



# Risk of asthma exacerbation in adolescent users of electronic nicotine delivery systems: a systematic review and meta-analysis

*Risco de exacerbação de asma em adolescentes usuários de dispositivos eletrônicos de liberação de nicotina: uma revisão sistemática e metanálise*

Anne Karoline Cardozo da Rocha<sup>1</sup>, Andresa Emy Miyawaki<sup>1</sup>, Marina Alves Trombini<sup>1</sup>, Victória Augusta Cavassim Costa Rosa<sup>1</sup>, Raul Cesar Santos Prestes<sup>1</sup>, Thamires Bezerra Costa<sup>1</sup>, Herberto José Chong-Neto<sup>2</sup>, Marilyn Urrutia-Pereira<sup>3</sup>, Dirceu Solé<sup>4</sup>, Nelson Augusto Rosário-Filho<sup>2</sup>, Miguel Morita Fernandes-Silva<sup>1</sup>, Débora Carla Chong-Silva<sup>2</sup>

## ABSTRACT

This study aims to investigate the association between electronic cigarette use and lung disease in adolescents. A systematic review was conducted in PubMed. We used the MeSH terms “Electronic Nicotine Delivery Systems” and “Lung Diseases” as well as synonyms in the title and abstract, with the age filter “child: birth - 18 years” to search for articles related to electronic cigarette use and lung disease in adolescents. The eligibility criteria consisted of adolescent users and exposure to e-cigarettes that resulted in lung disease. The articles were selected by independent assessment, reading first the titles and abstracts, then the full text of the selected articles. The Newcastle-Ottawa Scale was used to assess study quality, and the included studies received between 5 and 7 stars. Finally, the data were extracted for meta-analysis. Initially, 61 articles were found and 6 were considered eligible, all of which were cross-sectional and applied questionnaires. The meta-analysis found a significant association between electronic cigarette use and asthma exacerbation (adjusted OR 1.44 95% CI 1.17 - 1.76). However, no studies evaluated the association with other lung diseases, including electronic cigarette or vaping product use-associated lung injury in adolescents. The meta-analysis revealed a significant association between e-cigarette use and asthma exacerbation among adolescents with chronic asthma, as well as among their previously healthy peers.

**Keywords:** Asthma, adolescent, electronic nicotine delivery systems, lung diseases.

## RESUMO

Este trabalho tem como objetivo investigar a associação entre o uso dos cigarros eletrônicos e doenças pulmonares em adolescentes. Foi realizada uma revisão sistemática na base de dados PubMed. Os termos Mesh incluídos na busca foram “Electronic Nicotine Delivery Systems” e “Lung Diseases” e sinônimos no título e abstract, com o filtro de idade “child: birth - 18 years”, para buscar artigos relacionados ao uso de cigarros eletrônicos e doenças pulmonares em adolescentes. Os critérios de elegibilidade consistiram em: usuários adolescentes, exposição ao cigarro eletrônico e doença pulmonar como desfecho. Os artigos foram selecionados por uma revisão pareada de maneira independente, primeiramente com a leitura dos títulos e resumos, seguida da leitura integral dos artigos selecionados, os quais foram analisados pela ferramenta New Castle-Ottawa quanto sua qualidade, e receberam entre 5 e 7 estrelas. Os dados encontrados foram extraídos para a realização da metanálise. Inicialmente foram encontrados 61 artigos, sendo seis considerados elegíveis, todos transversais e com aplicação de questionários. Na metanálise foi encontrada uma associação significativa entre o uso de cigarro eletrônico e exacerbação de asma (OR ajustado 1,44; IC 95% 1,17–1,76). Não foram encontrados estudos que avaliassem a associação do cigarro eletrônico e outras doenças pulmonares, incluindo EVALI (*E-cigarette or Vaping product use-Associated Lung Injury*), em adolescentes. Na metanálise foi encontrada uma associação significativa entre exacerbações de asma e uso de cigarros eletrônicos em adolescentes com asma crônica e nos previamente hígidos.

