CHAPTER 3

EXTREMELY LOW PREVALENCE OF EPINEPHRINE AUTOINJECTORS IN HIGH-RISK FOOD-ALLERGIC ADOLESCENTS IN DUTCH HIGH SCHOOLS

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ABSTRACT
The aim of the study was to estimate the prevalence of probable food allergy in adolescents aged 11–20 and to examine the frequency of epinephrine autoinjector (EAI) ownership among high-risk individuals. Adolescents were screened followed by a more detailed telephone questionnaire inquiring about suspected food(s), symptoms, diagnosis, and use of an EAI. The participating adolescents were classified as probably or unlikely to be food-allergic. The need for an EAI was assessed. In total, 2284 adolescents completed the screening questionnaire, of which 396 indicated food to be a problem and 168 agreed to be interviewed. Forty-eight adolescents were classified as probably food-allergic, of which eight were not aware of their food allergy. Twenty-three adolescents were considered candidates for an EAI, whereas only two of them had been prescribed this medication. The calculated questionnaire-based prevalence of EAI need was 3.0% (minimal prevalence at least 1.0%), whereas the EAI ownership was 0.09%. In conclusion, we found an alarming under prescription of EAI in school-going adolescents.

INTRODUCTION
A number of studies suggest that the prevalence of food allergy is increasing.1-3 The only proven forms of treatment for food allergy are strict avoidance of the food(s) involved and medication for emergency treatment.4 When a severe allergic reaction occurs, prompt administration of epinephrine is essential.5 Therefore, all food-allergic patients at risk for severe allergic reactions should carry an epinephrine autoinjector (EAI). However, there is no definite international consensus on whom should be prescribed an EAI6 and the prevalence of EAI ownership may vary between countries.7,8 The aim of this study was to estimate the prevalence of probable food allergy and EAI ownership in adolescents aged 11-20. In addition, the prevalence of probably as well as self-perceived food allergy among adolescents in Dutch high schools was estimated.

METHODS
STUDY DESIGN
Adolescents aged 11–20 from four high schools in four different provinces of the Netherlands were asked to complete a screening questionnaire. This questionnaire consisted of four screening questions: (i) Do you have a food allergy or do you think you have a food allergy? (ii) Do you get symptoms from certain foods? (iii) Do you avoid certain foods to prevent symptoms? (iv) Do you have an EpiPen or Anapen (Or ever had one)? Pictures of the EpiPen and Anapen were shown on the screening questionnaire. Adolescents, who answered ‘yes’ to one or more of the screening questions and agreed to be contacted, were interviewed using a detailed telephone questionnaire.

The telephone questionnaire included questions concerning the suspected food(s), symptoms, the person responsible for the food allergy diagnosis, and the need for an EAI. The foods named were based on the EU directive on labeling of pre-packaged products (EU
Directives 2003/89/EC amending Directive 2000/13/EC relevant in the Netherlands, i.e., peanut, nuts, milk, egg, wheat, soy, sesame seed, fish, shell fish, and celery. In addition, fruits and vegetables were named. The questionnaire also inquired about 37 specific symptoms of the mouth, nose, eyes, skin, gastrointestinal tract, respiratory tract, and cardiovascular tract. Other reported foods and symptoms were recorded as well. Only recent (past 2 yr) allergic reactions to foods were recorded. The person responsible for the food allergy diagnosis was recorded, i.e., the adolescents themselves, general practitioner (GP), dietician, allergist, dermatologist, pediatrician, alternative medicine practitioner (i.e., any practitioner of medicine without the use of conventional diagnostic methods or drugs, which may involve herbal medicines, homeopathy, self-awareness, biofeedback, or acupuncture), or other person. To assess the need for an EAI, we asked whether the adolescent ever had a life-threatening anaphylactic reaction to a food requiring emergency treatment or hospitalization as a result, whether there was coexistent asthma, and whether there had been clear systemic reactions to traces of food (i.e., itchy palms, food soles and/or generalized itch, urticaria, swelling of face and/or body, asthmatic symptoms, dizziness, gastrointestinal, or cardiovascular symptoms).

