuts for those with allergy to other foods and no history of prior ingestion or reaction to cashew. We have previously reported that up to half of those with egg and peanut allergy can be sensitized on SPT to tree nuts as early as 1 year of age.[1] The diagnostic gold standard is to perform an oral food challenge (OFC); however, this is time and labor intensive, limited in availability in many tertiary allergy services, and exposes the child to the risk of severe reactions.[9] This can result in patients being advised to avoid multiple tree nuts based on sensitization alone, which, given recently published evidence of the protective effect of early allergen introduction, may increase their risk of developing tree nut allergy.[10]

SPT and sIgE thresholds above which the individual has a 95% probability of being clinically allergic (95% positive predictive value [PPV]) have been used as a tool for clinicians to determine when an OFC should be performed. In Australia, SPTs are performed in preference to sIgE in most pediatric allergy clinics. PPVs are dependent on the underlying prevalence of disease (in other words, the pretest probability of food allergy), which is likely to depend on factors such as age, SPT method, and the population in which the allergy testing is being performed.[11,12] Clinic-based PPV studies often do not report the reason for challenge; however, in our experience, most OFCs in the clinical setting are undertaken to determine resolution of allergy (tolerance) rather than a diagnostic challenge. Those at higher risk of reaction, such as those with high SPT wheal sizes, are not offered an OFC, which impacts the pretest probability of food allergy.

PPVs for SPT have now been widely published for peanut, egg, milk, and sesame in both clinical and population cohorts.[13-25] There is limited data on tree nut PPVs and no data derived from population cohorts.[15,26] With the possibility of increasing prevalence and severity of cashew allergy there is an urgent need for more accurate, timely, and cost-effective diagnostic methods.

We aimed to establish the SPT wheal size that correlated with 95% PPV to a positive OFC for cashew in a population-based cohort of children and a clinic-based cohort of children. We also aimed to explore if these thresholds differ when stratified by known risk factors for cashew allergy (coexisting peanut or other food allergy, coexisting atopy, previous reaction history, age, and sex).

## METHODS

### Study populations

The population cohort of this study comprised participants who underwent cashew OFC as part of the HealthNuts and SchoolNuts studies. The HealthNuts and SchoolNuts studies are 2 large population-based allergy studies performed at the Murdoch Children's Research Institute. Both studies recruited participants from the community. Cashew OFCs were performed at 4-year-old and 6-year-old follow-up in the HealthNuts study, whereas the SchoolNuts study assessed students aged 10 to 14 years. The study populations are outlined in further detail below.

The HealthNuts study is a population-representative longitudinal study of 5276 children recruited at age 1 and followed up to age 6 years. The study methods have been described in detail previously.[27-29]

At age 4 years, all participants were followed up via questionnaire (83% participation) and those who reported a new food allergy reaction, and those who had any food allergy at age 1 year, were invited for clinic assessment that included SPT to a predetermined panel of 8 foods (milk, egg, peanut, wheat, sesame, cashew, almond, and hazelnut). All those with an SPT $\geq$1 mm were offered an OFC.

At age 6 years, the entire cohort (n = 5276) was invited to participate in questionnaire and SPT assessment. Questionnaires were mailed to all participants capturing demographic details, history of food allergy and new food reactions, common allergen exposure information, and history of asthma/wheeze and eczema. All participants were invited for an allergy/health assessment that included SPT to the same predetermined panel of 8 foods as age 4 years (60.5% participation). All those with a positive SPT ($\geq$1 mm) were offered a cashew OFC except those who had a cashew positive OFC at age 4 years and a cashew SPT $\geq$8 mm at 6 years or a recent history of IgE-mediated reaction.

The SchoolNuts study is a cross-sectional population-based study that aimed to determine the population prevalence of challenge-proven food allergy in early adolescence. The study methods have been described in detail previously.[2,30] Briefly, recruitment was via stratified random population-based sampling of schools in Melbourne (n = 9663) from 2011 to 2014. Questionnaires with phone follow-up were used to identify students with potential IgE-mediated food allergy. Students with potential IgE-mediated food allergy were invited to attend a clinic assessment for allergy testing (SPT) to a panel of 15 food allergens (egg white, cow's milk, soy, peanut, cashew, almond, hazelnut, walnut, pistachio, macadamia, pecan, brazil nut, pine nut, sesame, shellfish) and a panel of environmental allergens.

Students were eligible for OFC if they had a positive SPT result (≥3 mm) to a food that they had a history of reaction to and were currently avoiding, or that they had never eaten. OFC were not performed if participants met any one of the following criteria: (1) were sensitized (≥3 mm) and had a past history of a severe reaction requiring multiple doses of epinephrine, (2) reported an episode of anaphylaxis when older than 10 years of age, (3) reported a food reaction in the past 12 months consistent with an IgE-mediated food allergy reaction, or (4) were highly sensitized (≥8 mm) and reported a past history of reaction consistent with IgE-mediated food allergy.

The clinic cohort of this study comprised patients who had undergone a cashew OFC as part of the allergy clinic at the Royal Children's Hospital (RCH) between 2011 and 2016 and a private allergy clinic based at RCH, the Melbourne Allergy and Children's Centre (MACCS), that opened in 2015 and had an OFC database established from 2016. We conducted a retrospective analysis of all sequential open cashew OFCs undertaken at both sites. Patients undergoing cashew OFC were identified from the electronic medical records databases at both the RCH and MACCS. Cashew SPT wheal size, coexisting food allergy, current and resolved comorbid allergic disease, and food and environmental allergen sensitization were extracted via chart review. Those with their most recent cashew SPT conducted more than 3 months before OFC were excluded.

### Skin prick testing

All SPT performed at RCH, MACCS, and the HealthNuts study were performed on the child's back, whereas the SchoolNuts study used the volar aspect of the student's forearm. Wheal size was measured after 15 minutes and calculated by subtracting the negative control from the average of the longest diameter and the diameter perpendicular to it. SPTs for MACCS and RCH were performed with Quintip device (Stallergenes, Antony, France) and the HealthNuts and SchoolNuts studies were performed with single-tine lancets (Stallergenes) using cashew extract along with a positive and negative saline control. Extracts for the HealthNuts and SchoolNuts studies were ALK-Abello SA, Madrid, Spain, and RCH and MACCS Hollister-Stier, Stallergenes, Antony, France. All SPTs were performed within 3 months before cashew OFC.

