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Development of a screening questionnaire for the study of food allergy in adults

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ABSTRACT

Background & aims: As far as we know, no screening questionnaire has been developed and validated for identification of adverse food reactions in Portuguese-speaking adults, as an initial approach towards the investigation of cases of possible food allergy. Thus, the objective of this study was to develop and validate a screening questionnaire of food allergy in adult Portuguese-speaking patients.

Methods: This was a multicentre, cross-sectional study using a simple random sample of 186 adults between 18 and 82 years old from various parts of the centre of Portugal. Intelligibility of the questionnaire was first assessed in 24 patients with confirmed IgE- or non-IgE-mediated food allergy, and in 24 volunteers without food allergies. The 17-item questionnaire was subsequently applied by phone to 78 food allergic patients (66 IgE-mediated and 12 non-IgE mediated) and to 60 non-food allergic volunteers, with subsequent reassessment (re-test). Face and content validity, intelligibility, construct validity, and test-retest reliability (temporal stability) were analysed.

Results: Face and content validity allowed item reduction from 30 to 17 items with adequate content validity index $>$0.78. Construct validity was confirmed in the 66 confirmed IgE-mediated food allergic patients, 12 non-IgE-mediated food allergic patients, and 60 non-allergic patients. Test-Retest Reliability (general temporal stability) of the test had a Spearman correlation coefficient value of 0.845 for the retest. Cohen's Kappa values for the relevant questions were greater than 0.890 for almost all items. No differences were found when sex, age, and volunteers' recruitment origin were analysed. An inverse relationship was found between reliability and retest time interval.

Conclusions: Due to the quick and easy implementation, confirmation of face, content and construct validity as well as high temporal reproducibility, this screening questionnaire may be a useful study tool for an initial approach to detection of food allergies in adults.

Keywords: Adults, Adverse food reactions, Food allergy, Questionnaire, Validation

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INTRODUCTION

Food allergy is an important health problem in western countries as reflected in the appearance of numerous publications in this field over the past years.[1] For instance, in the United States, up to 20% of the population has been shown to change their diet due to the development of food allergy or other type of adverse reaction to food.[2] Nevertheless, the values for the prevalence of food allergy in the general population, particularly in adults, are not well known. In fact, various meta-analyses[3–5] and other recent studies[6,7] estimate that the prevalence of food allergy may vary according to the methodology used: 6–13% of adults and 6–38% of children when based upon self-reports, and 1–3% at all ages when oral food challenges are performed. Independently of using or not other diagnostic tests, namely oral provocation procedures, most studies on the prevalence of food allergies in the general population have been based upon an initial step involving the application of a questionnaire, which must be validated in order to be useful in terms of analysis.[8–12]

Thus far, only one study on the prevalence of food allergies in the general population has been performed in Portugal, limited to a sample of 659 adult participants older than 39 years old, where the authors performed a large, health and nutrition questionnaire, including questions not only related with food allergy, but also to demographic characteristics and social dietary habits.[13] Furthermore, as far as we know, no validated questionnaires, or clinical history screening questionnaires for epidemiological studies of adverse food reactions (AFR) as an initial approach to the study of food allergies in adults have been developed in Portuguese speaking countries. In fact, there is a lack of validated questionnaires or other clinical screening tools for the study of food allergies in adults, worldwide. Therefore, this is a pilot study, aimed at developing a clinical history screening questionnaire to be specifically applied in adults and studying its validity and reliability.

MATERIALS AND METHODS

Setting

This study was carried out at 3 healthcare centres in the central region of Portugal and at the allergy outpatient clinics of the central hospitals of Castelo Branco Local Health Unit and Cova da Beira University Hospital Centre, serving a population of 180,000 inhabitants older than 15 years old.[14] It was carried out between 2012 and 2015.