**Descritores:** Asma, adolescente, sistemas eletrônicos de liberação de nicotina, pneumopatias.

1. Pontifícia Universidade Católica do Paraná, Medical School - Curitiba, PR, Brazil.

2. Universidade Federal do Paraná, Pediatric Allergy, Immunology, and Pulmonology Service - Curitiba, PR, Brazil.

3. Universidade Federal do Pampa, Medical School - Uruguaiana, RS, Brazil.

4. Universidade Federal de São Paulo, Allergy, Immunology, and Rheumatology Service, Pediatrics Department - São Paulo, SP, Brazil.

## Introduction

Electronic nicotine delivery systems (ENDS), commonly referred to as electronic cigarettes (e-cigarettes), have gained popularity since their introduction in the United States in 2007.<sup>1</sup> These devices consist of three components: a battery, a heating coil, and a reservoir containing the liquid to be heated. The e-liquid generally contains a solvent (propylene glycol or vegetable glycerin), varying levels of nicotine, and flavorings. This mixture is heated, converted into an aerosol, and then inhaled through the mouthpiece.<sup>2</sup>

There is a special concern about ENDS, as their dissemination and consequent popularization may be affecting the nonsmoking population.<sup>2</sup> E-cigarette use has grown substantially among adolescents and young adults,<sup>3</sup> and one explanation is that these devices have been widely publicized on digital media.<sup>1</sup> Unlike conventional cigarettes, e-cigarettes do not burn. Therefore, they do not produce many of the toxic products generated by conventional cigarettes.<sup>1</sup> For this reason, although the effects of ENDS are not well understood, some public health scholars<sup>4</sup> and e-cigarette supporters claim that they would be a safe option to conventional cigarettes as well as an effective alternative for those who are trying to stop smoking.<sup>5</sup>

Studies reveal, however, that e-cigarettes are not risk-free. Negative effects have been demonstrated, such as increased oxidative stress, decreased cell proliferation, and DNA damage in cell cultures exposed to aerosols from e-cigarettes.<sup>2</sup> There is also a concern about known tobacco carcinogens found within the vapor of most e-cigarettes. Heating propylene glycol also generates toxic aldehydes such as formaldehyde, acetaldehyde, and acrolein.<sup>2,6</sup>

E-cigarette nicotine vapor reaches the airways in the same manner as conventional cigarette vapor, which makes both products equally addictive. In addition to dependency, the neurocognitive actions of nicotine are a cause for concern. The observed effects on adolescents and young adults are especially related to reduced reflexes, attention and reasoning deficits, and mood disorders.<sup>1</sup> Tom Frieden, director at the Centers for Disease Control and Prevention (CDC), says adolescence is a critical period for brain development. Nicotine exposure at a young age may cause permanent brain damage, promote addiction, and lead to sustained tobacco use.<sup>7</sup>

Another alarming factor related to e-cigarette use, shown in a 2017 study conducted by Soneji et al., is that these devices may contribute to cigarette smoking initiation. Likelihood was 30.4% for e-cigarette users versus 7.9% for those who had never used the device. These data refute the notion that e-cigarettes are an option for smoking cessation – on the contrary, they are a risk factor for initiation.<sup>1,8</sup> Also, a longitudinal study focusing on the evaluation of an adolescent population showed that e-cigarette use by nonsmokers is associated with an increased risk of them becoming conventional cigarette smokers, even after assessing demographic, psychosocial, and risk factors.<sup>8</sup>

In Brazil, there are no data regarding the number of young e-cigarette users, but a United States study showed that the use of this device has increased significantly among adolescents. According to the 2014 National Youth Tobacco Survey, conducted by the CDC, there are currently 4.6 million student tobacco users, and approximately half of them (2.4 million) reported e-cigarette use.<sup>9</sup> The survey also found that e-cigarette use by high school students increased approximately 800% from 2011 to 2014.<sup>9</sup>

Regarding the trade and import of ENDS in Brazil, both were prohibited in 2009<sup>10</sup> by the National Health Surveillance Agency (Anvisa), given the lack of knowledge about safety and efficacy of the product. However, e-cigarettes can be easily purchased from e-commerce websites and even street stores, with prices starting at R\$49.00 for the simplest models.<sup>1</sup>

This study seeks to evaluate the occurrence of e-cigarette or vaping product use-associated lung injury (EVALI) and other lung diseases in adolescents.

