

## THE PREVALENCE OF EXERCISE-INDUCED BRONCHOCONSTRICTION IN NON-ASTHMATIC SWIMMERS: A SYSTEMATIC REVIEW AND META-ANALYSIS

### PREVALÊNCIA DA BRONCOCONSTRICÇÃO INDUZIDA PELO EXERCÍCIO EM NADADORES NÃO ASMÁTICOS: UMA REVISÃO SISTEMÁTICA E META-ANÁLISE

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#### RESUMO

**Objetivo:** Avaliar a prevalência de broncoconstrição induzida por exercício (BIE) em nadadores não asmáticos. **Métodos:** Foram pesquisadas as bases de dados BVS/LILACS, MEDLINE/PubMed, Web of Science, Scopus, SPORTDiscus e dois repositórios (BDTD e OATD) até julho de 2023. Foi utilizada uma combinação de descritores MeSH e palavras de texto. Os estudos originais relatando casos de BIE, diagnosticados por teste objetivo foram selecionados. Avaliou-se a qualidade metodológica dos estudos com o instrumento para prevalência Joanna Briggs e meta-análises de efeitos aleatórios com análise planejada de subgrupos foram conduzidas. **Resultados:** Esta revisão recuperou 33 estudos (700 nadadores não asmáticos, 250 casos de BIE). A prevalência do BIE foi de 34% (IC 95%: 25-45%) com heterogeneidade significativa ( $I^2 = 68\%$ ), a qual foi parcialmente explicada pela análise de subgrupos para método diagnóstico. O teste de metacolina apresentou maior prevalência (51%, IC 95%: 43-59%) com baixa heterogeneidade ( $I^2 = 28\%$ ). Apenas três estudos (90,1%) foram considerados de baixo risco de viés, enquanto os 30 restantes (90,9%), como moderado. Os resultados indicam que nadadores não asmáticos apresentam prevalência expressiva de BIE, principalmente com teste de metacolina. **Conclusão:** A melhor compreensão da prevalência do BIE entre nadadores não asmáticos, estimada em 34% nesta revisão, deve ser considerada um alerta para os profissionais envolvidos no treinamento e para os formuladores de políticas de saúde. São necessárias intervenções de saúde pública para prevenção. Além disso, a heterogeneidade substancial entre os estudos destaca a necessidade de estudos melhor desenhados.

**Palavras-chave:** Prevalência. Asma induzida por exercício. Hipersensibilidade respiratória. Natação.

#### ABSTRACT

**Objective:** To evaluate the prevalence of exercise-induced bronchoconstriction (EIB) in non-asthmatic swimmers. **Methods:** We searched BVS/LILACS, MEDLINE/PubMed, Web of Science, Scopus, SPORTDiscus databases, and two repositories (BDTD and OATD) up to July 2023. A combination of MeSH descriptors and text words were used. We selected original studies reporting cases of EIB diagnosed by objective test in non-asthmatic swimmers. We assessed the quality of the included studies for bias with Joanna Briggs checklist for prevalence, and conducted random-effects meta-analyses with planned subgroup analysis. **Results:** This review retrieved 33 studies (700 non-asthmatics swimmers, 250 cases of EIB). The EIB prevalence was 34% (95% CI: 25-45%) with a significant heterogeneity ( $I^2 = 68\%$ ), which was partially explained by the subgroup analysis for diagnostic method used. The methacholine test showed a higher prevalence (51%, 95% CI: 43-59%) with a low heterogeneity ( $I^2 = 28\%$ ). Only three studies (90.1%) were considered as low risk of bias, while the remaining 30 (90.9%), as moderate. The results indicate that non-asthmatic swimmers have an expressive prevalence of EIB, especially when performing methacholine test. **Conclusion:** The better understanding of the prevalence of EIB among non-asthmatic swimmers, estimated in 34% in this review, should be considered a warning to professionals involved in training and health policymakers. Public health interventions for prevention are required. Also, the substantial heterogeneity between studies highlights the need for better designed studies.

**Keywords:** Prevalence. Asthma, exercise-induced. Respiratory hypersensitivity. Swimming.

#### Introduction

Regular physical activity is an effective health promotion measure recommended by all main health care systems<sup>1</sup>. Among the various sports, swimming is one of the most

popular worldwide for recreational and competitive purposes<sup>2</sup>. Furthermore, it is the second in number of athletes in the Olympic Games, featuring at every modern edition<sup>2</sup>.

Although it is considered beneficial to health, swimming brings unique challenges due to high respiratory rate and exposure to specific environmental factors, such as chlorine, its metabolites and poor air circulation in indoor settings<sup>3,4</sup>. As a result, respiratory problems such as exercise-induced bronchoconstriction (EIB) may arise<sup>1,3</sup>. Its definition comprises a transient obstruction of the airway caliber that usually occurs during exercise or just after and resolves spontaneously in approximately 60 minutes<sup>1,3,4</sup>.

Exercise-induced bronchoconstriction tends to cause limitations in physical activities, which impact negatively the quality of life and the performance of athletes. In this way, proper diagnosis and management lead to healthy lifestyle and make sports careers feasible, allowing competition at elite level<sup>1,5</sup>.

For a long time, this condition was called exercise-induced asthma (EIA) as it was thought that only asthmatics were committed. Later on, the term has been renamed to EIB, although used as synonym for EIA<sup>3,4</sup>. However, this use should avoid inasmuch as EIB can be observed in cases without asthma, and also because it may imply that exercise causes rather than triggers or exacerbates asthma symptoms. The underlying mechanisms, diagnosis and management strategies of EIB may differ from EIA. To clarify this debate, the American Thoracic Society Clinical Practice Guideline suggested using the terminology EIB without asthma (EIB<sub>wa</sub>) and EIB with asthma (EIB<sub>a</sub>), instead of EIA<sup>4</sup>.

The prevalence of EIB can vary widely depending on several factors, including the population studied and diagnostic method used, among others<sup>1,3,4</sup>. It is estimated that the general population has a prevalence of approximately 5-20%, while higher rates are observed in athletes, ranging from 3.7 to 70%<sup>1,5</sup>. The most common sports associated with EIB are cycling, running, and swimming in summer and cross-country, ice hockey, and ice skating in winter<sup>3</sup>. Swimming, for instance, has a similar wide distribution, ranging from 11% to 68% in competitive ones<sup>6,7</sup>. However, there is currently a dearth of scientific literature, addressing the actual prevalence of EIB<sub>wa</sub> in general and specifically among swimmers<sup>5</sup>. Most of the data available do not differentiate asthmatics from non-asthmatics in their analysis, which may impact the assessment of prevalence, as many as 90% of asthmatics have EIB<sup>3,5</sup>.