Volunteers and study design

Overall, we studied 186 volunteers, as shown in the Fig. 1 flowchart. Initially, we recruited 4 groups of adult volunteers into 2 clusters with characteristics similar to those of subjects in whom a future study on food allergy will be carried out. The first cluster ("Intelligibility study groups-ISG") was formed by 2 groups of individuals: a series of 24 non-food allergic volunteers from the general population (randomly recruited from general practicioners' files of participating healthcare centres and other hospital clinical services doctors files), and another series of 24 randomly recruited patients with food allergy confirmed by clinical history, specific IgE levels, cutaneous tests, and double-blind placebo-controlled food challenges (DBPCFC) (patients with IgE-mediated food allergy), with 2 of them being patients with positive clinical history and DBPCFC but negative specific IgE levels and cutaneous tests (patients with non-IgE-mediated food allergy), belonging to a database of food allergic patients, prepared from the medical records of the allergy outpatient clinics of the central hospital of the Castelo Branco Local Health Unit and Cova da Beira University Hospital Centre. This intelligibility study group was used for piloting purposes.

The second cluster of volunteers (case patients and control individuals) was different from the ISG groups, and was used for validity testing, namely test-re-testing, and included a total of 138 volunteers. This cluster included 66 randomly recruited adult patients with IgE-mediated food allergies, not previously selected for the first cluster, confirmed according to the same protocol used for the ISG patient group (clinical history, specific IgE levels, cutaneous tests and DBPCFC). Patients were randomly recruited from the previously mentioned database of food allergic patients of the Allergy Outpatient Clinic of the Castelo Branco Local Health Unit and Cova da Beira University Hospital Centre ("Case Group-IgE"). An extra group of 12 patients with positive DBPCFC but

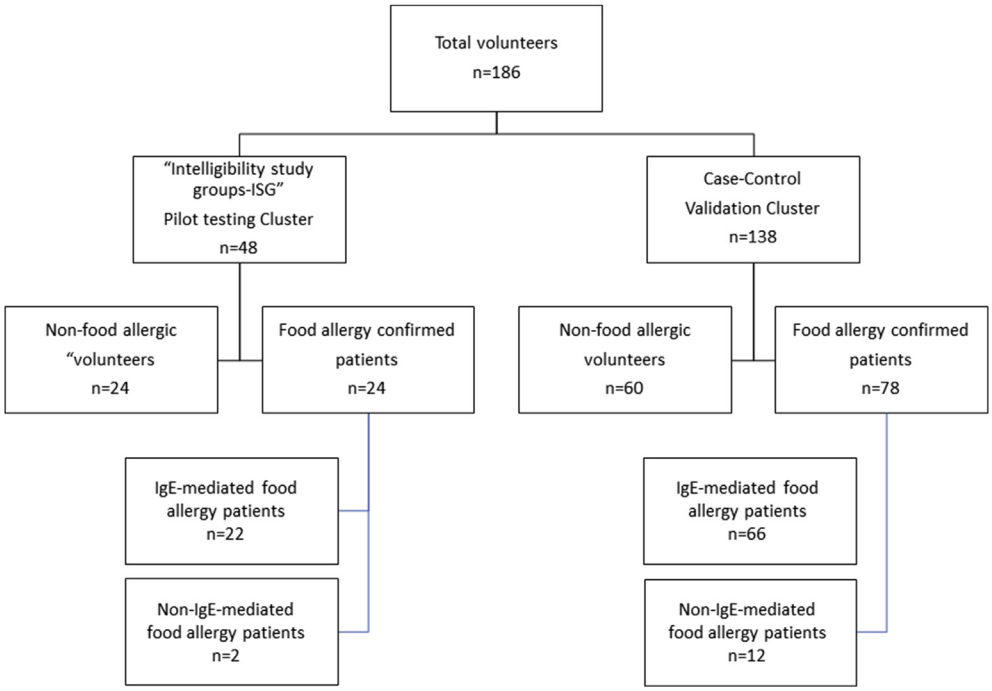

Fig. 1 Flowchart of study methodology steps

negative food-specific IgE and SPT were also recruited from the same database, and these patients constituted a non-IgE-mediated food allergy group. Non-food allergic volunteers (n = 60) from the general population were also randomly selected from the files of general practitioners belonging to the participating healthcare centres and who were invited to take part in the study ("Control Group").