## Methods

### **Data source and search strategy**

The PubMed database was searched using specific descriptors and synonyms found in the title and abstract, based on the following Medical Subject Headings (MeSH) terms: “electronic nicotine delivery systems,” “lung diseases,” “child,” “pediatrics,” “birth – 18 years,” and variations. The search strategy was limited to the pre-pandemic period, as the new coronavirus pandemic could influence the findings and deserves to be evaluated separately. Only articles written in English were considered. No search filters were used for the date of articles published until 2020.

### **Study selection**

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (Prisma) checklist recommendations.<sup>11</sup> The process of article selection began with removal of duplicates; then, two raters independently screened the titles and abstracts; subsequently, the pair of raters came to an agreement for choosing the articles that fit the eligibility criteria. When there was no consensus, a third rater was consulted for making the decision. The previously selected articles were then screened in full text and, finally, were elected for the review. The eligibility criteria were adolescent users, exposure to e-cigarettes, and, as an outcome, lung disease.

### **Inclusion and exclusion process**

Randomized and nonrandomized cross-sectional studies reporting analyses of respiratory conditions in adolescent ENDS users were included. Incomplete texts and studies related to diagnosis of diseases other than respiratory diseases were excluded. Articles that evaluated consequences other than the respiratory outcome and those that addressed exposure to tobacco products other than ENDS were also excluded.

### **Data extraction**

As recommended by the Prisma checklist,<sup>11</sup> two raters extracted and analyzed data from the selected articles. Authorship, year of publication, nationality, study design, sample size, sex, age group, and other epidemiological data were extracted from the selected studies.

### **Quality assessment**

Two independent raters assessed the methodology of the selected studies using the New Castle-Ottawa Scale (NOS),<sup>12</sup> which was designed to score the quality of nonrandomized studies between 0 and 9 stars. NOS can be used either as a checklist or a scale. A Delphi process was used to develop the tool, which was then tested in systematic reviews and refined. It consists of eight items, divided into three categories, including selection, comparability, and, depending on study type, outcome (cohort studies) or exposure (case-control studies). For each item, a series of response options is provided. A star system is used to allow a semiquantitative assessment of

study quality, so that studies receive one star for each item if they meet the requirement for that item, except for the comparability item, which allows two stars being assigned.<sup>12</sup>

### **Results**

In total, 257 articles were found during initial database search with the descriptors “electronic nicotine delivery systems” and “lung diseases,” all in English language. After the filter for the desired age group was applied, 74 articles were obtained. Thirteen duplicates were excluded, and then the screening process for the 61 selected articles began (Table 1).

Full-text articles were screened using the Prisma method,<sup>11</sup> as previously reported, and 55 articles were excluded from the final analysis for one of the following reasons: including other age groups; evaluating e-cigarette consequences other than the respiratory outcome; including tobacco products other than e-cigarettes; and, in some cases, not being available in full text. Therefore, 6 articles were selected in the eligibility analysis and were then submitted to the New Castle-Ottawa Scale,<sup>12</sup> which scores the quality of nonrandomized studies between 0 and 9 stars (Figure 1).

The studies selected for this systematic review received between 5 and 7 stars, were all cross-sectional, and administered questionnaires as part of their methodology, as shown in Table 2.

A single article – Bayly (2019)<sup>13</sup> – received 5 stars and, for this reason, was not included in the meta-analysis. Schweitzer (2017)<sup>14</sup> received 6 stars, and the others – Cho (2016),<sup>15</sup> Choi (2016),<sup>16</sup> Kim (2017),<sup>17</sup> and McConnell (2017)<sup>18</sup> – received 7 stars.