CLASSIFICATION
Adolescents were classified as probably food allergic when they reported allergic symptoms after eating known allergenic foods (occurring within maximally 1 h and to a daily serving or less). The foods named above were considered as being allergenic. Symptoms of the face (i.e., mouth, nose, eyes), skin, gastrointestinal tract, respiratory tract, or cardiovascular tract were considered as allergic symptoms. The presence of only subjective gastrointestinal symptoms (i.e., stomach ache, nausea) without other symptoms or inconsistent symptoms after repeated ingestion were not classified as food allergy.

The need for an EAI was assessed using a risk factor-based protocol.9 This protocol considers an EAI to be indicated if a patient has had a previous severe anaphylactic reaction to a food, or food allergy is suspected or confirmed and the patient has two or more of the following risk factors: adolescent to young adult age, asthma, previous reaction to trace amounts of a food, and (possible) allergy to peanuts or tree nuts. Allergy only to fruits or vegetables with these risk factors did not constitute an indication for an EAI.

All doubtful cases concerning food allergy and EAI classification were discussed with an allergist (AEJD).

STATISTICS
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. 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. In addition, the minimal prevalence was calculated without extrapolation. The diagnostic accuracy and sources of ‘correct’ and ‘incorrect’ diagnoses were investigated by calculating percentages. 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’. 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’.

RESULTS

CLASSIFICATION

In total, 2284 adolescents were screened, of which 396 answered ‘yes’ to one or more of the screening questions (Fig. 1). Of these, 168 agreed to be contacted by phone, resulting in 120 adolescents (mean age 14.4, s.d. 1.9 yr) that could be contacted and were further evaluated. Of the interviewed adolescents, 70 thought that they were food allergic, whereas 48 adolescents were classified as probably food allergic. Most adolescents in the ‘probably food-allergic’ group reported symptoms from fruits (39%), tree nuts (23%), and peanuts (16%). Most adolescents in the ‘unlikely to be food-allergic’ group reported symptoms from ‘other foods’ (such as meat or ice tea) (56%), milk (22%), and fruits (15%). Importantly, 23 of the probably food-allergic adolescents were considered candidates for an EAI, but only two of these individuals had actually been prescribed one. Both EAI prescriptions were considered appropriate as both had four risk factors for anaphylaxis. Of the 21 high-risk adolescents with no EAI prescribed, two were hospitalized previously for their food allergy, 11 had asthma, eight had previous reaction to trace amounts of a food, 19 had a (possible) allergy to peanuts or tree nuts, and all were adolescent to young adult age. Eight adolescents with no perceived food allergy were classified as probably food allergic. Thus, these adolescent were not aware of their food allergy, and four of them were also considered candidates for an EAI.

PREVALENCE

The calculated questionnaire-based prevalence of probable food allergy was 6.2%, and for perceived food allergy classified as unlikely to be food allergic, it was almost as high as 4.0%. The prevalence of food allergy requiring an EAI was 3.0%, but only in 0.09% (2/2284) had an EAI been prescribed. The minimal prevalence of probable food allergy was at least 2.1%. The minimal prevalence of perceived food allergy classified as unlikely to be food allergic was at least 1.3% and of food allergy requiring an EAI was at least 1.0%.

DIAGNOSIS

Diagnostic accuracy was highest for GPs and specialists, respectively, 70% and 100% (Table 1, columns). Most adolescents were not physician-diagnosed, and the most ‘incorrect’ diagnoses (i.e., adolescent thought themselves to be food allergic but classified in this study as unlikely to be food allergic) came from the adolescents themselves (63%) (Table 1, rows). Although GPs and alternative medicine practitioners made an ‘incorrect’ diagnosis in a comparable number of cases (20% vs. 17%), the GPs made a ‘correct’ diagnosis five times more often than the alternative medicine practitioners (35% vs. 7.5%) (Table 1, rows). Of the 21 high-risk adolescents with no EAI prescribed, the food allergy was diagnosed by a specialist in two
Prevalence of EAs in food-allergic adolescents - Chapter 3

PART II

that they were food allergic and who were subsequently classified as probably food allergic were referred to in this study as ‘correctly diagnosed’. 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’.