Development of the clinical screening questionnaire

The initial step consisted of a bibliographical search for published validated questionnaires for screening food allergies in adults and was performed on PubMed using terms such as "questionnaire", "survey", "food allergy", "food hypersensitivity", "history", "tool", and "diagnosis". Published reports, namely EuroPrevall studies, did not include full questionnaires or did not mention any validation data. In addition, possible cultural adaptations might be needed. Although international consensus agrees that the allergy-focused history is a key part of the diagnostic pathway, there is no agreement regarding the type of questions to be asked, or the typified clinical history, as highlighted by Skypala et al.[15] For these reasons, we decided to develop a clinical history screening questionnaire for our study. Its design was based upon specific principles, as defined by a panel of experts in line with principles previously used in other publications using questionnaires in other fields of study,[16-18] as well as taking into account Portuguese[19] and European guidelines.[20] It was also based upon a questionnaire previously applied to children with food allergies,[21] with an adequate sample size calculated in accordance with appropriate recommendations.[22,23] The questionnaire aimed at screening for the presence of adverse food reactions and their risk factors. It also included the main clinical manifestations of adverse reactions to foods which are crucial to its diagnosis, as well as demographic data such as age, gender, and healthcare centre of referral. The questions were designed in an objective way in 7 domains, in a procedure similar to that used in a questionnaire developed and validated by our group, for detecting children with food allergies.[24] The first questions focused on the identification of the volunteer (assigning an identification code for data anonymisation, gender, and age) and request to answer the questionnaire (questions 1–4). In addition, item 17, asked volunteers about willingness to carry out a food allergy study in a specialized centre. Domain #1 focused on confirmation of the

presence of a previous adverse reaction to food (item 5). We must stress that the questionnaire only proceeded on from this point in case of a positive answer to this question. Domain #2 aimed at identifying the food which triggered the adverse reaction (question 6). Domain #3 focused on characterisation of the reaction to suspect food(s), and included questions 7 and 8. These questions were answered separately for each identified trigger food, and they included evaluation of reported symptoms and their severity, as well as definition of the reaction as immediate or delayed. Domain #4 included questions 9 and 10 and asked the need for treatment and procedures followed in response to the reaction. Domain #5 involved questions about previous reactions and how long ago the last reaction had taken place (items 11 and 12). Domain #6 studied the accessibility to diagnosis of food allergy, focusing as well on medical specialty care versus general practitioner care (questions 13 and 14). Domain #7 included questions 15 and 16, on personal and family history of allergy, as risk factors.

Analysis of theoretical construct: face and content validity

This initial version was analysed by a panel of 3 medical experts with experience in food allergy, who checked the questionnaire in terms of face validity, bearing in mind food allergy concepts and guidelines (Table 1). Analysis of content validity was performed by submitting the questionnaire for review to a team of nine medical specialists in allergy with recognized clinical and research experience in food allergy, who rated the relevance of each question in terms of current guidelines and knowledge (1-not relevant; 2-somewhat relevant; 3-quite relevant; 4-highly relevant).[25] The Item Content Validity Index (I-CVI) was calculated for each question, as the number of experts that gave a rating of 3 or 4, divided by the total number of experts, and I-CVI was regarded as significant if its value was 0.78 or above [26](Table 1). In addition, the experts also suggested modifications deemed as relevant, proposed the inclusion of new aspects and reviewed semantics as well, in a procedure similar to that previously performed by Lyra et al.[21] The questionnaire was then converted into a Google Docs format in order to facilitate collection of data via a phone call.