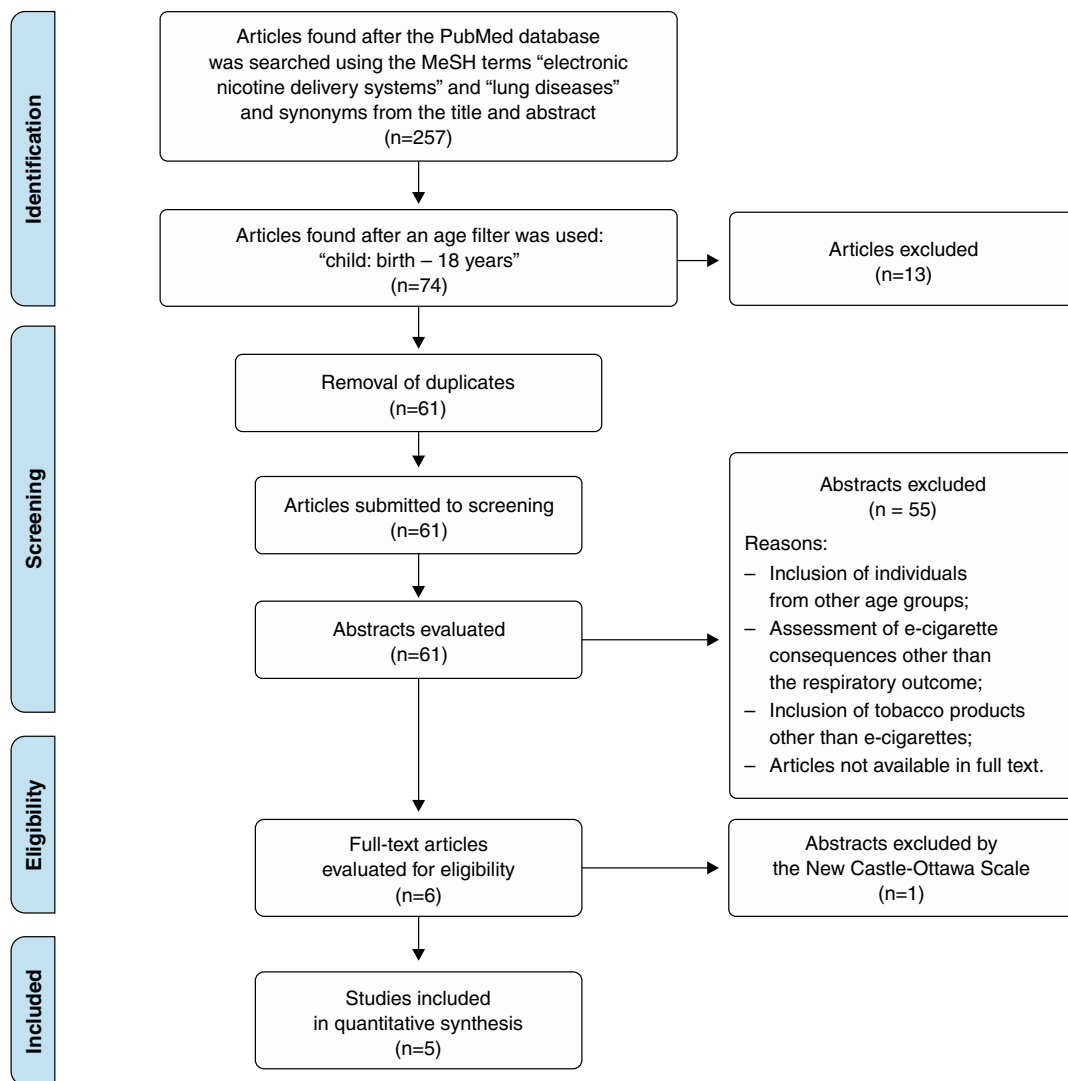
The data reported in the 5 articles included in the final sample were extracted into a table, for subsequent systematic review and meta-analysis. The meta-analysis consisted of an analysis of data expressed as odds ratio (OR).

Most studies reported a population of adolescents aged 11 to 18 years, with the same proportion of female and male participants. Two studies were conducted in South Korea, and the rest in the United States, in the states of Florida and California. Four studies evaluated adolescents with a previous diagnosis of asthma, while the others assessed healthy people. Only 2 studies asked the adolescents about previous tobacco use. Three articles discussed sociodemographic issues, such as ethnicity, physical activity, parents'

**Table 1**  
Description of inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Studies evaluating age group up to 18 years	Language other than English
Studies evaluating vaping use	Age groups other than children and adolescents
Articles evaluating respiratory outcomes	Articles evaluating outcomes other than respiratory outcomes
Detailed description of methods used	Tobacco products other than ENDS
	Studies not available in full text or available in other forms (abstract, thesis, dissertation)

ENDS = electronic nicotine delivery systems.