In this scenario, the present study aims to better estimate the prevalence of EIB among non-asthmatic swimmers, based on available data. By better understanding its frequency, policies regarding screening and management of this condition may allow improvement in lifestyle, quality of life and athletic performance.

## Methods

### *Study design and protocol*

The present study is a systematic review and meta-analysis. We followed the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) to conduct and report this review<sup>8</sup>. In addition, the study protocol was submitted to the International Prospective Register of Systematic Reviews (PROSPERO) and approved on the 13th of September 2023, under registration number CRD42023460070.

### *Sources of information and search strategies*

To retrieve all published reports describing the prevalence of EIB among non-asthmatic swimmers, we consulted BVS/LILACS, MEDLINE/PubMed, Scopus, SPORTDiscus/EBSCOhost and Web of Science databases, and two repositories (Biblioteca Digital Brasileira de Teses e Dissertações [BDTD] and Open Access Theses and Dissertations [OATD]) until July 31<sup>st</sup> of 2023. We structured search strategy as blocks, based

on checking the descriptors in the Medical Subject Headings (MeSH by PubMed), combined with the text words (tw) to Boolean operators (AND, OR). The first block encompassed “swimming”[MeSH Terms] OR “swimmer”[tw], and the second block, “bronchoconstriction”[MeSH Terms] OR “asthma, exercise-induced”[MeSH Terms] OR “exercise-induced bronchoconstriction”[tw] OR “exercise-induced bronchospasm”[tw] OR “respiratory hypersensitivity”[MeSH Terms] OR “airway hyper-responsiveness”[tw].

### *Eligibility criteria*

Articles were considered for inclusion based on PICOT strategy, where Participants comprised all types of swimmers (elite and non-elite); Indicator included assessment of EIB through a complementary exam such as direct (inhaled methacholine) and/or indirect challenge (field-based or laboratory exercise challenges and surrogate testing, such as EVH or hyperosmolar tests with saline or mannitol). For the former, a definition of a positive test was as a drop of 20% or greater in forced expiratory volume in 1 second (FEV1) observed in the post-test, and for the latter, it was a drop of 10% or greater in FEV1 observed in the post-test<sup>3,4</sup>. Comparison included non-asthmatics swimmers without EIB; Outcome comprised the EIB prevalence in non-asthmatic swimmers, and Type of studies enrolled original articles with no language restriction and published from inception to 31<sup>st</sup> July 2023. We excluded any article that did not present the term “exercise-induced bronchospasm”, “exercise-induced bronchoconstriction”, or used “exercise-induced asthma” as a synonym for EIB without any differentiation between asthmatic and non-asthmatic participants. Also, editorial articles, author's opinion, book, experimental studies (animal and in vitro), and review were excluded. The MEDLINE/PubMed database was the reference for cases of duplicate articles.

We considered two types of athletes: elite and non-elite. The definition of the former was highly competitive persons who train and compete consistently at higher levels (*e.g.*, Olympics or professional)<sup>4</sup>. These data were obtained from the author's report.

The diagnosis of asthma was based on the criteria reported by the authors, and included questionnaire and/or medical diagnosis.

### *Study selection*

Two reviewers (MJDL and JV) independently assessed the entire study selection process. Records were screened by title and abstract to determine initial eligibility. The full texts of the remaining records were then retrieved and assessed for inclusion in the review. Any disagreements were resolved by discussion and a consultation with a third reviewer (ASV) if necessary.

Finally, we also checked the reference lists of eligible papers to identify additional relevant studies.

### *Quality control assessment*

Two reviewers (ASV and NSP) independently assessed the quality of each eligible study according to the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Studies Reporting Prevalence Data (University of Adelaide, Australia)<sup>9</sup>. This checklist contains nine questions encompassing sampling, reporting, validation of the method used, execution, and statistical analysis. There are four possible answers (“yes”, “no”, “unclear” or “not applicable”). An overall score for each article was achieved, ranging from 1 to 9 “yes” answer. We rated the risk of bias as high, (1 to 3 “yes”), moderate (4 to 6 “yes”) or low (7 to 9 “yes”).

### *Data extraction*

Two reviewers (MJDL and JV) extracted data from each eligible study using a standardized extraction sheet. It included: 1. Study identification: name of the first author, year of publication, country of study; 2. Study characteristics: design and sample size; 3. Participants: non-asthmatic swimmers and its characteristics, including type of athlete (elite or non-elite), number of cases, sex, and age; 4. Comparison: non-asthmatic swimmer without EIB diagnosis; 5. Diagnostic method: complementary exams that assessed EIB, and 6. Prevalence. Another reviewer (ASV) checked this step.