Logical (intelligibility) analysis of the questionnaire

In order to assess its intelligibility, adequacy, logic, and comprehension of the questions and duration, as well as the eventual need to modify some of the terms for the sake of clarity and adequate data collection, a pilot study was performed, with the questionnaire being applied to the 2 volunteer groups, matched in terms of socioeconomic status and degree of literacy ("Intelligibility study groups-ISG"). In 50% of cases, the questionnaire was applied by phone, and in the other 50% it was applied in a written form. Time taken to complete the questionnaire was measured in both groups. In addition, these volunteers were asked for an opinion about the degree of difficulty and pertinence of the questionnaire items. With the feedback obtained, some of the questions were simplified.

Subsequently, the questionnaire was again sent to a panel of 3 allergists with experience in food allergy, who agreed upon the final version of the questionnaire. Thus, literature review, allergy experts, and non-food allergic volunteers as well as patients with DBPCFC-confirmed food allergy contributed to content validity of the questionnaire.

Analysis of empirical construct: construct validity

In order to assess construct validity, the 17-item questionnaire was analysed in terms of known-group validity. We specifically wanted to test our hypotheses that the test would discriminate between: a) food allergic patients and non-food allergic individuals; b) IgE-mediated and non-IgE-mediated food allergic patients. Known-group validity analysis was based on analysis of the agreement between positive replies to its questions and the actual presence of food allergy in patients with previously confirmed food allergy (positive food-specific skin tests, positive food allergen-specific IgE, and positive DBPCFC), as well as differences in replies between patients with IgE-mediated and non-IgE-mediated food allergy.[22]

Question number	Item	Item CVI
1	Identity Code of volunteer	**1**
3	Gender	**0.888**
3	Age in years	**0.888**
4	Do you want to answer this questionnaire?	**1**
5	*Ethnicity*	0.222
6	*Social grade (occupation)*	0.111
7	*Literacy*	0.111
8	*Do you have any systemic disease?*	0.111
9	Do you have any adverse food reaction?	**1**
10	What kind of food causes your reaction?	**1**
11	*How much food caused the reaction?*	0.333
12	*Was the food that caused the reaction cooked (or not)?*	0.222
13	What kind of reaction did you have?	**1**
14	*Where did you have the reaction?*	0.111
15	How long after food ingestion did the reactions appear?	**0.888**
16	Did you need medical treatment?	**1**
17	If answer was "yes" for item 9, Where did you receive medical treatment?	**0.888**
18	*What kind of treatment did you receive (intravenous, oral)?*	0.333
19	*Did food ingestion occur on an empty stomach?*	0.111
20	*Was food ingestion associated with exercise?*	0.222
21	*Was food ingestion associated with any drug treatment?*	0.111
22	*Did you drink alcohol beverages during food ingestion?*	0.222
23	Have you had any previous episodes with the same food?	**1**
24	How long ago did the previous reaction take place?	**1**
25	*Have you had subsequent episodes with the same food?*	0.333
26	Have you been previously diagnosed with food allergy?	**1**

(continued)

Question number	Item	Item CVI
27	Have you ever been to a specialty appointment by an Allergist doctor?	**1**
28	Do you have any other allergic disease? (personal history of atopy)	**1**
29	Does anybody in your family have an allergic disease?	**0.888**
30	Would you want to be followed up at a specialty clinic?	**1**

Table 1. (Continued) Initial 30 items screening questionnaire and Item Content Validity Index (I-CVI) average performed by the nine experts medical specialists in allergy. Italic*: Items deleted in final versionItems highlighted in bold had a high I-CVI score (high level of concordance among experts).*

Test-retest reliability (temporal stability) of the questionnaire

The questionnaire was analysed in terms of reliability, using a test-retest approach. The questionnaire was applied via a phone call by a trained technician under allergist supervision, to the case and control groups as previously defined in the "volunteers" section and re-applied via a phone call to the case and control groups, on a second contact ("test-retest" technique)[22] after the first phone call.

Statistical analysis

Spearman's correlation coefficient (*Spearman's Rho value*) was used for determination of temporal stability, regarding values > 0.70 in absolute value as a strong correlation.