**Figure 1**  
Prisma algorithm for study selection process

educational level, socioeconomic status, and region of residence. The 6 studies reported, as an outcome, asthma exacerbation in people previously diagnosed with asthma and asthma symptoms in previously healthy people.

The meta-analysis found a significant association between e-cigarette use and asthma exacerbation (adjusted OR 1.44; 95% CI 1.17-1.76). Five studies were statistically relevant, and all showed that e-cigarette use may exacerbate asthma. Only one study – McConnell et al. – crossed the vertical line in the forest plot, which reduced its statistical relevance for the research (Figure 2).

## Discussion

The number of e-cigarette users has grown alarmingly around the world, particularly among young people.<sup>1</sup> In the United States, these devices have been addressed as a serious public health problem in recent years.<sup>1,3</sup> Although epidemiological data referring to Brazil are lacking and free dissemination and marketing of these products are banned, the perception that vaping use has been increasing among Brazilian youth is undeniable.<sup>10,19,20</sup>

One suggested explanation for such growth is the mistaken notion that these devices are harmless. Also, e-cigarettes have become synonymous with social acceptance and ostentation among adolescents and young adults.<sup>9,20</sup>

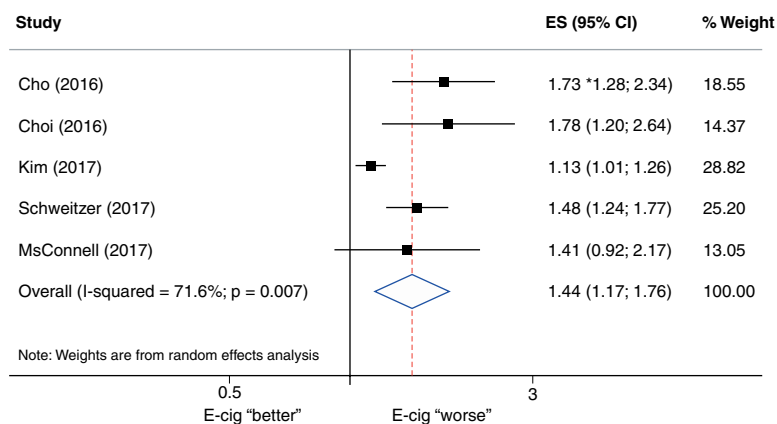
Although the effects of ENDS are not well understood, it is known that they are an important risk factor for cardiovascular and lung diseases.<sup>21</sup> In addition to chemical dependency, there are some concerns about the deleterious neurocognitive actions of nicotine, confirmed production of carcinogens, and effects on the vascular endothelium with a consequent impact on cardiovascular diseases.<sup>2,6,7,21</sup>

Compared to conventional cigarettes, e-cigarette vapor reaches the airways in the same manner and is equally addictive.<sup>2,6,7</sup>

Regarding local aggressive action on the respiratory epithelium, many studies indicate specific inflammatory effects and confirm the impairment of innate immune response in the lungs. Exposure to ENDS flavorings results in abnormal activation of lung epithelial cells and  $\beta$ -defensins, dysfunction of macrophage phagocytic activity, increased mucin levels (MUC5AC), and abnormal activation of neutrophil response (NETosis).<sup>22,23</sup> Menthol flavorings disrupt

