Updated threshold dose-distribution data for sesame

To the Editor,

Sesame is classified as a "major" food allergen for which mandatory disclosure is required. Understanding reaction thresholds and how these vary within the allergic population is crucial in providing appropriate dietary advice to patients, providing guidance to the food industry, and informing dosing regimens for oral food challenges (FC). However, the largest data series used to derive a threshold dose-distribution for sesame included blinded challenge data from just 40 individuals. Data from low-dose, open FC can be used to supplement that from blinded FC, reducing uncertainty in estimating threshold dose-distributions for allergenic foods which otherwise lack sufficient data. We, therefore, undertook a systematic search of the literature and performed dose-distribution modelling of individual patient FC data (including open FC) to update estimated eliciting doses for sesame.

Eleven studies were included (Table S1), representing data from 246 positive FC. The discrete and cumulative eliciting dose predicted to provoke reactions in 5% of the sesame-allergic population (ED_{05}) were 2.4 (95% CI 1.0–7.7) and 2.5 (95% CI 0.9–9.5) mg sesame protein, respectively. Dose-distributions are shown in Figure 1 and Table S1. These estimates are reassuringly similar to those previously reported, only with much greater precision reflecting the increased number of datapoints (Table 1). Furthermore, these estimates were robust at sensitivity analyses when excluding data from unblinded food challenges or studies with a significant proportion of "first dose reactors" (Table 1).

With this analysis, the dataset for sesame is now similar to that used to inform eliciting doses for other food allergens, and sufficient to inform public policy despite the potential limitations of analyses using FC data. The CODEX committee of the Food and Agricultural Organization of the United Nations and the World Health Organization recently commissioned an Expert Consultation which recommended the inclusion of sesame as a global "priority" allergen. The data presented here will be used to inform a reference dose which might be recommended to guide the use of precautionary allergen ("may contain") labelling. Given that ED values remain robust at sensitivity analysis when limited to blinded FC in the ED_{01}-ED_{10} range, we recommend using ED values based on the blinded FC dataset for risk assessment and risk management purposes, to maintain consistency with approaches for other food allergens.

A strength of this dataset is the inclusion of cohorts spanning four of the six global CODEX regions. These data were mostly generated from FC using ground sesame or tahini and may not be directly

**Figure 1** Eliciting dose curves from the model averaged population threshold dose-distributions for sesame, based on (A) discrete and (B) cumulative dose datasets. Doses are expressed in mg sesame seed protein, and are compared to equivalent data reported by Houben et al. used to inform VITAL 3.0 reference doses.

**Abbreviations:** 95% CI, 95% confidence interval; DBPCFC, Double-blind placebo-controlled food challenge; ED, Eliciting dose; FC, Food challenge; LOAEL, Lowest-observed adverse effect level; NOAEL, No observed adverse effect level.

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Ovadia et al. recently reported a cohort of 51 sesame-allergic endosperm proteins, resulting in a much lower exposure to sesame al-
mastication, and thus, swallowed whole; this prevents the release of
baked into the surface of bread rolls are frequently not broken during
commonly used in food preparation. For example, sesame seeds when
extrapolated to the consumption of whole sesame seeds which are
~exposure, implying tolerance in
a top dose of 1 g protein (around 4 g of tahini paste,
strong taste can create difficulties, particularly in younger children. Our
commonly used for the higher doses used at sesame- FC; however, the
(as recommended by PRACTALL) is appropriate for sesame. Tahini is
It is, therefore, unclear whether baked sesame seeds are tolerated
due to the low level of allergen exposure, the lower bioavailability of
sesame seed protein with this form of consumption, or both.
Finally, these data confirm that a semi-log dosing regimen for FC
(this analysis (limited to
DBPCFC only, n = 67)
This analysis (excluding studies with significant left-
censoring a, n = 172)
Note: Discrete dosing schemes are reported as the mg protein amount of each separate dose within a food challenge when determining the individual
NOAEL and LOAEL. Cumulative dosing schemes are reported as the cumulative sum of all prior doses within a food challenge when calculating the individual NOAEL and LOAEL. Population dose-distributions were determined using “Stacked Model Averaging” as previously described.12
aLeft-censoring of data occurs when participants react to the first dose of the challenge protocol, and is more likely to occur in those studies with a
higher initial challenge dose. All doses are presented as mg sesame protein.
extrapolated to the consumption of whole sesame seeds which are
commonly used in food preparation. For example, sesame seeds when
baked into the surface of bread rolls are frequently not broken during
mastication, and thus, swallowed whole; this prevents the release of
endosperm proteins, resulting in a much lower exposure to sesame al-
lergens. Ovadia et al. recently reported a cohort of 51 sesame-allergic
children, of whom 41 (80%) were able to tolerate 3 pretzels with
sesame seeds (total exposure approximately 36 mg sesame protein)
baked into the surface.6 This would be equivalent to an ED25 level of
objective symptoms in someone unable to ingest a higher dose at FC.

Data that support the findings of this study are available from
the corresponding author upon reasonable request, but may be sub-
ject to non-disclosure agreements.
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