Analysis of concordance and reproducibility of the questionnaire was performed using Cohen's Kappa Test for each question. Cohen's Kappa results and their 95% confidence intervals were accepted as having good concordance if Kappa values were >0.60, and as having almost perfect concordance for levels of Kappa >0.80.[22] Data were studied using SPSS 22.0 (SPSS Inc., Chicago, IL, USA).[27] A level of significance of less than 0.05 was regarded as statistically significant.

Ethical aspects

This study was conducted in accordance with the guidelines laid down in the Declaration of Helsinki, and all procedures involving subjects/patients were approved by the Ethics Committees of the Amato Lusitano Hospital (Castelo Branco Local Health Unit), the Cova da Beira University Hospital Centre, and the Sub-Regional Health Authorities of Castelo Branco. Written informed consent was obtained from all subjects/patients.

RESULTS

Face and content validity

From the initial 30 questions, only 17 were kept (Table 2), with 0.967 being the final mean of the I-CVIs for the 17 scale items (mean I-CVI). These 17 items were regarded as essential for obtaining adequate information from the patients (Supplementary Material 1), and distributed by 7 domains.

Demographics of the study volunteers

Intelligibility study groups-ISG (pilot testing)

The 24 non-food allergic volunteers included in the "ISG-NFA" group were randomly recruited from the medical files of general population registed at participating primary care centres (50% females, median age of 45 $\pm$ 7 years). The 24 volunteers with confirmed food allergy (positive clinical history, specific IgE, skin tests, DBPCFC), randomly recruited from the Allergy outpatient clinics belonging to both hospitals (83% females, median age of 36 $\pm$ 11 years), were included in the "ISG-FA" group. These 2 groups were matched in terms of age, gender, Graffar scale, and degree of literacy.

Case and controls groups (validation testing)

The 66 patients with previously confirmed (positive clinical history, specific IgE, skin tests, and

Question number	Item	References
1	Identity Code of volunteer	19
3	Gender	9,10,12,18,19,21,31,32,39
3	Age in years	9-12,18,19,21,31,32,39
4	Do you want to answer this questionnaire?	9,10
5	Do you have any adverse food reaction?	9,10,12,18,19,21,31,32
6	What kind of food causes your reaction?	9,10-12,18-21,31,32,39,41
7	What kind of reaction did you have?	9-12,19-21,31,32,39-41
8	How long after food ingestion did the reactions appear?	9,10,12,19-21,31,39-41
9	Did you need medical treatment?	10,21,31,41
10	If answer was "yes" for item 9, Where did you receive medical treatment?	10,31
11	Have you had any previous episodes with the same food?	20,21,39,41
12	How long ago did the previous reaction take place?	10,20,21,39,41
13	Have you been previously diagnosed with food allergy?	10,11,31
14	Have you ever been to a specialty appointment by an Allergist doctor?	10,11,31
15	Do you have any other allergic disease? (personal history of atopy)	9-12,18,20,21,31,39,41
16	Does anybody in your family have an allergic disease?	9,10,11,20,40,41
17	Would you want to be followed up at a specialty clinic?	9,10

Table 2. Screening questionnaire and references used in its design

DBPCFC) food allergies were aged between 18 and 74 years (mean = 38.27 ± 9.3 years; 73% female). Forty-six of these patients reported symptoms related to one single foodstuff, and the other 20 were sensitised to more than one food. Implicated foodstuffs were seafood (32 cases), fresh fruits (26 cases), tree nuts (11 cases), peanut (8 cases), vegetables, chicken and egg (4 cases each), and other foodstuffs (8 cases). The 12 patients with previously confirmed (positive clinical history and DBPCFC, but negative specific IgE and skin tests) non-IgE mediated food allergies were aged between 27 and 68 years (mean = 46.58 ± 11.5 years; 67% female). Seventy-five percent of these patients reported symptoms related to one single foodstuff, and the other 25% were sensitised to more than one food. Implicated foodstuffs were seafood (11 cases), fresh fruits (2 cases), and other foodstuffs (8 cases). The 60 non-food allergic volunteers recruited from the general population were aged between 18 and 82 years (mean = 50 ± 14.21 years; 55% female). These 3 groups were matched in terms of age, gender, Graffar scale, and degree of literacy.