**Table 2**  
Scores of selected studies in the New Castle-Ottawa Scale

	Selection			Comparability		Outcome		Total (9/9)
	Representativeness of the sample	Sample size	Non-respondents	Ascertainment of the exposure	Comparability	Assessment of the outcome	Statistical test	
McConnell et al., 2017 <sup>18</sup>	★	★	0	★	★★	★	★	7/9
Choi K et al., 2016 <sup>16</sup>	★	★	0	★	★★	★	★	7/9
Cho JH et al., 2016 <sup>15</sup>	★	★	0	★	★★	★	★	7/9
Bayly JE et al., 2019 <sup>13</sup>	★	★	0	★	0	★	★	5/9
Kim SY et al., 2017 <sup>17</sup>	★	★	0	★	★★	★	★	7/9
Schweitzer RJ et al., 2017 <sup>14</sup>	★	★	0	★	★	★	★	6/9



**Figure 2**  
Meta-analysis of asthma exacerbation and e-cigarette (e-cig) use

innate immune responses and may be associated with allergies and asthma through activation of the transient receptor potential ankyrin 1 (TRAP1).<sup>23</sup> A potential effect on the respiratory microbiota of ENDS users has also been studied.<sup>23</sup>

More recently, studies showing a positive association between ENDS use and viral respiratory infections have gained prominence. Cigarette users showed a consistent change in antiviral response, with a decreased production of defense cytokines (IFN $\gamma$ , IL-6, and IL-12p40) when exposed to live-attenuated influenza virus, and failed to increase influenza-specific IgA levels, significantly differing from the nonsmoking group.<sup>24</sup>

This study reported a relevant finding: an increased risk of asthma exacerbation in e-cigarette users, which was detected in those with chronic asthma but also in healthy adolescents.

Asthma is one of the most common chronic diseases of childhood and adolescence, with increasing prevalence, high number of admissions, and high social burden.<sup>25</sup> It is a worldwide health problem that affects approximately 300 million individuals. Twenty million live in Brazil, accounting for a prevalence of 10% of the population. The rate increases when it comes to school-aged children and adolescents, reaching up to 20%.<sup>25</sup> The negative impact of exposure to conventional cigarette smoke on asthma symptoms has already been proven.

Asthmatic children and adolescents exposed to passive smoking have moderately severe asthma, require inhaled corticosteroids more often, and show a greater frequency of daytime symptoms compared to those who are free from exposure.<sup>26</sup>

It is not difficult to imagine that, because asthma is a disease that causes inflammation of the airways, environmental exposure to allergens and irritating agents such as cigarette smoke generates hyper-responsiveness, with reduced ventilatory flow and consequent exacerbation of the disease.<sup>25,26</sup> The present study showed that heated vapor and e-cigarette-generated products have the same ability to trigger a dreaded asthma exacerbation.

A study evaluating immediate local effect showed an increase in airway resistance at 5 Hz and at 20 Hz, measured by impulse oscillometry, after use of an e-cigarette for 5 minutes. This effect was also described for use of conventional cigarettes, suggesting that they are potential constrictors.<sup>27</sup> The study found a significant increase in oxidative stress in the e-cigarette group, proven by a decrease in fraction of exhaled nitric oxide.<sup>27</sup>

EVALIs were not found in this systematic review when the age group was restricted to adolescents. However, recent studies showing a positive association between ENDS use and a positive COVID-19 diagnosis revealed that young users of e-cigarettes only were 5 times more likely (95% CI: 1.82-13.96) of

having a positive diagnosis; when both e-cigarettes and conventional cigarettes were used, likelihood was even greater, almost 7 times (95% CI: 1.98-24.55), compared to young nonsmokers.<sup>28</sup>

The results of this review and meta-analysis indicate that e-cigarette use causes a real harm in adolescents. Preventive measures that ensure education, information, and action plans to fight e-cigarette use must be adopted by educators, health professionals, and managers, aiming to stop the growing adherence to these devices by young people.

Pediatricians and other professionals who assist adolescents in daily practice need to provide the asthmatic population with special attention, which includes investigating e-cigarette use during history taking and giving firm and precise guidance on the harm that these devices may cause.