### *Statistical analysis*

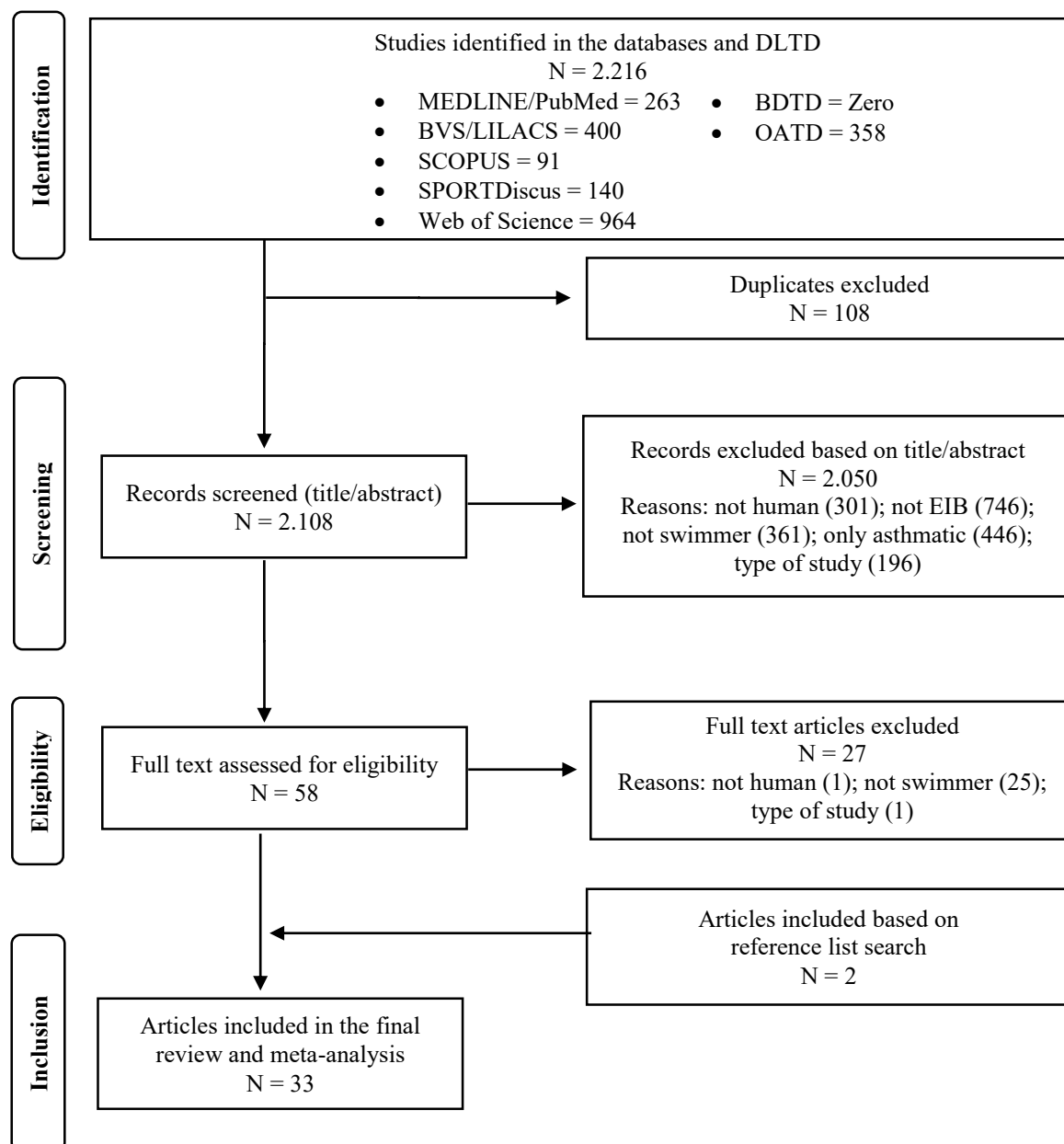
We performed a proportion meta-analysis, only if at least two studies reported the outcome. Summary estimates, along with their 95% confidence intervals (CI), were calculated for the prevalence of EIB among non-asthmatic swimmers, using random effects models. Whenever a study used more than one diagnostic method, we selected the highest result, after calculation it for each method. We chose this strategy, in order to avoid data entry errors by including data from the same study several times, which would promote an overestimation.

The assessment of study heterogeneity occurred through the Cochran's Q and the  $I^2$  statistic and it was considered statistically significant if  $p < 0.10$  for Cochran's Q test and  $I^2 > 50\%$ . We conducted a subgroup analysis on study design, quality (risk of bias), geographic area (continent), type of athlete (elite or non-elite), and diagnostic method used, in order to investigate the causes of heterogeneity.

We constructed forest plots to visually display the study results. To determine the risk of publication bias, we used a funnel plot and the Egger test if  $\geq 10$  studies were available for an association. Asymmetry of the funnel plot, plus a  $p$  value  $< 0.10$  for Egger test, was considered indicative of a potential publication bias. All meta-analysis were performed in R language and environment for statistical computing (version 4.1.2, The R foundation for Statistical Computing, Vienna, Austria), using the commands "metaprop" for pooling EIB prevalence, "metafunnel" for producing funnel plot, and "metabias" for Egger test.

## **Results**

Our search strategy retrieved 2.216 records, published until 31<sup>st</sup> July 2023. After removing 108 duplicates, a total of 2.108 remained. The systematically review of all titles/abstracts and full-text studies, yielded 31 records that met our inclusion criteria, 26 from the databases, and five from OATD repository. The inclusion of two other records from the manual reference query totaled 33. All documents were published between 1990 and 2022. The reasons for exclusion were irrelevant content and lack of EIB evaluation (746, 35.9%) followed by no differentiation between asthmatics and non-asthmatics populations (446, 21.5%), not swimmer (386, 18.6%), not human (302, 14.5%), and type of study (197, 9.5%). Figure 1 displays the flowchart of the search and screening process.



**Figure 1.** PRISMA flowchart of the study selection process.

**Note:** DLTD – Digital Library of Theses and Dissertations; BVS/LILACS – Biblioteca Virtual em Saúde/Literatura Latino-Americana e do Caribe em Ciências da Saúde; WOS – Web of Science; BDTD – Biblioteca Digital Brasileira de Teses e Dissertações; OATD – Open Access Theses and Dissertations.

**Source:** Authors

Out of 33 selected studies, one was an experimental study (randomized clinical trial)<sup>10</sup>, and 32 were observational including 26 cross-sectional<sup>6,11-34</sup>, five cohorts<sup>35-39</sup>, and one case series<sup>40</sup>, all written in English. They covered 932 swimmers, and 700 of them were

non-asthmatics. The conduction of these researches took place on four continents encompassing sixteen countries (eight in Canada, four in Belgium, three in the USA, two in Brazil, Denmark, Italy, England, and Scotland, and one in Austria, Australia, Germany, New Zealand, Norway, Slovenia, South Africa and Sweden).

Concerning the participants' activity profile, 434 (62%) were elite swimmers, 248 (35.4%) were non-elite, and there was no discrimination in 20 (2.9%). Among the non-elite swimmers, only 29 (4.1%) practice swimming in recreational level.

The participants had the following characteristics: 157 (22.4%) were men, 147 (21%) were women, and there was no report in 398 (56.9%). Fifteen studies reported the age, with a mean of 16.9 years<sup>6,10-13,15,17,23,26,27,29,31,37,39,40</sup>. None of the 33 articles reported the ethnicity of its participants. Also, none of the 700 used any anti-asthma medication, and we could not retrieve solid information about smoking.