## ORAL FOOD CHALLENGES

### Criteria for undergoing cashew oral food challenges

HealthNuts participants with a cashew SPT ≥1 mm or a parent-reported reaction consistent with an IgE-mediated allergy were invited for a clinic appointment with a specialist allergy nurse and OFC. The low SPT cutoff for sensitization was applied in the HealthNuts study to ensure that all potential cases of food allergy were detected. Cashew OFCs were offered at both the 4-year-old and 6-year-old follow-up.

SchoolNuts participants with a parent-reported history of an adverse food reaction consistent with IgE-mediated food allergy were invited to participate in an allergy assessment that included cashew SPT. Those with a cashew SPT ≥3 mm were invited for cashew OFC.

### Cashew OFC protocols

OFC dosage protocols for all sites were consistent with those of the Australian Society of Clinical Immunology and Allergy using graded, incremental doses administered at 15- to 20-minute intervals with a top dose of 2 teaspoons of crushed cashew. OFC protocols for the HealthNuts and SchoolNuts studies have been previously described.[2,31] An OFC was deemed positive if it met at least one of the following predefined criteria: (1) 3 or more concurrent noncontact urticaria lasting at least 5 minutes; (2) severe persistent vomiting; (3) peri-oral or peri-orbital angioedema; or (4) anaphylaxis (evidence of circulatory or respiratory involvement) within 2 hours of the last challenge dose in the presence of IgE sensitization. For the SchoolNuts study, additional criteria based on persistent subjective symptoms in the upper airways or the gastrointestinal tract were included because of the older age of participants. In the absence of objective signs, if subjective symptoms (itchy mouth or throat, abdominal pain or nausea, tightness in throat, difficulty talking, or difficulty breathing) continued up to the timing of the next dose, the previous dose was repeated. If the above symptoms persisted for a total of more than 40 minutes or reoccurred on 2 doses, the challenge was considered positive.

OFCs were deemed negative at all sites if a patient or participant tolerated a top dose of 2 teaspoons of crushed cashew nut on the day of the OFC and did not report any positive reactions during continued daily intake of 2 teaspoons at home in the week after the OFC.

RCH and MACCS cashew OFCs were performed in a clinical allergy setting with the recommendation to undertake an OFC based on the clinical expertise of the attending allergist. In this setting, OFCs are not routinely performed if there is a high likelihood of reaction such as those with high-level sensitization or a recent history of reaction. Therefore, OFCs are largely performed to determine tolerance rather than diagnose food allergy. Occasionally, an OFC may be performed despite a highly positive SPT if there is a recent history of tolerance to a partial ingestion of cashew. All RCH and MACCS OFCs had symptoms retrospectively reassessed and those not meeting OFC stopping criteria as outlined by PRACTALL guidelines were excluded (n = 2).[32]

## STATISTICAL METHODS

Continuously valued variables are summarized using means (and standard deviations) or medians (and range), with frequencies reported as percentages with 95% confidence intervals (CIs) based on the binomial distribution. A 2-sample comparison of the prevalence of positive OFC within the clinic cohorts showed little evidence that these samples were drawn from populations with different prevalence of cashew allergy ($P = .24$) and similarly for the population-based cohorts ($P = .24$). There was also no evidence against the null hypothesis that the magnitude of the relationship between SPT wheal size and positive OFC was the same for (1) RCH and MACCS; and (2) HealthNuts and SchoolNuts (Table E1, available in this article's Online Repository at www.jaci-inpractice.org), therefore these were combined for all analyses.

There was no evidence against the null hypothesis of a linear relationship between the SPT wheal size and the log-odds of a positive OFC based on data from any of the cohorts, so we assumed linear association throughout our analyses (data not shown).

In light of these results, we combined data for the 2 clinic cohorts RCH and MACCS to form a clinic cohort and for the 2 population-based cohorts HealthNuts and SchoolNuts to form a population cohort for all analyses. All analyses were conducted for the population and clinic cohorts separately. The capacity of the cashew SPT to diagnose OFC-confirmed cashew allergy was assessed using receiver operating characteristic curves and the area under the curve (AUC) was used to quantify the accuracy of the