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<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Adolescent¹</th>
<th>GP²</th>
<th>Specialist³</th>
<th>AMP⁴</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correct*</td>
<td>16 (46%C, 40%R)</td>
<td>14 (70%C, 35%R)</td>
<td>7 (100%C, 17.5%R)</td>
<td>3 (38%C, 7.5%R)</td>
<td>40</td>
</tr>
<tr>
<td>Incorrect*</td>
<td>19 (54%C, 63%R)</td>
<td>6 (30%C, 20%R)</td>
<td>0 (0%C, 0%R)</td>
<td>5 (62%C, 17%R)</td>
<td>30</td>
</tr>
<tr>
<td>Total</td>
<td>35</td>
<td>20</td>
<td>7</td>
<td>8</td>
<td>70</td>
</tr>
</tbody>
</table>

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, %R= percentage row)
* Correct = adolescent thought themselves to be food allergic and classified in this study as probably food allergic
** Incorrect = adolescent thought themselves to be food allergic but classified in this study as unlikely to be food allergic
¹ adolescent or parent;
² general practitioner.
³ allergist, dermatologist, paediatrician, dietician
⁴ alternative medical practitioner
FIGURE 1
Flow chart of the study*.
*Percentages represent those of the previous step in the chart.
DISCUSSION

This study shows that there is an alarming under prescription of EAI in food-allergic adolescents (11–20 yr) in Dutch high schools. Using a relatively restrictive risk factor–based protocol,9 approximately 3.0% of the study participants were found to have a food allergy requiring an EAI. Less than 1 in 30 of these adolescents had actually been prescribed this potentially lifesaving device. Based on the Dutch population aged 11–20, 3% represents 54,000 individuals. In addition, inappropriate self-diagnosis of ‘food allergy’ was found almost as often as probable food allergy.

The calculated questionnaire-based prevalence of probable food allergy in this age group was 6.2%. Allergy testing was not performed in this study and could have assisted accurate diagnosis. Moreover, it is likely that a considerable number of these cases would be found to be non-allergic if double-blind food challenges were used for diagnosis.2 However, even if the prevalence found was halved, the prevalence of food allergy requiring an EAI would still be 1.5%, which represents 27,000 individuals aged 11–20 at high risk in the Netherlands.

Regarding the accuracy of diagnosis, alternative medical practitioners (AMPs) were actually no more accurate than patients themselves and considerably less accurate than trained medical practitioners. Because the term ‘food allergy’ may be used loosely by AMPs, education of these practitioners to refer patients with IgE-mediated food allergy is important given the proportion of the general population who consult AMPs for advice.

A limitation of this study may be selection bias, in that more than half of the adolescents with a ‘yes-answer’ on the screening questionnaire did not agree to be contacted by phone for the follow-up questionnaire. However, of the adolescents that did agree to be contacted, we reached more than 80%. Additionally, adolescents were included from four schools from four different parts of the Netherlands, and a considerable part of all adolescents from these four schools were screened (2284 of approximately 4500). The minimal prevalence of food allergy requiring an EAI, calculated without extrapolation, was at least 1.0%, which still represents 16,200 individuals aged 11–20 at high risk in the Netherlands.

The under prescription of EAs and the high prevalence of self-diagnosis found in this study show that a considerable part of food-allergic adolescents is not being reached by health care providers and thus lack proper care. These adolescent likely lack proper education on, and awareness of, food allergy and may either be at high risk for severe allergic reactions without appropriate avoidance strategies and appropriate action plans or may unnecessarily eliminate certain foods from their diet. This warrants promotion of education and awareness concerning food allergy and EAs for health care providers10 as well as the wider community.
REFERENCES