Nine studies measured chlorine in the environment<sup>7,10,13,17,18,22,23,31,37</sup>. Out of these, eight did it in the water<sup>7,10,13,17,18,23,31,37</sup>, and one in the air<sup>22</sup>.

Concerning the diagnostic method used, 694 participants (99.1%) performed it. Of these, 403 (58.1%) did just one test, as foreseen in the twenty study protocols<sup>6,7,10,11,17,23,25,26,28-32,34-40</sup>. The indirect challenges were the most used as a diagnostic method for EIB, comprising 29 studies<sup>6,7,10,12-22,24-30,32-36,38-40</sup> with 580 participants (83.6%). The EVH challenge and the exercise challenge tests were the commonest (17 studies each). Two hundred and fifty swimmers had a positive test for EIB. Table 1 displays the characteristics of the selected studies.

**Table 1.** Characteristics of the selected studies

Author (et al.), Year, Location	Study characteristics (design; total of participants [number of swimmers])	Swimmer characteristics				Diagnostic Method**	EIB prevalence Cases/total (%) **
		Total (n)	Type (n)	Sex (n)	Age (mean)		
Zwick, 1990, Austria <sup>11</sup>	CS, n = 28 [14]	(14)	Non-elite (14)	M (7) F (7)	15.2y	MCT	11/14 (79%)
Potts, 1994, Canada <sup>12</sup>	CS, n = 51 [35]	(17)	Elite (17)	NR	19.2y	ECT (swim) MCT	2/17 (12%) 10/17 (59%)
Bonsignore, 2003, Italy <sup>13</sup>	CS, n = 17 [7]	(7)	Non-elite (7)	NR	23.3y	ECT (swim) MCT	0/7 (0%) 1/7 (14%)
Williams, 2004, South Africa <sup>10</sup>	CT, n = 42 [41]	(21)	Non-elite (21)	M (12) F (9)	15y	ECT (run) ECT (swim)	2/21 (10%) 9/15 (60%)
Pedersen <sup>a</sup> , 2008, Denmark <sup>42</sup>	CS, n = 33 [33]	(28)	Elite (28)	NR	NR	EVH MCT	11/28 (39%) NR
Pedersen <sup>b</sup> , 2008, Denmark <sup>53</sup>	CS, n = 16 [16]	(16)	Elite (16)	M (0) F (16)	18.3y	ECT (lab) ECT (swim) EVH MCT	4/16 (25%) 4/16 (25%) 5/16 (31%) 3/16 (19%)
Castricum, 2010, Australia <sup>64</sup>	CS, n = 33 [33]	(20)	Elite (20)	NR	NR	ECT (cycle) ECT (swim) EVH	1/20 (5%) 0/20 (0%) 7/20 (35%)
Clearie <sup>a</sup> , 2010,	CS, n = 36 [36]	(28)	Elite (28)	M (12) F (16)	13y	ECT (swim)	10/28 (36%)

Author (et al.), Year, Location	Study characteristics (design; total of participants [number of swimmers])	Swimmer characteristics				Diagnostic Method**	EIB prevalence Cases/total (%) **
		Non-asthmatic					
		Total (n)	Type (n)	Sex (n)	Age (mean)		
<i>Scotland<sup>17</sup></i>							
<i>Clearie<sup>b</sup>, 2010, Scotland<sup>18</sup></i>	CS, n = 61 [57]	(49)	Elite (49)	NR	NR	<b>ECT (swim)</b> Mannitol	<b>7/47 (15%)</b> 5/49 (10%)
<i>Stadelmann, 2011, Norway<sup>19</sup></i>	CS, n = 24 [24]	(20)	Elite (20)	NR	NR	<b>EVH</b> MCT	<b>8/20 (40%)</b> 8/20 (40%)
<i>Bougault, 2012, Canada<sup>20</sup></i>	CS, n = 33 [23]	(20)	Elite (20)	NR	NR	EVH <b>MCT</b>	6/19 (32%) <b>9/20 (45%)</b>
<i>Hanks, 2012, USA<sup>35</sup></i>	CO, n = 148 [26]	(18)	NR (18)	NR	NR	<b>EVH</b>	<b>15/18 (83%)</b>
<i>Labreche, 2012, Canada<sup>21</sup></i>	CS, n = 21 [21]	(16)	Non-elite (16)	M (9) F (7)	NR	ECT (swim) <b>EVH</b>	2/16 (13%) <b>6/16 (38%)</b>
<i>Romberg, 2012, Sweden<sup>22</sup></i>	CS, n = 101 [101]	(41)	Elite (41)	NR	NR	ECT (swim) <b>Mannitol</b>	4/39 (10%) <b>5/41 (12%)</b>
<i>Silvestri, 2012, Italy<sup>23</sup></i>	CS, n = 34 [34]	(34)	Non-elite (34)	M (28) F (6)	13y	<b>MCT</b>	<b>18/33 (55%)</b>
<i>Turmel, 2012, Canada<sup>24</sup></i>	CS, n = 133 [50]	(40)	Elite (40)	NR	NR	<b>EVH</b> MCT	<b>20/40 (50%)</b> NR
<i>Seys, 2014, Belgium<sup>25</sup></i>	CS, n = 58 [12]	(11)	Elite (11)	NR	NR	<b>EVH</b>	<b>3/11 (27%)</b>
<i>Morissette, 2015, Canada<sup>26</sup></i>	CS, n = 29 [23]	(23)	Non-elite (23)	NR	19y	<b>ECT (swim)</b>	<b>1/23 (4%)</b>
<i>Seys, 2015, Belgium<sup>27</sup></i>	CS, n = 72 [41]	(26)	Elite (26)	M (16) F (10)	16.5y	ECT (swim) <b>EVH</b>	2/26 (8%) <b>6/26 (23%)</b>
<i>Levai, 2016, England<sup>7</sup></i>	CS, n = 82 [44]	(28)	Elite (28)	NR	NR	<b>EVH</b>	<b>19/27 (70%)</b>
<i>Van der Eycken, 2016, Belgium<sup>36</sup></i>	CO, n = 52 [12]	(8)	Elite (8)	NR	NR	<b>EVH</b>	<b>5/8 (63%)</b>
<i>Bohm, 2017, Germany<sup>37</sup></i>	CO, n = 50 [25]	(25)	Elite (25)	M (15) F (10)	18y	<b>MCT</b>	<b>13/25 (52%)</b>
<i>Kennedy, 2017, Canada<sup>28</sup></i>	CS, n = 25 [25]	(24)	Non-elite (24)	M (14) F (10)	NR	<b>ECT (run)</b> ECT (swim)	<b>1/24 (4%)</b> 0/24 (0%)
<i>Mata, 2017, Brazil<sup>29</sup></i>	CS, n = 40 [18]	(18)	Non- elite* (18)	M (12) F (6)	16.3y	<b>ECT (run)</b>	<b>0/18 (0%)</b>

