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# **AQUA® Questionnaire as prediction tool for atopy in young elite athletes**

**Author's full names:** Anne-Charlotte Jonckheere (1); Sven F Seys (2); Ellen Dilissen (1); Gudrun Marijsse (1); An-Sofie Schelpe (1); Sarah Van der Eycken (1); Tulasi Verhalle (1); Vincent Vanbelle (3); Sven Aertgeerts (4); Thierry Troosters (5); Koen Peers (6); Lieven J Dupont (7,8); Dominique MA Bullens (1,9)

## **Author's affiliation(s):**

- (1) Laboratory of Paediatric Immunology, KU Leuven, Belgium
- (2) Laboratory of Clinical Immunology, KU Leuven, Belgium
- (3) Flemish Swimming Federation, Merelbeke, Belgium
- (4) Academic Centre for General Practitioners, KU Leuven, Belgium
- (5) Department of Rehabilitation Sciences, KU Leuven, Belgium
- (6) Sport Medical Advice Centre, University Hospitals of Leuven, Belgium
- (7) Clinical division of Respiratory Medicine, University Hospitals of Leuven, Belgium
- (8) Laboratory of Pneumology, KU Leuven, Belgium
- (9) Clinical division of Paediatrics, University Hospitals of Leuven, Belgium

## **Corresponding author:**

Anne-Charlotte Jonckheere.

Herestraat 49 bus 811, 3000 Leuven.

annecharlotte.jonckheere@kuleuven.be

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## LETTER TO THE EDITOR

To the editor,

Several studies have already identified atopy as a risk factor for the development of exercise-induced bronchoconstriction (EIB) in adult elite athletes (1–3). Skin prick test or serum specific IgE to common aero-allergens is used to determine the patient's atopy status (4). In 2009, Bonini M *et al.* introduced a screening tool to predict atopy in elite adult athletes, namely the Allergy Questionnaire for Athletes or short the AQUA<sup>®</sup> questionnaire (5). This questionnaire was validated in soccer players (5) and elite marathon runners (6) and concluded that a total AQUA<sup>®</sup> score of 5 or higher had the best predictive value for atopy with a specificity of 97.1% and a sensitivity of 58.3% (5). Both validation studies were performed in adult elite athletes (16-50 years old). Here, we studied whether the AQUA<sup>®</sup> questionnaire (with permission) can be used to predict atopy in young elite athletes (12-14 years old). To that extent, we recruited 24 basketball players and 44 football players from the Belgian elite sport high-school in addition to 44 swimmers from the Flemish Future team to complete the AQUA<sup>®</sup> questionnaire. The study was approved by the institutional review board and registered at clinicaltrials.gov (NCT02432183). Subject characteristics are summarized in table 1. The total AQUA<sup>®</sup> score was determined by scoring the questions related to allergy (Q4 to Q13 as well as Q15) and summing the scores of the individual questions as described in table 2 (5). To objectify the atopy status in our cohort of elite sport high school athletes, a skin prick test was performed for 9 common aero-allergens (grass pollen, weed pollen, birch pollen, mixed tree pollen (hazel, birch and alder), house dust mite (*Dermatophagoides pteronyssinus*), cat, dog, *Alternaria alternaria* and *Aspergillus fumigatus*), together with a histamine control and a negative control. A person was considered atopic if at least one allergen was positive during the skin prick test (wheal  $\geq$  3 mm and at least the size of the histamine control) (4). Forty of the 112 athletes (35.7%) were considered atopic with a higher prevalence of atopy in swimmers (40.4%) compared to other disciplines (table 1). To study the value of the AQUA<sup>®</sup> questionnaire to predict atopy in young elite athletes, a

receiver operating curve (ROC) analysis was performed with the AQUA<sup>®</sup> score and atopic status of all young elite athletes. The scores of the AQUA<sup>®</sup> questionnaire ranged from 0 up to 27. Several cut-off values were evaluated in our cohort to identify the AQUA<sup>®</sup> score with the best specificity and sensitivity for the prediction of allergy (table 3). The highest sensitivity (79%) was obtained with a cut-off value of 4 corresponding with the lowest specificity (64%). A cut-off value of 6 had the highest combination of both specificity (74%) and sensitivity (71%) in our cohort. Using the same cut-off value of 5 as in adult athletes yielded a similar sensitivity of 71%, but had a lower specificity (69%). This means that in young elite athletes an AQUA<sup>®</sup> score  $\geq 6$  is the best to be used to predict atopy. We furthermore need to mention that the AQUA questionnaire mainly consists of questions related to the clinical representation of allergic disease, which might be discordant from the evaluation of the atopic state of the subject studied by specific IgE and/or SPT (7). Another reason for the difference in cut-off value between our study and others, can possibly be explained by the age difference between our cohort (12-14 years old) and the cohort (20-50 years old) used to validate the AQUA<sup>®</sup> questionnaire or by the relatively limited number of subjects that were studied (5,6). However, Belgium (Flanders) only has a limited number of young athletes performing at elite levels in the respective sport disciplines, who almost all participated in this study. A validation study might be necessary in a bigger cohort of young elite athletes or a cohort containing children and adults to confirm or deny our results. The need for a larger cohort validation was already mentioned in the original paper (5). The likelihood ratio (LR) of every question to predict atopy (see table 2) was also calculated as described in the original article by Bonini *et al.* (5). The LR of question 6 and 10 (see table 2) was higher than in the original study (5). This might be due to the use of different sport disciplines in this study or the age difference with the original study. Despite these differences, we decided to use the original scoring system for its validation in young athletes. One specific question (question 9, table 2) from the AQUA<sup>®</sup> questionnaire scores 5 points which corresponds with the cut-off value to predict atopy in adult athletes (5). This means that all adult subjects who respond positively to that question already screen positive for atopy. We separately investigated this