Intelligibility and testing of the questionnaire

All volunteers in the ISG-NFA and ISG-FA groups confirmed the intelligibility and adequacy of the 17 questionnaire items. It was estimated that the questionnaire, when applied to volunteers without AFR, would take 1 min to complete for the written form, and 2 min for the phone-applied form. In case of food allergy-confirmed volunteers, it took between 2 and 10 min (mean of

4.5 ± 1.5 min), for the written form and 2 min for the phone-applied form, respectively.

Analysis of empirical construct: construct validity

The 17-item questionnaire was analysed in terms of known-group validity in 3 different groups: a) a group of 66 patients with previously confirmed IgE-mediated food allergy, b) a group of 12 patients with previously confirmed non IgE-mediated food allergy, and c) a group of 60 non-food allergic volunteers.

Questionnaire items 5 (main), as well as 6–8, consistently identified food-allergic patients (both IgE-mediated and non-IgE-mediated) with excellent discrimination from non-food allergic controls (sensitivity 100%; specificity 100%), and being a "percentage of agreement" indicator. Furthermore, item 8 ("How long after food ingestion did the reactions appear?") also discriminated between patients with confirmed classical IgE-mediated food allergy (all had reactions in less than 2 h after food ingestion) and patients with non-IgE-mediated food allergy (who had reaction more than 2 h after food ingestion) with high sensitivity (100%) and specificity (100%).

Test-retest reliability (temporal stability)

In the case-control validation cluster groups (IgE- and non-IgE-mediated analysed together), mean re-application time value was 7 ± 9 weeks (range: 2–38 weeks; median and mode: 2 weeks). In the control group, mean re-application time was 8 ± 7 weeks (range: 2–34 weeks; median and mode: 2 weeks), thereby allowing analysis of the variability of replies to each of the items of the questionnaire. Temporal stability was calculated by determining *Spearman's Rho* correlation coefficient for 8 items (items number 5, 9, 11–15, 17) which were regarded as indispensable, since they objectively characterized the development of adverse food reactions, and due to the "yes-no" binary answer type. The set of 8 previously mentioned items, both globally and also taking gender, age, time interval between test and retest, as well as the volunteers' source of referral (diagnosed patients and Health Care Centres) into account are shown in Table 3. Five patients had new reactions between test and re-test phases, by

Parameter	Parameter classes	Rho spearman's values	*p* value (*)
Sex	Female	0.927	$p < 0.001$
	Male	0.898	$p < 0.001$
Age (years)	<25	0.724	$p < 0.001$
	25–50	0.986	$p < 0.001$
	>50	0.713	$p < 0.001$
Test-retest time interval (weeks)	<8	0.947	$p < 0.001$
	9–30	0.614	$p < 0.010$
	>30	0.500	$p < 0.050$
Volunteers' local of origin	Hospital Patients	0.489	$p < 0.100$
	Out of Hospital Patients	0.667	$p < 0.001$
	Community Healthcare Centre #1	0.733	$p < 0.010$
	Community Healthcare Centre #2	0.450	$p < 0.100$
	Community Healthcare Centre #3	0.758	$p < 0.001$

Table 3. Temporal Stability for Relevant questions by sex, age, time interval and local origin. *(*) p value indicates statistical significance of Spearman's Rho for each different subgroup*

inadvertent ingestion of suspect foods or ingestion by self-initiative to see whether they could tolerate the foods. No differences were found in temporal stability when sex, age, and volunteer origin were analysed. An inverse relationship was found between reliability and retest time interval.