## References

- Sociedade Brasileira de Pediatria. Departamentos Científicos de Pneumologia Toxicologia e Otorrinolaringologia. Dispositivos eletrônicos de entrega de nicotina (cigarros eletrônicos e similares): "Lobos em pele de cordeiro?". Out. 2018 [Internet]. Available at: [www.sbp.com.br](http://www.sbp.com.br).
- Sood AK, Kesic MJ, Hernandez ML. Electronic cigarettes: One size does not fit all. *J Allergy Clin Immunol*. 2018 Jun;141(6):1973-82. doi: 10.1016/j.jaci.2018.02.029.
- Bunnell RE, Agaku IT, Arrazola RA, Apelberg BJ, Caraballo RS, Corey CG, et al. Intentions to smoke cigarettes among never-smoking US middle and high school electronic cigarette users: National Youth Tobacco Survey, 2011-2013. *Nicotine Tob Res*. 2015 Feb;17(2):228-35. doi: 10.1093/ntr/ntu166.
- Riahi F, Rajkumar S, Yach D. Tobacco smoking and nicotine delivery alternatives: patterns of product use and perceptions in 13 countries. *F1000Res*. 2019 Jan 21;8:80. doi: 10.12688/f1000research.17635.2.
- Ghosh S, Drummond MB. Electronic cigarettes as smoking cessation tool: are we there? *Curr Opin Pulm Med*. 2017 Mar;23(2):111-116. doi: 10.1097/MCP.0000000000000348.
- Cobb NK, Sonti R. E-Cigarettes: The Science Behind the Smoke and Mirrors. *Respir Care*. 2016 Aug;61(8):1122-8. doi: 10.4187/respcare.04944.
- Centers for Disease Control and Prevention. E-cigarette use triples among middle and high school students in just one year [Internet]. 2015. Available at: <https://www.cdc.gov/media/releases/2015/p0416-E-cigarette-use.html>.
- Soneji S, Barrington-Trimis JL, Wills TA, Leventhal AM, Unger JB, Gibson LA, et al. Association Between Initial Use of e-Cigarettes and Subsequent Cigarette Smoking Among Adolescents and Young Adults: A Systematic Review and Meta-analysis. *JAMA Pediatr*. 2017 Aug 1;171(8):788-797. doi: 10.1001/jamapediatrics.2017.1488. Erratum in: *JAMA Pediatr*. 2018 Jan 1;172(1):92-93. Erratum in: *JAMA Pediatr*. 2018 Jan 1;172(1):98. Erratum in: *JAMA Pediatr*. 2020 May 1;174(5):509.
- US Food & Drug Administration [Internet]. Youth Tobacco Use - Results from the 2014 National Youth Tobacco Survey. Available at: [http://www.smchd.org/wp-content/uploads/NYTS\\_YouthTobaccoUse\\_508.pdf](http://www.smchd.org/wp-content/uploads/NYTS_YouthTobaccoUse_508.pdf).
- Cavalcante TM, Szklo AS, Perez CA, Thrasher JF, Szklo M, Ouimet J, et al. Electronic cigarette awareness, use, and perception of harmfulness in Brazil: findings from a country that has strict regulatory requirements. *Cad Saude Publica*. 2017;33(Suppl 3):e00074416.
- Moher D, Liberati A, Tetzlaff J, Altman DG. PRISMA Group. Preferred reporting items for systematic reviews. *Ann Intern Med*. 2009;151:264-9.
- Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality if nonrandomized studies in meta-analyses [Internet]. 2008. Available at: URL: [http://www.ohri.ca/programs/clinical\\_epidemiology/oxford.htm](http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm). Accessed in: november/2021.
- Bayly JE, Bernat D, Porter L, Choi K. Secondhand Exposure to Aerosols From Electronic Nicotine Delivery Systems and Asthma Exacerbations Among Youth With Asthma. *Chest*. 2019;155(1):88-93. doi: 10.1016/j.chest.2018.10.005.
- Schweitzer RJ, Wills TA, Tam E, Pagano I, Choi K. E-cigarette use and asthma in a multiethnic sample of adolescents. *Prev Med*. 2017;105:226-31. doi: 10.1016/j.ypmed.2017.09.023.
