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Probabilistic risk assessment model for allergens in food: sensitivity analysis of the minimum eliciting dose and food consumption

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Abstract

Previously, TNO developed a probabilistic model to predict the likelihood of an allergic reaction, resulting in a quantitative assessment of the risk associated with unintended exposure to food allergens. The likelihood is estimated by including in the model the proportion of the population who is allergic, the proportion consuming the food and the amount consumed, the likelihood of the food containing an adventitious allergen and its concentration, and the minimum eliciting dose (MED) distribution for the allergen. In the present work a sensitivity analysis was performed to identify which parts of the model most influence the output.

A shift in the distribution of the MED reflecting a more potent allergen, and an increase in the proportion of the population consuming a food, increased the number of estimated allergic reactions considerably. In contrast, the number of estimated allergic reactions hardly changed when the MEDs were based on a more severe response, or when the amount of food consumed was increased.

Development of this work will help to generate a more accurate picture of the potential public health impact of allergens. It highlights areas where research is best focused, specifically the determination of minimum eliciting doses and understanding of the food choices of allergic individuals.

Keywords: Probabilistic model; Allergens; Food; Sensitivity analyses; Modelling

1. Introduction

To assess the risk arising from unintended exposure to food allergens a deterministic approach may be applied, where point estimates are used to calculate the outcome (Spanjersberg et al., 2007). In worst case scenarios usually the observed values of high percentiles, for example, the 97.5th percentiles or maximum are used. In less worst case scenarios mean values may be used. This approach often leads to conclusions such as "an allergic reaction cannot be excluded", which is a poor basis for decision making in risk management. Furthermore, in this approach neither variability (for example, heterogeneity over different members of a population) nor uncertainty (for example, lack of knowledge about the true value) can be taken into account. In probabilistic modelling, distributions are used to represent the input parameters, making it possible to account for both variability and uncertainty and to quantify the risk.

A risk assessment model for allergens in food based on probabilistic techniques resulting in a quantitative

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assessment of the risk and detailed information on the predicted number of allergic reactions has been developed at TNO (Spanjersberg et al., 2007). This approach is now recognized as a way forward in allergen risk assessment (Health Council of the Netherlands, 2007; Europrevall & FSA, 2007). In summary, in this model several input parameters can be identified, such as the proportion of the population who is allergic to a specific allergen, the likelihood that an allergic person consumes a certain product and if so in what amount, the likelihood that the food accidentally contains the allergen and if so the concentration of the allergen. These input parameters determine the distribution of intake of the allergen. By combining the distribution of allergen intake with the distribution of minimum eliciting doses (MED) among the population, the number of allergic reactions can be estimated more realistically.

In most probabilistic assessments, the majority of the variance in the output distribution is attributable to variability and/or uncertainty in a selected number of inputs. The identification of significant contributors to output variance has useful implications for future research. It makes it possible to target resources to a small number of important inputs, rather than spread the resources across the entire set of inputs (Cullen and Frey, 1999). Sensitivity analysis of a model is used to identify these key contributors to variability and uncertainty in model outputs by describing the change in output as a function of the change in the input variable. By comparing the magnitude of changes it is possible to identify those inputs which have the most influence on the output.

Validation of the model by a comparison of the predictions with observational data is not possible at this moment due to the lack of observational (incidence) data. Nothing it known about how the incidence of allergic reactions in a specific population relates to the consumption of a food containing an adventitious allergen.

This model has been developed to assess the risk associated with a given allergen concentration in a food. This means that an established allergen concentration (distribution) will be the starting input parameter. With these sensitivity analyses we wanted to investigate the major sources of variance and uncertainty affecting the risk associated with such given concentration (distribution). Therefore, we performed sensitivity analyses, involving different scenarios in which the input parameters of the MED part and the food consumption part of the model were varied.

2. Methods

As the basis for the sensitivity analyses, a case study was used for the probabilistic risk assessment model. The probabilistic model and case study have been described in more detail by Spanjersberg et al. (2007). The model consists of two elements: the distribution of allergen intake and the distribution of MEDs within a population. Within the model the values of these two factors relative to each other, and the shape of their distributions determine the probability of an allergic reaction. The reference model that was used as a basis for the sensitivity analyses calculated the frequency of an allergic reaction associated with the presence of hazelnut proteins in chocolate spread due to cross-contact at the production facilities. The mean number of allergic reactions calculated was approximately 5 per 10,000 persons at breakfast in the reference model (Spanjersberg et al., 2007). It should be noted that some worst case assumptions were made in our reference model. However, the risks calculated from these sensitivity analyses are only meant to determine the relative influence of the input parameters on the output and should not be interpreted as actual risk estimates for the population in question, due to the various assumptions made.

In the case study, data on food consumption were derived from the third Dutch National Food Consumption Survey (Anonymous, 1998), in which a representative sample of 6250 individuals recorded their food consumption for two consecutive days. For the modeling, data from male subjects older than 18 years were used, because males were found to be higher consumers of the food under study. IgE-mediated allergic reactions to food are generally accepted to occur within minutes to about 2 h after exposure. Therefore, we calculated the predicted risk of an allergic reaction using one eating occasion, since the allergic complaints are linked to single eating occasions. Breakfast and lunch were selected since these were found to be eating occasions with the highest consumption of the potentially contaminated food product, in this case chocolate spread (Anonymous,1998). Table 1a describes the input parameters in the case study, the reference model, that were used to estimate the number of persons that would suffer from an allergic reaction as a result of unintended allergen consumption.

2.1. Description of input parameters identical in all models

Three factors were identical in all scenarios examined: the proportion of the population who are food allergic (the prevalence), the likelihood that a food accidentally contains an allergen and the distribution of the concentration of the allergen in the product (Spanjersberg et al., 2007). The concentration of the allergen was kept identical since this model was developed to assess the risk associated with unintended exposure to food allergens taking the allergen concentration as the starting point.

Table 1a
The reference model

Input parameters in reference model	
Proportion of allergic persons in population	5.4% (Hupkens, 1999)
Proportion of population consuming chocolate spread at breakfast	2% (50/2155) (Anonymous, 1998)
Amount of chocolate spread eaten at breakfast (g)	Lognormal (19, 12) (Anonymous, 1998)
Proportion of population consuming chocolate spread at lunch	1% (29/2155) (Anonymous, 1998)
Amount of chocolate spread eaten at lunch (g)	Lognormal(17, 11) (Anonymous, 1998)
Likelihood product is contaminated	100% (Koppelman et al., 1999)
Concentration if contaminated (mg/g)	Lognormal (0.3, 0.4) (Koppelman et al., 1999)
MED (mg)	Raw data (Wensing et al., 2002a)

Input parameters estimating the number of persons in which an allergic reaction would occur as a result of unintended allergen consumption.