**TABLE I.** Demographic and clinical characteristics, stratified by cashew OFC cohort

| | Clinic cohort (n = 386) | | Population cohort (n = 145) | |
|---|---|---|---|---|
| | RCH (n = 343) | MACCS (n = 43) | HealthNuts (n = 108) | SchoolNuts (n = 37) |
| Gender, male, n (%) | 210 (61.2) | 26 (60.5) | 62 (57.4) | 22 (59.5) |
| Mean age at OFC, y (SD) | 8.0 (4.4) | 7.2 (4.9) | 5.2 (1.1) | 12.9 (1.1) |
| Challenge outcome, n (%) | | | | |
| Positive | 65 (18.9) | 12 (27.9) | 68 (62.9) | 22 (59.4) |
| Negative | 260 (75.8) | 31 (72.1) | 39 (36.1) | 12 (32.4) |
| Equivocal | 14 (4.1) | 0 | 1 (0.9) | 3 (5.4) |
| Missing | 4 (1.2) | 0 | 0 | 0 |
| Median SPT, mm (interquartile range) | | | | |
| Overall SPT | 3 (1-5) | 3 (1-4) | 8 (4-12) | 6 (2-9) |
| SPT, positive challenge | 6 (4-8) | 6 (4-8) | 11 (8-14) | 8 (6-10) |
| SPT, negative challenge | 3 (0-4) | 3 (0-4) | 4 (0-6) | 1 (0-4) |
| Reason for cashew OFC, n (%) | | | | |
| Not cashew sens (<3 mm) or allergic but allergy to other nut/s | 35 (10.2) | 3 (7.0) | 1 (0.9) | 5 (13.5) |
| Not cashew sens (<3 mm) or allergic, other non-nut allergies | 24 (7.0) | 5 (11.6) | 3 (2.8) | 0 |
| Not cashew sens (<3 mm) or allergic, no other food allergies | 25 (7.3) | 1 (2.3) | 14* (13.0) | 0 |
| Sensitized 3-8 mm, never eaten cashew | 144 (42.1) | 16 (37.2) | 29 (26.9) | 6 (16.2) |
| Sensitized >8 mm, never eaten cashew | 20 (5.9) | 2 (4.7) | 50 (46.3) | 11 (29.7) |
| Previous cashew reaction | 70 (20.5) | 11 (25.6) | 9 (8.3) | 14 (37.8) |
| Reaction to an unknown trigger | 14 (4.1) | 5 (11.7) | 0 | 0 |
| Unable to determine OFC reason | 10 (2.9) | 0 | 2 (1.9) | 1 (2.7) |
| Food allergy details, n (%) | | | | |
| No other food allergies | 124 (29.0) | 15 (34.9) | 58 (53.7) | 13 (35.1) |
| Coexisting food allergy | 220 (64.0) | 25 (58.1) | 50 (46.3) | 24 (64.9) |
| Peanut allergy | 76 (22.2) | 8 (18.8) | 23 (21.3) | 11 (29.7) |
| Other tree nut† | 36 (10.5) | 3 (7.0) | 2 (1.9) | 10 (27.0) |
| Egg allergy | 54 (15.7) | 8 (18.6) | 11 (10.2) | 2 (5.4) |
| Other allergies‡ | 53 (15.5) | 9 (20.9) | 13 (12.0) | 1 (2.7) |
| Food sensitization details, n (%) | | | | |
| Peanut 3-8 mm | 5 (4.3) | 1 (4.3) | 3 (6.8) | 1 (4.2) |
| Peanut >8 mm | 5 (17.2) | 1 (14.3) | 5 (19.2) | 1 (20.0) |
| Any tree nut 3-8 mm§ | 80 (68.4) | 18 (78.3) | 31 (70.5) | 11 (45.9) |
| Any tree nut >8 mm¶ | 18 (62.1) | 6 (85.7) | 19 (10.5) | 3 (60.0) |
| Egg 3-8 mm | 4 (3.4) | 0 | 3 (60.0) | 1 (4.2) |
| Egg >8 mm | 0 | 0 | 0 | 0 |
| Sesame 3-8 mm | 8 (6.8) | 2 (8.7) | 3 (6.8) | 3 (12.5) |
| Sesame >8 mm | 5 (17.2) | 0 | 1 (3.9) | 0 |
| Milk 3-8 mm | 0 | 0 | 1 (3.9) | 2 |
| Milk >8 mm | 0 | 0 | 0 | 0 |
| Shellfish 3-8 mm | 1 (3.4) | 0 | 3 (6.8) | 0 |
| Shellfish >8 mm | 0 | 0 | 0 | 1 (20.0) |
| Allergic disease history, n (%)# | | | | |
| Current eczema | 194 (56.6) | 17 (39.5) | 60 (55.6) | 20 (54.1) |
| Current asthma | 197 (57.4) | 30 (69.8) | 29 (26.9) | 14 (37.8) |
| Current rhinitis | 157 (45.8) | 27 (62.8) | 16 (14.8) | 7 (18.9) |

*MACCS*, Melbourne Allergy and Children's Centre; *OFC*, oral food challenge; *RCH*, Royal Children's Hospital; *SPT*, skin prick test.

*HealthNuts study protocol was to offer all participants with SPT ≥1 mm an OFC to ensure that all potential cases of food allergy were captured.

†Tree nut allergy: defined as a positive OFC or history of reaction and sensitized (≥3 mm). Does not include those with SPT ≥8 mm defined as probable allergy in the HealthNuts (n = 19) and SchoolNuts studies (n = 3). Individual tree nut allergy details—almond = 2, hazelnut = 8, macadamia = 7, pecan = 4, pistachio = 14, and walnut = 29.

‡Other food allergies: milk = 26, sesame = 23, fish = 11, shellfish = 4, wheat = 4, and kiwifruit = 9.

§Tree nut sensitization 3-8 mm: almond = 18, hazelnut = 30, macadamia = 11, pecan = 16, pistachio = 72, and walnut = 44.

¶Tree nut sensitization >8 mm: almond = 3, hazelnut = 15, macadamia = 1, pecan = 5, pistachio = 21, and walnut = 15.

#Current eczema, current asthma, current rhinitis = parent report of doctor-diagnosed eczema, asthma, and rhinitis.

test. Logistic regression was used to model the association between the SPT wheal size in millimeters and the risk of cashew allergy. The assumption that the logarithm of the odds of food allergy was linearly related to the SPT wheal size was assessed using the likelihood ratio (LR) test to compare the linear model with a more general "saturated" model that made no assumption about the shape of the relationship between SPT wheal size and the risk of food allergy. A fitted probability of food allergy was produced for each study participant given their SPT wheal size and used to replace the observed binary outcome in the standard formula for the PPV, that is, a modeled PPV for each level of SPT wheal size was produced by taking the average of the fitted probability of cashew allergy for all infants with an SPT wheal size of greater than the given level. This method produces a smooth nondecreasing curve for the PPV across the range of SPT wheal sizes, therefore overcoming fluctuations (sampling variation) in the observed proportion of infants with cashew allergy for increasing SPT. To quantify the precision of estimation of the PPVs, we used bootstrapping, a method of deriving SEs and CIs from repeated samples drawn with replacement from the original dataset. One hundred bootstrap replications were used to determine the variability of parameter estimates and to calculate 95% CIs for the thresholds with 95% PPVs to food allergy.

The analysis was stratified on known risk factors for food allergy/positive tree nut challenge: sex, coexisting peanut allergy, coexisting tree nut allergies, coexisting non-nut allergies, other allergic disease, and previous reaction history. All analyses were done using Stata 15.0 (release 15.0; StatCorp, College Station, Tex).

