

Safety Benefits of an Increased Threshold in Milk-Allergic Patients: A Quantitative Risk Assessment Study

Ben Remington,^{1*} Tanja Krone,¹ Stef Koppelman²

¹TNO, The Hague, The Netherlands; ²Food Allergy Research and Resource Program, University of Nebraska, Lincoln, NE, USA

*Current affiliations: Food Allergy Research and Resource Program, University of Nebraska, Lincoln, USA and the Remington Consulting Group B.V., Utrecht, The Netherlands



RATIONALE

- The prevalence of IgE-mediated cow's milk allergy in children is high, especially in younger age groups¹
- This can be particularly concerning as cow's milk protein (CMP) is a frequently detected unintended allergen in food products^{2,3}
- Because of its ubiquitous distribution in foods and common consumption, it is particularly difficult to avoid cow's milk
- Accidental exposures can occur due to ingestion of food products that do not intentionally contain CMP but are contaminated with cow's milk, or by accidental ingestion of food products that contain cow's milk by recipe⁴
- Therefore, cow's milk allergic (CMA) patients may be at a high risk of allergic reactions as a result of accidental allergen exposure^{2,3}
- Food immunotherapy can increase the eliciting dose (ED) threshold, which may reduce risk of reaction to CMP following unintended exposure

OBJECTIVE

- To assess the risk of experiencing an allergic reaction and to quantify safety benefits of increased ED thresholds in CMA patients by modeling the exposure to milk in 2 scenarios (accidental exposures and accidental ingestions) and comparing these with set ED threshold values in CMA patients

METHODS

Quantitative Risk Assessment (QRA)

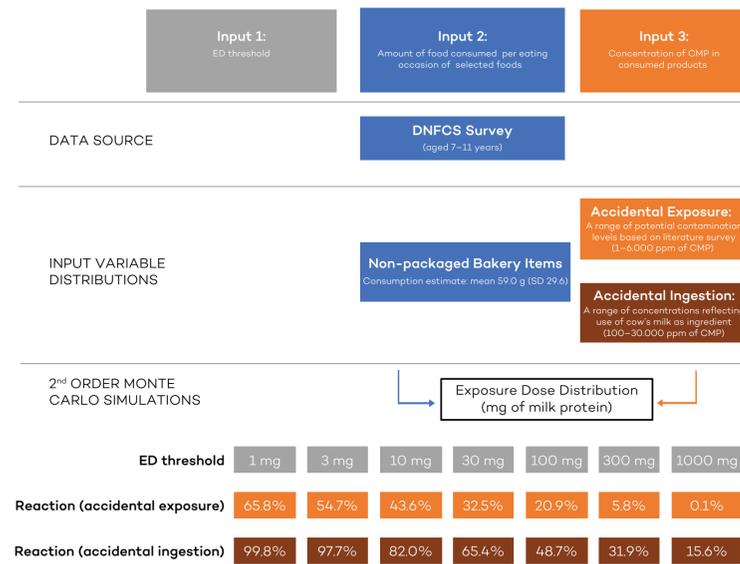
- Consumption summary statistics for children aged 7–11 years from the 2007–2010 Dutch National Food Consumption Survey (DNFCS) and concentration of CMP in the consumed products were used to model exposures to milk protein in 5 food categories: bakery items, boxed cheesecake mixes, dark chocolate, seasonings, and water ice
- These data were used as inputs and incorporated into a Monte Carlo framework to model the probability of an allergic reaction in 2 scenarios (**Figure 1**):
 - Accidental exposures to food products contaminated with cow's milk
 - Accidental ingestions of food products that contain cow's milk as an ingredient

Risk Reduction

- Modeled risks were used to calculate individual risk reductions for CMA children with increased ED threshold associated with immunotherapy
- Relative risk reductions were calculated using the following formula:

$$\left(1 - \frac{\text{Risk at POST-immunotherapy mg milk protein threshold}}{\text{Risk at baseline PRE-immunotherapy mg milk protein threshold}} \right) \times 100\% = \text{Percentage decrease in risk (\%)}$$

Figure 1. Illustration of Risk Assessment Model (using non-packaged bakery items)



CMP=cow's milk protein; ED=eliciting dose; DNFCS=Dutch National Food Consumption Survey; SD=standard deviation.