question in our cohort to look if a positive answer to question 9, also strongly influences the score in our cohort. Fifty athletes had an AQUA<sup>®</sup> score  $\geq 6$  of which 26 (52%) answered yes to question 9. Statistical analysis concludes that question 9 could predict an AQUA<sup>®</sup> score  $\geq 6$  with a specificity of 97.3% and a sensitivity of 52% ( $P < 0.0001$ ; Fisher exact two-tailed test). Because of the low sensitivity, it is more plausible that a combination of different questions leads to an AQUA<sup>®</sup> score  $\geq 6$ . In the future, the AQUA<sup>®</sup> questionnaire probably can be reduced to a few key questions as already suggested by Bonini *et al.* (5), of which question 9 is one of these, that predict atopy with the same specificity and sensitivity as answering the 11 AQUA<sup>®</sup> questions (table 1) and calculating the total AQUA<sup>®</sup> score.

To conclude, our study shows the presence of atopy in 35.7% of the young elite athletes at the age of 12-13 years old, which is slightly higher than in the general adolescent population in Europe (15-20%; 8). We also show that the AQUA<sup>®</sup> questionnaire can be used as a prediction tool for atopy in a population of young elite athletes and therefore might be an interesting tool to predict the risk for EIB in young elite athletes. However, this should be subject of further studies. An AQUA<sup>®</sup> score  $\geq 6$  is proposed to predict atopy in young elite athletes with a specificity of 74% and a sensitivity of 71%. Alternatively, a positive answer to question 9 might also predict atopy with a high specificity though low sensitivity.

Anne-Charlotte Jonckheere<sup>1</sup>

Sven Seys<sup>2</sup>

Ellen Dilissen<sup>1</sup>

Gudrun Marijsse<sup>1</sup>

An-Sofie Schelpe<sup>1</sup>

Sarah Van der Eycken<sup>1</sup>

Tulasi Verhalle<sup>1</sup>

Vincent Vanbelle<sup>3</sup>

Sven Aertgeerts<sup>4</sup>

Thierry Troosters<sup>5</sup>

Koen Peers<sup>6</sup>

Lieven Dupont<sup>7,8</sup>

Dominique Bullens<sup>1,9</sup>

<sup>1</sup>Laboratory of Paediatric Immunology, KU Leuven, Belgium

<sup>2</sup>Laboratory of Clinical Immunology, KU Leuven, Belgium

<sup>3</sup>Flemish Swimming Federation, Merelbeke, Belgium

<sup>4</sup>Academic Centre for General Practitioners, KU Leuven, Belgium

<sup>5</sup>Department of Rehabilitation Sciences, KU Leuven, Belgium

<sup>6</sup>Sport Medical Advice Centre, University Hospitals of Leuven, Belgium

<sup>7</sup>Clinical division of Respiratory Medicine, University Hospitals of Leuven, Belgium

<sup>8</sup>Laboratory of Pneumonology, KU Leuven, Belgium

<sup>9</sup>Clinical division of Paediatrics, University Hospitals of Leuven, Belgium

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Table 1: Subject characteristics

	Basketball players	Football players	Swimmers	P-value*
Number (n=)	26	44	47	
Age (years)	12.19 ± 0.57	13.05 ± 0.91	12.13 ± 0.77	
Gender (M/F)	14/12	37/7	36/11	
Atopy (n=)	6 (23.1%)	14 (31.8%)	19 (40.4%)	0.2424
Mono-sensitized	3	8	10	
Poly-sensitized	3	6	9	
(> 1 sensitization)				

\* P-value was determined via Chi square test.

Table 2: AQUA© questions for determination of AQUA© score together with likelihood ratio (LR)

	Question	Scoring points	Likelihood ratio (LR)
Q4	Has a doctor ever diagnosed you with an allergic condition?	Yes = 4 No = 0	3,120
Q5	Do you suspect to suffer from allergy, independently from any medical diagnosis?	Yes = 4 No = 0	3,744
Q6	Did you ever use anti-allergic drugs (antihistamines, topical steroids, “allergy vaccines”)?	Yes = 3 No = 0	8,111
Q7	Is there any allergic subject in your family?	Mother and Father = 3 Mother or Father = 2 Other relatives = 1	Not applicable* 1,921 1,842
Q8	Have you frequently red eyes with tearing and itching?	Yes = 2 No = 0	4,368
Q9	Do you frequently sneeze, have a running or itchy nose (apart from colds)?	Yes = 5 No = 0	4,132
Q10	Do you suffer from wheezing or chest tightness?	Yes = 2 No = 0	5,615
Q11	Have you ever had itchy skin eruptions?	Yes = 2 No = 0	3,522
Q12	Have you ever had severe allergic or anaphylactic reactions?	Yes = 2 No = 0	1,123
Q13	Have you ever had shortness of breath, cough and/or itching of the throat following exercise?	Yes = 2 No = 0	0,887
Q15	Have you ever had allergic reactions to foods?	Yes = 3 No = 0	1,872

\* No subject who was atopic answered “mother and father” to this question in our cohort.



Table 3: Validation of different AQUA-scores in young elite athletes

AQUA-score	Atopic	Non-atopic	P-value*	Specificity	Sensitivity
≥ 4	27	27	< 0.0001	64%	79%
< 4	7	47			
≥ 5	24	23	0.0002	69%	71%
< 5	10	51			
≥ 6	24	19	< 0.0001	74%	71%
< 6	10	55			
≥ 7	23	15	< 0.0001	80%	68%
< 7	11	59			

\* P-value, specificity and sensitivity were determined via a Fisher exact two-tailed test.