## ETHICS

Approval to conduct the HealthNuts study was obtained from the Victorian State Government Office for Children (reference no. CDF/07/492), the Victorian State Government Department of Human Services (reference no. 10/07), and the RCH Human Research Ethics Committee (reference no. 27047). For the SchoolNuts study, ethics approval was obtained from the RCH Human Research Ethics Committee (HREC number 31079), the Department of Education, and Early Childhood and the Catholic Education Office. All parents provided written informed consent.

Ethics approval for the use of deidentified clinic data from RCH and MACCS was obtained from the RCH Human Research Ethics Committee (HREC number 37076A).

## RESULTS

### Study populations

Demographic and clinical characteristics stratified by the cashew OFC cohort are outlined in Table I. A total of 386 cashew OFCs were performed in a clinical setting (RCH: n = 343, MACCS: n = 43) and 145 cashew OFCs were performed as part of the population-based studies (HealthNuts: n = 108, SchoolNuts: n = 37). Age stratified demographic and clinical characteristics for the clinic cohort are outlined in Table E2 (available in this article's Online Repository at www.jaci-inpractice.org).

### Results of cashew OFC

Among the clinic cohort, 19.9% (n = 77) of cashew OFCs were positive compared with 62.1% (n = 90) of the population cohort challenges. The most common reason for cashew OFC among both cohorts was cashew sensitization without a history of cashew ingestion, 46.6% of those in the clinic cohort and 67.7% of those among the population cohort. Among the population cohort, 91% (n = 61) of those with an SPT ≥8 mm and no history of cashew exposure had a positive cashew OFC compared with 59% (n = 22) of those among the clinic cohort.

**TABLE II.** Characteristics of positive cashew oral food challenges, stratified by cohort

| | Clinic cohort (n = 77) | Population cohort (n = 90) |
|---|---|---|
| Mean age at OFC, y (SD) | 7.8 (4.3) | 7.1 (3.5) |
| Median SPT, mm (interquartile range) | 6.0 (4-8) | 10.0 (7-13) |
| OFC top dose | | |
| Crumb/smear | 0 | 47* (52.2) |
| 1/16 | 3 (3.9) | 9 (10.0) |
| 1/8 tsp | 1 (1.3) | 11 (12.2) |
| 1/4 tsp | 11 (14.3) | 8 (8.9) |
| 1/2 tsp | 6 (7.8) | 10 (11.1) |
| 1 tsp | 22 (28.6) | 1 (1.1) |
| 2 tsp | 25 (32.5) | 4 (4.4) |
| Missing | 9 (11.7) | 0 |
| Symptoms | | |
| Skin (pruritus, hives, rash) | 58 (75.4) | 54 (60.0) |
| Angioedema | 16 (20.8) | 55 (61.1) |
| Oropharyngeal (sneezing, itchy mouth/throat, eye/nose rubbing, rhinorrhea) | 29 (37.7) | 44 (48.9) |
| Respiratory (wheeze, cough, stridor) | 18 (23.4)† | 12 (13.3)‡ |
| Gastrointestinal (nausea, abdo pain, vomiting) | 37 (48.1) | 32 (35.6) |
| Cardiovascular (tachycardia, dizziness, BP drop) | 0 | 0 |
| Other (distress, decreased activity) | 3 (3.9) | 2 (1.1) |
| Treatment | | |
| Nil | 15 (19.5) | 67 (77.4) |
| Antihistamine | 60 (77.9) | 20 (22.2) |
| Epinephrine | 8 (10.4) | 1 (1.1) |
| Salbutamol | 3 (3.9) | 5 (5.6) |
| Steroid | 1 (1.3) | 0 |
| Other | 0 | 0 |

*OFC*, Oral food challenge; *SPT*, skin prick test.
*Population cohort reaction details to crumb/smear dose: skin = 1, angioedema = 8, oropharyngeal = 19, respiratory = 3, gastrointestinal = 15, and other = 3.
†Clinic cohort respiratory symptom details: 8 = intermittent cough, 2 = throat clearing, 4 = wheeze, and 4 = persistent cough.
‡Population cohort respiratory symptom details: 9 = intermittent cough, 2 = throat clearing, and 1 = wheeze.

### Characteristics of the positive cashew OFCs

Characteristics of positive cashew challenges stratified by cohort are outlined in Table II. Among those in the clinic cohort with a positive cashew challenge (n = 77), the most common symptoms were skin (75%), gastrointestinal (48%), and oropharyngeal (38%). Among those in the population cohort with a positive cashew challenge (n = 90), the most common symptoms were angioedema (61%), skin (60%), and oropharyngeal (50%). There were marked differences in reported treatments between the clinic and population cohorts. Among those with a positive cashew OFC in the population cohort (n = 90), 77% required no treatment, 22% antihistamine, and 5.6% salbutamol. Among those with a positive cashew OFC in

**TABLE III.** Details of the participants with a positive OFC that required epinephrine (n = 9)

| | Cohort | Age at OFC (y) | Cashew SPT (mm) | OFC reason | Other coexisting food allergy | Other allergic disease | OFC top dose (g) |
|---|---|---|---|---|---|---|---|
| 1 | RCH | 12 | 1 | Previous IgE-mediated reaction | None | Eczema | 10 |
| 2 | RCH | 3 | 2 | Reaction to unknown trigger | None | Eczema | 10 |
| 3 | MACCS | 10 | 4 | Previous IgE-mediated reaction | None | Rhinitis | 10 |
| 4 | RCH | 3 | 5 | Previous anaphylaxis to cashew | None | Eczema | NA |
| 5 | RCH | 8 | 5 | Sensitized, never eaten | Sesame | Eczema | NA |
| 6 | RCH | 2 | 6 | Sensitized, never eaten | Other tree nut | Eczema | 2.5 |
| 7 | RCH | 9 | 9 | Sensitized, never eaten | Milk | Eczema | 10 |
| 8 | RCH | 16 | 12 | Sensitized, never eaten | Milk | Rhinitis | 2.5 |
| 9 | HealthNuts | 7 | 17.5 | Sensitized, never eaten | Sesame | Eczema | 0.31 |

*MACCS*, Melbourne Allergy and Children's Centre; *OFC*, oral food challenge; *RCH*, Royal Children's Hospital; *SPT*, skin prick test.

the clinic cohort (n = 77), 19.5% required no treatment, 78% antihistamine, 3.4% salbutamol, and 1.3% oral steroid.

