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The prevalence of food allergy and epinephrine auto-injectors in Dutch food-allergic adolescents

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To the Editor:

Food-induced anaphylaxis continues to be increasing across all ages, and the risk of fatal food-induced anaphylaxis is disproportionately high in adolescents(1,2). Effective management of food-induced anaphylaxis must include both prompt acute, emergency treatment and long-term care. When a severe food-allergic reaction occurs, prompt administration of epinephrine may be life-saving. Therefore, all food-allergic patients at high-risk of anaphylaxis should carry an epinephrine auto-injector (EAI) at all times. However, a previous study in 2009 showed that there was an alarming underprescription of EAI to high-risk food-allergic adolescents (11-20 years) in Dutch high schools(3). Less than 1 in 30 of these adolescents had actually been prescribed an EAI. Recent guidelines for food allergy and anaphylaxis by the European Academy of Allergy and Clinical Immunology (EAACI)(4) gave recommendations about risk assessment and management of patients who are at high-risk of experiencing anaphylaxis to improve the care for food-allergic patients. With the prevalence of food allergies and anaphylaxis increasing, it is therefore of interest to investigate if the situation in the Netherlands has changed over the years.

Therefore, the aim of this study was to estimate the prevalence of probable and self-perceived food allergy, EAI need and ownership in adolescents aged 11-20 in Dutch high schools and to compare this data with the findings of 2009.

The study population were adolescents aged 11–20 from four high schools in four different provinces of the Netherlands. The same study design was used as in 2009(3). High schools who participated in 2009 were contacted again to participate in this study(3). Participants were asked to complete a (digital) screening questionnaire(Figure 1)(3). Adolescents, who answered 'yes' to one or more of the screening questions and agreed to be contacted, were interviewed using a telephone questionnaire. The telephone questionnaire included questions concerning the suspected food(s), allergic symptoms, the person responsible for the food allergy diagnosis, and the need for an EAI(3). Only allergic reactions to foods that occurred in the last 2 years were recorded. Adolescents were classified as probably food-allergic when they reported allergic symptoms after eating known allergenic foods (occurring within maximally 1 hour and to a daily serving or less.

The need for an EAI was assessed using a risk factor based protocol(3,4). This protocol considers an EAI to be indicated if a patient has had (a) a previous severe anaphylactic reaction to a food, or (b) food allergy is suspected or confirmed and the patient has two or more of the following risk factors: (1) adolescent to young adult age, (2) asthma, (3) previous reaction to trace amounts of a food, and (4) (possible) allergy to peanuts or tree nuts.

For calculation of the questionnaire-based prevalence, it was assumed that the prevalence of food allergy in the group of adolescents that refused or could not be contacted was the same as in the group of adolescents that could be contacted(3). Prevalence was calculated based on extrapolation of the data from the

adolescents that were contacted and are shown as percentage of the total number of screened adolescents(3). In addition, the minimal prevalence was calculated without extrapolation(3). The diagnostic accuracy and sources of 'correct' and 'incorrect' diagnoses were investigated by calculating percentages(3). Adolescents who thought that they were food-allergic and who were subsequently classified as probably food-allergic were referred to in this study as '*correctly diagnosed*'(3). Adolescents who thought that they were food-allergic and who were subsequently classified as unlikely to be food-allergic were referred to in this study as '*incorrectly diagnosed*'(3).

The calculated questionnaire-based prevalence of probable food allergy of present study was compared to the calculated questionnaire-based prevalence of 2009 to calculate either an increase or decrease in prevalence. Fisher exact test was used to investigate differences in prevalence of food allergy and EAI ownership between 2009 and 2016. Data entry and statistical analyses were conducted using SPSS version 23.0 (SPSS Inc. Chicago, IL, USA).

Two high schools who participated in 2009 refused to participate again in this study and were replaced for high schools with similar characteristics and located in the same province.

In total, 2632 adolescents were screened between November 2015 and February 2016, of which 592 answered 'yes' to one or more of the screening questions (Figure 2). Of these, 112 agreed to be contacted by phone. In total 15 adolescents could not be contacted and 31 were not suitable for analysis due to incorrect information. Therefore, 66 adolescents were suitable to be evaluated further. Of these 66 adolescents, 35 thought that they were food-allergic and 31 thought that they were not food-allergic. In total 25 adolescents were classified as

probably food-allergic. Most adolescents in the *probably food-allergic* group reported symptoms from fruits (28%), milk (10%), and nuts (9%). The most frequently reported symptoms of this group were skin symptoms (37%).