- Cho JH, Paik SY. Association between Electronic Cigarette Use and Asthma among High School Students in South Korea. *PLoS ONE* 11(3):e0151022. doi: 10.1371/journal.pone.0151022.
- Choi K, Bernat D. E-cigarette use among Florida youth with and without asthma. *Am J Prev Med*. 2016 October;51(4):446-53. doi: 10.1016/j.amepre.2016.03.010.
- Kim SY, Sim S, Choi HG. Active, passive, and electronic cigarette smoking is associated with asthma in adolescents. *Sci Rep*. 2017;7(1):17789. doi: 10.1038/s41598-017-17958-y.
- MacConnell R, Barrington-Trimis JL, Wang K, Urman R, Hong H, Unger J, et al. Electronic Cigarette Use and Respiratory Symptoms in Adolescents. *J Respir Crit Care Med*. 2017;195(8):1043-9. doi: 10.1164/rccm.201604-0804OC.
- Brasil - Agência Nacional de Vigilância Sanitária (ANVISA) [Internet]. Painel Debate Dispositivos Eletrônicos para Fumar. Available at: <https://www.gov.br/anvisa/pt-br/assuntos/noticias-anvisa/2018/painel-debate-dispositivos-eletronicos-para-fumar>. Accessed in: november/2021.
- O Globo [Internet]. Usuários driblam proibição de venda de cigarro eletrônico no Brasil. Available at: <https://oglobo.globo.com/sociedade/saude/usuarios-driblam-proibicao-de-venda-de-cigarro-eletronico-no-brasil-16182500>. Accessed in: november/2021.
- Münzel T, Hahad O, Kuntic M, Keaney JF, Deanfield JE, Daiber A. Effects of tobacco cigarettes, e-cigarettes, and waterpipe smoking on endothelial function and clinical outcomes. *Eur Heart J*. 2020 Nov 1;41(41):4057-70. doi: 10.1093/eurheartj/ehaa460.
- Reidel B, Radicioni G, Clapp PW, Ford AA, Abdelwahab S, Rebuli ME, et al. E-Cigarette Use Causes a Unique Innate Immune Response in the Lung, Involving Increased Neutrophilic Activation and Altered Mucin Secretion. *Am J Respir Crit Care Med*. 2018;197(4):492-501. doi: 10.1164/rccm.201708-1590OC.
- Quinones Tavares Z, Li D, Croft DP, Gill SR, Ossip DJ, Rahman I. The Interplay Between Respiratory Microbiota and Innate Immunity in Flavor E-Cigarette Vaping Induced Lung Dysfunction. *Front Microbiol*. 2020;11:589501. doi: 10.3389/fmicb.2020.589501.
- Rebuli ME, Glista-Baker E, Hoffman JR, Duffney PF, Robinette C, Speen AM, et al. Electronic-Cigarette Use Alters Nasal Mucosal Immune Response to Live-attenuated Influenza Virus. A Clinical Trial. *Am J Respir Cell Mol Biol*. 2021;64(1):126-37. doi: 10.1165/rcmb.2020-0164OC.
- Global Initiative for Asthma (GINA) [Internet]. Global Strategy for Asthma Management and Prevention. 2021 – update. Available at: <https://ginasthma.org/wp-content/uploads/2021/05/GINA-Main-Report-2021-V2-WMS.pdf>. Accessed in: november/2021.
- Pilato EL, Filla TFL, Couto LC, Rosário CS, Neto HJC, Riedi CA, et al. Impacto do tabagismo passivo nos sintomas da asma na infância. *Arq Asma Alerg Imunol*. 2020;4(2):190-7.

27. Vardavas GI, Anagnostopoulos N, Kougias M, Evangelopoulou V, Connolly GN, Behrakis PK. Short-term pulmonary effects of using an electronic cigarette: impact on respiratory flow resistance, impedance, and exhaled nitric oxide. *Chest*. 2012;141(6):1400-6. doi: 10.1378/chest.11-2443.
28. Gaiha SM, Cheng J, Halpern-Felsher B. Association Between Youth Smoking, Electronic Cigarette Use, and COVID-19. *J Adolesc Health*. 2020;67(4):519-23. doi: 10.1016/j.jadohealth.2020.07.002.

---

No conflicts of interest declared concerning the publication of this article.

Corresponding author:  
Débora Carla Chong-Silva  
E-mail: debchong@uol.com.br