Among the 168 positive cashew challenges in the population and clinic cohorts, 9 children required epinephrine (5.3%). Interestingly, the majority of these had an SPT that was lower than 10 mm and more than half had never ingested cashew. Table III summarizes the details of the 9 patients requiring epinephrine. Five had no history of cashew ingestion and 3 had a previous history of cashew reaction (1 anaphylaxis), and cashew SPT wheal sizes ranged from 1 to 18 mm. Five had coexisting food allergy (milk 2, sesame 2, and another tree nut 1).

The majority of reactions among the population cohort occurred with a crumb (52%, n = 47), whereas reaction doses in the clinic population tended to be higher with 29 of 77 (38%) occurring at the top dose (2 teaspoons) (Table II).

## Diagnostic capacity of cashew SPT for challenge confirmed cashew allergy

There were marked differences in the prevalence of cashew allergy between the population- and clinic-based cohorts, 62.1% and 19.5%, respectively (see Table I), which we believe is due to differences in the selection of participants for cashew challenge between the 2 cohorts. Patients in the allergy services from which the clinic cohort is drawn are less likely to have undergone an OFC if the attending clinician determines that they are more likely to have a positive result, such as patients with high-level sensitization (>8 mm SPT). This is not the case for the population-based cohorts, where OFCs were offered to all participants with a detectable SPT (wheal size ≥1 mm except those with a recent history of a reaction consistent with IgE-mediated food allergy). This is further supported by the difference in median SPT between the 2 cohorts (clinic cohort = 3 mm; interquartile range [IQR], 1-5; and population cohort = 7.5 mm; IQR, 4-11). The SPT threshold with 95% PPV for cashew allergy also varied between the population- and clinic-based cohorts, 10 mm or greater (95% CI, 7.5-12.0) and 14 mm or greater (95% CI, 9.5-unknown), respectively. AUC was 0.89 (95% CI, 0.83-0.95) for the population cohort and 0.81 (0.76-0.87) for the clinic cohort (Figure 1). SPT thresholds with 95% PPV for cashew allergy, along with sensitivity, specificity, negative predictive value (NPV), positive, and negative LR at the reported thresholds are presented in Table IV. A 50% NPV could not be generated for the clinic cohort, and among the population cohort, a 50% NPV of 10 mm or less (95% CI, 9-14) was determined.

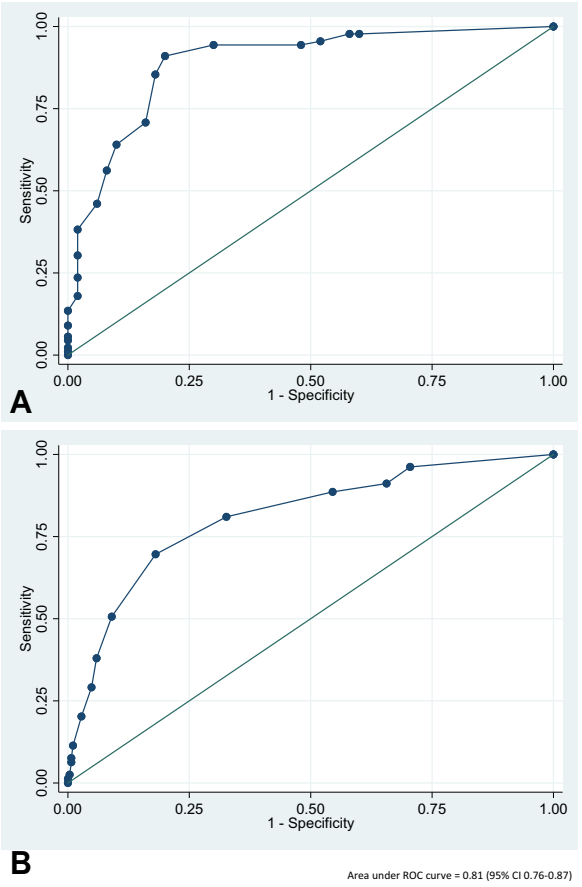


**FIGURE 1. A**, ROC curve for cashew SPT wheal size, population cohort. **B**, ROC curve for cashew SPT wheal size, clinic cohort. Area under ROC curve = 0.81 (95% CI, 0.76-0.87). *CI*, Confidence interval; *ROC*, receiver operating characteristic; *SPT*, skin prick test.

There were 11 participants in the population cohort who were defined as cashew allergic but did not have an OFC performed (n = 11, sensitized and recent reaction consistent with IgE-mediated food allergy). We undertook a sensitivity analysis including these participants and determined a 95% PPV of 10 mm (95% CI, 8-12).

When stratified by risk factors for cashew allergy, 95% PPVs could not be generated for the clinic cohort. For the population

**TABLE IV.** Diagnostic capacity of SPTs to challenge-confirmed cashew allergy

| | 95% PPV, mm (95% CI) | NPV, % (95% CI) | Sensitivity, % (95% CI) | Specificity, % (95% CI) | Positive LR (95% CI) | Negative LR (95% CI) | AUC (95% CI) |
|---|---|---|---|---|---|---|---|
| Population cohort (HealthNuts and SchoolNuts) | 10 (7.5-12) | 47.5 (37.3-57.8) | 42.9 (32.5-53.7) | 97.9 (88.9-99.9) | 20.6 (2.9-145.2) | 0.6 (0.5-0.7) | 0.89 (0.83-0.95 |
| Clinic cohort (RCH and MACCS) | 14 (9.5-unknown) | 79.7 (75.1-83.7) | 7.6 (2.8-15.8) | 99.3 (97.5-99.9) | 10.9 (2.2-53.1) | 0.9 (0.87-0.99) | 0.81 (0.76-0.87) |

*AUC*, Area under the curve; *CI*, confidence interval; *LR*, likelihood ratio; *MACCS*, Melbourne Allergy and Children's Centre; *NPV*, negative predictive value; *PPV*, positive predictive value; *RCH*, Royal Children's Hospital; *SPT*, skin prick test.