Of the 25 adolescents classified as probably food-allergic, ten were considered candidates for an EAI. Two of these ten adolescents had actually been prescribed an EAI. These two prescriptions were considered appropriate as both had more than two risk factors for anaphylaxis. Of the eight adolescents who had not been prescribed an EAI all of them had two or more risk factors and were considered high-risk patients.

Out of the 35 adolescents who had a food allergy in their own perception, twenty-one adolescents were classified as *probably food-allergic* (correct diagnosis) and fourteen adolescents were classified as *unlikely to be food-allergic* (incorrect diagnosis). Out of the 31 adolescents who did not have a food allergy in their own perception, four adolescents were classified as *probably food-allergic* (missed diagnosis). Most adolescents were not physician-diagnosed and adolescents with an incorrect diagnosis diagnosed themselves. Table 1 shows the diagnostic accuracy of adolescents and health care providers and sources of correct and incorrect diagnosis.

The calculated questionnaire-based prevalence of probable food allergy in 2016 was 6.2%. In 2009 the calculated questionnaire-based prevalence of probable food allergy was 6.2%. The minimal prevalence of probable food allergy in 2016 was at least 0.95%. In 2009 the minimal prevalence of probable food allergy was at least 2.1%. There were no differences in characteristics between the group of adolescents that refused or could not be contacted and the group of adolescents that could be

contacted. The difference of prevalence of probable food allergy between 2009 and 2016 was not significant ($p=0.755$).

The calculated questionnaire-based prevalence for perceived food allergy classified as unlikely to be food-allergic in 2016 was 4.4%. In 2009 the calculated questionnaire-based prevalence for perceived food allergy classified as unlikely to be food-allergic was 4.0%.

The prevalence of food allergy requiring an EAI in 2016 was 2.5% and 0.5% had been prescribed an EAI. In 2009 the prevalence of food allergy requiring an EAI was 3.0% and 0.3% had been prescribed an EAI. The minimal prevalence of food allergy requiring an EAI in 2016 was at least 0.08%. In 2009 the minimal prevalence of food allergy requiring an EAI was at least 0.09%. The differences of food allergy requiring an EAI between 2009 and 2016 was not significant ($p=0.378$).

This study shows that the prevalence of (high-risk) food allergy in Dutch adolescents has not increased in the last six years. Even though EAI ownership has improved marginally, there is still a substantial under prescription of EAIs in high-risk food-allergic adolescents in the Netherlands.

The calculated questionnaire-based prevalence of probable food allergy did not change in comparison to 2009, in both years the prevalence was 6.2%. This is not in keeping with other studies which report that the prevalence of food allergy is increasing(1,5). These studies also report a higher self-reported food allergy prevalence than our study varying from an increase of 1.7% to 4.2% for a time interval of about 6 years.

EAI ownership has improved marginally in comparison to 2009. Even though this improvement was not significant and may therefore not be generalizable, there is ultimately still a substantial under prescription of EAIs in food-allergic adolescents in

Dutch high schools at high-risk for anaphylaxis. The reason for this under prescription may be that adolescents with problems with food are not visiting their general practitioner, and are consequently ignorant of the fact that they are at high-risk for food-induced anaphylaxis. Also the high rate of inaccurate diagnoses of food allergy by adolescents themselves and alternative medical practitioners may contribute to the under prescription. Another reason may also be that general practitioners and other specialists are not prescribing EAls to adolescents for whom it would be appropriate to do so even though their diagnosis is accurate(6,7).

The under prescription of EAls in high-risk food-allergic adolescents and the number of self-reported probable food-allergic adolescents found in this study show that awareness about food allergy, anaphylaxis and its management still need to be increased. In recent years the Dutch government has made an effort to increase public awareness of several health-related topics through the use of government-sponsored campaigns. However, no specific campaigns to improve the management and treatment of food allergies and anaphylaxis have been undertaken. In June 2012 the European Academy of Allergy and Clinical Immunology (EAACI) launched its *Stop Anaphylaxis!* Food Allergy Campaign(8). This campaign aimed at educating the European public in the recognition of the symptoms and triggers of anaphylaxis as well as measures to be implemented in emergency situations. Now, three years on and despite these efforts, little seems to have changed and opportunities still exist for improving awareness about food allergy, anaphylaxis and its management in the Netherlands.