REFERENCES

- Nwaru BI, et al. *Allergy*. 2014;69(8):992-1007.
- Blom WM, et al. *J Allergy Clin Immunol*. 2018;142(3):865-875.
- Crotty MP, Taylor SL. *J Allergy Clin Immunol*. 2010;125(4):935-937.
- Boyano-Martinez T, et al. *J Allergy Clin Immunol*. 2009;123(4):883-888.

ACKNOWLEDGMENTS

This study was sponsored by DBV Technologies. Editorial support for the preparation of this poster was provided by International Meetings & Science (IMsci), funded by DBV Technologies.

RESULTS

Accidental Exposure Scenario

- Percentage of eating occasions predicted to result in allergic reaction for accidental exposure to non-packaged bakery items contaminated with cow's milk (**Figure 1**) were used to calculate relative risk reductions
- For non-packaged bakery products, a relative risk reduction of at least 82.3% was achieved when the ED threshold was increased from ≤30 mg to 300 mg, and up to 99.8% when increased to 1,000 mg (**Figure 2**)
- Similar results were seen for the other food categories (74.2% to 97.6% when the ED threshold was increased from ≤30 mg to 300 mg, and 96.9% to >99% when the ED threshold was increased to 1,000 mg, regardless of the initial threshold)

Figure 2. Relative Risk Reductions for Allergic Reactions Due to Accidental Exposure to Non-packaged Bakery Products Contaminated With Cow's Milk in CMA Children With Raised ED Threshold

Baseline ED Threshold (mg of CMP)	ED Threshold – Post Immunotherapy Treatment (mg of CMP)						
	1	3	10	30	100	300	1000
1	0.0%	16.8%	33.8%	50.7%	68.2%	91.2%	99.8%
3		0.0%	20.4%	40.7%	61.8%	85.9%	99.8%
10			0.0%	25.5%	52.0%	86.8%	99.7%
30				0.0%	35.6%	82.3%	99.7%
100					0.0%	72.4%	99.5%
300						0.0%	98.1%
1000							0.0%

Accidental Ingestion Scenario

- For products that contained cow's milk as an ingredient, relative risk reductions were lower but still clinically relevant compared with accidental exposures
- For non-packaged bakery products, a relative risk reduction of at least 51.1% was achieved when the ED threshold was increased from ≤30 mg to 300 mg, and up to 84.4% when increased to 1,000 mg (**Figure 3**)
- The relative risk reductions were similar for other food categories (48.8% to 89.2% when the ED threshold was increased from ≤30 mg to 300 mg, and 47.8% to >99% when the ED threshold was increased to 1,000 mg, regardless of the initial threshold)

Figure 3. Relative Risk Reductions for Allergic Reactions Due to Accidental Ingestion of Non-packaged Bakery Products That Contained Cow's Milk in CMA Children With Raised ED Threshold

Baseline ED Threshold (mg of CMP)	ED Threshold – Post Immunotherapy Treatment (mg of CMP)						
	1	3	10	30	100	300	1000
1	0.0%	2.1%	17.8%	34.5%	51.2%	68.0%	84.4%
3		0.0%	16.1%	33.1%	50.2%	67.3%	84.1%
10			0.0%	20.3%	40.6%	61.0%	81.0%
30				0.0%	25.5%	51.1%	76.2%
100					0.0%	34.4%	68.0%
300						0.0%	51.3%
1000							0.0%

CONCLUSIONS

- In CMA children, accidental exposure or ingestion of products containing cow's milk can pose substantial risk for experiencing an allergic reaction
- Increasing a milk-allergic patient's ED threshold to 300 mg or 1,000 mg of CMP resulted in a clinically relevant reduction of modeled risk for a reaction to cow's milk-contaminated food products
- For food products that contain dairy as an intended ingredient, the modeled risk reduction for an allergic reaction upon accidental ingestion by increasing the ED threshold to 300 or 1,000 mg of CMP was less pronounced, yet still potentially clinically meaningful