**TABLE V.** Diagnostic capacity of commonly applied SPT thresholds (<3 mm and >8 mm) to challenge-confirmed cashew allergy

| | SPT wheal size (mm) | PPV, % (95% CI) | NPV, % (95% CI) | Sensitivity, % (95% CI) | Specificity, % (95% CI) | Positive LR (95% CI) | Negative LR (95% CI) | AUC (95% CI) |
|---|---|---|---|---|---|---|---|---|
| Population cohort | 3 | 76.6 (67.6-84.1) | 85.7 (67.3-96.0) | 95.5 (88.9-98.8) | 48.0 (33.7-62.6) | 1.84 (1.40-2.41) | 0.09 (0.03-0.25) | 0.72 (0.64-0.79) |
| | 8 | 88.7 (79.0-95.0) | 61.8 (49.2-73.3) | 70.8 (60.2-79.9) | 84.0 (70.9-92.8) | 4.42 (2.31-8.47) | 0.35 (0.25-0.49) | 0.77 (0.70-0.84) |
| Clinic cohort | 3 | 30.8 (24.9-37.3) | 93.6 (88.1-97.0) | 88.6 (79.5-94.7) | 45.5 (39.6-51.4) | 1.63 (1.42-1.85) | 0.25 (0.13-0.47) | 0.67 (0.63-0.72) |
| | 8 | 62.2 (44.8-77.5) | 83.0 (78.5-86.9) | 29.1 (19.4-40.4) | 95.1 (92.0-97.3) | 6.0 (3.2-11.1) | 0.75 (0.65-0.86) | 0.62 (0.57-0.67) |

*AUC*, Area under the curve; *CI*, confidence interval; *LR*, likelihood ratio; *NPV*, negative predictive value; *PPV*, positive predictive value; *SPT*, skin prick test.

cohort some differences were noted but with overlapping CIs there is little evidence to support differences in 95% PPVs between the groups at the population level (Table E3, available in this article's Online Repository at www.jaci-inpractice.org). There was no evidence of differences in population-level 95% PPVs based on analyses after stratification on other known risk factors for food allergy or age (data not shown).

The commonly applied SPT thresholds of less than 3 and 8 mm and above are presented in Table V. The 3-mm threshold performed as expected with high sensitivity and low specificity for the population- and clinic-based cohorts. Sensitivity and specificity for other SPT wheal sizes are shown in Table E4 (available in this article's Online Repository at www.jaci-inpractice.org).

## DISCUSSION

To our knowledge, this is the largest series of OFCs for cashew allergy reported and the first study to report 95% PPVs for cashew SPT. We found the SPT threshold for 95% PPV among a clinic cohort of 14 mm and a population cohort of 10 mm with marked differences in cashew allergy prevalence between the clinic and population cohorts.

The strengths of this study are the large number of cashew OFCs and the development of SPT thresholds with 95% PPVs for cashew allergy using data contributed from population- and allergy clinic-based samples of children in the same city. The population-based cohorts provide cashew OFC outcomes based on predetermined stopping criteria irrespective of SPT wheal size.

There are also a number of limitations. Similar to other studies based on data from allergy clinics, the results of our analyses of data from the clinic-based cohorts are affected by 2 types of selection bias because patients are likely to have (1) more severe allergic disease when compared with individuals from population cohorts of children; and (2) been offered OFC only if the allergist deemed them to be at low risk of reacting. As a result, the clinical cohort has a limited number of OFCs represented with high-level sensitization (>8 mm), a lower median SPT, and the majority of reactions were to the top OFC dose. The clinic cohort data are also likely to have suffered from a type of information bias, because details were obtained from a retrospective record review and OFC outcomes were not standardized. All challenge outcomes were, however, reviewed and those that did not meet the PRACTALL criteria[32] for a positive OFC were excluded from analysis. Both the population and clinic cohorts have a limited number of cashew OFCs performed in children less than 2 years of age that is the age that children typically present with food allergy and when 95% PPV estimates for cashew SPT would be most useful to guide cashew introduction recommendations.

It should also be noted when making comparisons between the 2 cohorts in our study that there are SPT device and extract differences. Our center has previously shown that there is little variation between the Quintip and single-tine lancet SPT devices.[33] However, performance variability between the 2 extracts is unknown and was not undertaken as part of this study.

Comparison of our thresholds for cashew SPT response with other studies is difficult due to the limited number of studies to date. One study reported that SPT wheal diameters ≥8 mm predicted a positive food challenge with >95% accuracy individually for cashew, hazelnut, walnut, and sesame. This study was, however, from a highly selected clinic population and included lower numbers of cashew OFC (n = 89).[15] A more recent study that retrospectively reported outcomes of tree nut challenges from the University of Michigan Allergy clinic included 28 cashew challenges and fitted a single predictive model that combined cashew and pistachio OFCs to generate a 50% NPV of 6.5 mm.

If the sensitivity and specificity of SPT thresholds for OFC allergy are assumed not to vary between populations, then PPVs and NPVs will be dependent on the underlying prevalence of food allergy. It has been previously argued that PPVs for sIgE derived from clinic populations cannot be meaningfully applied to general populations, although this question has not yet been addressed using relevant data on SPT wheal size.[12] Our data demonstrate a similar variation of PPVs based on different populations and highlight that PPVs based on clinic cohorts are more likely to include those with a lower prevalence of food

allergy due, most likely, to selection bias related to physician decisions around who is offered an OFC, and therefore generate artificially higher PPV thresholds. On the basis of our results, we propose that an SPT wheal size of 10 mm may be more appropriate than the commonly used 8 mm cutoff to guide clinical decisions around when to perform OFC for cashew. However, our results also support the limitation of SPT to predict reaction severity with the majority of those requiring epinephrine having an SPT <10mm.

It has been proposed that LRs, which compare the probability of a positive SPT result in patients with and without food allergy, should be the tool of choice to determine the probability of allergic disease as they have the potential to be independent of the disease prevalence.[34] The calculation and appropriate application of LRs does, however, require several steps, which may explain why this procedure has received limited use in clinical practice. In the present study, we have included both positive and negative LRs to assist clinicians with applying our data to their own settings.