DISCUSSION

In the present study, we developed and analysed in terms of face, content and construct (known-group) validity and reliability (temporal stability), for the first time in the Portuguese language, a screening questionnaire of adverse food reactions in the general adult population. This questionnaire was rapid and easily applicable, and showed excellent known-group validity, as well as a high degree of temporal stability. On the other hand, there was no variability in results when gender, age, and extra-hospital referral source of the volunteers were taken into account. In addition, *Spearman's Rho* correlation coefficient did not show significant differences across health care centres where control, non-food allergic volunteers were recruited.

Although, after the pilot study, we only analysed 138 volunteers (60 randomly selected non-food allergic controls, 64 patients with confirmed IgE-mediated food allergies, and 12 patients with confirmed non-IgE-mediated food allergies), this number is well within what is accepted as an appropriate sample size for this type of studies.[23]

For the assessment of the questionnaire, we studied reproducibility (test-retest stability) of the questionnaire, which was very high in global terms, as expressed in Spearman's Rho values of 0.80. Furthermore, reproducibility of specific items showed Cohen's Kappa values greater than 0.80 for most items, which is very good given the number of analysed items.[22,28] However, again items 12: "time elapsed since the previous episode", 11:"existence previous episodes of food allergy", item 15: "personal history of atopy" and 17: "Would you want to be followed up at specialty clinic?" significantly varied with time, between test and retest. This may have been due to memory bias, as reported by other studies,[29] or may have been due to the fact that volunteers might not be aware of the co-existence of other allergic diseases in them or did not report them either during test or re-test phase. In addition, in the case of item 12, discrepancy may arise from the fact that adverse food reactions may develop between test and retest, as a result of accidental exposure[30,31] or as self-initiative to test a minor portion of food, as actually happened in a small proportion of the patients (n = 5) in our study, or inversely by development of tolerance, which was unlikely in our study, given the short period of time between test and re-test.[32] In addition, volunteers with food allergies may develop novel reactions to new foodstuffs not mentioned in the first test, as may happen with patients sensitised to various food families (fruits, fish, seafood, egg, milk, etc)[30,33] thereby potentially affecting items 11 and 12.

Low temporal stability was found for items 15 and 17, ("Do you have any other allergic disease?" and "Would you want to be followed up at specialty clinic?"), with a value for Cohen's Kappa of 0.441 and 0.296 respectively (Table 4). This may have been due to the fact that a proportion of patients either became aware that they had an allergic disease or had a confirmed diagnosis of allergic disease between test and retest, as was observed in some cases. On the other hand, since food allergic patients were already being followed up at a clinic and the remainder of the volunteers were non-food allergic, this may have been associated with confusion regarding the need to be re-evaluated. In fact, non-food allergic volunteers who changed their answers between test and re-test, had mild symptoms they interpreted as possible rhinitis, conjunctivitis or dermatitis, which waxed and waned, which may have been associated with such changes in answers to item 17. Finally, the low temporal stability may also have been due to a memory bias as previously referred, since it was not possible to analyse this item separately from the variability between groups (non-food allergic controls versus patients with food allergies) using Spearman's coefficient, given the relatively limited size of the sample. In spite of these aforementioned factors potentially affecting the "8 crucial questions" (items 5,9,11–15,17), 6 of these questions maintained an optimal degree of temporal stability which afforded the whole of the test a high level of reproducibility.

Question number	Item	Cohen's Kappa Value (Test-ReTest reliability: intraclass correlation)
5	Do you have any adverse food reaction?	0.914
9	Did you have medical treatment?	0.830
11	Have you had any previous episodes with the same food?	0.696
12	How long ago did the previous reaction take place?	0.641
13	Have you been previously diagnosed a food allergy?	0.886
14	Have you ever been to a specialty appointment by an Allergist doctor?	0.892
15	Do you have any other allergic disease?	0.441
17	Would you want to be followed up at specialty clinic?	0.296

Table 4. Analysis of temporal stability (test- Re-test reliability). *$p < 0.05$ for all values*

In our study, although most patients were retested within 2 weeks of the initial test, there was high amplitude of time intervals, with a few of the patients being retested after 30 weeks. We acknowledge that this may be a limitation of our study since current guidelines for the performance of this type of study state that the ideal interval should be between 4 weeks and 6 months (ideally between 15 and 45 days).[34–36] Nevertheless, our study followed COSMIN guidelines,[37] and allowed the study of reliability (internal consistency and some aspects of reliability).