Author (et al.), Year, Location	Study characteristics (design; total of participants [number of swimmers])	Swimmer characteristics				Diagnostic Method**	EIB prevalence Cases/total (%) **
		Total (n)	Type (n)	Sex (n)	Age (mean)		
Wang, 2017, New Zealand <sup>30</sup>	CS, n = 22 [22]	(11)	Non- elite* (11)	NR	NR	<b>EVH</b>	<b>1/11 (9%)</b>
Davies, 2018, Canada <sup>6</sup>	CS, n = 8 [8]	(7)	Non-elite (7)	M (4) F (3)	16y	<b>EVH</b>	<b>6/7 (86%)</b>
Jackson, 2018, England <sup>38</sup>	CO, n = 14 [14]	(13)	Elite (13)	NR	NR	<b>EVH</b>	<b>7/10 (70%)</b>
Škrgat, 2018, Slovenia <sup>31</sup>	CS, n = 41 [41]	(41)	Non-elite (41)	M (18) F (23)	16y	<b>MCT</b>	<b>18/41 (44%)</b>
Snyder, 2018, USA <sup>39</sup>	CO, n = 13 [13]	(13)	Non-elite (13)	M (1) F (12)	20.3y	<b>ECT (run)</b>	<b>2/13 (15%)</b>
Jonckheere, 2019, Belgium <sup>32</sup>	CS, n = 134 [45]	(42)	Elite (42)	NR	NR	<b>EVH</b>	<b>14/42 (33%)</b>
Robinson, 2019, USA <sup>40</sup>	Case series, n = 4 [4]	(2)	Elite (2)	M (0) F (2)	14.5y	<b>ECT (swim)</b>	<b>1/2 (50%)</b>
Leahy, 2020, Canada <sup>33</sup>	CS, n = 15 [15]	(12)	Non-elite (12)	M (4) F (8)	NR	ECT (swim) <b>EVH</b>	1/12 (8%) <b>1/12 (8%)</b>
Santos, 2022, Brazil <sup>34</sup>	CS, n = 19 [19]	(7)	Non-elite (7)	M (5) F (2)	NR	<b>ECT (swim)</b>	<b>0/7 (0%)</b>

**Note:** CS – cross-sectional; CO – cohort; CT – clinical trial; M – male; F- female; y – years; NR – not reported; MCT – Methacholine challenge test; ECT - exercise challenge test; EVH – eucapnic voluntary hypercapnia; Lab – laboratory; \*Non-elite (recreational); \*\*Bold letter – method and result that were chosen.

**Source:** Authors

Thirty-two studies reported the cut-off value of percent fall in FEV1. According to the diagnostic method employed, the levels changed. All that used a direct challenge (inhaled methacholine), applied a 20% fall<sup>11-15,19,20,23,24,31,37</sup>. In the other hand, the indirect challenge (ECT, EVH or mannitol) showed different levels of cut-off. All 17 studies that used EVH<sup>6,7,14-16,19-21,24,25,27,30,32,33,35,36,38</sup> and 14 studies that used ECT<sup>10,15-18,21,22,27-29,33,34,39,40</sup>, applied  $\geq 10\%$  fall, while two studies that also used ECT, applied  $\geq 12\%$  fall<sup>26</sup>, and  $\geq 15\%$  fall<sup>12</sup>, each. Finally, two studies that used mannitol, applied  $\geq 15\%$  fall<sup>18,22</sup>.

Eighteen studies<sup>10,11,13-15,17-19,21-24,26,28,29,32,33,37</sup> reported the training volume prescribed (54.5%%), ranging on average from at least 10 hours/week to 22.2 hours/week. Out of 18, seven studies<sup>20,21,28,31,33,34,40</sup> informed the athlete 's periodization and only one<sup>6</sup> addressed the effect of training loads on health.

The JBI Checklist for Prevalence Studies to assess the quality revealed that 30 (90,9%) achieved an overall moderate risk of bias, and only three (9.1%) were considered as low risk. The main flaws referred to question 3 (adequacy of sample size; n = 32 studies)<sup>7,10-40</sup>, and question 2 (participants' sampling; n = 29)<sup>7,10-23,25-29,31-37,39-40</sup>. Table 2 depicts the methodological quality assessment of the selected studies.



**Table 2.** Methodological quality assessment of the selected studies

Author (s), Year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Total score	Overall risk of bias
Zwick et al., 1990 <sup>11</sup>	●	●	●	●	●	●	●	●	NA	5	Moderate
Potts, 1994 <sup>12</sup>	●	●	●	●	●	●	●	●	NA	5	Moderate
Bonsignore et al., 2003 <sup>13</sup>	●	●	●	●	●	●	●	●	NA	5	Moderate
Williams, 2004 <sup>10</sup>	●	●	●	●	●	●	●	●	NA	6	Moderate
Pedersen <sup>a</sup> et al., 2008 <sup>14</sup>	●	●	●	●	●	●	●	●	NA	5	Moderate
Pedersen <sup>b</sup> et al., 2008 <sup>15</sup>	●	●	●	●	●	●	●	●	NA	5	Moderate
Castricum et al., 2010 <sup>16</sup>	●	●	●	●	●	●	●	●	NA	6	Moderate
Clearie <sup>a</sup> et al., 2010 <sup>17</sup>	●	●	●	●	●	●	●	●	NA	6	Moderate
Clearie <sup>b</sup> et al., 2010 <sup>18</sup>	●	●	●	●	●	●	●	●	NA	5	Moderate
Stadelmann et al., 2011 <sup>19</sup>	●	●	●	●	●	●	●	●	NA	6	Moderate
Bougault et al., 2012 <sup>20</sup>	●	●	●	●	●	●	●	●	NA	6	Moderate
Hanks et al., 2012 <sup>35</sup>	●	●	●	●	●	●	●	●	NA	4	Moderate
Labreche, 2012 <sup>21</sup>	●	●	●	●	●	●	●	●	NA	6	Moderate
Romberg et al., 2012 <sup>22</sup>	●	●	●	●	●	●	●	●	NA	6	Moderate
Silvestri et al., 2012 <sup>23</sup>	●	●	●	●	●	●	●	●	NA	6	Moderate
Turnel et al., 2012 <sup>24</sup>	●	●	●	●	●	●	●	●	NA	7	Low
Seys et al., 2014 <sup>25</sup>	●	●	●	●	●	●	●	●	NA	4	Moderate
Morissette et al., 2015 <sup>26</sup>	●	●	●	●	●	●	●	●	NA	5	Moderate