## CONCLUSION

Within a population-based cohort we have established a 95% PPV for cashew SPT of 10 mm. It is known that 95% PPVs can vary depending on the population they are generated from and this study has demonstrated considerable variability between clinic- and population-based cohorts for the 95% PPV for cashew SPT. To improve tree nut allergy diagnosis and management, further work is required using data based on OFC-confirmed outcomes with OFC offered to all sensitized individuals irrespective of wheal size to generate 95% PPVs for the additional tree nuts.

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## ONLINE REPOSITORY

**TABLE E1.** Estimated odds ratios of positive OFC for a 1 mm increase in SPT wheal size from study-specific logistic regression models

| | Estimate | 95% confidence interval | *P* value for the null hypothesis that the true parameter value is 1.00 |
|---|---|---|---|
| RCH | 1.50 | 1.34-1.69 | <.001 |
| MACCS | 1.74 | 1.18-2.56 | .005 |
| HealthNuts | 1.44 | 1.25-1.66 | <.001 |
| SchoolNuts | 1.67 | 1.21-2.32 | .002 |
| Ratio: MACCS to RCH | 1.16 | 0.77-1.73 | .48 |
| Ratio: SN to HN | 1.16 | 0.81-1.65 | .41 |

The coefficients from study-specific logistic regression models of positive OFC on SPT wheal size were estimated. There was no evidence against the null hypothesis that the magnitude of the relationship between positive OFC and SPT wheal size was the same for (1) RCH and MACCS; and (2) HealthNuts and SchoolNuts. In both cases the ratio of estimate log-odds ratios for a 1 mm increase in SPT wheal size was 1.16. The *P* values for the null hypothesis that the population ratio is 1.00, that is, the relationship is the same for RCH and MACCS, and similarly for HealthNuts and SchoolNuts, are .48 and .41, respectively.
*HN*, HealthNuts; *MACCS*, Melbourne Allergy and Children's Centre; *OFC*, oral food challenge; *RCH*, Royal Children's Hospital; *SN*, SchoolNuts; *SPT*, skin prick test.

**TABLE E2.** Demographic and clinical characteristics of the clinic cohort (RCH and MACCS), stratified by age

| | 0-2 y (n = 50) | 3-9 y (n = 304) | 10-14 y (n = 137) | 15-18 y (n = 40) |
|---|---|---|---|---|
| Gender, male, n (%) | 36 (72.0) | 107 (54.6) | 65 (63.7) | 28 (75.7) |
| Challenge outcome | | | | |
| Positive | 11 (22.0) | 39 (19.9) | 22 (21.6) | 5 (13.2) |
| Negative | 35 (70.0) | 150 (76.5) | 74 (72.6) | 32 (84.2) |
| Equivocal | 3 (6.0) | 5 (2.6) | 5 (4.9) | 1 (2.6) |
| Missing | 1 (2.0) | 2 (1.0) | 1 (1.0) | 0 |
| Median SPT, mm (interquartile range) | 3 (3-4) | 3 (0-5) | 3 (1-5) | 4 (2-5) |
| Reason for cashew OFC, n (%) | | | | |
| Not cashew sens (<3 mm) or allergic but allergy to other nut/s | 4 (8.0) | 24 (12.2) | 8 (7.9) | 2 (5.3) |
| Not cashew sens (<3 mm) or allergic, other non-nut allergies | 4 (8.0) | 12 (6.1) | 11 (10.9) | 2 (5.3) |
| Not cashew sens (<3 mm) or allergic, no other food allergies | 0 | 16 (8.2) | 7 (6.9) | 3 (7.9) |
| Sensitized 3-8 mm, never eaten cashew | 34 (68.0) | 75 (38.3) | 36 (35.6) | 15 (39.5) |
| Sensitized >8 mm, never eaten cashew | 2 (4.0) | 11 (5.6) | 8 (7.9) | 1 (2.6) |
| Previous cashew reaction | 4 (8.0) | 40 (20.0) | 24 (23.8) | 13 (34.2) |
| Reaction to an unknown trigger | 1 (2.0) | 11 (5.6) | 6 (5.9) | 1 (2.6) |
| Unable to determine OFC reason | 1 (2.0) | 7 (3.6) | 1 (1.0) | 1 (2.6) |
| Food allergy details, n (%) | | | | |
| No other food allergies | 5 (10.0) | 82 (41.8) | 37 (36.3) | 15 (39.5) |
| Coexisting food allergy | | | | |
| Peanut allergy | 8 (16.0) | 37 (18.9) | 28 (27.5) | 11 (28.9) |
| Other tree nut | 7 (14.0) | 21 (10.7) | 9 (8.8) | 2 (5.6) |
| Egg allergy | 20 (40.0) | 27 (13.8) | 12 (11.8) | 3 (7.9) |
| Other allergies* | 10 (25.0) | 28 (9.2) | 16 (11.7) | 7 (17.5) |
| Allergic disease history, n (%)† | | | | |
| Current eczema | 37 (77.1) | 110 (52.3) | 47 (47.0) | 15 (46.0) |
| Current asthma | 8 (16.6) | 76 (39.0) | 51 (51.0) | 17 (46.0) |
| Current rhinitis | 7 (14.6) | 89 (46.3) | 72 (72.0) | 25 (67.6) |

*MACCS*, Melbourne Allergy and Children's Centre; *OFC*, oral food challenge; *RCH*, Royal Children's Hospital; *SPT*, skin prick test.
*Other food allergies: milk = 26, sesame = 23, fish = 11, shellfish = 4, wheat = 4, and kiwifruit = 9.
†Current eczema, current asthma, current rhinitis = parent report of doctor-diagnosed eczema, asthma, and rhinitis.