Most food-allergic accidents happen outside the home. Twenty percent of food allergy reactions occur in schools. It is therefore important that schools are prepared for the management of food-allergic children. Previous studies show that in

reality many schools are poorly prepared: preventive measures of food allergen exposure are missing, teachers have little knowledge of food allergy and anaphylaxis, and EAls(9,10). The preparedness of Dutch high schools have not yet been investigated, it would be of interest to investigate how prepared they are.

A limitation of this study may be that adolescents classified as probably food-allergic were not referred for further testing for an objective diagnosis of food allergy. However, if all probably food-allergic adolescents underwent the gold standard double blind, placebo-controlled food challenge, our experience is that approximately half of those adolescents would have a positive test outcome. Ultimately, adolescents reporting having experienced a (severe) allergic reaction would still require an EAI until challenge tests could be done, and overestimation of the need for EAls would thus only be apparent after such tests had been completed. Our findings may thus eventually be an overestimation of the problem of under prescription of EAls to high-risk food-allergic patients to some degree.

Another limitation of this study may be selection bias, in that a large number of the adolescents with problems with foods did not agree to be contacted by telephone for the follow-up questionnaire. However, of those who agreed to be contacted we reached 86% of them. Adolescence is a period of developmental transition between childhood and adulthood, involving multiple physical, intellectual, personality, and social developmental changes. Therefore, there may be a variety of reasons why adolescents with problems with food did not agree to be contacted. Our reported calculated questionnaire-based prevalence may be an underestimation.

A further limitation of this study may be recall bias, to which retrospective self-reported data are prone. We limited patient reporting to the last two years in order to

limit recall bias. Moreover, we used the exact same methods as were used in the study by Flokstra-de Blok et al in 2009(3).

In summary, the calculated questionnaire-based prevalence of probable food allergy is still the same as in 2009 (6.2%) and the EAI ownership has marginally improved. However, there is still an under prescription of EAIs in high-risk food-allergic adolescents in Dutch high schools. There are still opportunities to raise food allergy awareness in communities, especially in schools, and also among health-care providers to improve the care for food-allergic adolescents at high-risk for anaphylaxis.

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CONFLICT OF INTEREST

All authors have no declared conflict of interest.

STATEMENT OF CONTRIBUTION

All authors declare to have contributed significantly to the research and preparation, revision and final production of the manuscript and approve its submission to the journal. All authors take public responsibility for appropriate portions of the content. The contents of the manuscript have not been previously published and are not currently submitted elsewhere.