Seys et al., 2015 <sup>27</sup>	●	●	●	●	●	●	●	●	NA	6	Moderate
Levai et al., 2016 <sup>7</sup>	●	●	●	●	●	●	●	●	NA	6	Moderate
Van der Eycken et al., 2016 <sup>36</sup>	●	●	●	●	●	●	●	●	NA	4	Moderate
Bohm et al., 2017 <sup>37</sup>	●	●	●	●	●	●	●	●	NA	6	Moderate
Kennedy et al., 2017 <sup>28</sup>	●	●	●	●	●	●	●	●	NA	6	Moderate
Mata et al., 2017 <sup>29</sup>	●	●	●	●	●	●	●	●	NA	6	Moderate
Wang et al., 2017 <sup>30</sup>	●	●	●	●	●	●	●	●	NA	6	Moderate
Davies et al., 2018 <sup>6</sup>	●	●	●	●	●	●	●	●	NA	8	Low
Jackson, 2018 <sup>38</sup>	●	●	●	●	●	●	●	●	NA	7	Low
Škr gat et al., 2018 <sup>31</sup>	●	●	●	●	●	●	●	●	NA	5	Moderate
Snyder et al., 2018 <sup>39</sup>	●	●	●	●	●	●	●	●	NA	6	Moderate
Jonckheere et al., 2019 <sup>32</sup>	●	●	●	●	●	●	●	●	NA	4	Moderate
Robinson et al., 2019 <sup>40</sup>	●	●	●	●	●	●	●	●	NA	5	Moderate
Leahy et al., 2020 <sup>33</sup>	●	●	●	●	●	●	●	●	NA	6	Moderate
Santos et al., 2022 <sup>34</sup>	●	●	●	●	●	●	●	●	NA	5	Moderate

**Note:** ● - yes; ● - no; ● unclear; NA - not applicable

Questions for the Joanna Briggs Institute Checklist for Prevalence Studies:

Q1 - Was the sample frame appropriate to address the target population?

Q2 - Were study participants sampled in an appropriate way?

Q3 - Was the sample size adequate?

Q4 - Were the study subjects and the setting described in detail?

Q5 - Was the data analysis conducted with sufficient coverage of the identified sample?

Q6 - Were valid methods used for the identification of the condition?

Q7 - Was the condition measured in a standard, reliable way for all participants?

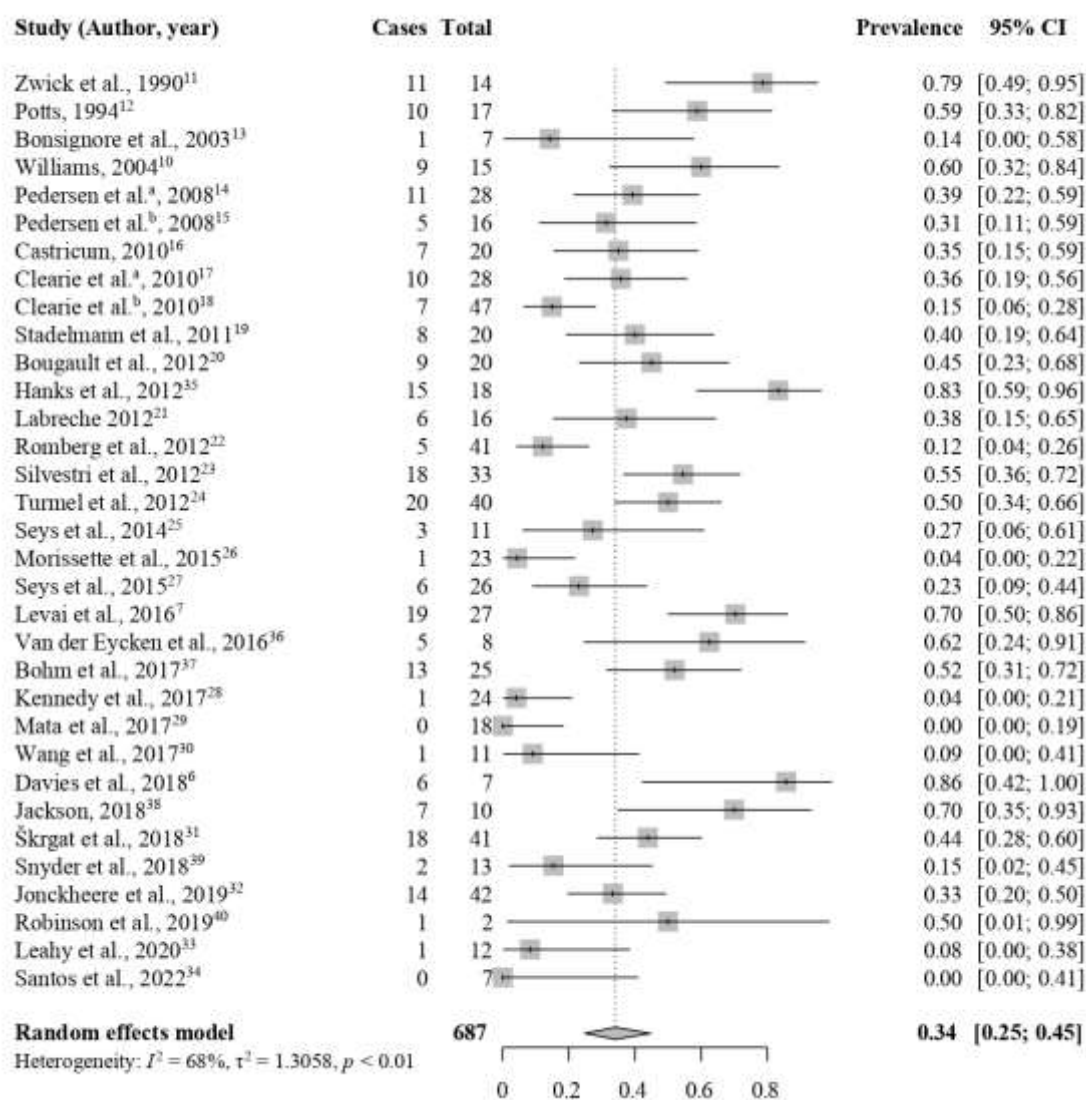
Q8 - Was there appropriate statistical analysis?