**TABLE E3.** Diagnostic capacity of SPTs to challenge confirmed cashew allergy stratified by risk factors for cashew allergy, population cohorts (HealthNuts and SchoolNuts)

| Risk factor | 95% PPV, mm (95% CI) | Sensitivity, % (95% CI) | Specificity, % (95% CI) | Positive LR | Negative LR |
|---|---|---|---|---|---|
| Sex | | | | | |
| Male (n = 84) | 13 (7.5-16.0) | 22.4 (12.5-35.3) | 97.9 (88.9-99.9) | 10.8 (1.5-79.3) | 0.79 (0.69-0.92) |
| Female (n = 61) | 8 (5.35-9.0) | 66.7 (51.0-80.0) | 96.8 (83.3-99.9) | 20.7 (2.9-144) | 0.34 (0.23-0.52) |
| Current food allergy | | | | | |
| Yes (n = 75) | 9 (7.0-11.0) | 58.3 (44.9-70.9) | 92.0 (78.6-98.3) | 7.4 (2.4 (22.4) | 0.45 (0.33-0.62) |
| No (n = 65) | 13 (7.0-16.0) | 20.5 (10.0-36.0) | 97.5 (86.8-99.9) | 8.2 (1.1-62.6) | 0.82 (0.69-0.96) |
| Type food allergy | | | | | |
| None (n = 70) | 13 (7.0-16.0) | 32.6 (19.1-48.5) | 97.3 (85.8-99.9) | 8.2 (1.1-62.6) | 0.82 (0.69-0.96) |
| Any nut allergy (n = 58) | 8 (5.0-10.0) | 65.9 (50.0-79.5) | 93.1 (77.2-99.2) | 9.6 (2.5-37) | 0.34 (0.24-0.56) |
| Any non-nut allergy (n = 17) | 11 (4.0-16.0) | 25 (7.3-52.4) | 91.7 (61.5-99.8) | 3 (0.4, 23.5) | 0.82 (0.57, 1.14) |
| Past history of cashew reaction | | | | | |
| Yes (n = 23) | Unable to achieve | | | | |
| No (n = 122) | 10 (7.5-11.5) | 47.7 (36.8-58.7) | 95.3 (86.9-99.0) | 10.2 (3.3-31.4) | 0.55 (0.45-0.65) |

*CI*, Confidence interval; *LR*, likelihood ratio; *PPV*, positive predictive value; *SPT*, skin prick test.

**TABLE E4.** Cashew OFC outcomes by SPT wheal size, stratified by OFC cohort

| | Clinical cohort (RCH/MACCS) (n = 370) | | | | Population cohort (HealthNuts/SchoolNuts) (n = 142) | | | |
|---|---|---|---|---|---|---|---|---|
| SPT wheal size (mm) | Cashew tolerant, n (%) | Cashew allergic, n (%) | Sensitivity (%) | Specificity (%) | Cashew tolerant, n (%) | Cashew allergic, n (%) | Sensitivity (%) | Specificity (%) |
| 0 | 85 (96.6 | 3 (3.4) | 100.0 | 0 | 20 (90.9) | 2 (9.1) | 100.0 | 0 |
| 1 | 14 (77.8) | 4 (22.2) | 96.2 | 29.5 | 1 (100.0) | 0 | 97.8 | 40.0 |
| 2 | 32 (94.1) | 2 (5.9) | 91.4 | 34.4 | 3 (60.0 | 2 (40.0) | 97.8 | 42.0 |
| 3 | 63 (91.3) | 6 (8.7) | 88.6 | 45.5 | 2 (66.7) | 1 (33.3) | 95.5 | 48.0 |
| 4 | 42 (82.4) | 9 (17.6) | 81.0 | 67.4 | 9 (100) | 0 | 94.4 | 52.0 |
| 5 | 26 (63.4) | 15 (36.6) | 69.6 | 81.9 | 5 (62.5) | 3 (37.5) | 94.4 | 70.0 |
| 6 | 9 (47.3) | 10 (52.6) | 50.6 | 91.0 | 1 (28.6) | 5 (71.4) | 91.0 | 80.0 |
| 7 | 3 (42.9) | 7 (57.1) | 37.9 | 94.1 | 1 (5.9) | 13 (94.1) | 85.4 | 82.0 |
| 8 | 6 (50.0) | 7 (50.0) | 29.1 | 95.1 | 3 (30.0) | 6 (70.0) | 70.8 | 84.0 |
| 9 | 5 (40.0) | 7 (50.0) | 20.2 | 97.2 | 1 (16.6) | 7 (87.4) | 64.0 | 90.0 |
| 10 | 1 (25.0) | 3 (75.0) | 11.4 | 98.9 | 1 (10.0) | 9 (90.0) | 56.2 | 92.0 |
| 11 | 0 | 1 (100.0) | 7.6 | 99.3 | 2 (22.2) | 7 (77.8) | 46.1 | 94.0 |
| 12 | 1 (25.0) | 3 (75.0) | 6.3 | 99.3 | 0 | 7 (100.0) | 38.2 | 98.0 |
| 13 | 0 | 0 | 2.5 | 99.6 | 0 | 6 (100.0) | 30.3 | 98.0 |
| 14 | 1 (50.0) | 1 (50.0) | 1.3 | 100.0 | 0 | 5 (100.0) | 23.6 | 98.0 |
| 15 | | | | | 1 (20.0) | 4 (80.0) | 18.0 | 98.0 |
| 16 | | | | | 0 | 4 (100.0) | 13.5 | 100.0 |
| 17 | | | | | 0 | 0 | | |
| 18 | | | | | 0 | 3 (100.0) | 9.0 | 100.0 |
| 19 | | | | | 0 | 1 (100.0) | 5.6 | 100.0 |
| 20 | | | | | 0 | 0 | | |
| 21 | | | | | 0 | 2 (100.0) | 4.5 | 100.0 |
| 22 | | | | | 0 | 0 | | |
| 23 | | | | | 0 | 1 (100.0) | 2.3 | 100.0 |
| 24 | | | | | 0 | 1 (100.0) | 1.1 | 100.0 |
| Missing | 3 | 0 | | | 1 | 2* | | |

*MACCS*, Melbourne Allergy and Children's Centre; *OFC*, oral food challenge; *RCH*, Royal Children's Hospital; *SPT*, skin prick test.
Clinic cohort: n = 16 excluded as equivocal OFC outcome.
Population cohort: n = 3 excluded as equivocal OFC outcome.
*Had positive sIgE and negative SPT.