One important feature of our screening questionnaire is the fact that it is short and quick to apply. This is highly relevant to its application in clinical settings as well as in studies involving large samples, since it has been shown that volunteers' attention time span decreases as the length of a questionnaire increases.[38] In addition, our questionnaire adequately discriminated patients with confirmed food allergies from those without food allergies. It also discriminated between patients with IgE-mediated food allergies ($n = 22$, for the intelligility phase and $n = 66$ for the other validity assessment phases) from those with non-IgE-mediated food allergies ($n = 12$), on the basis of item 8, regarding timing of development of reactions upon food ingestion. However, the latter group only included 12 patients, which is a limitation of our study, and we are also aware that some patients with non-IgE-mediated food allergies may also have early onset symptoms.

Our study had other limitations. Firstly, it is a pilot study that needs a larger sample to improve its performance, applicability, and generalizability. Although, based on the sociodemographic features of our samples of patients and controls, we believe that these were representative of the Portuguese population for the age range in question, we still have to adequately study its generalizability to other Portuguese speaking countries. Secondly, although we used the acknowledge known-groups validity with 2 groups of food-allergic patients (IgE- and non-IgE-mediated) and 1 group of non-food allergic individuals to assess construct validity, due to the type of questions being asked, and the format of replies, it was not possible to carry out factor analysis or internal stability procedures. In addition, our questionnaire needs to be further studied with a higher sample, in terms of its limits for discriminating between classical IgE-mediated and non-IgE-mediated food allergies.

In spite of the limitations, our study also has new and consistent results. Firstly, our results do suggest that this screening questionnaire is essentially useful for screening of food allergies in cross-sectional studies but may need to be optimized for the

follow-up of patients over time. Furthermore, this questionnaire is the first one developed and validated in the Portuguese language for adults with food allergies, and we believe it may be applied in all Portuguese speaking countries worldwide (250 million people). In addition, our questionnaire is simple and quickly applicable and also fully based upon accepted criteria for a sensitive collection of the clinical history of food allergies.[39,40] We also believe that it is easily adaptable to other languages, particularly because not many clinical screening questionnaires are available for the study of adverse food reactions as an initial approach to the investigation of food allergy in adults. Our study was an alternative to the validation, in Portuguese, of the clinical history section of the EuroPrevall questionnaires and one of our future projects will be to assess the validity of our questionnaire in comparison with such EuroPrevall approach, regarded as a quality reference.

In conclusion, we developed, for the first time in the Portuguese language, a screening questionnaire for the study of adverse food reactions in adults, which showed high reproducibility and good potential to be a useful screening test in potentially different settings.

Consent for publication
All authors gave their written consent for publication.

Authors' contributions
CLI participated in the study design, data collection and analysis; AR participated in data collection; JB carried out the statistical analyses; LTB, RMA and HP supervised the whole project and participated in study design and data analysis. All authors participated in writing the manuscript.

Availability of data and materials
Please contact corresponding author for primary data requests.

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Declaration of competing interest
The authors declare no conflict of interests.

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Appendix ASupplementary data
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Abbreviations

AFR
Adverse Food ReactionsCOSMIN
Consensus-based Standards for the selection of health Measurement INstrumentsDBPCFC
Double-Blind Placebo-Controlled Food ChallengeI-CVI
Item Content Validity IndexIgE
Immunoglobulin EISG
Intelligibility Study GroupsISG-FA
Intelligibility Study Groups–Food AllergicISG-NFA
Intelligibility Study Groups–Non Food Allergic