Q9 - Was the response rate adequate, and if not, was the low response rate managed appropriately?

**Source:** Authors

*Prevalence of exercise-induced bronchoconstriction in non-asthmatics swimmers*

Meta-analysis assessment revealed a pooled prevalence of EIB in non-asthmatics swimmers of 34% (95%CI: 25-45%) with a significant heterogeneity among the analyzed studies ( $I^2 = 68\%$ ,  $p < 0.01$ ) (Figure 2).



**Figure 2.** Forest plot for analysis of EIB prevalence in non-asthmatic swimmers

Source: RStudio project

It could not be fully explained by the subgroup analysis done for geographic location and type of athlete. However, on the other hand, there are statistically significant subgroup effect for study design, quality (risk of bias), and diagnostic method, which results we should interpret with caution. First, the test for study design ( $p = 0.03$ ) suggested that it modify the prevalence of EIB, favoring the cohort study (57%, 95% IC: 34-78%;  $I^2 = 67\%$ ,  $p = 0.02$ ). However, a far smaller number of studies and participants contributed data to the cohort subgroup (5 studies, 74 participants) than to the cross-sectional subgroup (26 studies, 596 participants), meaning that the analysis is unlikely to produce useful findings. Second, the test for quality ( $p = 0.04$ ), also suggested that it modify the prevalence of EIB, favoring the studies with low risk of bias. However, the same line of reasoning applied to study design

serves to this case. Finally, the test for diagnostic method ( $p < 0.01$ ), suggested that it significantly modifies the EIB prevalence, favoring methacholine (51%, 95% CI: 43-59%) and EVH (43%, 95% CI: 31-55%), over ECT (12%, 95% CI: 4-30%). A sufficient number of studies ( $> 7$ ) and participants ( $> 150$ ) were included in each subgroup, so the covariate distribution is not concerning for this subgroup analysis. However, there is substantial unexplained heterogeneity between studies within the EVH ( $I^2 = 63\%$ ) and ECT ( $I^2 = 62\%$ ) subgroups, that does not appear to justify the heterogeneity. The same cannot be said about the methacholine subgroup ( $I^2 = 28\%$ ). This analysis shows a relatively small amount of heterogeneity between results from the studies evaluated, explaining it. Table 3 displays the results of the subgroup analysis for the prevalence of EIB in non-asthmatic swimmers.

**Table 3.** Subgroup analysis on prevalence of EIB in non-asthmatic swimmers.

Subgroup	Number of studies	Number of participants	Random-effects model		Heterogeneity between subgroups*
			Prevalence	95% CI	
<b>Overall</b>	<b>33</b>	<b>687</b>	<b>34%</b>	<b>25-45%</b>	<b><math>I^2 = 68\%</math>, <math>p &lt; 0.01</math></b>
<b>Study design<sup>A</sup></b>					$\chi^2 = 4.61$ , $p = 0.03$
Cross-sectional	26	596	29%	20-40%	$I^2 = 67\%$ , $p < 0.01$
Cohort	5	74	57%	34-78%	$I^2 = 67\%$ , $p = 0.02$
<b>Quality (bias)</b>					$\chi^2 = 4.31$ , $p = 0.04$
Low risk	3	57	60%	35-81%	$I^2 = 41\%$ , $p = 0.18$
Moderate risk	30	630	31%	22-42%	$I^2 = 68\%$ , $p < 0.01$
<b>Continent<sup>B</sup></b>					$\chi^2 = 2.47$ , $p = 0.29$
Europe	17	422	39%	29-50%	$I^2 = 70\%$ , $p < 0.01$
America	13	216	23%	9-48%	$I^2 = 69\%$ , $p < 0.01$
Asia-Pacific	2	31	25%	10-50%	$I^2 = 53\%$ , $p = 0.14$
<b>Type of athlete</b>					$\chi^2 = 2.57$ , $p = 0.11$
Elite	18	428	39%	31-48%	$I^2 = 63\%$ , $p < 0.01$
Non-elite	14	241	21%	8-42%	$I^2 = 69\%$ , $p < 0.01$
<b>Diagnostic method<sup>C</sup></b>					$\chi^2 = 11.77$ , $p < 0.01$
MCT	7	157	51%	43-59%	$I^2 = 28\%$ , $p = 0.22$
EVH	16	312	43%	31-55%	$I^2 = 63\%$ , $p < 0.01$
ECT	9	177	12%	4-30%	$I^2 = 62\%$ , $p < 0.01$

**Note:** MCT – methacholine challenge test; ECT - exercise challenge test; EVH – eucapnic voluntary hypercapnia.

<sup>A</sup> two articles excluded<sup>10,40</sup>

<sup>B</sup> one article excluded<sup>10</sup>

<sup>C</sup> one article excluded<sup>22</sup>

\* $p < 0.1$  was considered statistically significant for subgroup comparison.

**Source:** Authors

It is worth noting that, due to lack of adequate information, other variables associated to EIB prevalence, such as age, sex, ethnicity, and environmental condition, were not addressed.

There was no indication of publication bias in the funnel plot and Egger test ( $p=0.1221$ ).