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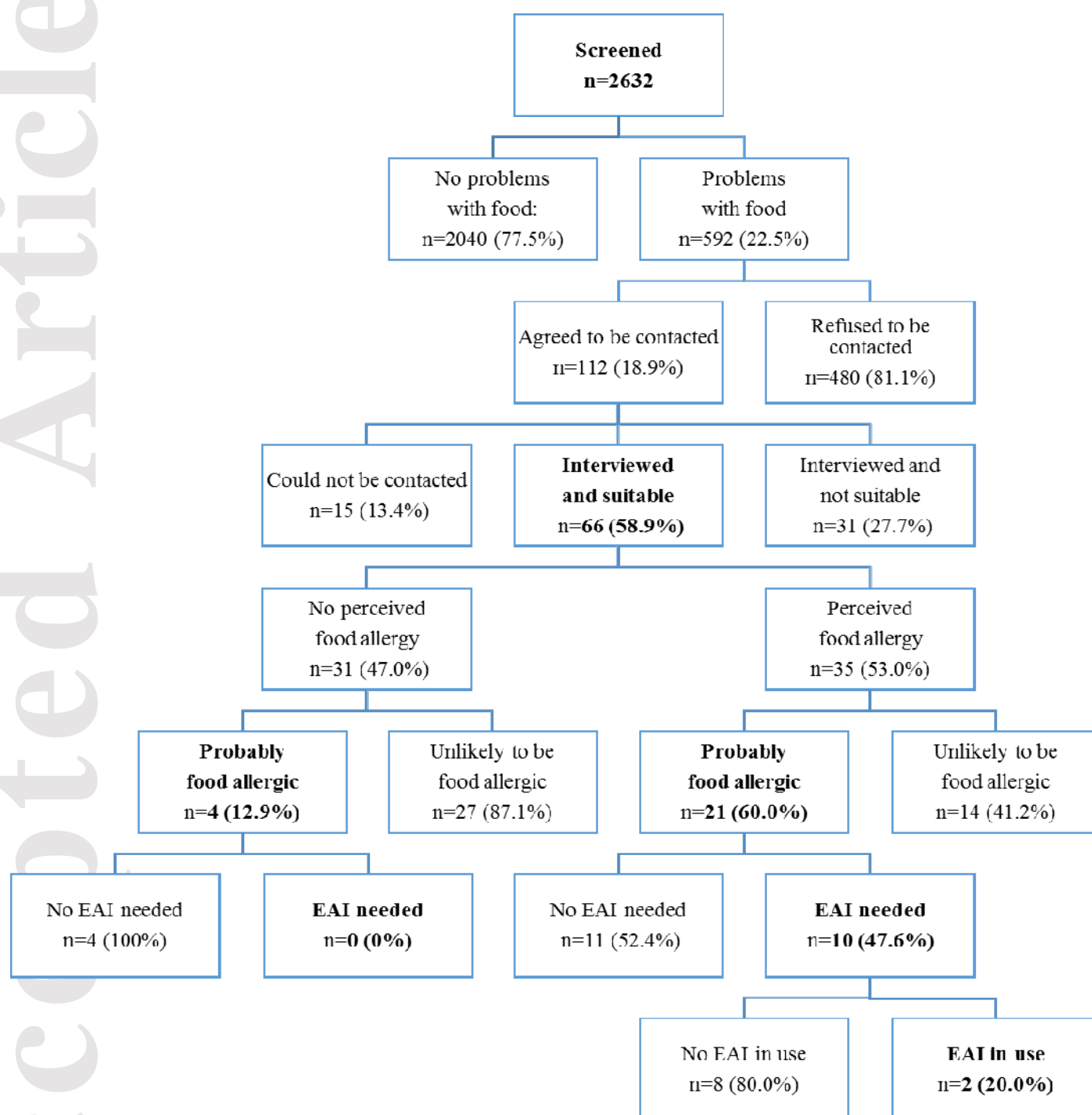
Figure 1. Screening questionnaire questions

Screening questions	Yes	No
1. Do you have a food allergy or do you think you have a food allergy?	☐	☐
2. Do you get symptoms from certain foods?	☐	☐
3. Do you avoid certain foods to prevent symptoms?	☐	☐
4. Do you have an Epipen® or Jext® (or ever had one?)*	☐	☐
Other questions		
What is your age?	☐	☐
Can we contact you for further questions?	☐	☐
If yes, please write down your phonenumber below		

Legend Figure 1. Screening questionnaire questions

*pictures of Anapen®, Epipen® and Jext ® were shown

Figure 2. Flow chart of study



Legend Figure 2. Flow chart of study

*Percentages represent those of the previous step in the chart

Table 1. Diagnostic accuracy of adolescents and health care providers (columns) and sources of ‘correct’ and ‘incorrect’ diagnoses (rows)

Diagnosis	<i>Adolescents or parent</i>	<i>General practitioner</i>	<i>Specialist*</i>	<i>Alternative medical practitioner</i>	Total
Correct§	11 (48% C, 52% R)	4 (80% C, 19% R)	5 (100% C, 24% R)	1 (50% C, 5% R)	21
Incorrect¶	12 (52% C, 86% R)	1 (20% C, 7% R)	0 (0% C, 0% R)	1 (50% C, 7%)	14
Total	23	5	5	2	35

Legend Table 1. Diagnostic accuracy of adolescents and health care providers (columns) and sources of ‘correct’ and ‘incorrect’ diagnoses (rows)

Percentages shown as % C, percentage column and % R, percentage row. *allergist, dermatologist, paediatrician, dietician.

§adolescent thought themselves to be food allergic and classified in this study as probably food allergic. ¶Adolescent thought themselves to be food allergic but classified in this study as unlikely to be food allergic.