## Discussion

In this systematic review and meta-analysis, we undertook an exhaustive literature search on the prevalence of EIB among non-asthmatic swimmers. After pooling the results of 33 studies, encompassing 700 non-asthmatic swimmers from 16 countries worldwide, we found that EIB affects 34% of them (95% CI: 25-45%) with a substantial heterogeneity ( $I^2 = 68\%$ ). It was partially explained by the subgroup analysis that identified diagnostic method as the main factor associated with the prevalence of EIB ( $p < 0.01$ ). Studies, especially those using Methacholine challenge test (MCT), had a higher calculated summary estimate for the prevalence (53%, 95% CI: 43-59%).

Exercise-induced bronchoconstriction has obvious implications on physical activities, promoting limitations, and affecting health lifestyle, quality of life, and competitiveness. One of the most frequent sports associated with EIB is swimming, reaching rates up 68%<sup>7</sup>. However, there is a dearth in the scientific literature about its prevalence in non-asthmatic swimmers. As the underlying mechanisms, diagnosis and management strategies for EIB<sub>a</sub> and EIB<sub>wa</sub> may differ, understanding how much is attributable to asthmatic and non-asthmatics, is of utmost importance<sup>4,5</sup>. Furthermore, there is an assumption that asthmatics are the primarily responsible for the higher rates of EIB, as many as 90% of them have this condition. In the literature, there is lack of information concerning the differentiation between asthmatics and non-asthmatics<sup>5</sup>. Indeed, in this review, we could observe it at the selection process, where as many as 21.5% of the retrieved studies, did not report the difference between them. In an unprecedented way, our findings allow to better understand the frequency of a significant problem among non-asthmatic swimmers.

The expressive prevalence of EIB reported in this study may reflect a combination of factors deemed to cause it<sup>4</sup>. Besides the release of inflammatory mediators and stimulation of sensory nerves responsible for bronchoconstriction (osmotic and thermal hypotheses), environmental factors represented by inhalation of air saturated with chloramine from water associated with poorly conditioned air during exercise, has been hypothesised as contributor factor for EIB<sub>wa</sub>, especially in swimmers<sup>4,5,16</sup>.

Some factors can influence the prevalence of EIB<sup>3-5</sup>. However, still the role of age, sex, ethnicity, and environmental condition on this topic remained poorly understood, as there was a lack of adequate information to run the meta-analysis. On the other hand, while the subgroup analysis performed for the type of athlete, used as a proxy for training, showed no significant differences in the prevalence of EIB, the diagnostic method used revealed that it significantly modified it ( $p < 0.01$ ). This finding is line with the current consensus statement from the scientific literature, which considers diagnostic method used, the most significant factor that can influence the prevalence of EIB<sup>4</sup>.

Although, there is no gold standard for diagnosis EIB, it is well established that its prevalence varies with the type of challenge (level of evidence: A)<sup>4</sup>. Therefore, it should be diagnosed by means of a direct (eg, methacholine) or an indirect (eg, exercise challenge or surrogate testing, such as EVH or mannitol) challenge, where the latter is more sensitive for detection of EIB than the former (level of evidence: B)<sup>4</sup>. Nevertheless, there is debate about the overall efficacy of a screening program for EIB, athletes should be evaluated with objective testing due the potential implications on their performance and strict regulations concerning the use of medications<sup>3-5</sup>. The International Olympic Committee considers EVH the best test for athletes, as the MCT has a sensitivity as low as 40% for athletes engaged in summer competition<sup>3,4</sup>. However, in our review, it was studies using MCT that had a higher calculated summary estimate for prevalence (51%) with a better degree of certainty ( $I^2 = 28\%$ ), when compared to studies using EVH (43%,  $I^2 = 63\%$ ).

A strength of our review relies on a complete, systematic overview of the current body of evidence, that included five different electronic databases and grey literature, regarding the prevalence of EIB among non-asthmatic swimmers. In addition, to our knowledge, this is the first to conduct a meta-analysis addressing this topic. It retrieved and included a large number of studies from four geographical regions, providing an evidence-based estimation of global burden of EIB in non-asthmatic swimmers. Although, there was a substantial heterogeneity in the calculated summary estimate for prevalence, it was partly explained by the subgroup analysis for diagnostic method used.

However, some limitations should be taken into account, when interpreting the results of this review. Firstly, we observed a limited data addressing specifically the topic, although swimming is one of the most popular sports worldwide. Secondly, in most of the retrieved studies, we had to calculate the prevalence of EIB. Furthermore, there were substantial variations across studies regarding geographical location, type of athlete, exercise protocol (ECT), and study sample size that may affect the results. Most studies were conducted in Europe (17) and American (13) continents, especially in the northern countries (11). The lack of studies from other regions, especially Asian and developing countries, represents a significant gap in the literature, which may hamper the comparison of the prevalence of EIB between geographical regions. Thirdly, there was a lack of adequate information regarding the role of age, sex, ethnicity and environmental conditions on the prevalence of EIB, precluding their assessment as possible explanations for the substantial heterogeneity reported. Finally, the tool used for quality assessment revealed a moderate risk of bias in 90.9% of studies. Issues related to insufficient or inadequate study subjects and setting description, and/or a limited or inappropriate sampling frame to reliably assess the population of non-asthmatic swimmers were observed.

The impact and implication of this meta-analytic study of 700 non-asthmatic swimmers rely on the estimation of prevalence of EIB in 34% with a significant difference by diagnostic method used. With this rate, the popularity of swimming as a sport, and the negative impact of EIB on the quality of life and athletic performance, the focus of public health interventions should remain on its prevention through proper screening and treatment options, that should include reevaluation of training prescription.

## Conclusion

This systematic review and meta-analysis addressed 700 non-asthmatic swimmers and estimated a prevalence of EIB of 34%. There was a substantial heterogeneity partially explained by the subgroup analysis for diagnostic method used. Indeed, the MCT had significantly a higher prevalence (51%). These results should be considered a warning for professional involved in training and health policymakers due to the importance of swimming worldwide and the negative impact of EIB on lifestyle. As 90.9% of studies had a moderate risk of bias, along with the substantial heterogeneity, it is clear that better-designed studies addressing properly sociodemographic and environmental variables, as well as differentiating asthmatics from non-asthmatics, and establishing standard diagnosis tests, will contribute to a better understanding of this topic. New studies such as these add to the unique information provided by our review can help policymakers in determining which their interventions for prevention are needed.

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